

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, October 17, 2018 11:43:21 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration,
Bryscen Prothero APRN-Rx

From: [REDACTED]
To: [REDACTED]
Subject: In support of HAR 11-157
Date: Wednesday, October 17, 2018 3:27:42 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Mahalo, Maile Walters

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, October 17, 2018 11:50:55 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.
Dr. Celeste Baldwin, PhD, APRN, CNS

Hawaii Immunization Coalition Board Member

From: [REDACTED]
To: [REDACTED]
Subject: support for HAR 11-157
Date: Wednesday, October 17, 2018 11:55:39 AM

I support HAR 11-157 regarding immunizations for school entry. I would also recommend that parents who claim a religious exemption provide a letter from the head of the church or temple and that the organization be a registered entity.

-Gail Nakaichi, D.O.
pediatrics

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, October 17, 2018 5:10:45 PM

Thank you for this opportunity to provide testimony. As a community member, public health advocate, and parent of a student who will be affected by these changes, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Gail Ogawa

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Support Bill
Date: Friday, October 19, 2018 7:01:40 AM

Hi

My name is Janelle Jinbo. I am a medical provider in the state of Hawaii and have been for more than 10 years. I am a strong supporter of immunizations. Immunizations are one of the easiest things to do to prevent many diseases that increase rates of morbidity and mortality in Hawaii today. Vaccinations not only help prevent the individual from getting diseases, but also those around them. The state of Hawaii has lagged behind the rest of the nation in its laws to support the use of recommended vaccinations in childhood.

Thus, I thank you for this opportunity to provide testimony. I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Janelle Jinbo, PhD, APRN



Date: October 21, 2018

To: Department of Health

From: Jessica Yamauchi, Executive Director, Hawai'i Public Health Institute

Re: **Strong Support for HAR 11-157**

Hrg: November 1, 2018 at 3:00 pm at Kinau Hale Boardroom

Thank you for the opportunity to offer testimony in strong support of the HAR 11-157 proposed rules update.

The Hawai'i Public Health Institute (HIPHI) brings community organizations, government, academia, foundations, and businesses together to advance policy and systems change to reduce disparities and improve the health of Hawai'i residents.

The proposed changes in HAR 11-157 will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

HPV prevents cancer. I respectfully request that the proposed changes to HAR 11-157 be passed and adopted for the health of all of our communities.

Thank you for the opportunity to provide testimony.

A handwritten signature in black ink that reads 'Jessica Yamauchi'.

Jessica Yamauchi, MA
Executive Director

From: [REDACTED]
To: [REDACTED]
Subject: Please help us make vaccination mandatory!
Date: Monday, October 22, 2018 7:21:34 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,
Patrick Walters

From:

To:

[REDACTED];
[REDACTED] US;

Subject:

Testimony HAR

Date:

Monday, October 22, 2018 8:59:15 AM

To Whom it may concern,

My name is Annalisa and I am the Health Aide at Farrington High School, my Hawaii Keiki Nurse had forwarded the testimony to me because vaccinations are a BIG issue in my school.

Heres some of the issues I run into:

* A lot of my students are coming from Philippines and Micronesia so I rely on the HAR often. What I find is the State of Hawaii and the CDC run differently for vaccine timelines. This is an issue because as I'm telling my student's they are non-complaint they go to the clinic and they go off CDC Guidelines.

* I wish the "Catch-up" schedule was written in the HAR. As I'm sure most will assume students in high school should have all vaccines that's NOT the case for this district.

* As of right now I have 40 student's non-complaint and the only thing that truly helps me is entering the student as a Provisional and them having to have an appointment card to enroll in school.

* Often they make an appointment but DO NOT go to appointment. As the health aide at Farrington High I hand deliver a reminder Provisional to the student with a copy of their appointment card, then I call parent to remind them as well and I mail a copy home. If they were to do a no show for there appointment this can cause a delay with other vaccines such as Dtap 2 & 3 and Polio 2 & 3 since both vaccines require 6 months between doses.

* I wish it was written in HAR that all students on EPI 12 A or B at end of school year will be EXCLUSION for the following school year.

* Having students start their school year with a Provisional then they attend and update Health Room they are served Provisional again which causes procrastination on complying in vaccines. I feel only one Provisional should be served and then there time starts. As long as they continue to receive vaccines on time no EXCLUSION should be served.

Thank you for your time,

Annalisa Felt
Health Aide

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 Testimony
Date: Tuesday, October 23, 2018 5:09:41 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Pat Cheng

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Tuesday, October 23, 2018 2:10:19 PM

Dear DOH,

My name is Nicholas Tsoi, I am a student pharmacist at the [REDACTED]
[REDACTED]. I support the amendments proposed for Title 11, Chapter 157
"Examination and Immunization" as this would help to increase the health of our students and
community.

Sincerely,
--Nicholas Tsoi

--
Nicholas Tsoi

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11, Chapter 157 Examination and Immunization
Date: Tuesday, October 23, 2018 3:25:24 PM

Dear Department of Health representatives,

I am on faculty at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. These immunizations have been shown to decrease the risk of several types of cancer in the population.

Thank you for the opportunity to submit testimony.

Deborah Taira

--

Deborah Taira, ScD

[REDACTED]

CONFIDENTIALITY NOTICE: The contents of this email message and any attachments are intended solely for the addressee(s) and may contain confidential and/or privileged information and may be legally protected from disclosure. If you are not the intended recipient of this message or their agent, or if this message has been addressed to you in error, please immediately alert the sender by reply email and then delete this message and any attachments. If you are not the intended recipient, you are hereby notified that any use, dissemination, copying, or storage of this message or its attachments is strictly prohibited.

From: [REDACTED]
To: [REDACTED]
Subject: SUPPORT HAR 11-157
Date: Tuesday, October 23, 2018 11:45:33 PM

Aloha,

I am writing to state my SUPPORT of vaccination and examination requirements for the protection of Hawaii keiki. I am in a homeschool group where a parent is working to mobilize others to oppose this bill. I believe the idea of informed consent for vaccinations is not based on credible science and could put other children at risk of spreading preventable diseases by making the choice to not vaccinate their children while participating in a learning community. If I understand correctly, I am happy that the state is working to require that these individuals would vaccinate their children if they intend to have their children participate in the public/private/charter/homeschool community of Hawaii. If they choose to not vaccinate their children, I believe those of us who do take medically and scientifically based precautions to protect our keiki, especially those that are too young for vaccinations and especially vulnerable, that we should also have the choice to not expose our children to potentially life threatening preventable disease that these unvaccinated children could spread because their parents are not basing their decision on the overwhelming scientific advice and opinion of the medical community that vaccinations are safe and effective at preventing the spread of preventable disease.

Thank you!
A concerned parent

Sent from my iPhone

October 23, 2018

Bruce Anderson, PH.D.
Director of Health
Hawaii State Department of Health

SUBJECT: Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization"

Dear Dr. Anderson:

Thank you for this opportunity to provide testimony on the proposed rules. I strongly support the HAR 11-157 proposed rule changes.

This update of the Administrative Rules would establish immunization requirements for school, post-secondary school, and child care facility attendance in Hawaii. The State of Hawaii, through the Hawaii State Department of Health, Immunization Branch, monitors the immunization levels of public and private individuals in the state, and is proposing these changes to HAR 11-157.

Why monitor and insist on high student immunization levels in Hawaii?

- More than 3 million persons die from vaccine-preventable diseases every year. A vaccine-preventable disease can be minimized or prevented through immunization.
- Vaccine-preventable diseases are passed through the school community by person-to-person contact.
- Vaccination of students – both for attendance and at registration – is a critical strategy for keeping schools and communities safe for children who **can** get vaccinated and for those who **cannot** because of medical reasons.
- School immunization regulations rely on **herd or community immunity** that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who cannot be vaccinated.
- Vaccine-preventable diseases have a costly impact, resulting in doctor's visits, hospitalizations, and premature deaths. Sick children can also cause parents to lose time from work.

The Centers for Disease Control and Prevention (CDC) clearly states:

- State and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases (VPDs).
- Studies have shown that vaccine exemptions tend to cluster geographically, making communities with more vaccine exemptions at greater risk for disease outbreaks.

I respectfully request that the Hawaii Administrative Rule 11-157 be supported and passed for the reasons noted above.

Signed:

Judy Strait-Jones, MPH, MED

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Tuesday, October 23, 2018 10:22:54 AM

Thank you for the opportunity to provide testimony. As a community member, public health advocate, former immunization program educator for this Department and current member of the Hawaii Immunization Coalition, I strongly support the HAR 11-157 proposed rules update.

The proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the ACIP. It is challenging enough to meet the immunization goals set for the public without administrative infrastructure to support the provider community. We need to have our rules as current as the information on a national level indicates.

Hawaii is lagging in desired immunization levels once children enter 7th grade and this lag continues throughout the adult and senior years. This is true both for vaccines which address communicable diseases such as HPV, MCV, and Tdap, and for those which prevent disease in adults with underlying diseases such as diabetes, cancer, heart and lung disease in the case of Pneumococcal vaccine.

Limiting exemptions for those who are able to receive vaccines is the responsible approach for minimizing exposure for those who are medically contraindicated to receive certain vaccines. Health care providers and health program administrators site the lack of strict requirements as a major barrier to carrying out ACIP recommendations and achieving the goals set by the CDC.

Please support the proposed changes to HAR 11-157.

Thank you,

Marian Phillipson
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Wednesday, October 24, 2018 6:48:10 AM

Dear DOH:

I am an Assistant Professor of Pharmacy Practice at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community.

Pharmacists are one of the most accessible health care providers in the community. Many times accessibility and convenience play a large part in facilitating immunizations. Thank you very much for your consideration.

Best wishes,

Chad

Chad Kawakami Pharm.D., BCPS, CDE
[REDACTED]

CONFIDENTIALITY NOTICE: The contents of this email message and any attachments are intended solely for the addressee(s) and may contain confidential and/or privileged information and may be legally protected from disclosure. If you are not the intended recipient of this message or their agent, or if this message has been addressed to you in error, please immediately alert the sender by reply email and then delete this message and any attachments. If you are not the intended recipient, you are hereby notified that any use, dissemination, copying, or storage of this message or its attachments is strictly prohibited.

From: [REDACTED]
To: [REDACTED]
Subject: testimony against HAR Title 11, Chapter 157, "Examination and Immunization."
Date: Wednesday, October 24, 2018 9:28:27 PM

This email is public testimony against HEARING DOCKET NO. R-157-18-07 (Amendment to Hawaii Administrative Rules Title 11, Chapter 157, "Examination and Immunization.")

I am adamantly opposed to adding more vaccines to the vaccine schedule. The research has not been done to assess what the impacts are to children of adding more and more vaccines to the schedule.

Specifically, I am VERY STRONGLY OPPOSED to mandating the annual flu shot and the HPV vaccine. These vaccines are available if someone chooses it in consultation with their physician. I have discussed the HPV vaccine in depth with my doctor and she is not in agreement that the research exists to prove that this vaccine is safe. The vaccine only protects against 4 strains of the virus when there are over 200 strains of HPV, and there have been far too many injuries for it to be worth the risk. Further HPV is curable when treated and annual pelvic exams are effective for diagnosis.

The American College of Pediatricians has issued strong and serious warnings against HPV. They warn against the methods used for testing the vaccine safety and the health risks associated with HPV vaccine includes infertility due to premature ovarian failure among other health affects, including death.

Further, HPV is not a communicable disease that children might 'catch' at school simply by attending school.

Allow me to clarify that my children are vaccinated. However, I have done my research on the HPV vaccine and am convinced that this vaccine was rushed to market and is not safe. Its sole purpose is for pharmaceutical industry profits (\$300 per shot x 3 shots/student = many multi millions of dollars for the industry).

Again, I OPPOSE this Amendment of Chapter 11-157 of Hawaii Administrative Rules.

Mahalo,
Irene Kelly
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, October 24, 2018 10:43:19 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Lauren H. Stuart, MD

**Pediatric Department Chair
Pediatric Hospitalist**



From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Thursday, October 25, 2018 10:28:15 AM

Dear DOH:

I am a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community.

Aloha,
Rachel Randall

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony on proposed Hawaii Administrative Rules (HAR 11-157)
Date: Thursday, October 25, 2018 4:42:26 PM

To Whom it May Concern:

I am writing in strong support of the update on school immunization proposed in the proposed HAR 11-157. As a concerned citizen and parent, I support the change in the list of vaccinations required for 7th grade attendance to include HPV (Human Papillomavirus Vaccine), MCV (Meningococcal Conjugate Vaccine), and Tdap (Tetanus-diphtheria-acellular pertussis vaccine). Adolescents are at high risk of being infected with these viruses and bacteria which have the potential of producing serious, acute illness (MCV and Tdap) or the development of cancers (HPV). These vaccines have been shown to be safe and effective and are of great benefit to the community.

Sincerely,

Sandra P. Chang
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: TESTIMONY (HAR) Title 11, Chapter 157, "Examination and Immunization"
Date: Thursday, October 25, 2018 12:47:50 PM

To Whom It May Concern (i.e. which is all of us),

Re: Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

I'm writing in response to the proposed addition of the following vaccines to the vaccine schedule here in Hawaii:

Hepatitis A, PCV, Rotavirus and Flu Vaccines for those attending childcare.
Hepatitis A, HPV, MCV and Tdap booster in 7th grade for K-12 students.
Tdap and Varicella for all college students and MCV (Meningococcal Conjugate Vaccine) for 1st year college students living in dorms.

Why are more vaccines being added to the list when the vaccine schedule as whole has NEVER been tested for safety or efficacy? Not one study.

Vaccines have also never been tested to determine if they cause cancer, even though they contain cancer causing ingredients. And what are the repercussions of injecting female DNA into males, and male DNA into females? Vaccines grown on aborted fetal tissue contain the DNA from what would have been that child. That aborted fetal DNA can insert into our own children's DNA (it's called Insertional Mutagenesis). We don't know what the repercussions are because it's never been tested.

You'll just keep adding more and more vaccines to the schedule without the proper testing having been done. When is it going to be enough? How many more children need to be maimed or killed until we choose the children over Big Pharma profits?

If you haven't figured it out yet, I am completely against adding more vaccines to the current Hawaii schedule. The proposed amendment to add more vaccines should be denied.

Stephanie Whaley
Sent from [Mail](#) for Windows 10

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Friday, October 26, 2018 10:20:33 PM

Dear DOH:

I am Mia Tran, a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. As a student pharmacist and a pharmacy intern at one of the local community pharmacies, I believe that this would be very important to me.

Thank you for your time and consideration.

Sincerely,

Mia Tran

--

Mia M. C. Tran

[REDACTED]

VINCE YAMASHIROYA, M.D., FAAP
GENERAL PEDIATRICS

October 26, 2018

To Whom It May Concern:

Thank you for this opportunity to provide testimony. As a pediatrician and strong advocate for immunizations, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

One could make the argument that schools should not have the HPV vaccine mandatory since it does not have the same transmissibility as other respiratory infections. However, sexual experimentation does occur in the teen years and early HPV vaccination not only is proven to prevent genital warts and other HPV-related cancers but will also confer better protection compared if given later. HPV vaccination has been proven to be safe despite what one may hear about unproven neurological side effects and it does not make a teenager promiscuous.

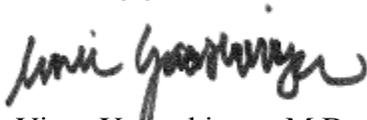
The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely yours,



Vince Yamashiroya, M.D.

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]
Subject: HAR-157
Date: Saturday, October 27, 2018 10:15:09 AM

Re: STRONG OPPOSITION TO HAR-157

Aloha,

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of [REDACTED] and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.

2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question “are you allergic to eggs?” asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind.

5. Stop re-defining what a “group” is – Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that's one thing, but many, many, many of us have opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven't. We have created our own options because there is no “one size fits all” when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don't know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

Sent from my iPad

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines
Date: Saturday, October 27, 2018 9:34:45 AM

Aloha, My name is Sarah Silva

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of Kauai and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.

2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question “are you allergic to eggs?” asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind.

5. Stop re-defining what a “group” is – Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that's one thing, but many, many, many of us have

opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven’t. We have created our own options because there is no “one size fits all” when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don’t know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

Sincerely,

Sarah Silva



From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]
Subject: Please do not mandate vaccines
Date: Saturday, October 27, 2018 4:15:40 PM

Please do not mandate vaccines. They have been implicated in so much injury, disability and death. 3.9 billion paid out to vaccine injured families. Do not mandate or increase your vaccine schedule. I have been a RN for 8 years and I was 1 year away from graduating from Marquette as a Nurse practitioner when my son was vaccine injured at his first set of vaccines. They injected him with 7 vaccines in 3 shots and one oral. He screamed for 18 months. His body was so stiff. He banged his head and did not relax into our arms until 18 months. Do not mandate these vaccines. The rate of death from any of these diseases was already down 90% by the time the first vaccine came to market. Please go to Learntherisk.org, watch Vaccines Revealed, watch Vaxxed, Listen to Dr. Seneff from MIT. You do not want to be part of these permanent injuries, disabilities and deaths.

Thank you for reading this,

Tracy Navar

From: [REDACTED]
To: [REDACTED]
Subject: STRONG OPPOSITION TO HAR-157
Date: Saturday, October 27, 2018 3:04:26 PM

Aloha,

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of Oahu and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.
2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of

gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question "are you allergic to eggs?" asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind.

5. Stop re-defining what a "group" is – Your wording about what a "school" is concerns me. It now defines "school" as a "congregate setting for educational purposes." That is too general. Even if you listed "exceptions" in a later paragraph, this definition is too vague and I ask that it be changed to "public school." If you want to have rules for public school, that's one thing, but many, many, many of us have opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a "one size fits all" mold, we would send them to public school. But we haven't. We have created our own options because there is no "one size fits all" when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don't know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you

believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

Sincerely,
Wainani Young

From: [REDACTED]
To: [REDACTED]
Subject: Re: STRONG OPPOSITION TO HAR-157
Date: Saturday, October 27, 2018 7:40:48 PM

Aloha,

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of [REDACTED] and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.

2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question “are you allergic to eggs?” asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind.

5. Stop re-defining what a “group” is – Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that's one thing, but many, many, many of us have opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public

school. But we haven't. We have created our own options because there is no "one size fits all" when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don't know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Sunday, October 28, 2018 6:27:37 PM

To Whom It May Concern,

Thank you for this opportunity to provide testimony. As a nurse, community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update**, as these proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Recent outbreaks of vaccine-preventable diseases in our state and across our country can be attributed to the decrease in vaccination uptake in our community, thus illustrating the importance and value of vaccinations.

The effectiveness of vaccinations in our community depends on those that are blessed in being healthy enough to receive vaccinations, as those whose immune systems are compromised--our most vulnerable (newborns, elderly, and the immunocompromised), are not able to receive vaccinations.

The health of our community is interdependent. In order for vaccinations to work in preventing disease outbreaks, a concept called, herd immunity is necessary. Herd immunity, indirect protection from a contagious disease, occurs only when a high percentage of the population is immune to the disease, often through vaccination.

Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized. Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration,
Nagisa Kimura, RN, MPH

From: [REDACTED]
To: [REDACTED]
Subject: legislation to increase vaccination requirements
Date: Sunday, October 28, 2018 7:27:19 AM

I have recently become aware that the Hawaii Department of Health is considering legislation to greatly increase the vaccination requirements for children to include HPV and Meningococcal vaccine in seventh grade, Hepatitis A for all children, additional doses of MMR, and flu vaccine for young children. All of these proposed changes are in the wrong direction. Already the childhood vaccination schedule includes an excessive burden of aluminum exposure. Aluminum is present in high amounts and in an especially toxic formulation in the HPV vaccine. Aluminum is also used as an adjuvant in Meningococcal and Hepatitis A vaccine. The flu vaccine often contains mercury, possibly the most neurotoxic metal known to biology. While MMR contains neither aluminum nor mercury, my research on MMR and that of others have shown that MMR is statistically linked to autism. I believe the causal link is due in part to the fact that MMR has been found to contain glyphosate as a contaminant. Glyphosate works synergistically with the glutamate present in the vaccine to cause neurotoxicity.

We face an epidemic in autism, ADHD, food allergies and autoimmune diseases among our children today, and I believe that excessive vaccination is playing a critical role in that epidemic. HPV vaccine in particular has had a very checkered history, with many reports showing up on the web of severe adverse effects leading to either death or a permanent severe disability among affected children. Japan has made the very wise decision to stop recommending HPV. Our country should be following their lead.

Given the rising awareness of the toxic effects of over-vaccination, Hawaii should be considering dropping requirements for some of the already existing vaccines on the schedule. Instead, there is a long list of new vaccines being proposed. In the interest of safeguarding our keiki, I urge you not to introduce any new vaccines on the schedule.

Thank you for your consideration.

Stephanie

[REDACTED]

--

Stephanie Seneff
Senior Research Scientist

[REDACTED]

From: Brad Roon
To: [REDACTED]; [REDACTED]; [REDACTED]
Subject: HPV and vaccines.
Date: Sunday, October 28, 2018 10:24:07 AM

Agammammunoglobulinaemia. Big word - from the middle of the last century, before almost all vaccines existed. No Polio vax, no measles, mumps, meningitis, rubella (chicken pox) HPV, Hep A, B, or C....etc.

This agammammunoglobulinaemia was the condition found in which many people cannot make antibodies - this is a little tricky and requires logic and retention so some don't make it through this train of thought/logic/facts.

The definition of "vaccine effectiveness" (a legal term with no relationship between health, disease curing or prevention and effectiveness in those matters) is "antigen response" So first: What is an antigen?

An antigen is a substance in your body that your body desperately works to get rid of - it could be an allergen like pollen, dander, or a food substance. It could be a toxin. A pathogen. It could be dead cells carried away from a cut, scrape or wound - and EVERY substance in EVERY vaccine is an antigen - your body DOES NOT WANT IT INSIDE OF YOU!

So the body makes antibodies to remove those substances if possible. Not all antibodies are alike. The antibody to remove one of the 4 or 9 out of over 120 HP viruses will not remove the aluminum the shot just shoved into your muscle tissues. Nor will it remove the carcinogenic and neurotoxic formaldehyde in your vaccine, or the Polysorbate 80 (or 20) that will damage your blood-brain barrier and allow toxins to enter your brain which shouldn't get there. That's why you HAVE a blood/brain barrier.

So you get injected with a group of toxins - some neurotoxic, some plain poisonous, some carcinogenic, some genetics from insect slurry, dog parts, calf pieces, egg goo, monkey chunks, and the ever popular aborted human baby genetic line of cells. In the case of HPV vaccines - they use GENETICALLY MODIFIED (never proven safe*) yeast - i'm sure every woman's friend - and viruses which have NEVER BEEN PROVEN TO CAUSE CERVICAL OR ANY CANCERS - EVER!!!!

These people with agammammunoglobulinaemia developed the same childhood diseases as everyone else - at the same rates. More interesting is that they cured their selves in the same time frame and with the same cure rates as people that can make antibodies.

SO ANTIBODIES ARE NOT WHAT CURES DISEASES AND LIKELY DOESN'T PREVENT THEM either in many cases. Since the vaccine crowd (i call them JABBERS for obvious and ambiguous reasons) believes that antibodies are necessary for the immune function to work - THEY ARE WRONG - flat out wrong.

So basically, the HPV shot is a stupid GUESS. The university in Vancouver used Mercks own statistics and proved protection as claimed was absolutely impossible. They also proved that the children that die from anaphylactic shock and those getting headaches develop swelling in their lower brain stem. If severe enough, that can shut down all your motor functions - no heartbeat, breathing, muscle control - and results in situations like that poor girl who got her HPV shot, LITERALLY TOOK SIX STEPS, AND THEN DIED!!!

The HPV is causing - PROVEN to cause reproductive harm to females. In Australia, one girl took her HPV shots at age 14 and entered menopause at age 16. Proven to be caused by the Gardasil. She is not the only one.

So not only is there no proof that HPV viruses cause cancer and that the obverse is shown in studies, not only is there no proven effectiveness of the HPV vaccines to prevent cancer, or even HPV infections - people taking the HPV vaccines are PROVEN to have more likelihood to develop other HPV infections. Proven.

So the shot is targeted wrong, doesn't work as claimed and has the highest degree of damages to the victims of "immunizations" of any vaccine - ever. And we thought Smallpox was bad...That vaccine may not have killed and damaged (reproductively, but mostly neurologically) as much on a per-capita basis as this HPV [REDACTED] does...

So to mandate this vaccine, and violate human rights to self-determination is an abomination, a crime, a psychopathic power play by your group. When one realizes that THERE IS NO POSSIBLE HERD IMMUNITY FROM VACCINES your stupid and erroneous assertion/argument that it's needed for the "good of the herd" goes down the drain. In China there is 99% vax compliance for measles and 707 outbreaks in one year. Total herd immunity failure. In S Korea (2005) it was decided that they had a "chicken pox problem" and in multiple steps increased vaccine compliance. By 2015 they estimated the general populace had 95% compliance, and the under 18 month age group was at 97% vax compliance for chicken pox. Their chicken pox and chicken pox outbreak rate had not only increased MORE than each increase in vaccination - their end result is NOT herd immunity - as the chicken pox rate is TRIPLE what it had been in 2005. Statistically, when one vaccinates - that disease increases.

So you violate the constitutionally recognized human right (they don't come from govt - so govt has no right to take those rights away. If you conversely argue that you are in fact a corporation as you are in reality - no corporation has any regulatory authority over any human being at all - in both cases your arguments are [REDACTED]) unlawfully - which makes YOU treasonous. You literally turn the state into a literal dictator and them into literal slaves - which is no doubt your intent. You have the state practicing medicine without a license - and using the most ignorant, stupid, dangerous, and insane diagnostic criterion of "one size fits all". Thus you show imbecility, spiritual retardation, ignorance of the highest laws of the land, and psychopathic control issues.

[REDACTED] you - i won't even be vacationing in your damn state again if this passes. Only done so twice, but not again, if.....

Bradley S Roon - non corporation (Notice the name is not in ALL CAPS which always ALWAYS designates corporations when used by fictitious legal entities. Note - fictitious legal entity - corporate HAWAII - literally DOES NOT EXIST. It is simply a mind construct agreed upon by some people.)

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Monday, October 29, 2018 5:49:27 PM

Aloha,

My name is Lyndee Sprenger and parent of 4 toddler and elementary age children. All of my children have inherited genetic mutations that make it difficult for them to process chemicals, manufactured and processed foods and other environmental pollutants that many children have no problem detoxing out of their systems. They may look normal and appear healthy, but their genetic makeup allows for them to be more susceptible to even "normal" substances and can cause violent reactions.

Unfortunately we only became aware of this information after severe allergic reactions to vaccination which led to autoimmune issues in both of my older children causing medical as well as other impairment. While we have personally researched long and hard to find the cause of injury, many medical professionals do not recognize the genetic mutations listed yet, and will not support our refusal on medical means to continue to vaccinate our children. This has led to strong beliefs on our part, where we have had to cling to FAITH and the only way we have been able to protect our children is to state we will not vaccinate for their safety based on our religious beliefs. This is true in our case, however it should NOT be the only way we can have our children educated and also choose not to vaccinate. We are making informed decisions about the health and safety of our children based on the science and knowledge we have. Much of this knowledge is learned from personal experience and deep research learned from these sometimes traumatic experiences.

Please allow us the freedom to make choices for our children based on what we believe is safe for them. Medicine is changing and advancing everyday. Things we thought we knew 20 years ago are proving to be wrong today. Please don't let our children be an experiment. Let us as parents decide what is best for our children.

Please do not mandate HAR11-157.

Lyndee Sprenger

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Monday, October 29, 2018 4:47:36 PM

Aloha,

I am writing to you to oppose HAR 11-157 which is a violation of our health care privacy, rights and freedom. I am a stern believer in body autonomy. And I am very concerned Hawaii might follow California's lead in taking that right away from its citizens. Forcing children and healthcare workers to inject themselves with something that the government has deemed critical to society's health at large is a scary thought. I find it interesting that the government has not deemed clean drinking water to the residents of Flint, Michigan and other cities around the nation, important to their health? Yet when a new vaccine can be mandated to the vaccine schedule, and billions of dollars are to be made off that introduction, it seems VERY important to our health. lol. Money aside lets consider the vaccines being questioned, the Hep A and HPV vaccine, If you spend any time doing real research you will find that HPV and Hep A are low on the list of medical concerns. And if you research the HPV vaccine and the injuries resulting from that vaccine it far outweighs the lives saved. Japan and Denmark did not pull that vaccine for no reason. And finally as a parent and healthcare worker I know that NO research has ever been done on the effect of the magnitude of vaccines children receive in America today. When I was a child we received a handful before entering school, today the number these small children have received is astronomical and continues to grow. It is irresponsible medicine. And unfortunately pharmaceutical companies have a heavy hand in Healthcare and government today. But as government elected officials I plead with you not to take their handouts and to really do your research. Please help protect Hawaii's keiki. I am not anti-vaccination, I am for choice in vaccination. Please protect our choice. And do your research. Thank you very much, Tara Mattes

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Monday, October 29, 2018 11:15:46 AM

Thank you for providing the opportunity for me to provide testimony. I am a community pediatrician in East Hawai'i, and i would like to voice my strong support for the HAR 11-157 proposed rules change. We have a large unvaccinated population and visitors from every corner of the world. I tire of treating serious and vaccine-preventable diseases and of seeing children and young adults with life-threatening conditions that might have been avoided, like cervical cancer. Given the history of infectious diseases in these islands, and how the ravages of diseases now vaccine-preventable helped lead to the collapse of the Hawaiian Kingdom, I cannot strongly enough encourage the Immunization Branch of the Department of Health to adopt this common-sense rules update.

Thank you for your consideration.

--

Michael Treece, MD
Pediatrician



[REDACTED] Notice: This Email message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Any unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 proposed rules update
Date: Monday, October 29, 2018 5:48:24 PM

Aloha,

As a practicing pediatrician and public health advocate, I am on the front lines of keeping our keiki healthy and disease-free.

I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

I have seen preventable diseases such as measles, mumps, hepatitis A, hepatitis B, pertussis, and tetanus impact children significantly. The benefit of vaccination is for everyone to remain healthy, while exemptions of any kind put everyone at risk, but significantly increase the risk of the most vulnerable.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,
Bryan Mih, MD MPH FAAP
[REDACTED]



This email was seamlessly encrypted for your privacy and security by [Paubox](#)

Russell Ruderman

10/29/18

To whom it may concern,

I am a state senator for [REDACTED].

I oppose any increase in mandatory vaccinations for any category of workers, students, or people.

The total vaccination schedule today includes about ten times as many vaccinations as we had 20 years ago, and more come on line every year. Yet the combinations of vaccines given have never been proven safe or effective. The sum total of heavy metals in the adjuvants to all these vaccines amounts to a clear health hazard. It has not been proven safe.

I am not an 'anti-vaxxer,' and I am also not 'anti-science.' I am pro-freedom and pro-individual liberty. Like many others I also believe in natural health which does not come from chemicals, but from one's inherent, God-given powers to grow, heal, and maintain health when free from harmful influences, such as pharmaceuticals. You may not feel the same; That is your right, but you do not have the right to take this health freedom away from others.

In fact I have a degree in biology and respect science greatly. One of the primary principles of science is the precautionary principle; if you are unsure of the consequences of an action, proceed cautiously or not at all. This scientific principle should be applied here, instead of the reckless promotion of untested vaccine protocols.

The adjuvants in vaccines have never been proven safe, either in individual doses or in the large combinations of vaccines given today. The active ingredients have also never been proven safe or effective in the same sense that any modern medicine must be proven. The very fact that vaccine manufacturers have been granted immunity from liability is telling: the only other industry granted such immunity is the nuclear industry. The logic is that the liability is so vast and the public need so great that special immunity is needed. But as with nuclear industry, there is no true need and the protection comes from political power and financial influence, not from public safety concerns.

Some say we must compel vaccines to protect ourselves and our kids. But if vaccines really worked, then one wouldn't care if my child or your teacher is vaccinated or not; one's vaccines would protect one. I am aware of the 'herd-immunity' argument here, and I am also aware of its scientific fallacy.

The pharmaceutical industry is free to promote its products, despite lack of safety studies. And you are free to accept them if you wish. But you have no right to compel any one to submit to such hazards, and to take away anyone's freedom of choice regarding how they care for their own body.

The number of vaccines recommended or required in this country is much greater than in other modern countries, such as the E.U. Is this because the other countries are not as 'scientific' as the U.S.? Or is it possible that what we accept as 'scientifically justified' is influenced by the massive outreach of the pharmaceutical industry in our country? And is it possible that you are being used as a marketing device of this pharmaceutical industry?

If there is any question about this, then further compelling the use of vaccines is irresponsible and immoral. You must stop doing so.

Russell Ruderman

[REDACTED] or [REDACTED]

[REDACTED]
[REDACTED]



Submitted electronically to: [REDACTED]

October 29, 2018

Bruce Anderson, PhD
Director of Health
Hawaii Department of Health
335 Merchant Street, Rm. 213
Honolulu, Hawaii 96813

Re: *Notice of Public Hearing Docket No. R-157-18-07*

Aloha Director Anderson,

Kaiser Permanente Hawaii appreciates the opportunity provide the following comments for the proposed amendments to Hawaii Administrative Rules (“HAR”) Title 11, Chapter 157, “Examination and Immunization”. Kaiser Permanente Hawaii supports the proposed amendments given that they update the immunizations required for schools, post-secondary schools, and child-care facilities as well as the manner and frequency of their administration in accordance with current recognized standard medical practices.

Kaiser Permanente Hawaii provides and coordinates complete health care services for over 253,000 members through 21 medical office buildings in the state. We are a total health organization composed of Kaiser Foundation Health Plan Hawaii Region, Inc., Kaiser Foundation Hospitals, which provides hospital services to our patients, and the Hawaii Permanente Medical Group, comprised of approximately 600 physicians who provide or arrange care for patients throughout the region.

The enactment of Act 231, Session Laws of Hawaii 2013, allowed more rapid compliance with federal recommendations for vaccinations. The current state rules process for updating the immunization school entry requirements is very lengthy and can take years. The Centers for Disease Control (CDC) Advisory Committee on Immunization Practices (ACIP) meets three times a year to ensure immunization schedules and vaccine administration guidelines, are providing the best protection against infectious diseases in the population. These proposed amendments by the Department of Health are being done pursuant to Act 231 and adhere to the CDC’s ACIP recommendations as they apply to the specific list of vaccines as required for school entry and attendance in the state.

We note that HAR Title 11, Chapter 157 was last updated in 2001. Therefore, the “*Guide to Hawaii Pediatric Immunization Requirements*” is obsolete and is not in alignment with the CDC’s ACIP schedule. This has led to confusion in terminology, which has in turn led to duplication in vaccine administration. A notable example is inconsistencies in administration of the hepatitis B vaccine. The ACIP recommendation states, “the final dose in the hep B vaccine series should be administered no earlier than 24 weeks,”. In contrast, the “*Guide to Hawaii*

Pediatric Immunization Requirements” states the third (and final) dose should be given, “not before 6 months”. This difference between the ACIP recommendation and the “*Guide to Hawaii Pediatric Immunization Requirement*” has led to infants needing an extra injection, which leads to increased cost and time for the family as well as increased cost and time to the health care system, not to mention added discomfort to the child.

In conclusion, Kaiser Permanente Hawaii strongly supports the proposed amendments to HAR Title 11, Chapter 157 because they conform and align to the CDC’s ACIP recommendations. We believe that the recommended vaccines are a safe, efficient and cost-effective way to protect against vaccine-preventable diseases.

Thank you for your time and consideration. Please do not hesitate to contact Jonathan Ching, Specialist, Government Relations at [REDACTED] or [REDACTED] if you have any questions or require additional information.

October 29, 2018

DOCD, DOH

[REDACTED]

[REDACTED]

Hawaii Department of Health, [REDACTED]

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter157, “Examination and Immunization.”

Strongly **Oppose** Administrative Rules (HAR) Title 11, Chapter157, “Examination and Immunization.” Taking on the ACIP guidelines is not in the best interest of our Keiki’s overall health or best practice of health guidelines for the State of Hawaii.

Dear Hawaii Department of Health,

Thank you for taking the time to read my testimony completely and taking into strong considerations of my testimony. My Name is Dawn Poiani and I am a mother of 3 boys and a health advocate residing in the State of Hawaii. I strongly **oppose** the state of Hawaii taking on the ACIP guidelines as their best practice for immunization. I see serious issues with this proposed rule as there are some inherent flaws in the ACIP vaccine recommendations and . If the state of Hawaii follows the ACIP Vaccine schedule guidelines we are adding multiple new vaccines to our already vaccine burdened schedule. These additional vaccine recommendations have never been tested for safety and synergistic affects of against our current schedule. I have watched hours of multiple different hearings of ACIP and witnessed how new vaccines are approved, and I must say, these hearings are disturbing to watching. I witnessed the ACIP gleefully and irresponsibly approve more vaccines to the pediatric schedule using weak vaccine science and underpowered correlation studies. Every vaccine is approved solely on the safety of the vaccine and if the vaccine will affect the serology of the other vaccines. An example is of the ACIP approval process of approving a new adjuvant in the Hep B vaccine. There are no safety studies done on the new adjuvant given with the currently used adjuvants or the safety of adding it to the schedule as well as there were some risk concerns that the ACIP voted to watch after the Hep B was put on the market. Watch this video and you will get the sense of how

vaccine safety is an after-market concern. https://youtu.be/L_JJMpe00mM. Do we really want to make our children the test subject for the safety of every vaccine that the ACIP recommends adding to our children's vaccine schedule? I don't, these are our children our future! The US Government HHS (Health and Human Services) has never conducted a single safety study as part of the fulfillment of the National Childhood Vaccine Injury Act of 1986 which grants legal immunity to vaccine makers. These safety studies were assigned to HHS in an effort to be the checks and balances over pharmaceutical safety studies and recommendations, because they have no liability for vaccine injuries and death. HHS was also to conduct and report these findings every two years to Congress; these studies have never been done! Exposure to viral particles and adjuvant (aluminum) in vaccines, along with routine exposures to other immune disruptors are '**antigen overload**' for the immune system that could shift the induction of chronic health problems (e.g., increased asthma, ocular or skin allergies, ovarian failure, gastrointestinal conditions or neurological and autoimmune diseases). We are seeing a rapid rise in chronic disease and neurological disorders in the State of Hawaii and across the world. There is only one environmental exposure that can be found in most states as well as most other countries, and that is vaccines. So are vaccines the potential cause of the rise of chronic disease and neurological issues? Are we trading the prevention of a handful of diseases for chronic health issues and neurological problems? We don't know because there has never been an effective study done looking at the vaccine schedule. It is claimed that it is unethical to do a study like that, so the solution is to just put the next new vaccine on the schedule, and see what happens. The ACIP continues to add vaccines to the schedule based on information and studies they receive from vaccine makers that can and do tweak data and find new ways to record reactions and data, in their studies, in an effort to make their vaccines look safer and or more effective (ex. <http://probeinternational.org/library/wp-content/uploads/2014/09/chatom-v-merck.pdf>, <https://www.classaction.com/zostavax/lawsuit/>). Additionally, ACIP calls on VAER to report vaccine injuries as their source of safety once the vaccine is on the market, but VAERS is voluntary and dismally under used for reporting (estimated between 1-10%) yet this is the safety science? There are over 200 vaccines currently being developed, how many more will they add to the schedule without any safety studies against our schedule, how many will be approved gleefully

with poor science? There is only one ingredient and one vaccine adequately studied. From these two studies the mantra has been “the science has been settled that vaccines are safe and effective.” **If the dose makes the poison**, at what point do the trace amounts of aluminum, Antibiotics, Egg protein, Formaldehyde, Monosodium Glutamate, Thimerosal and many many antigens become the tipping point and destroy our children’s health and vitality? I cannot understand how any doctor, immunologist, or virologist can emphatically say that adding to our vaccine schedule is safe. The State of Hawaii should set it’s own schedule based on a **Core Group** of vaccines that are specifically targeted to protect our demographics and geographical tendencies. We have no idea how any vaccine will affect our diverse ethnic population or the affect of our keiki’s overall health by more vaccines to the schedule. It is medically unethical and irresponsible. Are we really going to play a Russian roulette game on our Keiki? The future health of Hawaii deserves better than that. These additional vaccine recommendations do not provide the strength of the benefit to risk ratio to recommend adding further vaccines to the schedule.

By adding the HPV vaccine to the schedule requirements for school entry at 7th grade provides absolutely no benefit to the spread of disease in a school environment. The HPV is a cancer preventative vaccine that may or may not protect the student 20-40 years later from cancer. Additionally, there are serious issues with the way the HPV vaccine studies have been conducted. Manufacturers, did not have to prove that vaccine prevented cancer and were allowed to use precancerous lesions as “surrogate endpoints” in the clinical trials. Scientists do not know if the decline in cases of precancerous lesions will translate into fewer cases of cervical cancer in 20-30 years. None of the participants in the original pre-approval clinical trials received a true saline placebo, an aluminum containing adjuvant was used. Manufacturers never tested HPV vaccines on human fertility (acknowledged in the package insert). Manufacturers never tested HPV vaccine to discover if they might cause cancer (package insert say vaccine has never been tested for “carcinogenicity”). <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>. The original Gardasil clinical trials used a new metric, “**New Medical Conditions**,” as a way to claim that serious health problems after vaccination were unrelated to the vaccine or aluminum-containing placebo.

More than 50 percent of all clinical trial participants reported “new medical conditions,” including infections, reproductive disorders, neurological syndromes, and autoimmune conditions. The FDA never questioned this novel metric. Lawsuits have been filed against Merck, GlaxoSmithKline, and government health agencies around the world, including the US, India, Columbia, Japan, Spain and France. The US government earns royalties from Merck and GSK for licensing HPV vaccine technology (this is an egregious conflict of interest!). Why would the state of Hawaii mandate the HPV vaccine, when the vaccine carries these kinds of flaws in the HPV vaccine safety assurance? As of June 2018, the VICP paid out or settled 126 HPV vaccine claims. A total of 49 people received \$5.8 million after the U.S. Court of Federal Claims found Gardasil injured them <https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-june-2018.pdf>. “The HPV Vaccine On Trial: Seeking Justice for a Generation Betrayed” by Mary Holland. Let the HPV be an optional vaccine and not mandated to the required school entry **Core Vaccines**.

According to the manufacture’s package inserts, the rate of “**serious adverse events**” **from meningitis B vaccine are 2.1% for Bexsero (Novartis)**, <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm431447.pdf> and **1.8% for Trumenba, (Pfizer)**, <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm421139.pdf>. Based on this information, if the roughly 58,000 HI college and undergraduate students receive either of these vaccinations, approximately 1,218 students will experience “severe adverse events,” including death. In 2016, there were 2 cases at Rutgers University, treated with antibiotics and fully recovered. The risk of “**SERIOUS ADVERSE EVENTS**” from the vaccine is much higher than the risk of becoming ill with bacterial meningitis. At a cost of \$100-125 a dose, this is a serious cost to the State of Hawaii. Although Bacterial Meningitis can be a serious disease, it is not common and is very difficult to acquire. The best outcomes in cases of bacterial meningitis occur when the infection is detected early and antibiotics are administered. Public Health initiatives to enhance the awareness of the early symptoms of the infection and the importance of securing appropriate treatment would be impactful. There is no public health situation present that warrants infringing on a person’s right

to decide what medical treatment and intervention is appropriate for him/her and allowing doctors and students to make these decisions for health care is essential.

Hep A cannot become chronic disease and most (70%) of infections in children younger than age 6 are not accompanied by symptoms according to the CDC. To avoid “**antigen overload,**” the Hep A Vaccination should only be recommended for individuals in high-risk settings and not for the requirement of school attendance.

Examples would include people that are at increased risk for acquiring hepatitis A virus (HAV) infection?

- Persons with direct contact with persons who have hepatitis A
- Travelers to countries with high or intermediate endemicity of HAV infection
- Men who have sex with men
- Users of injection and non-injection drugs
- Persons with clotting factor disorders
- Persons working with nonhuman primates
- Household members and other close personal contacts of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity
- People who have chronic liver disease.
- Homeless population.

The cases of Hep A we have seen in Hawaii in the past years have not spread from student to student in schools. Most of our Hep A cases were from food contamination. The healthier approach to preventing the spread of Hep A would be addressing the food importation issues into Hawaii. There is very minimal risk of Hep A spreading from student to student in schools.

The influenza vaccine from year to year is from 10% -60% effective according to the CDC. The flu vaccine, due to the innate natural drift nature of the virus and the absolute guess that the flu vaccine makers must make to pin point the prevalent strain the following year, this vaccine is not affective. The flu vaccine is one of the leading reported vaccines for adverse events according to VAERS. This risk/benefit ratio to require this vaccine for school just doesn't add up. Additionally this vaccine continues to have trace amounts of mercury (Thimerosal),

according to the FDA vaccines with trace amounts of thimerosal contain 1 microgram or less of mercury per dose.: the manufacturers best effort to wash the mercury out is not 100% effective. However mercury in conjunction with aluminum creates a heavier neurotoxic load which comes with risk. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344667/>
<https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>
<http://vaccineimpact.com/wp-content/uploads/sites/5/2017/09/DOJ-Report-9.8.17.pdf>

The requirement of a standardized medical exemption is flawed and it is a direct effort to restrict our medical rights. A standardized medical form may intimidate or discouraging a Physician to use their best precautionary principles and medical judgement for each patient. Physicians need to be allowed to write their medical evaluations and exemptions on their own letter head and freely decide if a vaccine is truly appropriate using the best medical judgement for each patient. It is not in the best interest of the patient or the physician to create additional paperwork, road blocks or exemption restrictions to a physicians best medical practice.

The Hawaii Vaccine Coalition is promoting the idea that restricting or even eliminating Religious Exemptions would improve vaccinations rates, which are already higher than the national average. Article I section 4 of the bill of rights “No law shall be enacted respecting an establishment of religion, or prohibiting the free exercise thereof, or abridging the freedom of speech or of the press or the right of the people peaceably to assemble and to petition the government for a redress of grievances. [Ren and am Const Con 1978 and election Nov 7, 1978]. There are inherent constitutional issues of restricting religious exemptions or challenging a persons spiritual beliefs.

Mandatory school reporting of all students with vaccine exemptions may be a violation of FERPA (Federal Educational Rights and Privacy Act) as well create additional financial burden on schools. <https://www.mbm-law.net/newsletter-articles/“ferpa-trumps-hipaa-in-immunization-disclosure”/1020/>

Oppose Administrative Rules (HAR) Title 11, Chapter157

Thank you for the time you took to read my testimony. **I strongly OPPOSE HAR 11-157 rule changes.** These rule changes are not in the best interest of our Keiki's health or the best interest of promoting a healthy child in the State of Hawaii. My uncle is a Surgeon/doctor and he once said "before I prescribe any medication I always ask myself will this drug cause more harm than the disease it is trying to cure?". These rule changes squash our freedom and the fundamental principles of effective and safe medicine - "First Do No Harm." Please host a public hearing statewide to fairly hear all testimony on all islands.

Sincerely,

Dawn Poiani

████████████████████

██

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Monday, October 29, 2018 8:47:49 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration

Dr Kara Wong Ramsey
Neonatologist at [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: TESTIMONY IN SUPPORT OF HA11-157
Date: Monday, October 29, 2018 12:13:33 PM

Thank you for this opportunity to provide testimony. **As a pediatrician, parent, community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Malia A.L. Shimokawa, MD
Pediatrics

[REDACTED]

[REDACTED]

[REDACTED]
[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Tuesday, October 30, 2018 5:05:27 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Dennis Inouye

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Tuesday, October 30, 2018 5:58:58 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

L. Inouye

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 proposed rules update
Date: Tuesday, October 30, 2018 12:01:29 PM

To the Hawaii DOH:

I am writing to strongly support the HAR 11-157 rules update. I have practiced community pediatrics on Kauai for over 40 years, long enough that I have been witness to the enormous benefits that have occurred with the introduction of the Varicella, Hemophilus, and Pneumococcal vaccines, to name just a few of the vaccines that have been developed and have become the standard of care over my practicing lifetime. I cannot stress strongly enough how gratifying it is to see the virtual elimination of bacterial meningitis, epiglottitis, and pneumococcal pneumonia, which in the past caused severe morbidity and mortality. In addition, because of an over 90% immunization rate on most of Kauai, we no longer have to witness life-threatening varicella in immunocompromised children, and severe chicken pox in adolescents. We have seen even recently the effects of a Hepatitis A epidemic in the unimmunized population in Hawaii, and until Hepatitis B vaccine was introduced we were helpless to prevent the maternal-newborn transfer of the Hepatitis B virus, which was a cause of chronic Hepatitis B infection, cirrhosis, and liver cancer. I could go on, but these are just a few examples of the inestimable good that has accrued to the health of our keiki from a strong and diligent immunization program. I am happy to see the immunization standards for Hawaii being updated, as we have newer vaccines and recommended practices with the advent of the administration of Meningococcus, DTaP, and HPV vaccines to preteens. I also strongly support the emphatic language regarding school attendance vis-a-vis appropriate physical exams and documented immunizations or immune testing. As health workers, we must continue to support the best health measures for all of Hawaii's children, and we have plenty of data and strong recommendations from the CDC and AAP to support us in this endeavor.

Thank you so much for soliciting opinions from the pediatric community on this very important health issue.

Sincerely,
Linda J. Weiner, MD
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: I oppose additional vaccines being added to the childhood schedule.
Date: Tuesday, October 30, 2018 7:58:59 AM

Please consider your actions carefully. There is mounting scientific evidence that our over-bloated vaccine schedule is doing grave damage to a whole generation of our children.

Meningococcal vaccine for all seventh graders:

There is no question that meningococcal meningitis is a serious disease that can cause death and disability, but we need to ensure that the solution is not worse than the problem. There is every reason to believe that mandatory meningococcal B vaccines for all seventh graders could kill more students than the disease they protect against. Before we relinquish our rights, pay millions and sicken students, we should do the math.

http://www.dailycamera.com/guest-opinions/ci_28283397/robert-f-kennedy-jr-doing-math-meningitis-vaccinations

HPV vaccine for all seventh graders:

The HPV Vaccine on Trial: Seeking Justice for a Generation Betrayed paints a devastating picture of corporate and government conflicts of interest, negligence, and malfeasance in approving and promoting human papillomavirus (HPV) vaccines, touted to prevent cervical and other cancers. Coming out on the heels of recent New York Times revelations about astounding financial conflicts of interest at Memorial Sloan-Kettering Cancer Center, this groundbreaking book highlights the lack of transparency, manipulated science, and abuse of state power to market this medical juggernaut, already raking in over \$2.5 billion per year. Authors Holland, Rosenberg, and Iorio conclude:

- HPV vaccines have never been proven to prevent cancer of any kind.
- No participants in the original HPV clinical trials received true saline placebos.
- Japan no longer recommends HPV vaccines following a mass of injuries
- The clinical trials never investigated the vaccine's possible effects on human fertility or potential to cause cancer.
- The clinical trials show that the vaccines contribute to HPV lesions, and potentially cancer, in some women. Despite this, neither the manufacturers nor government agencies recommend prescreening to eliminate those with clear risk factors.
- Although the vaccine is targeted for 11-12-year-old children, and legal for children as young as 9, only a small fraction of clinical trial subjects was in this age range.
- Lawsuits against HPV vaccine manufacturers and government health agencies are progressing around the world, including the US, India, Japan, Colombia, Spain, and France.
- The US government earns millions in royalties from Merck and GSK, the vaccine manufacturers, for its role in the invention of HPV vaccine technology
- Although the US government proclaims HPV vaccines safe and effective, it has paid out millions of dollars to compensate families for death, brain injury, multiple sclerosis, ulcerative colitis, and other severe, debilitating conditions.

Influenza vaccine for all young children:

The influenza vaccine is a joke. It is very ineffective, usually less than 40% effective. And in multi-dose vials it contains mercury which can cause serious brain damage. Why are we risking the lives of our children with this vaccine, when the illness is not a threat to any healthy child. Keep our children healthy with hand washing and nutrition that includes adequate levels of vitamins A, C, and D.

Hepatitis A vaccine for all children:

The best tool for prevention of hepatitis A is to wash your hands with soap and water after using the bathroom, changing a diaper or preparing and eating food.

While I support the availability of hepatitis A vaccine for all who choose to use it, I oppose the mandated use of hepatitis A vaccine for the following reasons:

Hepatitis Does Not Cause Chronic Infection and Rarely Causes Death: Hepatitis A has a mortality rate of less than one percent (0.6) and over 70 percent of deaths occur in adults over the age of 49. Almost everyone who gets hepatitis A recovers from it without any treatment. Plus, it is so rarely fatal that the CDC does not show a record of deaths from it some years.

Hepatitis A Gives Lifelong Immunity But the Vaccine Does Not: Children often show no symptoms if they get hepatitis A and then develop lifelong immunity to the infection, but nobody knows how long vaccine-induced immunity will last. (All vaccines give only temporary immunity).

Child-to-Child Transmission in School is Rare: According to the CDC, "Child-to-child disease transmission [of hepatitis A] within the school setting is uncommon."

Hepatitis A Vaccine Can Cause Reactions: The vaccine can cause unpleasant or even health- or life-threatening conditions, such as Guillian-Barre Syndrome.

Additional dose of MMR for post-secondary school attendance and Meningococcal vaccine for all first-year students living in on-campus housing:

From 2003 to 2017 there were 127 deaths due to the MMR vaccine reported to VAERS, yet only 2 deaths due to natural measles during the same time period. Harvard School of Medicine estimates that only 1 to 10 percent of vaccine injuries are reported to VAERS. So actual VACCINE DEATHS could range from 1,270 to 12,700. Our ability to capture real data on the post-marketing occurrence of vaccine injury is appalling!

Please! for the sake of our children! Do not add any more vaccines to the childhood schedule.

Sincerely,
Susan Jorg
Oregonians for Vaccine Truth and Healthcare Choice

HAWAII YOUTH SERVICES NETWORK

677 Ala Moana Boulevard, Suite 904 Honolulu, Hawaii 96813

Phone: (808) 489-9549

Web site: <http://www.hysn.org> E-mail: [REDACTED]

Rick Collins, President

Judith F. Clark, Executive
Director

Bay Clinic

Big Brothers Big Sisters of
Hawaii

Bobby Benson Center

Child and Family Service

Coalition for a Drug Free Hawaii

Domestic Violence Action Center

EPIC, Inc.

Family Programs Hawaii

Family Support Hawaii

Friends of the Children of
West Hawaii

Hale Kipa, Inc.

Hale 'Opio Kauai, Inc.

Hawaii Children's Action
Network

Hawaii Student Television

Ho'ola Na Pua

Kahi Mohala

Kokua Kalihi Valley

Maui Youth and Family Services

P.A.R.E.N.T.S., Inc.

Parents and Children Together
(PACT)

Planned Parenthood of the
Great Northwest and
Hawaiian Islands

Salvation Army Family
Intervention Services

Sex Abuse Treatment Center

Susannah Wesley Community
Center

The Catalyst Group

October 30, 2018

To: Dr. Bruce Anderson
Hawaii Department of Health

Testimony in Support of Amendments to Immunization Policies

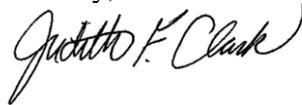
Hawaii Youth Services Network (HYSN) supports the proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization, which seek to codify the United States Department of Health and Human Services' Advisory Committee on Immunization Practices' General Best Practice Guidelines for Immunization.

A fully immunized population is our best protection to prevent the spread of communicable diseases. In particular, HYSN is pleased to see that HPV vaccine will be required for public school students.

HPV is so common that nearly all sexually-active men and women will get at least one type of HPV at some point in their lives. There is no cure for HPV - only treatment for related health problems. Yet, too few adolescents in Hawaii are receiving HPV vaccines.

Thank you for this opportunity to testify.

Sincerely,



Judith F. Clark, MPH
Executive Director

10/30/18

RE:

Public hearing notice: Proposed Changes to Hawaii Administrative Rules (HAR 11-157)

Re: NEW VACCINE REQUIREMENTS and REPORTING

Thursday November 1st 3:00-4:00 pm

Location: Hawaii Department of Health, Kinau Hale Boardroom, 1st Floor 1250 Punchbowl Street, Honolulu, HI 96813

To Whom It May Concern:

I would like to submit written testimony regarding the above.

I strongly OPPOSE HAR 11-157, for the following reasons:

This grave responsibility and power to make potentially life-altering decisions for Hawaii's Keiki, should not reside in the hands of a very few individuals, (if not a single individual: Chief of Disease Outbreak Control Division of the Hawaii DOH). The customary checks and balances of our Legislative Body should be restored, and the 2013 statute that allowed for this excessive control over health policy should be repealed. The Hawaii DOH should not be allowed to use such broad strokes in addressing important children's health policy. Notable important changes (too many) include: 1. The addition of multiple vaccines, some of which are not transmissible in a school setting (HPV). There are almost 300 vaccines currently in development, and ACIP blindly adds more vaccine requirements, when not one safety study has ever evaluated the potentially dangerous, synergistic or long term effects. How many is too many? See video here of an actual ACIP meeting to approve a new Hepatitis B vaccine—while acknowledging that data on a known "signal" of myocardial infarction [heart attack] will be collected from their consumer-guinea pigs, after sales begin 2. The requirement of a standardized Medical Exemption form could interfere with the doctor/patient relationship, restrict and discourage a physicians' best professional judgement regarding the patient-specific, "precautionary principle of medicine". 3. The requirement of a standardized Religious Exemption form may include wording that restricts religious freedoms. 4. Mandatory school reporting of all students with vaccine exemptions may be a violation of FERPA (Federal Educational Rights and Privacy Act). 5. New requirements for HPV (Human Papilloma Virus / trade name "Gardasil") and Influenza vaccines. Because neither have been deemed truly safe or effective, reports of extremely low voluntary uptake exists worldwide.

VAERS has paid out over \$3.7 billion to people for vaccine injuries. Vaccines are not completely safe. We have basic human rights. We should not be forced to vaccinate.

Sincerely,

Katherine M. Gravesen

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11 Chapter 157
Date: Tuesday, October 30, 2018 12:04:46 AM

Dear DOH:

I am a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. As a student pharmacist, I can help take the burden off of patients who do not have time to go and see their doctors. By having us easily accessible, more people can get vaccinated which means less chances of disease.

Respectfully,

Samantha Okubo

Student Pharmacist

Class of 2022

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Opposing HAR11-157
Date: Tuesday, October 30, 2018 7:44:27 AM

Aloha,

I'm a 25+ year resident of Hawaii and have two school age children. I absolutely oppose mandatory vaccinations.

Thank you,

Ano Hanamana

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines
Date: Tuesday, October 30, 2018 9:31:09 AM

Aloha, I'm writing in regards for my grandson Zechariah Kamaile- Shim. I adopted him at the age of 6months he's now 11yrs old . I'm grandma but legally mom. Single parent. He has autism, none verbal and extreme aggressive behaviors. At he meet all his milestones but had many ear inspection. So that time he missed having vaccine shot due to air infection and a cold coughing runny nose. So at 18 months old he was given his vaccine shot three days later No eye contact No laughing No sound from his mouth he was there and breathing normal but as if he'd turn into a zombie! All those months before he was he was a happy loving baby saying mama and baby talk. I know in my heart that those 4 shots made him this way and know he has to suffer for the rest of his life. I pray everyday for those people to understand what it feels like to be in those children's shoe and really know what they'd go through. God please bless your children for with your grace! In Jesus name Amen ..Thank you Renee and my grandson Zechy.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Zero mandatory vaccination
Date: Tuesday, October 30, 2018 11:32:18 AM

Until we test for MTFHR gene mutations which occur in up to 50% of the population and some mutations can inhibit detoxification in the body and cause reactions such as swelling on the brain in these individuals who cannot detoxify as easily as the rest of the population, so these toxins do greatly affect them, and not others...until we test everyone for this we cannot require everyone to take toxin containing vaccines....Ann Powers 868-9393

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Testimony on vaccinations
Date: Tuesday, October 30, 2018 12:25:21 PM

Aloha,

I am a parent and nanny. I did extensive research on vaccinations when my daughter was a baby, in the 1990s in California. At that time we still had the right to refuse vaccinations. Based on that research, we decided not to vaccinate my daughter. Primarily there were four issues for us: The use of Mercury in some vaccinations, the lack of proactive investigation and data gathering and study on the adverse impact of vaccinations on children, the studying of the influence of vaccinations in spreading disease, and the number of vaccines given to babies at one time. We chose to strengthen her immune system through the use of natural medicines.

Fast forward to 2018. As a nanny, I saw the adverse and potentially fatal effects of vaccination first hand, here on Maui. The 1 year old for whom I cared was vaccinated. The day after his visit to the doctor, he experienced shortness of breath which woke him from his nap. I called 911 and his mom, as he continued to struggle to breathe. Fortunately, I had Rescue Remedy with me, and administered it to him. Within seconds his chest shifted and his breathing became normal.

His father and the paramedics arrived. The head paramedic was questioning the father on health history. Father told him that he had his checkup the day before and he had been vaccinated (4 vaccinations at once). Not knowing this, I said oh, perhaps that's what caused it. The paramedic looked sternly at me and said " that's not possible.". I countered that in fact it was highly probable and that it should be noted. I also told his I gave the child Resue Remedy and it successfully cleared his breathing. He ignored this information.

The boy's mother took him to the doctor later that day and the doctor minimized the effect of the vaccinations. These attitudes by medical professionals are disturbing in that they lack interest in what is actually happening to children who have been vaccinated.

Also, please note that during the California whooping cough outbreak in 2010, 81% of pertussis cases under the age of 18 were fully vaccinated children. In a pertussis outbreak in Texas, the CDC statistics show that 81.5 percent of cases were fully vaccinated.

There are still big questions about vaccinations and their effectiveness, as well as their side effects. If medical professionals are trained to not even collect data and show interest in what is really going on, how can the public trust them. Parents should have the right to choose whether to vaccinate their children. And the state should ensure that the medical industry is researching the effects of vaccination in an unbiased way, and that the truth is being shared with the public.

Sincerely,
Rosemary Robinson
[REDACTED]

From: [Christopher Lawinski](#)
To: [DOH.Immunization](#)
Cc: [Don Daughtrey](#); [Amara Karuna](#); [Sally Boyd-Daughtrey](#)
Subject: Re: HAR-11-157
Date: Tuesday, October 30, 2018 3:12:55 PM

To Whom It May Concern,

Regarding HAR 11-157

I am a physician in private practice ([REDACTED]). I am strongly opposed to HAR 11-157. As a physician I have personally witnessed numerous vaccine related injuries, including neurological developmental injury, during routine vaccination as per the CDC recommend childhood vaccination schedule.

The risk of vaccination is not insignificant. To view the risk of vaccine injury, as documented by the Federal Health Resources and Services Administration, please see the following url: <https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-oct-2018.pdf>. Compensated injuries represented here are injuries that are permanent or fatal. The document represents a gross under reporting of vaccine injuries since it documents only those vaccine injuries filed in a federal court and represents only permanent, fatal and near fatal injuries. Vaccine injuries are real and they are much more common than published data suggest.

Any decision regarding a medical procedure that involves risk should be based upon an informed consent between the doctor and patient that involves assessment of the individualized benefits versus risk for any procedure. Mandatory vaccines in any form, as proposed by HAR-11-147 violate the basic right to make informed healthcare choices and place the citizens of Hawaii at increased risk for iatrogenic illness by enforcing a one sized fits all medical procedure. Medical interventions can be put in place to help protect from vaccine injury, but only if patients are properly informed of the risks and have a choice in the matter.

The HPV vaccine is particularly dangerous. The impact of the HPV vaccine seen in my patients includes damage to joints, cartilage and mobility which at this point seem to be permanent. This vaccine is untested in combination with other vaccines and is not necessary for community safety in a primary school setting as HPV is a sexually transmitted disease.

Please protect our children by opposing HAR-11-157.

Christopher S Lawinski, MD
[REDACTED]

[REDACTED]

CONFIDENTIALITY: This communication, including attachments, is for exclusive use of the addressee(s) and may contain proprietary, confidential or privileged information. If you are not the intended recipient, any use, copying, disclosure, or distribution or the taking of any action in reliance upon this information is strictly prohibited. If you are not the intended recipient, please notify the sender immediately and delete this communication and destroy all copies [v1.0.001].

On Tue, Oct 30, 2018 at 12:52 PM Sally Boyd-Daughtrey

[REDACTED] wrote:

To Whom It May Concern,

I am strongly opposed to HAR 11-157. As a physician I have seen numerous teenagers and young adults damaged by the HPV vaccine in particular. The impact of the HPV vaccine seen in my patients includes damage to joints, cartilage and mobility which at this point seem to be permanent. This vaccine is untested in combination with other vaccines and is not necessary for community safety in a primary school setting as HPV is a sexually transmitted disease.

Please protect our children by opposing HAR-11-157.

Sincerely,

Dr. Sally Daughtrey

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Regarding: NOTICE OF PUBLIC HEARING DOCKET NO. R-157-18-07
Date: Tuesday, October 30, 2018 4:40:27 PM

To Whom it May Concern within the Hawaii Department of Health:

It has come to my attention that the Hawaii Department of Health has a Public Hearing coming up on November 1st regarding proposed rule changes to include new vaccination requirements for Hawaii's children in order to attend school or daycare.

One of the vaccines that it appears may be added to the list of vaccines required for children includes the influenza vaccination. Is this committee aware that the National Vaccine Injury Compensation Program has paid out almost 4 billion dollars since the program began to those injured or killed by vaccines, many of whom received the Influenza vaccination? The current up to date payouts can be found here: <https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-oct-2018.pdf>

A recent press release stated that pharmaceutical companies who manufacture vaccines may reach an estimated 61 billion dollar profit by the year 2020. We have seen time and time again, pharmaceutical companies putting profits over the health of Americans. It is absolutely a proven fact that cannot be disputed. Why, then, are they given blanket immunity via the National Childhood Vaccine Injury Act of 1986 signed into law by President Reagan? Because vaccine manufacturers are not held liable for the injuries and or deaths they may cause, there is low incentive to create a safer vaccine.

The Advisory Committee on Immunization Practices is a committee within the CDC who recommends the vaccination schedule to the American people. Has anyone within the Hawaii Department of Health ever sat and watched the ACIP committee have discussions and make vaccine recommendations? Please see the video here for an example of ACIP's abhorrent and negligent decision-making process in action: https://www.youtube.com/watch?v=L_JJMpe00mM&feature=youtu.be

Also see this link here: <https://www.youtube.com/watch?v=vUPWRWTxj4s&feature=youtu.be> where you can watch the ACIP vote on its new vaccine schedule recommendations, unanimously-immediately after hearing the impassioned comments and criticisms by members of the public at their latest meeting.

Recently this past summer, the Informed Consent Action Network (ICAN) and Robert F. Kennedy Jr. sued the United States government and won in an issue regarding vaccine safety. According to a legal document entitled, "Mandate for Safer Childhood Vaccines" Health and Human Services (HHS) has openly admitted to not having filed any vaccine safety reports in over 30 years as they were required to by the National Childhood Vaccine Injury Act of 1986. See link here: <http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

If we cannot even trust our own government to do the studies that will show us whether vaccines are safe or not, how is it acceptable to continue to add more and more vaccines to the requirements in order for children to attend school or daycare?

I vehemently oppose the addition of any vaccination requirements proposed and discussed

during this public hearing. Until vaccine safety is removed from the CDC to an independent scientific board, I will never be in favor of any additional vaccines being added to the schedule. Vaccine safety should not be done by the very people who create the vaccines, and then recommend them to the public to purchase. The conflict of interest is huge, and our children and the American people deserve better. We MUST stop blindly following what the pharmaceutical companies desire. It is simply no longer acceptable.

Sincerely,
Tara Czachor

From: [REDACTED]
To: [REDACTED]
Subject: Re: Fwd: Hawaii Administrative Rules
Date: Tuesday, October 30, 2018 10:33:23 PM

"Always" with a smile...Nancy!

Begin forwarded message:

From: Curtis Ochiai [REDACTED]
Subject: Hawaii Administrative Rules
Date: October 30, 2018 at 3:54:19 PM HST
To: [REDACTED]

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Dear Dept of Health, I am writing to **strongly support the HAR 11-157 proposed rules update.**

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

Thank you for your consideration.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Nancy OConnor

From: [REDACTED]
To: [REDACTED]
Subject: Hawaii Administrative Rules
Date: Tuesday, October 30, 2018 3:54:26 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Curtis Y. Ochiai
Parent

From: [REDACTED]
To: [REDACTED]
Subject: Support of HAR 11-157
Date: Tuesday, October 30, 2018 8:58:27 AM

Thank you for this opportunity to provide testimony. As a community member, mother, and physician, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap vaccines.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, the vulnerable groups above whom pediatricians in Hawaii take care of, will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks, such as what we have seen recently in California prior to the change in their immunization requirements for school. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Kristyn Nishimoto, MD

From: [REDACTED]
To: [REDACTED]
Subject: Support of HAR 11-157 proposed rules update.
Date: Tuesday, October 30, 2018 7:13:24 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Kent Inouye
Grandparent

From: [REDACTED]
To: [REDACTED]
Subject: support the HAR 11-157 proposed rules update.
Date: Tuesday, October 30, 2018 7:15:30 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks.

--
Cynthia Inouye
[Grandmother and Parent](#)

October 30, 2018

Disease Outbreak Control Division (DOCD)

1250 Punchbowl Street, Room 443

Honolulu, Hawaii 96813

SUBJECT: Proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

Aloha,

As a parent of three children I OPPOSE the proposed amendments to the Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

There is no need to impose vaccines for sexually transmitted diseases for all students especially when some students are not sexually active. Please be mindful that ALL vaccines contain toxic ingredients and they ALL carry risks. I would appreciate if each family along with their medical advisor be allowed to weigh the pros and cons of each vaccines for themselves. The HPV vaccine in particular is highly controversial as many thousands of women have claimed injury from this vaccine. If there is a risk, there should be a choice and an opportunity for informed consent.

I would also like to request that a public hearing be held on every island for all families to be informed and participate in the hearing process.

Mahalo,

Mitsuko Hayakawa

Parent and Resident of [REDACTED]

Tarita Tehotu
Mother, Grandmother, Wellness & Health Advocate

[REDACTED]
October 30, 2018

Bruce S. Anderson, PhD., Director of Health
Hawaii Department of Health
1250 Punchbowl Street
Honolulu, HI 96813

Aloha Dr. Anderson,

I am in strong opposition to the proposed amendments to HAR Title 11, Ch 157. As a mom, grandma, registered nurse and health advocate, **a serious question** has arisen in my heart over the many years of attempting to understand the role and purpose of Hawaii's Department of Health: ***What causes a health agency like the Department of Health to develop and continue with perspectives, policies and rules that are questionable or detrimental to the health and welfare of the people of Hawaii?*** Is it pressure? Funding? Biased research? Fear? Power? Conflicts of interest? Misguided controlled information?

As stated on your website: "The mission statement of the Department of Health is to protect and improve the health and environment for all people in Hawaii", with goals to "promote health, well-being, healthy lifestyles in families, communities and workplaces." These are admirable intentions to be promoters of health and wellness for our beautiful islands. Yet, one of the department's guiding principles is to "ensure that federal mandates are satisfied."

Here is the major concern: Even if federal health recommendations or guidelines do NOT work or benefit the people of Hawaii, the DOH continues to follow and implement them. It is very disturbing that the current proposals for the DOH administrative rule continue to adopt the increasing vaccine schedule following the U.S. DHHS, CDC and ACIP guidelines. (Dept of Health & Human Services, Center for Disease Control, Advisory Committee for Immunization Practices).

Firstly, the following are researched and credible reasons (with resourced footnotes) to understand that adopting the recommendations of DHHS, CDC and ACIP is NOT in the best interest for Hawaii:

- The U.S. vaccine recommendations process is hopelessly compromised by conflicts of interests with vaccine manufacturers, the FDA and the CDC. (1)
- The U.S. Vaccination Policy Flow Chart shows how vaccine policies are made with questionable relationships between the vaccine industrial complex, FDA and the CDC's ACIP.
- Congressional records and transcripts indicate scientific and industry fraud including cover-ups of data that clearly show definitive links between vaccines and serious vaccine injuries. Yet, the U.S. Congress passed a law in 1986 shielding vaccine makers and doctors from liability for vaccine injuries and deaths. More CDC employees and other federal health agency whistleblowers are coming forth and exposing the corruption to the public via mass media and publications. (2)
- Recommendations may be given from the WHO, DHHS, CDC, ACIP and other global or federal health programs, but why is Hawaii's Department of Health **requiring** to adopt recommendations from these "experts" who appear NOT to have our best health interests?

Page 1 of 3

Secondly, public confidence in national and international vaccine policies is at an all time low obviously because of the following well-documented facts:

- We are facing the sickest generation and the U.S. Childhood Health statistics straight from the CDC's own website states:
 - 1 in 6 children with developmental disabilities. (3)
 - 1 in 59 children with Autism Spectrum Disorder (4)
 - 3,600 sudden unexpected infant deaths (SIDS) in 2016 (5)
 - Many other statistics from health agencies disclose phenomenal increases in childhood cancers, irritable bowel syndromes, arthritis, diabetes and other chronic conditions.
- The increasing vaccine schedule and lack of safety and efficacy studies ignore scientific evidence and valid testimonies of adverse vaccine reactions (see VAERS) at the expense of public health interests:
 - Increasing doses of 15 different vaccines with several added booster shots are now being given to our children from birth to age 18, with more vaccines being added to the schedule. Pregnant women are being vaccinated as well as the elderly with more toxic vaccines that compromise immune systems. Adverse reactions are sky-rocketing from neurodevelopmental disorders, allergies, seizures, paralysis, autism and others, worsening as the types and total number of vaccines required have expanded. (6)
 - The CDC's excipient list of vaccine ingredients reads like a toxic brew: from neuro-toxic aluminum, mercury, monosodium glutamate, formaldehyde, polysorbate 80 that causes cancer and infertility, human DNA from aborted babies, pig blood, horse blood, rabbit brains, dog kidneys, cow hearts, monkey kidneys, chick embryos, calf serum, sheep blood and more. (7)
 - Promoting mass vaccines is extremely profitable and big business. As the vaccine schedule continues to increase, global profits from the worldwide vaccine business climb to billions of dollars. Close to 300 more vaccines are in development.

Finally, is the adoption of these DOH administrative rules a violation to our health care privacy and freedoms?:

- Is there a violation of FERPA (Federal Educational Rights and Privacy Act – 20 U.S.C. Section 1232g; 34 CFR, Part 99) when requiring schools to report to the DOH the students/children names of those who have met the immunization requirements and those who have medical or religious exemptions (Section 11-157-64, pages 157-17)? This statewide violation would place Hawaii schools at risk of losing dollars in federal education support.
- Is there a violation of HIPAA (Health Insurance Portability and Accountability Act) as it allows health care providers to send copies of vaccine records to DOH (Section 11-157-5, pages 157-11&12)?
- These national FERPA and HIPAA standards are there to protect individual medical records and personal health information to safeguard the privacy of citizen information from being released to third parties such as local and state health departments.

There are rational perspectives and common sense advice for staying healthy as Hawaii's promoter for health and wellness. As Hawaii's Department of Health, you are encouraged to invest time, resources and energy in researching and promoting healthy lifestyles and health care to improve natural immunity, instead of adopting federal health policies that recommend and promote more toxic vaccinations.

Thank you for your consideration in this serious matter. Mahalo –
Tarita Tehotu



Footnotes:

1. <https://www.icis.com/resources/news/2000/08/23/119685/congress-hits-fda-cdc-on-vaccine-conflicts-of-interest/>
2. <http://vaxxedthemovie.com/>

3. <https://www.cdc.gov/ncbddd/developmentaldisabilities/features/birthdefects-dd-keyfindings.html>
4. <https://www.cdc.gov/ncbddd/autism/data.html>
5. <https://www.cdc.gov/sids/data.htm>
6. <https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-combined-schedule-bw.pdf>
7. <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf>

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 Support
Date: Wednesday, October 31, 2018 9:20:21 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

K. Nakamura
Parent

Laurie West, RN

██████████

██████████

October 31, 2018

Disease Outbreak Control Division (DOCD)
1250 Punchbowl Street
Room 443
Honolulu, Hawaii 96813

Re: **STRONG OPPOSITION TO PROPOSED RULE CHANGES
TO HAR 11-157**

Dear Disease Outbreak Division of Hawaii Department of Health:

I respectfully request that public hearings on these changes be held statewide prior to any decisions being rendered, since the sequelae of implementation of these rules are potentially health-endangering.

I **strongly oppose** the proposed rule changes to HAR 11-157, in general, pertaining to Hawaii vaccination policy, for several reasons, including, but not limited to the following:

- Bona fide double-blind, randomized, placebo-controlled studies—the “*Gold Standard*” of scientific inquiry—have NOT been done on individual vaccines, much to the surprise of healthcare workers tasked with administering them when apprised of this fact. It is alarming that substances like vaccines, with such demonstrated ability to alter the human body, are not held to the same testing standards as other drugs. Few, if any, vaccines have been tested using only relatively inert placebos, like sterile water or normal saline; instead, they are tested against other vaccines or aluminum-containing shots as the control, presumably to mask the deleterious health effects of vaccines, or why wouldn’t relatively inert placebos be used instead, exclusively?
- Furthermore, there has yet to be conducted a study on the safety and efficacy of the cumulative CDC-recommended vaccine schedule.

Where is the “vaxxed versus unvaxxed” data? It doesn’t yet exist. While we wait for such data, the people of Hawaii continue to be vaccinated.

We ought not be adding new vaccines to the schedule of vaccine requirements when they have not been adequately studied to demonstrate safety, either individually or cumulatively.

- Vaccines are contaminated with substances known to be toxic; People must retain the right to refuse any substance when there is a risk of injury.

Vaccine Excipient & Media Summary Excipients Included in U.S. Vaccines, by Vaccine

In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients or media.

Some excipients are added to a vaccine for a specific purpose. These include:

Preservatives, to prevent contamination. For example, thimerosal.

Adjuvants, to help stimulate a stronger immune response. For example, aluminum salts.

Stabilizers, to keep the vaccine potent during transportation and storage. For example, sugars or gelatin.

Others are residual trace amounts of materials that were used during the manufacturing process and removed. These include:

Cell culture materials, used to grow the vaccine antigens. For example, egg protein, various culture media.

Inactivating ingredients, used to kill viruses or inactivate toxins. For example, formaldehyde.

Antibiotics, used to prevent contamination by bacteria. For example, neomycin.

The following table lists all components, other than antigens, shown in the manufacturers’ package insert (PI) for each vaccine. Each of these PIs, which can be found on the FDA’s website (see below) contains a description of that vaccine’s manufacturing process, including the amount and purpose of each substance. In most PIs, this information is found in Section 11: “Description.”

All information was extracted from manufacturers’ package inserts.

If in doubt about whether a PI has been updated since this table was prepared, check the FDA’s website at <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm>

Vaccine	Contains
Adenovirus	human-diploid fibroblast cell cultures (strain WI-38), Dulbecco’s Modified Eagle’s Medium, fetal bovine serum, sodium bicarbonate, monosodium glutamate, sucrose, D-mannose, D-fructose, dextrose, human serum albumin, potassium phosphate, pladone C, anhydrous lactose, microcrystalline cellulose, polacrillin potassium, magnesium stearate, cellulose acetate phthalate, alcohol, acetone, castor oil, FD&C Yellow #6 aluminum lake dye
Anthrax (Biothrax)	amino acids, vitamins, inorganic salts, sugars, aluminum hydroxide, sodium chloride, benzethonium chloride, formaldehyde
BCG (Tice)	glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, iron ammonium citrate, lactose
Cholera (Vaxchora)	casamino acids, yeast extract, mineral salts, anti-foaming agent, ascorbic acid, hydrolyzed casein, sodium chloride, sucrose, dried lactose, sodium bicarbonate, sodium carbonate
DT (Sanofi)	aluminum phosphate, isotonic sodium chloride, formaldehyde, casein, cystine, maltose, uracil, inorganic salts, vitamins, dextrose
DTaP (Daptacel)	aluminum phosphate, formaldehyde, glutaraldehyde, 2-phenoxyethanol, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, Mueller’s growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion
DTaP (Infanrix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, sodium chloride, polysorbate 80 (Tween 80)
DTaP-IPV (Kinrix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, VERO cells, a continuous line of monkey kidney cells, Calf serum, lactalbumin hydrolysate, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B
DTaP-IPV (Quadacel)	modified Mueller’s growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion, formaldehyde, aluminum phosphate, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, MRC-5 cells, normal human diploid cells, CMRL 1969 medium supplemented with calf serum, Medium 199 without calf serum, 2-phenoxyethanol, polysorbate 80, glutaraldehyde, neomycin, polymyxin B sulfate

Vaccine	Contains
DTaP-HepB-IPV (Pediarix)	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, glutaraldehyde, modified Stainer-Scholte liquid medium, VERO cells, a continuous line of monkey kidney cells, calf serum and lactalbumin hydrolysate, aluminum hydroxide, aluminum phosphate, aluminum salts, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B, yeast protein.
DTaP-IPV/Hib (Pentacel)	aluminum phosphate, polysorbate 80, sucrose, formaldehyde, glutaraldehyde, bovine serum albumin, 2-phenoxyethanol, neomycin, polymyxin B sulfate, modified Mueller's growth medium, ammonium sulfate, modified Mueller-Miller casamino acid medium without beef heart infusion, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin. MRC-5 cells (a line of normal human diploid cells), CMRL 1969 medium supplemented with calf serum, Medium 199 without calf serum, modified Mueller and Miller medium
Hib (ActHIB)	sodium chloride, modified Mueller and Miller medium (the culture medium contains milk-derived raw materials [casein derivatives]), formaldehyde, sucrose
Hib (Hiberix)	saline, synthetic medium, formaldehyde, sodium chloride, lactose
Hib (PedvaxHIB)	complex fermentation media, amorphous aluminum hydroxyphosphate sulfate, sodium chloride
Hep A (Havrix)	MRC-5 human diploid cells, formalin, aluminum hydroxide, amino acid supplement, phosphate-buffered saline solution, polysorbate 20, neomycin sulfate, aminoglycoside antibiotic
Hep A (Vaqta)	MRC-5 diploid fibroblasts, amorphous aluminum hydroxyphosphate sulfate, non-viral protein, DNA, bovine albumin, formaldehyde, neomycin, sodium borate, sodium chloride
Hep B (Engerix-B)	aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
Hep B (Recombivax)	soy peptone, dextrose, amino acids, mineral salts, phosphate buffer, formaldehyde, potassium aluminum sulfate, amorphous aluminum hydroxyphosphate sulfate, yeast protein
Hep B (Hepelisav-B)	vitamins and mineral salts, yeast protein, yeast DNA, deoxycholate, phosphorothioate linked oligodeoxynucleotide, phosphate buffered saline, sodium phosphate, dibasic dodecahydrate, monobasic dehydrate, polysorbate 80
Hep A/Hep B (Twinrix)	MRC-5 human diploid cells, formalin, aluminum phosphate, aluminum hydroxide, amino acids, sodium chloride, phosphate buffer, polysorbate 20, neomycin sulfate, yeast protein
Human Papillomavirus (HPV) (Gardasil 9)	vitamins, amino acids, mineral salts, carbohydrates, amorphous aluminum hydroxyphosphate sulfate, sodium chloride, L-histidine, polysorbate 80, sodium borate, yeast protein
Influenza (Afluria) Trivalent & Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, monobasic potassium phosphate, potassium chloride, calcium chloride, sodium taurodeoxycholate, ovalbumin, sucrose, neomycin sulfate, polymyxin B, beta-propiolactone, thimerosal (multi-dose vials)
Influenza (Fluad)	squalene, polysorbate 80, sorbitan trioleate, sodium citrate dehydrate, citric acid monohydrate, neomycin, kanamycin, barium, egg proteins, cetyltrimethylammonium bromide (CTAB), formaldehyde
Influenza (Fluarix) Trivalent & Quadrivalent	octoxynol-10 (TRITON X-100), <i>alpha</i> -tocopheryl hydrogen succinate, polysorbate 80 (Tween 80), hydrocortisone, gentamicin sulfate, ovalbumin, formaldehyde, sodium deoxycholate, sodium phosphate-buffered isotonic sodium chloride
Influenza (Flublok) Trivalent & Quadrivalent	sodium chloride, monobasic sodium phosphate, dibasic sodium phosphate, polysorbate 20 (Tween 20), baculovirus and <i>Spodoptera frugiperda</i> cell proteins, baculovirus and cellular DNA, Triton X-100, lipids, vitamins, amino acids, mineral salts
Influenza (Flucelvax) Trivalent & Quadrivalent	Madin Darby Canine Kidney (MDCK) cell protein, protein other than HA, MDCK cell DNA, polysorbate 80, cetyltrimethylammonium bromide, and β -propiolactone
Influenza (Flulaval) Trivalent & Quadrivalent	ovalbumin, formaldehyde, sodium deoxycholate, <i>alpha</i> -tocopheryl hydrogen succinate, polysorbate 80, thimerosal (multi-dose vials)
Influenza (Fluvirin)	ovalbumin, polymyxin, neomycin, betapropiolactone, nonylphenol ethoxylate, thimerosal
Influenza (Fluzone) Quadrivalent	formaldehyde, egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, thimerosal (multi-dose vials), sucrose

Vaccine	Contains
Influenza (Fluzone) High Dose	egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, formaldehyde, sucrose
Influenza (Fluzone) Intradermal	formaldehyde, egg protein, octylphenol ethoxylate (Triton X-100), sodium phosphate-buffered isotonic sodium chloride solution, sucrose
Influenza (FluMist) Quadrivalent	monosodium glutamate, hydrolyzed porcine gelatin, arginine, sucrose, dibasic potassium phosphate, monobasic potassium phosphate, ovalbumin, gentamicin sulfate, ethylenediaminetetraacetic acid (EDTA)
Japanese Encephalitis (Ixiaro)	aluminum hydroxide, protamine sulfate, formaldehyde, bovine serum albumin, host cell DNA, sodium metabisulphite, host cell protein
Meningococcal (MenACWY-Menactra)	Watson Scherp media containing casamino acid, modified culture medium containing hydrolyzed casein, ammonium sulfate, sodium phosphate, formaldehyde, sodium chloride
Meningococcal (MenACWY-Menveo)	formaldehyde, amino acids, yeast extract, Franz complete medium, CY medium
Meningococcal (MenB – Bexsero)	aluminum hydroxide, <i>E. coli</i> , histidine, sucrose, deoxycholate, kanamycin
Meningococcal (MenB – Trumenba)	defined fermentation growth media, polysorbate 80, aluminum phosphate, histidine buffered saline
MMR (MMR-II)	chick embryo cell culture, WI-38 human diploid lung fibroblasts, vitamins, amino acids, fetal bovine serum, sucrose, glutamate, recombinant human albumin, neomycin, sorbitol, hydrolyzed gelatin, sodium phosphate, sodium chloride
MMRV (ProQuad) (Frozen)	chick embryo cell culture, WI-38 human diploid lung fibroblasts, MRC-5 cells, sucrose, hydrolyzed gelatin, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate dibasic, human albumin, sodium bicarbonate, potassium phosphate monobasic, potassium chloride; potassium phosphate dibasic, neomycin, bovine calf serum
MMRV (ProQuad) (Refrigerator Stable)	chick embryo cell culture, WI-38 human diploid lung fibroblasts, MRC-5 cells, sucrose, hydrolyzed gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, recombinant human albumin, sodium bicarbonate, potassium phosphate, potassium chloride, neomycin, bovine serum albumin
Pneumococcal (PCV13 – Prevnar 13)	soy peptone broth, casamino acids and yeast extract-based medium, CRM197 carrier protein, polysorbate 80, succinate buffer, aluminum phosphate
Pneumococcal (PPSV-23 – Pneumovax)	phenol
Polio (IPV – Ipol)	Eagle MEM modified medium, calf bovine serum, M-199 without calf bovine serum, vero cells (a continuous line of monkey kidney cells), phenoxyethanol, formaldehyde, neomycin, streptomycin, polymyxin B
Rabies (Imovax)	human albumin, neomycin sulfate, phenol red indicator, MRC-5 human diploid cells, beta-propiolactone
Rabies (RabAvert)	chicken fibroblasts, β-propiolactone, polygeline (processed bovine gelatin), human serum albumin, bovine serum, potassium glutamate, sodium EDTA, ovalbumin, neomycin, chlortetracycline, amphotericin B
Rotavirus (RotaTeq)	sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, fetal bovine serum, vero cells [DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.]
Rotavirus (Rotarix)	Vero cells, dextran, Dulbecco's Modified Eagle Medium (sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids solution, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red), sorbitol, sucrose, calcium carbonate, sterile water, xanthan [Porcine circovirus type 1 (PCV-1) is present in Rotarix. PCV-1 is not known to cause disease in humans.]
Smallpox (Vaccinia) (ACAM2000)	African Green Monkey kidney (Vero) cells, HEPES, 2% human serum albumin, 0.7% sodium chloride USP, 5% Mannitol USP, neomycin, polymyxin B, 50% Glycerin USP, 0.25% phenol USP

Vaccine	Contains
Td (Tenivac)	aluminum phosphate, formaldehyde, modified Mueller-Miller casamino acid medium without beef heart infusion, ammonium sulfate, sodium chloride, water
Td (Mass Biologics)	aluminum phosphate, formaldehyde, thimerosal, modified Mueller's media which contains bovine extracts, ammonium sulfate
Tdap (Adacel)	aluminum phosphate, formaldehyde, 2-phenoxyethanol, Stainer-Scholte medium, casamino acids, dimethyl-beta-cyclodextrin, glutaraldehyde, modified Mueller-Miller casamino acid medium without beef heart infusion, ammonium sulfate, modified Mueller's growth medium
Tdap (Boostrix)	modified Latham medium derived from bovine casein, Fenton medium containing a bovine extract, formaldehyde, modified Stainer-Scholte liquid medium, glutaraldehyde, aluminum hydroxide, sodium chloride, polysorbate 80
Typhoid (Typhim Vi)	hexadecyltrimethylammonium bromide, formaldehyde, phenol, polydimethylsiloxane, disodium phosphate, monosodium phosphate, semi-synthetic medium, sodium chloride
Typhoid (Vivotif Ty21a)	yeast extract, casein, dextrose, galactose, sucrose, ascorbic acid, amino acids, lactose, magnesium stearate, gelatin
Varicella (Varivax) Frozen	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, sodium phosphate monobasic, potassium phosphate monobasic, potassium chloride, EDTA, neomycin, fetal bovine serum
Varicella (Varivax) Refrigerator Stable	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed gelatin, sodium chloride, monosodium L-glutamate, urea, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum
Yellow Fever (YF-Vax)	sorbitol, gelatin, sodium chloride, egg protein
Zoster (Shingles) (Zostavax) Frozen	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride; neomycin, bovine calf serum
Zoster (Shingles) (Zostavax) Refrigerator Stable	MRC-5 human diploid cells, including DNA & protein, sucrose, hydrolyzed porcine gelatin, urea, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, neomycin, bovine calf serum
Zoster (Shingles) (Shingrix)	sucrose, sodium chloride, dioleoyl phosphatidylcholine (DOPC), potassium dihydrogen phosphate, cholesterol, sodium dihydrogen phosphate dihydrate, disodium phosphate anhydrous, dipotassium phosphate, polysorbate 80

A table listing vaccine excipients and media by excipient can be found in:

Grabenstein JD. *ImmunoFacts: Vaccines and Immunologic Drugs* – 2013 (38th revision). St Louis, MO: Wolters Kluwer Health, 2012.

The above Vaccine Excipient and Media Summary is posted on the CDC.gov website.

Where are the safety studies on injection of all of these contaminants into humans? Or are *we* the test subjects? The Gardasil vaccine, which is to be added to the requirement schedule for all seventh graders, contains an aluminum compound. Aluminum is recognized as a neurotoxin and is possibly a culprit in autism and other neurological disorders. Here are links to studies by Exley and Shaw.

We must not add any more vaccines to the schedule of school and daycare requirements until these concerns about aluminum and neurological disorders are better understood, so that a more balanced assessment of risks of vaccination versus benefits can be presented to the people of Hawaii.

- Gardasil testing, for example, used both an aluminum-containing placebo group and a saline placebo group, with most of the control subjects in the aluminum group. This vaccine is to become a requirement for all seventh graders, among the other vaccines in Exhibit A. I oppose this on the basis of inadequate safety data, and the many anecdotes of families reporting injury and death of their children not long after receiving HPV vaccine. Premature ovarian failure is another reported complication; [see also here].
- There is a disconnect between our public health officials on the one side, and on the other side people [including physicians] who recognize the increasing body of scientific literature implicating vaccines as culprits in burgeoning neurological and autoimmune disorders which have been rising concurrently with the additions to the vaccine schedule. Public health officials are reluctant or refuse to acknowledge science from sources without the stamp of approval from the Institute of Medicine [IOM] or other industry-connected scientific bodies. Industry-friendly sources mostly tout the “safety

and efficacy” of vaccines—which suits the industry’s bottom-line by downplaying potential hazards, while independent scientists who challenge the unproven mantra of safety and efficacy, and offer possible answers to victims of health deterioration post-vaccination are ignored by public health officials. This is a disservice to people who look to public health institutions as the ultimate arbiter of safe and effective vaccines.

- In a discussion earlier this year with Hawaii State Epidemiologist, Dr. Sarah Park of DOCD, I asked her if the Department of Health had any data on developmental disorders in Hawaii. She responded that she does *not* track such neurological disorders—“that’s not my area, I only deal with the infectious diseases.” This is alarming, considering that you in the Disease Outbreak Control Division are concerned only narrowly with communicable or “vaccine-preventable” diseases, and you are apparently not leading the way to discover more about the possible connections between vaccines and reportedly skyrocketing rates developmental and autoimmune disorders. Instead of pausing to investigate further, the Department of Health/DOCD seeks to add more vaccines to the schedule of requirements.

This is an unacceptable threat to public health in Hawaii. Other countries like Japan are banning Gardasil due to safety concerns, while we pile more on the list, with reportedly *hundreds* of more vaccines in the profitable pipeline. We need to avoid adding any new vaccines to the current schedule, until we have consulted with *unbiased* neurological disorder and autoimmunity experts who can give the “all-clear” that we are not condemning people to such afflictions in the name of winning the fight against “vaccine-preventable” diseases—some of which were far more benign prior to the commencement of the vaccine program than the neurological and autoimmune disorders which are reportedly increasing in incidence, commensurate with the increases to the vaccine schedule’s additions over the years.

- It is *unacceptable* for public health officials to cherry-pick only industry-friendly data which in effect gives plausible deniability that they've done their due diligence to maintain public safety by promoting "safe and effective" vaccines, based only on their chosen sources, while ignoring or disparaging studies critical of vaccine safety and efficacy. In our discussion this year referenced above, Dr. Park quoted a 2004 Institute of Medicine Report as being the authoritative source regarding my questioning of possible linkage of aluminum to developmental delays. Perhaps it's time to revisit this topic within the Department of Health, as there is emerging peer-reviewed science which offers different conclusions than the 2004 IOM Report.
- It is *never acceptable* to sacrifice someone else's health and well-being for another's. What is it that renders would-be victims of a communicable disease *more* worthy of protection than a potential victim of neurological or autoimmune disease? I hope it's not just industrial greed and control over our public health institutions. We must **NOW** cease the apparently never-ending additions of vaccine requirements *until* we have determined if *industry-independent science* supports or not possible vaccine component linkage to neurological and autoimmune disorders.
- We need legislation requiring full financial disclosure of studies serving as the underpinnings of our public health policy, with sworn assurances of the full disclosure, backed by penalties for insufficient disclosure. Perhaps public health officials ought to be required to cite the foundational studies they rely on in vaccine policy for open public viewing and review by independent experts. Informed consent proponents ought to welcome more debate and disclosure.
- We must protect our customary notion of informed consent. Our current medical and religious exemptions must be expanded—not curtailed. Elimination of non-medical exemptions is being promoted lately and frequently in nationwide media and public health talking

points. These proposed rule changes for reporting of exemptions place *unacceptable* limits on our **RIGHT** to informed consent by burdening the individual choosing to decline a vaccine with additional procedures and privacy violations which do not ultimately promote health.

- The people of Hawaii are looking to you to protect them and not cherry-pick only industry-approved “science.” We hope you are with us and champion the safety and well-being of all of us facing further potential vaccine injury, in addition to your focus on us as potential victims of “vaccine-preventable illnesses.”

Thank you for the opportunity to be heard.

**WHEN THERE IS RISK,
THERE MUST BE CHOICE!**

Sincerely,

Laurie West, RN

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, October 31, 2018 9:44:57 PM

Regarding Title 11, chapter 157:
I strongly oppose.

Thank you for the opportunity to oppose and submit a testimony.

I am asking you please to not remove or limit the exemptions for immunizations.

As long as the safety as well as the efficacy of vaccinations are not guaranteed, this should not be forced on anyone. No doubt, you are aware of that the manufactures of the vaccines have warnings about the potential serious side effects and even DEATHS. Even if the risk is low, it's still a risk and should never be forced on anyone. People who choose not to have their family or themselves vaccinated, have seriously and carefully studied the pros and cons of vaccinations and weighed the benefits against the risks or are people with strong religious convictions who's beliefs are not in harmony with inoculations. Should these people be stripped of their religious freedom in a free country?

Please do not punish the children, depriving them of their right to go to public school just because they are not willing to submit to medical procedures that are well documented to not always be safe.

Mahalo for taking the time to read my point of view on this topic.

Sincerely,
Maria Zuech
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR11-157
Date: Wednesday, October 31, 2018 4:21:36 PM

To: Dept of Health

It is with sadness that I learned that you are considering making immunization mandatory, removing medical as well as religious exemptions.

I would be totally pro-vaccination, if it was SAFE for all children. Regrettably, that is not the situation YET. No argument is needed. The manufacturer makes that clear. Serious side effects and deaths occur. I personally know of children that this has happened to.

With any medical procedure, a medical consent form is needed. With immunization, a cocktail of viruses, blood fractions and aborted fetus tissue is injected right into the body.

Is it really fair, that a child who for medical or conscience reasons cannot submit to this has to be deprived of an education?

I don't believe so. I am respectfully asking you to please, reconsider this bill!

Sincerely
Elisabeth Svanberg

Sent from my iPad

From: [REDACTED]
To: [REDACTED]
Subject: Hawaii Administrative Rules
Date: Wednesday, October 31, 2018 9:06:39 AM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Ann Inouye

From: [REDACTED]
To: [REDACTED]
Subject: Hawaii administrative rules
Date: Wednesday, October 31, 2018 7:20:20 AM

Dear Dept of Health,

I am writing to strongly support the HAR-11-57 proposed rules update.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all our communities.

Thank you for your consideration to this matter.

Sadako Shimai
Concerned citizen

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Hawaii vaccine policy
Date: Wednesday, October 31, 2018 5:27:00 PM

To whom it may concern,

I very strongly oppose the proposed changes to Hawaii's vaccine policy!!! I am a mother of 3 who homeschools my children and I see these proposed changes as cruel punishment!! You are proposing harsh requirements that I am not ok being required and forced to abide by.

DO NOT MAKE THESE CHANGES!!!

Sincerely,
Peniela Rand

Sent from my iPhone



UNIVERSITY OF HAWAI'I
CANCER CENTER

October 31, 2018

The University of Hawai'i Cancer Center strongly supports the addition of human papillomavirus (HPV) vaccination to the immunizations required for 7th grade school entry and attendance in the state of Hawai'i. Preventing cancer is a central mission of the UH Cancer Center and HPV vaccination remains a powerful tool in the effort to prevent cancers caused by HPV. HPV vaccines have proven to be highly efficacious and safe. Vaccine use in the US and other countries has been demonstrated to reduce HPV infections and reduce the development of pre-cancerous lesions.

HPV is a very common infection and is linked to multiple cancers including malignancies of the cervix, vagina, vulva, penis, anus, oropharynx and oral cavity. Our research with the National Cancer Institute and the Centers for Disease Control and Prevention has demonstrated that HPV contributes to substantial proportions of these cancers including nearly all cervical and anal cancers. The need for HPV vaccination in Hawai'i is underscored by the significant statewide increase in certain HPV-associated cancers including anal and vulvar tumors.

Although modest increases have been observed in HPV vaccination rates among boys and girls in Hawaii (55% receiving the recommended doses in 2017), vaccine uptake is well below the national goal of 80 percent coverage by year 2020. Our research among Hawai'i primary care providers has identified the lack of mandatory school-based HPV vaccination as a major barrier to immunization.

The University of Hawai'i Cancer Center affirms our support for school-based HPV vaccination in order to prevent HPV-associated cancers in our community.

Sincerely,

Randall F. Holcombe, MD, MBA
Randall F. Holcombe, MD, MBA
Director, University of Hawai'i Cancer Center

From: [REDACTED]
To: [REDACTED]
Subject: In strong opposition
Date: Wednesday, October 31, 2018 5:49:53 AM

I am writing in strong opposition to the regulations that HAR 11-157 would impose. When there is a risk, there should be a choice and I feel by making vaccinations mandatory, you are taking away our right to choose. Please re-consider these regulations.

Thank you,
Audrey Alvarez

[Sent from Yahoo Mail for iPhone](#)

October 31, 2018

DOCD, DOH immunization@doh.hawaii.gov
[\(808\) 586-8300](tel:8085868300)

Hawaii Department of Health
1250 Punchbowl St.
Honolulu, Hawaii 96813

I **strongly oppose** the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, “Examination and Immunization.”

Dear Hawaii Department of Health,

My name is Kim Haine, I am a Mother and StepMother to 5 children, and was a health care professional for 15 years. I oppose these amendments for several reasons, but primarily because it is not prudent health policy to vastly increase the school vaccine requirements without, acknowledgement and exploration of the **epidemic of chronic disease plaguing America’s children today**.

1. **I oppose the changes to the Medical and Religious Exemption requirements.**

Pertaining to **Religious Exemptions** being “in a format specified by the department” is vague and yet unspecified, therefore leaving room for egregious violations of our Constitutional, First Amendment Rights. It is not up to the government, nor certainly our DOH, to define spirituality or one’s relationship with God.

Medical Exemptions must now be “in a form or format specified by the department, that an immunization is medically contraindicated, due to a stated cause, for a specific period of time, in conformance with recognized standard medical practices”. A physician’s best professional judgement utilizing their intimate patient-specific, as well as family history knowledge, should be the sole determining factor in whether a medical exemption is warranted....period. The “Precautionary Principle of Medicine” must be upheld and not be restricted by bureaucratic oversight.

After evaluating ACIP's most recent General Best Practice Guidelines for Immunization; Section 4 "Contraindications and Precautions", Tables 4-1 and 4-2, it is abundantly clear that ACIP, and any Public Health Department that blindly follows such guidelines, care much more about the judicious uptake and militant adherence to the vaccination schedule, than the prevention of serious, life-long adverse reactions. All conditions listed have been absurdly minimized:

Pertussis Containing Vaccines

- DTaP (Dose 3 – Dose 4) minimum intervals (10/23/2017)
 - Prospective – 6 months
 - Retrospective – 4 months
 - 4 day grace period can be applied to 6 month interval prospectively
 - 4 day grace period can be applied to 4 month interval retrospectively
- Four precautions to DTaP removed
 - Fever $\geq 105^{\circ}$ F within 48 hrs following a dose of DTaP (09/20/18)
 - Persistent, inconsolable crying lasting ≥ 3 hrs within 48 hrs following a dose of DTaP (07/18/18)
 - Collapse or shock-like state with 48 hrs following a dose of DTaP (07/18/18)
 - Seizure within 72 hrs following a dose of DTaP (07/18/18)

See for example table to the left which lists known symptoms of "encephalitis" (brain swelling which can lead to autism), as no longer being a precaution to the DTaP vaccine, let alone a contraindication! There are hundreds of severe adverse reactions listed in ALL vaccine manufacture's package inserts, whether noted during clinical trials

OR post-marketing surveillance, that *should* qualify as a medical exemption, but they do not. **Vaccine Package Inserts** are never given out to patients as **true informed consent**, and most physicians have never even read them. *The Hippocratic Oath* that every American Medical Doctor is sworn in to "**FIRST DO NO HARM**" appears to have been forgotten as it relates to childhood vaccines. Please see a video clip of an actual ACIP vaccine approval meeting in progress here: https://www.youtube.com/watch?v=L_JJMpe00mM

2. I oppose mandatory physician and school reporting to the DOH, the names of children/students whom have not met their immunization requirements, or who have medical or religious exemptions.

The Federal and Educational Rights and Privacy Act (FERPA) and Health Insurance Portability and Accountability Act (HIPPA) standards are in place to protect personal health information and medical records; this would be a grave violation to the intentions of these privacy acts. The reporting of numbers of exemptions may be prudent, however names of students are not necessary, and feels more like a rule approaching communist China.

The only "mandatory reporting" that SHOULD be happening is the reporting by Health Care Professionals of vaccine injuries. We have a failed, passive reporting system in VAERS that, according to a Harvard study funded by our own DHHS, captures an estimated, pathetic 1% of actual vaccine injuries.

3. Finally, I stand in extreme opposition to the requirement of multiple new vaccines to attend daycare and all school institutions in Hawaii.

ACIP recommendations and guidelines are meant to be just that, recommendations, NOT mandates. The new proposed vaccine requirements for Hawaii's children would add approximately 17 doses of 7 new vaccines (including 35+ antigens) for those beginning in daycare. There are no urgent matters in our *school* settings warranting the use/addition of *any* of the proposed vaccines { Influenza; Rotavirus; PCV; Hep A; MCV; TDaP; and especially HPV}. There are also CDC statistics and abundant independent research to back up this claim, as well as facts proving that the risks far outweigh any benefits. HPV (Gardasil) vaccine especially, for a STD not highly communicable in a school setting, is one of the most controversial and dangerous vaccines ever recommended by ACIP. With debilitating autoimmune diseases, paralysis, and even death numbering 60,000 and counting, this vaccine should be pulled from market (as in other countries like Japan), not forced upon schoolchildren.

Important facts pertaining to vaccination:

1. Vaccination is a medical intervention, that carries risk of serious injury, death, and failure to prevent infection or transmission. There are genetic, biological and environmental risk factors rendering some more susceptible to vaccine reactions than others, yet doctors still cannot predict conclusively who will be harmed.
2. Section 13.1 on *every* manufacturer's package insert states that it has "not been evaluated for carcinogenic or mutagenic potentials, or impairment of fertility"
3. In 1986 Congress passed *The National Childhood Vaccine Injury Act* to shield vaccine manufacturers from civil product liability lawsuits for all harm caused by vaccines, including permanent disability and death (Public Law 99-660).
4. Since this 1986 ACT sheltered the vaccine manufacturers from liability, the childhood vaccination schedule has exploded to a current 74+ doses of 17 vaccines (given in pregnancy, on the first day of birth, up to 18 and beyond)
5. **What has also grown concurrently with the vaccination schedule is an epidemic of chronic illness in over half (54%) America's children.**

The gateway period that launched this decline was the late 1980's and early 1990's. Many chronic illnesses have doubled since that time:

- The “4-A” disorders— autism, attention deficit hyperactivity disorder, asthma and allergies—have experienced meteoric growth, affecting children's quality of life and contributing to premature mortality . The spike in autism prevalence has been particularly dramatic, with prevalence as high as 3% (one in 36 children) in some regions . Pediatric autoimmune conditions also are on the rise.
- U.S . children are far more likely to die before their first birthday than infants in other wealthy countries and life expectancy is falling, driven largely by rising death rates in adolescents and younger adults. Suicide is the second leading cause of death in teens, half of whom are reported to have at least one mental, emotional or behavioral disorder.
- The proportion of public school children using special education services is skyrocketing, with estimates ranging from 13% to 25% of school populations .
- The social and economic fallout from these health challenges is hitting home hard—with adverse impacts on intelligence, fertility, household and government finances, employment, productivity, military recruitment and more . The disproportionately high level of neurodevelopmental disability in males versus females is also reshaping society .

Mystifyingly, there is almost no outcry in medical, public health or government circles to find answers and solutions

The potentially dangerous, synergistic and long-term effects of the ever-growing childhood vaccination schedule has never been evaluated properly.

1. A 2013 study by the prestigious Institutes of Medicine (IOM) concluded that:

“ the key elements of the entire (childhood vaccine) schedule: the number, frequency, timing, order, and age of administration of vaccination have not been systematically examined in research studies”

2. In May 2017 Robert F Kennedy Jr.(childrenshealthdefense.org) & Del Bigtree (icandecide.org) filed a lawsuit against our U.S. Department of Health and Human Services suspecting it was not fulfilling its critical vaccine safety obligations.

DHHS is required by Congress as per the NCVIA of 1986, to assure “improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions”. The lawsuit revealed that

DHHS had never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety. <http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

The mission statement of the Hawaii Department of Health as stated is to “protect and improve the health and environment for all people of Hawaii.” Preventing the spread of infectious disease is important, but it appears that we may be trading infectious disease for chronic, life-long illnesses. Cigarettes were once proclaimed safe by the tobacco giants and supposedly did not cause cancer, while antibiotics have been absolute miracle drugs until mutations created resistant super-bugs like MRSA. It appears we may be in need of another great paradigm shift in medicine and public healthcare, or at the very least unbiased, ethical, independent research and regulation. The mantra “Vaccines are Safe & Effective” is losing support quickly in the eyes of astute Americans.

I am an advocate for improved vaccine safety, fully informed consent, and parental choice. These are essential if public confidence is to be restored, not further eroded.

Thank you for your attention to this serious matter,

Dr. Kimberly Haine

Hawaii for Informed Consent (HFIC)



From: [REDACTED]
To: [REDACTED]
Subject: Opposed to Title11, Chapter 157
Date: Wednesday, October 31, 2018 7:23:09 AM

Re: Public Testimony in opposition to Title 11, Chapter 157.

I am opposed to the changes submitted in this proposal. With a medical education and experience as a Registered nurse with my Master of Public Health degree, there should be a choice to ones health especially when there is clear risk involved.

In America, we have freedoms and a right to decide , these changes further take that away. There are numerous clinical studies that show that there can and has been danger in vaccines and that there are often no differences between disease rates of unvaccinated and vaccinated.

Drug/vaccine companies are not held accountable for any injury/harm or are not forced to make what we inject to our immune systems safe. Numerous vaccines are made for diseases that are natural and that pose minimal harm when allowed to naturally occur(i.e chickenpox vaccine). Financial compensation is a driver to force vaccines and many people have received untruths and act on them. The risk for ones child should be determined by their parent.

I plead that you do not pass this change for the sake of everyone's child and the health of our children. Not getting vaccines is not the problem and making people get them is not the answer. Please don't make a knee-jerk reaction with my child's life. Mandating such things could negatively impact people that may want to move and raise their children here(they would no longer come).

Amanda Wallace, CHES, MPH, RN
Cell-[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Opposition to HAR 11-157
Date: Wednesday, October 31, 2018 10:18:12 AM

October 31, 2018

Aloha,

Thank you for this opportunity to provide testimony. My family and I live on the island of Oahu. I am writing to **strongly oppose the HAR 11-157 proposed rules update**. The changes proposed in this update would have far reaching consequences to the families of Hawaii. We oppose the proposed rule changes for the following reasons:

1. Vaccines are known to cause harm and carry risk. **Where there is risk, there MUST be a choice.** If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box (<http://www.immunize.org/fda/#var>). Each vaccine administered to children was never evaluated for its ability to cause cancer, genetic mutation, or infertility. Also, there have never been studies regarding the effectiveness and safety for use of vaccines for people with autoimmune issues and/or MFTHR gene. It is wrong to mandate a medical procedure that is known to cause harm and carries risk, without informed consent. The MMR vaccine insert contains 42 paragraphs of warnings and adverse reactions, including seizures, encephalitis, pneumonia, deafness, and death (https://www.merck.com/product/usa/pi_circulars/m/mmr_ii/mmr_ii_pi.pdf pg. 4-9 Warnings, Precautions, Adverse Reactions). DTaP lists SIDS as a side effect (https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Infanrix/pdf/INFANRIX.PDF pg. 12 Section 6.2). The inserts for active/live virus vaccines state that recipients should avoid close contact with susceptible high-risk individuals for up to 6-weeks following vaccination (https://www.merck.com/product/usa/pi_circulars/v/varivax/varivax_pi.pdf, pg. 3 Section 5.4) (https://www.merck.com/product/usa/pi_circulars/p/proquad/proquad_pi_4171.pdf pg. 4, Section 5.8) (https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Rotarix/pdf/ROTARIX-PI-PIL.PDF pg. 5 Section 5.4) (https://www.emergentbiosolutions.com/sites/default/files/inline-files/ACAM2000%20Package%20Insert%20Version%202003_2018.pdf pg 8. Section 12.2.3). Unfortunately, the government does not know which individuals would be included in this group and would be forcing individuals that fall into those categories (immunocompromised, pregnant women, new infants, etc.) who work and attend the schools to exposure to those illnesses. Will the schools be accepting doctor's note for up to 6-week post vaccine absences?

2. The safety obligations from the 1986 National Childhood Vaccine Injury Act (<https://www.ncbi.nlm.nih.gov/books/NBK220067/>) are in place to protect our Keiki. It recently came to light that those safety obligations have never been upheld. We cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children. Why must parents have to harm their children to provide them an education. (It is essential to note that the total number of vaccine doses on the schedule has dramatically increased since the 1980s. This means children are expected to receive 72 doses between birth and age 18) (if the schedule is followed as written), as opposed to the 10 doses from 1980. This should make everyone question the effectiveness of the vaccines. (<https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications.html>)

There have been no studies showing the effects of the suggested vaccine schedule as a whole (birth to 18), let alone, how they are currently dosed. Attempting to mandate a medical procedure when there are no adequate safety studies in place is a blatant disregard for public safety. There are no check and balances in the vaccine program, as vaccines are classified differently than any other medications and are not subject to the rigorous scrutiny or the liability that comes along with putting new drugs on the market.

3. HPV is a sexually transmitted disease. It is appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. This is by far the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world. There have been numerous lawsuits across the world, including Spain, France, Japan, Colombia, India and right here in the US. The families injured by this vaccine has had their lives devastated, all in the name of money. We should be questioning why we are recommending a drug that has never been proven effective at the prevention of cancer. It has been linked to including but not limited to: ovarian failure, autoimmune disease, pancreatitis, infertility, seizures and disseminated encephalomyelitis, and death following vaccination (https://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf pgs. 4-10 Section 6, 6.1 and 6.2) . The median age for HPV-associated cervical cancer diagnosis is age 49 (<https://www.cdc.gov/cancer/hpv/statistics/age.htm>).

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Sadly, this information is not shared and the question “are you allergic to eggs?” is not always asked when the shot is administered (<http://labeling.seqirus.com/PI/US/FLUAD/EN/FLUAD-Prescribing-Information.pdf>, pg. 1 Contraindications). Couple this with the extremely low efficacy rate of the flu shot, its mind boggling that it would be add it to the list. This shows that the government and state entities do not have the best interest of children at heart. Earlier this year the CDC approved what they call an active/live virus flu vaccine. This active virus sheds post vaccine and flu shot clinics at the schools expose high-risk children, teachers, and aids to influenza. (<https://www.azpicentral.com/flumistquadrivalent/flumistquadrivalent.pdf#page=1>, pg 4 Section 12.2, 17.2)

5. Vaccine Excipient and Media. According to the CDC's publication “Vaccine Excipient & Media Summary” (https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf?fbclid=IwAR2_pFQdquuxZTD3-i3tHko0ATBNq4s_IWK1NOH6Joi7mAvQBi9JmifCYxw), “In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients or media.” These excipients include thimerosal (a form of mercury), aluminum (as amorphous aluminum hydroxy phosphate sulfate p/k/a aluminum hydroxide), aborted fetal cells, bovine extract, formaldehyde, monkey kidney cells, calf serum, chicken cells and polysorbate80 (breaks down the blood brain barrier).

6. Medical Freedom is our basic right. Health is very personal and varies between all individuals. Parents have the **right to informed consent**, allowing them to make educated decisions when it comes to vaccines. Stop acting as though you know the medical needs and concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know what is better than we do with regards to our children. Stop creating blanket rules based

on what you believe everyone should follow and believe in. Medical freedom should be protected so that INDIVIDUALS can make **EDUCATED INDIVIDUAL** decisions when it comes to their health. Stop trying to take that away from us.

I also question why our state epidemiologist, Dr. Park, who used to work for the CDC, isn't being investigated for the conflict of interest. She has stated that "giving parents full informed consent would hurt her flu shot program in the schools." How about the harm her program inflicts on the families that have adverse reactions?

For the reasons above, our religious beliefs, and many other reasons not covered in this testimony, I strongly oppose the HAR 11-157 proposed rule update. I strongly urge the committee to strike the proposed HAR 11-157 updates and do not take away our parental rights to make the right decision for our children. Thank you again for the opportunity to provide testimony.

Sincerely,

Amanda LaCasse

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Testimony to OPPOSE HAR 11-157
Date: Wednesday, October 31, 2018 12:44:53 PM

October 31, 2018

DOCD, DOH [REDACTED]

(808) 586-8300

Bruce S. Anderson, PhD, Director of Health
Hawaii Department of Health
1250 Punchbowl St.
Honolulu, Hawaii 96813

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter157, "Examination and Immunization."

Strongly **Oppose** the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter157, "Examination and Immunization." Taking on the ACIP guidelines is not in the best interest of our Keiki's overall health or best practice of health guidelines for the State of Hawaii.

Dear Hawaii Department of Health,

My name is Maly Gella and I am a Registered Nurse of 21 years. I am an aunty and a mother of a 23 year old daughter who was fully vaccinated as a child. I followed the vaccine schedule without question because I blindly trusted that her doctors were fully educated about vaccine safety, risk, and efficacy. I now know differently.

I strongly **oppose** the state of Hawaii taking on the ACIP guidelines as their best practice for immunization. I oppose these changes because I have spent hours watching ACIP (Advisory Committee for Immunization Practices) meetings and have done much research surrounding all aspects of vaccines; their history, ingredients, extensive side effects including death, the National Childhood Vaccine Injury Act of 1986 removing ALL pharmaceutical liability, the ever growing number of vaccines on the childhood vaccine schedule since the passing of this law, the giving of multiple vaccines at one time while assuring parents that it is safe yet having no safety studies to substantiate this, etc.

These safety studies were the responsibility of HHS after the 1986 Act was passed. These studies were to be conducted every 2 years and the findings reported to congress. ***In the last 30 years these studies were never done!*** A lawsuit was filed and won by ICAN (Informed Consent Action Network) and counsel Robert F. Kennedy Jr. Through this lawsuit HHS had to admit that they never submitted a single biennial report to Congress! So much for government oversight. Lawsuit link <https://goo.gl/1pNeaD>

I hope I have made it very clear why I have concerns. So now my questions to you Mr. Anderson, Dr. Sarah Park, and all parties involved in this decision making process; Do each of you regularly watch the ACIP meetings? If not then how can you confidently implement their recommendations on our children? If you have watched the ACIP meetings how can you in good conscience agree to follow their recommendations? I make these statements because I have watched these meetings and *while some on the committee may ask thought provoking questions and bring up safety concerns they still unanimously vote to proceed with the use of these vaccines!* One such example of this is the new hepatitis B vaccine which contains a new adjuvant. This new vaccine was shown to cause Myocardial Infarctions (MI=heart attacks) in 14 people while being tested. While one ACIP member brought it up as a concern he still voted to allow this vaccine to be used! The committee then said they would look to Post Marketing data for this "signal". In other words the public receiving this new vaccine will be their unknowing test subjects. The committee members

are waiting to see if a percentage will suffer heart attacks. I thought this was illegal based on the Nuremberg code.

I have deep concerns about this November 1st hearing process. We were told that we may ask questions but we will not get answers because the decision maker/s will not be present. So this raises questions for me; 1. Is this just a formality for the DOH? 2. Has the decision to implement these changes already been made and are you just checking off a box to remain compliant? If so this is unacceptable, these decisions personally affect our children and we need to have a say in any medical intervention imposed on them. Gone are the days that we blindly follow the medical establishment.

This whole process is disconcerting. It appears that assumptions have been made (or will be made) by the Hawaii DOH regarding ACIP. They are; 1. The DOH has confidence in adopting the ACIP recommendations because they assume ACIP has done their due diligence on each and every vaccine placed on the schedule. 2. The DOH believes that the safety of the vaccines have been established or ACIP would not recommend they be placed on the schedule. 3. ACIP is an independent, unbiased, conflict free entity. With a little bit of time and effort you will find these are all wrong assumptions. That being said we the public who stand in opposition of (HAR) Title 11, Chapter 157 place this responsibility back on you, the DOH. We need to know how you are making these decisions. We need to see the safety studies that you are basing your decisions on. We will no longer allow you to impose medical interventions on our children or our families that could have dire consequences. The government has already paid out \$3.9 billion to compensate for vaccine injury. We know the truth, vaccines have risk. Any denial of this on the part of the DOH is an outright lie.

We have done our homework and we have seen the injuries first hand. It is time that you the "Department of Health" do your homework, do your job, be advocates of health. With 54% of our children being affected by chronic illness and 1 in 6 children having some type of learning disability, it's time we work together and truly focus on improving the health of the children of Hawaii. We sincerely want to be part of the solution.

We insist that No changes be made to our current medical and religious exemptions. Doctor and patient confidentiality and confidence must be maintained. The DOH has no right in interfere with the doctor patient privilege nor do you have a right to infringe on anyones religious beliefs. A persons deep held religious beliefs are protected under the Constitution. Challenge this and you are opening up Pandoras box.

Lastly I am requesting that the Department of Health host public hearings Statewide on (HAR) Title 11, Chapter 157, "Examination and Immunization."

Thank you for taking the time to read my testimony

Maly Gella, RN



From: [REDACTED]
To: [REDACTED]
Subject: OPPOSE: MANDATORY Immunizations
Date: Wednesday, October 31, 2018 4:52:09 PM

I OPPOSE the mandatory immunizations.

There has been research on the side effects (due to the ingredients) of immunization for various segments of the population.

I would think that DOH could be held responsible for making this mandatory for those who would suffer greater illnesses and death caused by immunization.

Respectfully,

Sylvia Dolena

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: OPPOSITION TO HAR-157
Date: Wednesday, October 31, 2018 10:04:14 PM

Aloha,

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of Oahu and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. Please read the vaccine insert itself (not the generic “fact sheet” from the doctor), but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carry risk.

2. This rule changes will put more children at risk. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? There isn't one. There aren't any adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld.

We could not rely on our government to follow through with their promises when it comes to the health and safety of our children.

This bill makes it harder for parents to protect their children.

3. HPV is a sexually transmitted disease. It is appalling to require the HPV vaccine in order for children to attend school.

HPV is the most controversial vaccine because of its debilitating side effects. It has been known to ruin the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this. The information is most often not shared with patients.

The basic question of “Are you allergic to eggs?” is NOT asked before the shot is administered.

Additionally, this vaccine has been known to have very low efficacy rate. It does not appear that the children's best interest are kept in mind.

5. What you are proposing encroaches upon our rights.

Your definition of “school” as a “congregate setting for educational purposes.” is too broad a statement. Even if you listed “exceptions” in a later paragraph, this definition is too vague.

I wish to stop this bill.

However, at the very least, I ask that it be changed to “public school.” Many parents have opted to not send our children to public schools for a wide variety of reasons.

If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven't. We have created our own options. “One size fits all” does not work in most aspects of life, including education and medical decisions.

6. Medical Freedom is a basic right. You are attempting to regulate carte blanche without understanding the medical concerns, religious beliefs, or educational background of every individual.

Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and make educated decisions when it comes to vaccines. Please stop trying to take that away from parents.

Sincerely,
Tsu Osato

From: [REDACTED]
To: [REDACTED]
Subject: Rejecting mandatory immunization
Date: Wednesday, October 31, 2018 10:24:02 PM

Aloha,

I am writing this on behalf of my family of three. We reject the proposal of a mandatory immunization for children and adults. We believe in Body Sovereignty and we choose not to inject ourselves with any poisons that you deem mandatory. There is extensive research available to show that "herd immunity" has been proven incorrect. It's appalling that mandatory vaccinations are being considered in this state. This is poison whether space out or not, and it is our right to refuse any thing to enter into our bodies that we do not consent to, including vaccinations. We consider mandatory vaccination to be a form of assault, as it involves forceful penetration with a needle and injection of poisons carried out against a person without that person's consent. Those that would like to be vaccinated should be free to do so, and those that do not want to be vaccinated should be free to choose. Body Sovereignty for All.

Mahalo,
Danielle Holland and Family

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: RE: HAR 11-157
Date: Wednesday, October 31, 2018 10:57:19 PM

To: Hawaii State Department of Health, and whom it may concern.

Aloha, I am writing to express to you my extreme opposition to HAR 11-157. I live with my family on the Big Island of Hawaii and am strongly opposed to this shocking rule change.

To begin, I am most definitely not anti-vaccine. With some exceptions, I believe most vaccines can and do save lives. What I oppose is being FORCED to undergo an invasive medical procedure that carries with it the possibility of long term damage, injury or death. I am also particularly opposed to the flu vaccine and the HPV vaccine.

The flu vaccine is not only downright dangerous, it has a pathetically low success rate. My grandmother died very shortly after receiving this vaccine, both my parents became violently ill after being vaccinated for the flu, both saying never again, they would much rather take their chances with the actual flu bug. I know of several people here on this island who developed Guillain Barre Syndrome as a direct result of the vaccine and another who died within 6 hours of receiving it. Have you read the vaccine insert? The one that is in the box that the doctor NEVER shows you. Probably because it is about 3 ft long with listed side effects!

As for the HPV vaccine....Words fail me that you could even consider mandating such a hazardous and unnecessary vaccine for admittance to school! Recommendation for this vaccine was withdrawn in Japan due to the thousands of women and girls who had their bodies damaged and lives devastated. Some are paralyzed, some are brain-damaged. All have experienced immense physical, psychological and emotional pain. This has happened to countless females (and males) GLOBALLY. Then there are the many who have DIED from HPV vaccine, within hours or days of being injected. This is an atrocity.

There is no one size fits all, some bodies are sensitive or allergic to vaccine ingredients which include human and animal DNA and neurotoxic, carcinogenic chemicals. If an individual has an underlying genetic, metabolic or immune vulnerability, for example the common gene mutation MTHFR (which many people do not even know they have) a 'vaccine' could kill or seriously harm as the immune system reacts to the toxins and live viruses in vaccines and goes haywire.

This authoritarian overreach regarding unwarranted, mandatory vaccinations appears to be about money and control, NOT the well-being of our children. Pharmaceutical companies are making countless millions of dollars and using citizens, particularly the children, as human guinea-pigs. The 'safety' testing is rushed through, no long term safety studies are performed. The truth is covered up and the vaccine manufacturers are not held accountable.

It is a game of Russian roulette. It is **medical rape**. Please, consider our human rights and parental rights. Stop trying to take away medical freedom, religious freedom and informed consent. There should ALWAYS be choice NOT coercion! This is a violation of the Nuremberg Code. How can you expect we the people, to trust the government when you disregard our most basic rights as humans?

To finish, I thank you for the opportunity to submit written testimony, and I ask that you consider holding state-wide public hearings on every island, with enough public notice that EVERYONE gets the opportunity to hear of it and be able to testify should they decide they wish to do so.

Sincerely,

Nicole Yokoyama

(Registered voter, [REDACTED])

From: [REDACTED]
To: [REDACTED]
Subject: Aloha and Please: NO Mandatory Vaccinations
Date: Wednesday, October 31, 2018 2:29:27 PM

Dear Honorable Department of Health,

First I just want to say that the Food Handling Prep class I took a couple years ago with a retiring Health Department official was a GREAT class and I remember all the things he taught us, especially about time and temperature!

Health and cleanliness mean a lot to me, but that said, I am writing today to ask you to please not move forward with forcing a Mandatory Vaccine Schedule. Like most, I came from the point of view they were good until one day I met a woman who's 7 year old child was strapped to a way too small stroller and completely checked out. She stated that directly after his MMR, his eyes rolled up in his head and he had been a drooling, detached, mentally challenged child. Her boy never returned. This started me on a long research journey, which lead me to find out that Vaccines aren't required to have the rigorous years of testing as by-mouth pharmaceuticals and that is, in part, a reason for the proliferation of them.

I actually have reams of data to counter what I also thought seemed good medicine until I began to educate myself with more vaccine data and the absolute damage done by the ADJUVANTS used in the ingredients of vaccines with side effects sometimes more debilitating that what the vaccine is actually to prevent, but I won't go on in this vein.

Those that are vaccinated are safe from those who are not, so why would the public health require Nazi Regime forcing of ingredients into people who wish to maintain their right to consent. This is the greatest issue facing the Hawaii DOH, are you really willing to remove people's right to Body Sovereignty on an Island where the People have been marginalized and had their Sovereignty stolen in every other way.

Please do not continue pursuing taking away the individual rights of the many by pushing Mandatory vaccines.

Thank you for all you do for our community. Please don't take your sacred duties to the point of removing people from their sovereign right to informed consent and the right to chose for their own bodies. We may have lost our aloha, but must we really lose even our right to self care?

Respectfully submitted,

Susan

Susan Bambara
Kurtistown

From: [REDACTED]
To: [REDACTED]
Subject: FULL OPPOSITION!
Date: Wednesday, October 31, 2018 9:03:57 AM

I am in total OPPOSITION of this! We have a right to choose!

Please confirm receipt!

Mahalo!
Ilima Ho-Lastimoso

[REDACTED]



The Senate

STATE CAPITOL
HONOLULU, HAWAII 96813

October 31, 2018

To Whom It May Concern,

I am the State Senator for Puna and Ka'u.

I oppose any increase in mandatory vaccinations for any category of workers, students, or people, and I oppose adding additional vaccines to the childhood schedule for school acceptance.

The total vaccination schedule in the U.S. today includes about ten times as many vaccinations as we had 20 years ago, and more come on line every year. Yet the combinations of vaccines given have never been proven safe or effective. The sum total of heavy metals in the adjuvants to all these vaccines amounts to a clear health hazard. It has not been proven safe.

I am not an 'anti-vaxxer,' and I am also not 'anti-science.' I am pro-freedom and pro-individual liberty. Like many others I also believe in natural health which does not come from chemicals, but from one's inherent, God-given powers to grow, heal, and maintain health when free from harmful influences, such as pharmaceuticals. You may not feel the same; That is your right, but you do not have the right to take this health freedom away from others.

I have a degree in biology and respect science greatly. One of the primary principles of science is the precautionary principle; if you are unsure of the consequences of an action, proceed cautiously or not at all. This scientific principle should be applied here, instead of the reckless promotion of untested vaccine protocols.

The adjuvants in vaccines have never been proven safe, either in individual doses or in the large combinations of vaccines given today. The active ingredients have also never been proven safe or effective in the same sense that any modern medicine must be proven. The very fact that vaccine manufacturers have been granted immunity from liability is telling: the only other industry granted such immunity is the nuclear industry. The logic is that the liability is so vast and the public need so great that special immunity is needed. But as with nuclear industry, there is no true need and the protection comes from political power and financial influence, not from public safety concerns.

Some say we must compel vaccines to protect ourselves and our kids. But if vaccines really worked, then one wouldn't care if my child or your teacher is vaccinated or not; one's vaccines would protect one. I am aware of the 'herd-immunity' argument here, and I am also aware of its profound scientific fallacy.

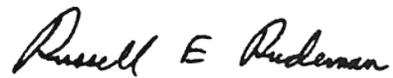
The pharmaceutical industry is free to promote its products, despite lack of safety studies. And you are free to accept them if you wish. But you have no right to compel any one to submit to such hazards, and to take away anyone's freedom of choice regarding how they care for their own body. Some of us don't want foreign biological agents or chemicals injected or otherwise introduced into our healthy bodies. A

The number of vaccines recommended or required in this country is much greater than in other modern countries, such as the E.U. Is this because the other countries are not as 'scientific' as the U.S.? Or is it possible that what we accept as 'scientifically justified' is influenced by the massive outreach of the pharmaceutical industry in our country? And is it possible that you are being used as a marketing device of this pharmaceutical industry?

Please note that these other modern countries, with much fewer vaccinations, have better infant mortality rates, fewer childhood diseases, and longer life expectancy than in the U.S. A scientific approach would take this combination of facts very seriously, and proceed cautiously with addition vaccine recommendations.

If there is any question about this, then further compelling the use of vaccines is irresponsible and immoral. You must stop doing so.

Sincerely,



Russell E. Ruderman, Senator
Hawaii State Senate
District #2: Puna - Ka`u



From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157 A'OLE "NO"
Date: Wednesday, October 31, 2018 11:01:56 AM

RE: HR 11-157

IM IN FULL OPPOSITION!

I am in total OPPOSITION of this! I/WE have a right to choose!
Please confirm receipt!

Tracy Pedrina

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: STRONG OPPOSITION TO HAR 11-157
Date: Wednesday, October 31, 2018 11:49:53 PM

Aloha,

Thank you for the opportunity to submit testimony. I oppose HAR 11-157 and urge you to take it off the table.

As a mother of three keiki, I care deeply about our health, and it begins with me. With my husband, we make all the decisions for our family: what we eat, what positive activities will consume our time, and what things we will put into our body when it comes to our health. When I speak with my doctors, I expect informed consent. I do not expect them to have all the answers but I do wish to know ALL the available facts. What I have come to learn is that doctors pass out “fact sheets” (Vaccine Information Sheets) which are far different from the actual vaccine package inserts (see [here](#)). When I dig deeper, I see that there is great risk. It is absolutely wrong to mandate medical procedures that are known to cause harm and carry risk. No vaccine or vaccine schedule is one-size-fits-all. No other medication is – why should vaccines be any different?

Where this is risk, there must be choice. Vaccination is a medical intervention that carries a risk of injury or death. As parents, we have the God-given human and legal right to say no about what goes into the bodies of our keiki. As taxpayers, we have the right to a public education for our keiki. We also have the right to homeschool our keiki as we see fit. That should NOT come at the cost of their health.

When it comes to the changes you are proposing, I have several disagreements. The HPV vaccine should NOT be mandated to attend school. HPV is a sexually transmitted disease. This has absolutely nothing to do with the educational environment. Leave those decisions up to the parents. Also, this particular vaccine has been shown to cause GREAT harm. Please see [all of these studies](#) done on the adverse affects of Gardasil. Did you know that when it was studied, it was only tested in young adults ages 16-26, yet it is recommended as young as 9 years old? There is literally no data on how it will affect our keiki in the short or long term. Our children are being used as guinea pigs.

Requiring the flu shot is also inappropriate. Given the ineffectiveness in recent years, you have a better chance of avoiding the flu by boosting your immune system naturally, washing your hands, and staying home if you are ill. Every year, it is a guessing game. I do not want my children or myself to be subjected to this.

In 2013, the Hawai'i State Legislation empowered the Hawai'i Department of Health with extensive, excessive latitude [to make and alter the health policy in the State](#). Now, only a few if not a single individual has the power to make decisions when it comes to our health. This is inappropriate and is devoid of the proper checks and balances. These individuals do not have

our best interests in mind. Where there is risk, there must be choice. And as parents, we have the right to decide what is best for our keiki.

There are countless victims who have experienced vaccine injury. You can hear their stories [here](#). My family member is one of them and his life was forever altered. Vaccine manufacturers are protected by law; no one is held accountable when injury happens. Taxpayers foot the bill when these (few) cases make it to the “vaccine court” (National Vaccine Injury Compensation Program). As of now in 2018, the U.S. Court of Claims [has awarded nearly \\$4 billion dollars](#) to vaccine victims for their catastrophic vaccine injuries, although two out of three applicants have been denied compensation. Currently, there are 76 vaccines on the childhood schedule. Many more are in the works. When will enough be enough? Who gets to put the cap on the number – the State? The ACIP? No. That decision should belong to the parents.

I respectfully request that the proposed changes to HAR 11-157 be removed for the health of all of our communities. Leave the decisions in the hands of parents who know what is best for their keiki.

Thank you for your consideration,

Aubrey Ae’a



From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: STRONGLY OPPOSE HAR 11-157
Date: Wednesday, October 31, 2018 4:15:16 AM

STRONGLY OPPOSE HAR 11-157

Thank you for the opportunity to submit testimony. I'm writing in strong opposition of HAR 11-157. In "all" fairness, public hearings should be hosted by DOH statewide on this rule. Shouldn't "all" the people be informed as this essentially will effect "all" people in one way or another? Vaccinations are approached as a one-size-fits-all and yet there in fact have been adverse consequences as a result of this approach and shouldn't we have learned this already that it doesn't "protect and improve the health for all people," as your mission statement maintains? The emphasis here is on "all," including "all" of those who may suffer adversely from being vaccinated – which goes directly against DOH's mission, and philosophy which also states, "– Health, that optimal state of physical, mental, social and environmental well-being, is a right and responsibility of all of Hawaii's people." How can the "people" exercise their "rights and responsibility" if it's being stripped away from them via forced vaccinations and without their knowledge?

With the multitude of reporting that has taken place and are still taking place, are these given any consideration, like those being documented by the Vaccine Adverse Events Reporting System (VAERS) in writing such a rule? Have all of those who are responsible for composing and proposing to implement HAR 11-157 read every vaccine inserts detailing all the possible adverse effects and at times very controversial ingredients? If side effects so indicated in the inserts exists, how can HAR 11-157 even be considered as not "all" will come away unscathed will they?

In addition, its common knowledge that the Vaccine Injury Compensation Program has paid out approximately \$3.9 Billion thus far, and it's inevitable that, that number will continue to rise, and that's just those who are lucky enough to have their cases heard, not factoring in those that haven't even had that opportunity to be heard, some claiming to still be waiting after an unjust number of years.

Now a days, systems are set up which groups and categorizes applications which just doesn't (at times), in the end produce the best outcomes for "all" that are forced into those "systems." Because medications go down a different road map/system, adverse reactions are known prior and reported and taken into consideration and are commonly discussed with a patient before dispensing/administering. When an adverse event occurs, the patient is listened to, medical interventions follow and so goes the medication road map/system. On the other hand, the vaccine road map/system never allows for disclosure of possible side-effects conveyed in the inserts prior to administration. Neither is one made aware of its controversial ingredients. Why is that? Parents/guardians have encountered a hostile environment in their quest to just have that right to know, or wish to wait, etc., or to be just heard. Why is that? And if a patient appears to have experienced any kind of problems following vaccination, its treated like that couldn't possibly be. Why is that? They are dismissed. They're treated with condescension. That's the current vaccine road map/system. What if it goes against your religious beliefs to have aborted fetal tissue, or other animal products, etc., injected into your person via vaccination, shouldn't you have that "right" to know prior and that "right" to refuse such an abomination? Wouldn't that be violating "people's rights" to reverence their religious beliefs?

My niece ended up in the emergency room, suffering from what she knew was an adverse reaction after receiving the HPV vaccine. When explaining this to the emergency room physician, he belittled her and dismissed anything that she might have been experiencing had anything to do with the HPV vaccination she was given. She was not heard that day. She was not listened to. Why was that? When her and her husband was expecting their first child, they were elated and couldn't wait to hold their baby in their arms. That was short lived when their baby died unexpectedly eight and half months into the pregnancy. She could no longer have children of her own. It's been several years since and she and her husband still honors that little life lost every anniversary. That was the vaccine

road map/system at work at that time. That same road map/system is still intact today given the horrendous vaccine schedule that has grown exponentially over a short period of time. When you follow that path of receiving feedback from patients about adverse, vaccine effects, the end of that path is denial, dismissiveness and condescension. It's that elephant in the room that's never acknowledged, never heard. It doesn't work for "all." It won't work for "all." What a dangerous path for "all" to keep going down on.

This system has created a rift between doctor and patient care that wasn't there before and now it's spilling over and creating unnecessary pressure into the public school environment. How can a system like that ever be to "protect and improve the health for all people," when people are not being listened to and are suffering as a result?" Shouldn't "all" lives matter? Shouldn't that road map/system change first before hastily implementing more forced, hostile mandates? Otherwise the "right" for "all of Hawaii's people" will be stripped by the very agency purporting to respect it. It isn't that hard to see.

Respectfully,
Mrs. L. Nakamura-Higa

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: STRONGLY OPPOSE HAR 11-157 rule changes to include new vaccine requirements
Date: Wednesday, October 31, 2018 1:09:09 AM

Aloha Dr. Bruce S. Anderson, Director Dept of Health Hawaii,
It with great concern that I STRONGLY OPPOSE HAR 11-157 rule changes to include new vaccine requirements. An increase in scheduled doses for our keiki without any liability on the part of the pharmaceuticals, the Center for Disease Control, the State of Hawaii or the doctors, in implementing the mandatory program is alarming and irresponsible. Having researched the toxic vaccine contaminants ie. thimerosal aka mercury, aluminum, formaldehyde, animal and/or human dna, one would wonder why the dept of health would consider a schedule increase when research shows incidents of detrimental neurological damage. Over the years it is noted that the vaccine schedule continues to escalate with a spike beginning in 1983 when the pharmaceutical companies were absolved of all liability for vaccine related injuries. When that occurred the burden of responsibility fell on the patient who would incur insurmountable medical bills in efforts to either detox the heavy metals or medicate vaccine injury symptoms. MMR is known to contribute to autism as covered up by the CDC. In 1962 only 5 vaccines were administered. Today in our efforts to "protect" our children, up to 72 + doses from infant to 18 are administered and yet our nations children are sicker than ever ie allergies, asthma, gut issues, ADD, ADHD, cancer, tumors. It is disturbing that this rule change requires all young children to take the influenza vaccine when its' efficacy is only 10%. Another alarming rule change is for all 7th graders be given the HPV aka gardasil when there are known injuries internationally; Japan, France and India have banned HPV gardasil.

All patients must be informed of vaccine contaminants and their side effects and given a CHOICE if there is a RISK and given the KNOWLEDGE that vaccine injuries can induce life-long medical issues.

The right to informed consent to any medical intervention that can kill or injure you or your child is a HUMAN RIGHT.

A healthy Hawaii, which is our goal, is an INFORMED Hawaii. Let's stop the implementation of HAR 11-157 till the pharmaceuticals, CDC, Dept of Health and our local clinics will take ownership of the potential vaccine injuries and take steps to inform EVERY patient of the RISK.

There is no such thing as a safe vaccine.

Sincerely,
Lois Young

--

Follow Me...

[REDACTED]

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: strongly opposing HAR11-157
Date: Wednesday, October 31, 2018 11:09:58 PM

Aloha,

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of [REDACTED], I work at In the medical field and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.

2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

Vaccines shed, therefore do not protect immuno compromised.

Newborns don't go to school. Also do alot of immuno compromised children go to school & how many % are immuno compromised?

All recent outbreaks has been in fully vaccinated individuals.

94 % of adults are not up to date with vaccines, so the 93% what they suggest have to be vaccinated is not even possible. Even if they were uptodate, vaccines have proven to weaken 2 to 5 years if they even worked at all. So that is completely false. To attack our exemptions is a uncalled for. Why do they keep mentioning elders and new borns. This is mandate for school, right? Also newborns, elderly and immuno compromised DO get vaccinated.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world. Abstinence needs to be taught in the schools more.

Cervical cancer has increased since the vaccine in the age group it was vaccinated for. Over 50.000 reportes adverse events and 325 deaths reported to VAERS. Fda admits only 1 to 10% even gets

What are the real reasons for these mandates? Hpv and Hep A is not something that would or should transfer in a school environment.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question “are you allergic to eggs?” asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind. Again, I work in the hospitals and I refuse to get this. A few of my kids that have not had all their shots are healthier than my ones that did. I have two vaccine injured children that I know of. Some are too young to know if there are effects or not.

5. Stop re-defining what a “group” is – Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that’s one thing, but many, many, many of us have opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven’t. We have created our own options because there is no “one size fits all” when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don’t know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

Use physicians for informed consent statement on that.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: strongly support the HAR 11-157 proposed rules update
Date: Wednesday, October 31, 2018 7:47:30 AM

October 31, 2018

To whom it may concern,

Thank you for this opportunity to provide testimony. As a parent of 3 children, and a pediatrician, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP)

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life. Some of these diseases are life-threatening. These diseases are preventable!

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Cristeta Ancog, M.D.

Certified, American Board of Pediatrics

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: strongly support the HAR 11-157 proposed rules update
Date: Wednesday, October 31, 2018 7:52:03 AM

Ocotober 31, 2018

To whom it may concern,

Thank you for this opportunity to provide testimony. As a parent of 3 fully immunized children, and a pediatrician with 30 years of experience, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP)

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life. Some of these diseases are life-threatening. These diseases are preventable!

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Bertram Weeks Jr, M.D.

Fellow, American Academy of Pediatrics

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Subject: Oppose HAR 11-157
Date: Wednesday, October 31, 2018 12:19:46 AM

Dear Hawai'i Department of Health,

I strongly oppose HAR 11-157.

The current vaccination schedule is Adequate as is.

Adding more to the schedule, especially vaccinations like HPV, which have not yet been researched fully and have had countless reports of adverse reactions, is unwise and irresponsible.

These mandates, and the reporting associated with exemptions, infringe upon personal liberties as well as violate the right to privacy concerning ones own health information and record.

Please respect and seriously consider the voices of those who oppose HAR 11-157 and do not move forward with these prescribed changes.

Thank you for listening,

Sandra Oda

From: [REDACTED]
To: [REDACTED]
Subject: support rule changes
Date: Wednesday, October 31, 2018 1:59:46 PM

I strongly SUPPORT the proposed rule changes. Our keiki deserve the herd immunity of having everyone vaccinated, and the recent outbreaks of diseases with vaccinations is evidence that current requirements should be strengthened.

Thank you for your time
Maxine Anderson

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Wednesday, October 31, 2018 8:17:49 AM

Aloha,

Thank you for allowing me to submit testimony. I oppose HAR 11-157. If there is a risk, there must be a choice. Informed Consent is meaningless without the right to say no. The one-size-fits-all vaccine schedule is not safe for every child. The proven negative side effects and dire consequences of many vaccines are far greater than the risks of the diseases the vaccines are claimed to prevent.

Vaccines never undergo long term, double-blind placebo-controlled tests for safety or efficacy. At best they are tested for 4-6 days and cleared of any harm by the manufacturers who profit off of them. This is a crime against humanity. The truth is that vaccines do harm and the damage typically surfaces after the manufacturer's extremely short safety study. This is not sound science, this is avoiding the elephant in the room. Vaccines do harm. Just look at the number of vaccine adverse reactions and deaths registered with VAERS each year. It is estimated that only 10% of injuries are even reported. The true number of vaccine injuries is staggering, and the injuries are often irreversible. This bill takes away the right of the parent to decide what is best for their children.

I am not anti-vaccine, I am pro-child, pro-family, pro-community. I am pro-science, I am pro-research. I am pro-health, pro-wellbeing, pro-safety. I am pro-government transparency. I am pro-pharmaceutical company accountability.

I am pro-honesty, I am pro-critical thinking. I am pro-freedom.

Please, I urge you to oppose HAR 11-157 for the sake of our child's health and her future. It is OUR decision, not the State's. The children are the future. We must not allow a healthy child to be harmed by unsafe vaccinations that are rushed to market by an industry that is not held legally liable for the harm their products cause. If HAR 11-157 passes, this is a blatant violation of the Nuremberg Code. It also goes against the Declaration of Geneva, where Doctors worldwide swear on oath, "I WILL NOT USE my medical knowledge to violate human rights and civil liberties, even under threat."

We're also asking you to hold public hearings statewide.

Signed,

Eric Day

Registered Voter



From: [REDACTED]
To: [REDACTED]
Subject: Testimony HAR 11-157
Date: Wednesday, October 31, 2018 3:02:57 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Gwen Navarrete Klapperich, CPLP

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, October 31, 2018 6:02:13 PM

To whom this may concern,

I'm born and raised on [REDACTED]. I have three children 10yrs and under. I am not in support of HAR-157. I strongly oppose this idea becoming a reality. Here are some of my concerns:

1. Where there is risk, there must be a choice. Vaccines carry risk. When I consent to medical treatment, I alone am assuming that risk. You cannot require anyone to receive medical treatment against their will. If I am forced to take the required vaccine and there is a side effect or harm that befalls me, will you assume that risk and liability? Do you become responsible for me now medically?

2. The logical fallacy that all vaccinations are equal and they work the same for all is not only illogical, but is putting the public at risk. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one.

How can you mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. HAR 11-157 makes it harder to protect our children.

3. HPV is a sexually transmitted disease. It is appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. It is the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world. Hepatitis B can only be transmitted by sex and needles, why does my child need to have four doses of this vaccine before they even start school?

4. Requiring the flu vaccine is absurd and so inappropriate! The efficacy rate of the flu vaccine is so low - how could it possibly be added to the list. I have personal testimony of my family members taking the flu shot, immediately getting sick and having long lasting effects like paralysis!!!! When we went back to the doctors, they assumed no fault, because it was the risk that WE took. Needless to say, none of us will ever take the flu shot again! You do not have the best interest of children in mind by requiring people to take the flu shot.

Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared. The basic question "are you allergic to eggs?" Is NOT asked when the shot is administered.

5. Stop re-defining what a “group” is. Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that’s one thing, but many, many, many of us have opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven’t. We have created our own options because there is no “one size fits all” when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don’t know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

7. Requiring adults who go to school to get vaccines but no other adults to get the same vaccines is discriminating against adult students.

I can understand the concern that we have about the spreading of communicable diseases! I am NOT against all vaccines all the time. But I strongly disagree with not having the liberty to choose what is best for me and my family, at what time! I DO NOT SUPPORT BILL HAR 11-157!

Thank you for your time.

Sincerely,

Shayna Bing



From: [REDACTED]
To: [REDACTED]
Subject: Hawaii Administrative Rules
Date: Tuesday, October 30, 2018 3:54:26 PM

Dear Dept of Health,

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Curtis Y. Ochiai
Parent

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Thursday, November 01, 2018 11:09:59 AM

Regarding the HAR 11-157 I strongly oppose!

Sincerely,
John Zuech

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Thursday, November 01, 2018 11:19:10 AM

Aloha kakou,

I write this as a citizen as a mother. I write this letter to advise you that I OPPOSE HAR 11-157. I do not believe HPV and flu shots should be mandatory!!! The flu shot is not effective as it is made out to be. It is a guess in the strain for that year. They have been many adverse reactions to HPV therefore I am not giving it to my kids!! I feel the rules are good the way it is! Please DO NOT pass this resolution!

Mahalo

Lela Kalama

[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Thursday, November 01, 2018 6:54:51 PM

I am writing to voice written testimony on HAR 11-157 as I am concerned about more mandatory vaccinations.

I am against this proposed Hawaii Administrative Rule to update the school vaccination and examination requirements. I am against HAR 11-157.

Thank you.

Aloha,
Faith LeLievre
Registered Voter
[REDACTED]



**Testimony Presented Before the
Department of Health, State of Hawaii
Thursday, November 1, 2018**

**By
Hali Robinett, MPH
President-Elect
Hawaii Public Health Association**

Hearing Docket No. R-157-18-07: PROPOSED AMENDMENTS TO HAR TITLE 11, CHAPTER 157

Thank you for the opportunity to provide testimony in support of the proposed amendments to Hawai'i Administrative Rules (HAR) Title 11, Chapter 157 regarding Examination and Immunization. These proposed amendments will bring Hawai'i's rules into compliance with the most current recommendations of the U.S. Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), and most importantly, protect our keiki and youth from life threatening diseases now and into the future.

The CDC advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases. The proposed rules update is especially important in this regard for students entering 7th grade (or higher) as the immunization requirements will help to prevent the spread of dangerous infectious diseases, as well as protect our youth from debilitating and life-threatening cancers caused by persistent human papillomavirus (HPV) infections.

Nearly 80 million Americans – one out of every four people – are infected with HPV, and of those millions, more than 31,000 will be diagnosed with an HPV-related cancer this year, namely malignancies of the cervix, vagina, vulva, penis, anus, oropharynx and oral cavity. Despite those staggering figures and the availability of a vaccine to prevent the infections that cause these cancers, HPV vaccination remains low in Hawaii and in the U.S., especially compared to other recommended adolescent vaccines: only 55% of Hawai'i's adolescents (males & females) have received the HPV vaccine compared to 86% who received the vaccine to prevent meningitis, 85% for tetanus booster and 90% for the measles-mumps-rubella booster (NIS-TEEN, 2017). This administrative rule change will greatly increase uptake of the HPV vaccine along with the other required vaccines, thereby protecting vulnerable groups in our community including the very young, the elderly and others with compromised immune systems who cannot be vaccinated.

Immunization is widely recognized as one of the greatest public health achievements of the twentieth century, and the HPV vaccine is considered one of the greatest achievements in cancer prevention in our lifetimes. As such, the Hawaii Public Health Association fully endorses the changes to HAR 11-157, for the health of all communities in Hawaii.

The Hawaii Public Health Association is a group of over 600 community members, public health professionals and organizations statewide dedicated to improving public health. HPHA also serves as a voice for public health professionals and as a repository for information about public health in the Pacific.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 Testimony
Date: Thursday, November 01, 2018 6:45:11 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157 STRONGLY SUPPORT
Date: Thursday, November 01, 2018 9:17:40 AM

Dear Madam/Sir,

My name is Nicole Miyahira and I am a community pharmacist on the Big Island. I earned my Bachelor of Science in Biology from Pacific University Oregon and subsequently earned my Doctorate of Pharmacy from the Daniel K Inouye College of Pharmacy in Hilo. I was born and raised by a working class family who did everything in their power to ensure I had the best education and opportunities possible. As a pharmacist, I feel responsible to protect the health of my local community who I serve nearly every day.

I am on the “front lines” so-to-speak in terms of serving our ohana from newborn to kupuna. As a pharmacist I am especially cognizant of the impacts of preventable diseases on our local community. When you witness a baby who was too young to be vaccinated die because a family member was not vaccinated for whooping cough-it changes your life as a medical professional. I feel that people of our generation are “spoiled” as we have not seen what a true preventable disease pandemic looks like and therefore do not understand the weight of importance vaccinations carry.

It is highly discouraging to witness so many individuals strongly oppose LIFE-SAVING vaccinations when they have little to no scientific education, lack any REPUTABLE resources to cite for their deluded views and are so aggressively pushing their message to you.

Ladies and gentlemen, I implore you to ensure that this extremely positive bill becomes law for the children of Hawaii. Mandatory vaccinations help protect the Keiki that are not old enough to receive theirs yet, supports herd immunity of our small communities and protects the kupuna whose immune systems are not as resilient any longer. It also helps to protect Keiki whose parents are misinformed and refuse to do what is in their best interest. It protects our Keiki who medically cannot be vaccinated because of severe medical conditions. There are so many amazing implications of this bill.

I want to show my strong support!

Mahalo for your time,

Nicole K. Miyahira, Pharm. D.

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157 strongly support
Date: Thursday, November 01, 2018 6:28:56 PM

Aloha,

I would like to share my very strong support for HAR11-157. Protecting our Keiki in the school setting and in turn their ohana is something I wholeheartedly agree with. Exemptions should only be for those who are medically unable to be vaccinated.

Thank you for your time,

John Rosner

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: HAR-11-157
Date: Thursday, November 01, 2018 10:29:37 AM

I strongly oppose bill HAR-11-157

Not only are immunization extremely dangerous but it is not for you to decide what is best for our children shame on you. Get your hands out of big pharm pockets at the expense of our children. Do your research people we don't need vaccine mandates in Hawaii!!!

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: HPV
Date: Sunday, November 11, 2018 3:08:10 PM

Aloha, I was reading about this required vaccine for school and I'm totally not comfortable with the HPV & Flu vaccine. I have 3 daughters ages 12, 10 & 3. I would never vaccinate my child with these 2. I'm not an anti-Vaccination parent either. My 2 oldest are fully vaccinated except for the 2 listed above. There just is not enough studies done to put this poison on my child especially the HPV. Adults I know who have been vaccinated with HPV (young adults) have tumors and that can't just be a coincidence. If this is a forced procedure done, my kids will not be going to school. My kids go to public school in Lahaina, Maui and I support vaccination but this makes me really not happy to support these 2 particular. STD vaccine is not an illness that can spread like Chicken pox or Measles, it's ridiculous that it would be treated like so. Please take this into consideration. Mahalo, April Colpas



Testimony Presented Before the
Department of Health, State of Hawaii
Thursday, November 1, 2018;

By

Jerris Hedges, MD
Professor and Dean

and

Lee E. Buenconsejo-Lum, MD, FAAFP
Designated Institutional Official (DIO) and GME Director
Professor of Family Medicine & Community Health

John A. Burns School of Medicine

Hearing Docket No. R-157-18-07: PROPOSED AMENDMENTS TO HAR TITLE 11,
CHAPTER 157

Thank you for the opportunity to provide testimony in support of the proposed amendments to Hawai'i Administrative Rules (HAR) Title 11, Chapter 157 regarding Examination and Immunization. The proposed amendments modernize and clarify the immunization and examination requirements for school, post-secondary school and child care facility attendance in Hawai'i by updating and expanding definitions, deleting unnecessary definitions and adding new definitions. Additionally, the amendments provide more guidance regarding school and post-secondary school provisional entrance and exclusion procedures.

At the University of Hawai'i John A. Burns, School of Medicine (JABSOM), we strive to teach and train high-quality physicians, biomedical scientists, and allied health workers for Hawai'i and the Pacific by providing an opportunity for a medical education previously unavailable to residents of Hawai'i and other Pacific nations. With Hawai'i's increasing need for medical services combined with growing workforce shortages for physicians and other health care providers, JABSOM plays a vital role in educating future generations of doctors to care for the people of the state.

Appropriate and timely immunizations are critical to the overall health and wellness of individuals as well as our community. Immunization against certain illnesses not only prevents the spread of dangerous contagious diseases, but also provides protection from certain cancers. The adoption of the CDC's recommended adolescent vaccinations for 7th grade entry includes the human papillomavirus (HPV) vaccine, which is the vaccine that has already been demonstrated worldwide to reduce pre-cancers in both females and males. Cervical cancer in Hawai'i disproportionately affects Native Hawaiians, Filipinos and Pacific Islanders. In Hawai'i, only 55% of adolescents receive the HPV vaccine, compared to 86% receiving the vaccine to prevent meningitis

(brain infection), 85% for tetanus booster and 90% receiving the measles-mumps-rubella booster shot. This administrative rule change will greatly facilitate receipt of the HPV vaccine along with the other required vaccines.

Doctors are key to assuring that needed immunizations are administered. Several research studies conducted by JABSOM, as well as the UH Cancer Center, have demonstrated that physician recommendation remains the most important factor in receiving the HPV vaccination. At JABSOM our students receive extensive training in immunization protocols, immunology and vaccinations. The students receive this information as part of illness prevention (public health) instruction and clinical skills development. Our Pediatrics, Family Medicine and Obstetrics-Gynecology residency programs have extensive training in HPV and provide immunizations in their clinics to many of Oahu's minority and underserved patients. Recognizing the importance of making necessary vaccinations available to everyone, JABSOM's staff and students have voluntarily provided immunization services to those who do not have a primary care physician and to the underserved population as part of the HOME Project.

JABSOM supports the proposed amendments to HAR Title 11, Chapter 157. Mahalo for the opportunity to provide testimony on this matter.

From: [REDACTED]
To: [REDACTED]
Subject: Oppose Mandate of Vaccinations
Date: Thursday, November 01, 2018 2:48:08 PM

Please do not force us and our keiki to take vaccines against our will.

Mahalo!

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: Oppose Mandatory vaccinations
Date: Thursday, November 01, 2018 6:36:23 AM

Aloha. As a resident of the big Island of Hawaii, I oppose any and all vaccinations being mandatory. The last thing we need is to be injecting heavy metals into ourselves and our children. If parents want to voluntarily have it done to their kids that's fine but for those who don't want it should not be forced to. There's too much evidence linking the toxic heavy metals to neurological damage. Mahalo for your time.

Sent from my iPhone

Testimony of Jennifer Kurrie
on behalf of
Walgreen Co.

DATE: November 1, 2018

TO: Director Bruce S. Anderson
Department of Health

RE: **Proposed Amendments to HAR Title 11, Chapter 157, Examination and Immunization**

Dear Director Anderson,

I am Jennifer Kurrie, government affairs director for Walgreen Co. (Walgreens). Walgreens operates stores at more than 8,200 locations in all 50 states, the District of Columbia, and Puerto Rico. In Hawaii, Walgreens now has 20 stores on the islands of Oahu, Maui, and Hawaii.

Walgreens **strongly supports** the proposed rules, which would bring Hawaii's school immunization requirements more fully in line with the current federal recommendations. The major amendments include: (1) expanding the definition of "student" to include persons enrolled and physically present on a post-secondary school campus; (2) excluding exclusively online schools from the definition of "school"; (3) incorporating the Federal Advisory Committee on Immunization Practices' (ACIP) 2017 best practices guidance including, by reference, a list of required vaccines; and (4) requiring schools to report to the Department of Health (DOH) the names of the students provisionally admitted, excluded for noncompliance, or exempted from vaccination requirements.

Walgreens commends the Department of Health's efforts to ensure that Hawaii's children receive all recommended vaccines. Walgreens believes that public health is best served by establishing a predictable environment for the uptake of vaccines that are critical to preventing devastating diseases and promoting the overall health of the community. The ACIP-recommended vaccine schedule ensures that vaccines will be administered at the ideal times to maximize their effectiveness in protecting children up through their post-secondary school years.

For these reasons, Walgreens strongly supports moving these proposed rules forward.

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: Oppose Mandatory vaccinations
Date: Thursday, November 01, 2018 6:36:23 AM

Aloha. As a resident of the big Island of Hawaii, I oppose any and all vaccinations being mandatory. The last thing we need is to be injecting heavy metals into ourselves and our children. If parents want to voluntarily have it done to their kids that's fine but for those who don't want it should not be forced to. There's too much evidence linking the toxic heavy metals to neurological damage. Mahalo for your time.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Please no mandatory vaccinations
Date: Thursday, November 01, 2018 7:21:09 AM

Please respect our right to choose.

A test for safety/efficacy of vaccines has never been performed.

Thank you.
~Ivory Kalber

Please excuse typos and brevity. Sent with aloha from my iPhone7.

From: [REDACTED]
To: [REDACTED]
Subject: Our body, our voice
Date: Thursday, November 01, 2018 7:54:27 AM

Aloha,

I am writing on behalf of my Kupuna, Makua and Ohana to let you know that we strongly oppose the proposal of mandatory vaccinations for all keiki and adults in Hawaii. As a native Hawaiian, born and raised on the islands it pains me to say that I have witnessed first hand family and friends who have taken their children to the doctor for a vaccination and suffered extreme side effects and even death following the injection of vaccinations. When you look at the growing number of autistic children in our community, one cant help but wonder "why all of a sudden?" Someone may challenge and say that "if its the vaccinations then why doesn't everyone who gets vaccinated react to the chemicals and poisons the same"? It is so important to understand that we are all born with different genes and a unique microbiome influenced by epigenetics which affects the way our bodies respond to the infectious diseases and pharmaceutical products like vaccines. What happened to island sustainability? Our Native ancestors built an ahupua'a system where the people could take care of themselves and used native plants to heal ailments and rid the body of sickness. I am asking as a Kanaka that you do NOT take away our rights to practice our indigenous Hawaiian Health healing modalities and do NOT move forward with making it mandatory for us to inject a foreign chemical into our bodies. So much have already been taken from the Native people, please DO NOT take away our right to body sovereignty.

Mahalo

Moani

From: [REDACTED]
To: [REDACTED]
Subject: Please do not require mandatory vaccinations for school children
Date: Wednesday, December 26, 2018 3:01:54 PM

Please do not require mandatory vaccinations for school children

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: testimony opposing HAR11-157 [REDACTED]
Date: Thursday, November 01, 2018 9:04:13 AM

To Whom It May Concern.

I am absolutely opposed to HAR11-157. I am not "Anti-Vaccine"; I am "Pro Choice". As an American citizen, I should have the right to choose what foreign substances are put into my body and the bodies of my children. If there is any shadow of a doubt that a substance may cause harm, it is my right to choose whether or not to willfully expose myself to that substance. As all vaccines have known risks associated with them, it is my right to choose which, if any, I am willing to receive.

Thank you for allowing me to submit testimony.

Aloha,

Sheryl Kincaid

From: [REDACTED]
To: [REDACTED]
Subject: School vaccinations and examinations updates testimony
Date: Thursday, November 01, 2018 9:18:30 AM
Attachments: [Dr_deZayas Memo 2 25 2018.pdf](#)

I, Elizabeth Sand, a mother, educator, and national, and domiciles in [REDACTED], testifies to the opposition of mandatory vaccination.

This testimony is for HAR 11-157. My name is Elizabeth Jean Sand and I am a United States citizen. I am a parent, educator and community contributor and I currently reside in [REDACTED].

As a United States citizen I am a protected person as defined by international criminal law in the Tadic judgment of 1999 by the International Criminal Tribunal for the Former Yugoslavia Appeals Chamber, which stated that civilians who are nationals of the occupying State are also protected persons because their allegiance while residing in the occupied State is, in this case, owed to the Hawaiian Kingdom and not the United States. Allegiance to the Hawaiian Kingdom by resident aliens is stated in Section 3, Chapter VI of the Hawaiian Kingdom Penal Code.

I too have come to learn that the Hawaiian Kingdom continues to exist as an independent and sovereign State that has been under an illegal and prolonged occupation by the United States since January 17, 1893. I am also aware that the United Nations Independent Expert Dr. Alfred deZayas sent a memorandum to members of the State of Hawai'i judiciary which stated "international laws (the Hague and Geneva Conventions) require that governance and legal matters within the occupied territory of the Hawaiian Islands must be administered by the application of the laws of the occupied state (in this case, the Hawaiian Kingdom), not the domestic laws of the occupier (the United States)." And according to Amnesty International, war crimes are crimes that violate the laws or customs of war defined by the Hague and Geneva Conventions.

Article 43 of the Hague Regulations and Article 64 of the Fourth Geneva Convention obligates the United States to administer Hawaiian Kingdom law, not United States law. This deliberate failure by the United States to administer Hawaiian Kingdom law has led to grave breaches under Article 147 of the Fourth Geneva Convention and international humanitarian law, which constitutes war crimes committed against me as a protected person. This body illegally enacts United States laws in violation of the Hague and Geneva Conventions and as a victim of war crimes that stem from this unlawful legislation, I demand that this body immediately cease and desist.

My name is Elizabeth Jean Sand and I am a United States citizen. I am a parent, educator, and community contributor and I currently reside in Mountain View. This body illegally enacts

United States laws in violation of the Hague and Geneva Conventions and as a victim of war crimes that stem from this unlawful legislation, I demand that this body immediately cease and desist.

If the Americans in America are learning about the illegal occupation of America in Hawaiian Kingdom, then the Americans in Hawaii should be abiding by international laws of occupation.

[The Illegal Overthrow of the Hawaiian Kingdom Government - NEA Today](#)

The Illegal Overthrow of the Hawaiian Kingdom Government - NEA Today

Status of the Hawaiian Kingdom under International Law In 2001, the Permanent Court of Arbitration's arbitral tribunal, in Larsen v.

[The U.S. Occupation of the Hawaiian Kingdom - NEA Today](#)

The U.S. Occupation of the Hawaiian Kingdom - NEA Today

In his message to the Congress on December 18, 1893, President Grover Cleveland acknowledged that the Hawaiian Kingdom was unlawfully

In case State of Hawaii vs. English, judicial notice has been taken that the Hawaiian Kingdom continues to exist.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Testimony OPPOSING HAR157 rule changes
Date: Thursday, November 01, 2018 10:00:15 AM

November 1, 2018

DOCD, DOH [REDACTED]

(808) 586-8300

Bruce S. Anderson, PhD, Director of Health
Hawaii Department of Health
1250 Punchbowl St.
Honolulu, Hawaii 96813

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

I strongly oppose the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

* I'm requesting that this hearing be held on EVERY island.

My name is Natasha Sky. I am a Hawaii resident, voter, mother, health advocate and member of Hawaii for Informed Consent. I'm writing today with my strong concern on the DOH planned changes on immunization policy.

Currently, 18 states allow philosophical exemptions for those who object to immunizations because of personal, moral or other beliefs. **In Virginia, parents can receive a personal exemption only for the HPV vaccine. If Hawaii mandates HPV for school attendance there should be a philosophical exemption available to opt out of this vaccine for a disease which is non communicable, no long-term safety studies and a higher reported number of incidences of adverse reactions than other vaccines. Please consider in the future to follow policy of these states and support adding a philosophical exemption.

HPV vaccine should not be required for school as it does not have any protection to prevention of an out break or being spread in a social setting.

When it comes to the changes on MEDICAL EXEMPTIONS please follow example of Illinois SB1410-

"A healthcare provider may consider including without limitation the nationally accepted recommendations from federal agencies such as the Advisory Committee on Immunization Practices, the information outlined in the relevant vaccine information statement, and vaccine package inserts, ALONG WITH THE HEALTHCARE PROVIDERS CLINICAL JUDGEMENT, to determine whether any child may be more susceptible to experiencing an adverse vaccine reaction than the general population, and if so, the healthcare provider may exempt the child from an immunization or adopt an individualized immunization schedule." We cannot remove the practitioners ability to use his/her judgement to issue medical exemptions. This infringes on the doctor patient relationship and violates a doctors right to do their job.

Mandating Medical exemptions to be filed with the DOH is a HIPPA violation.

Requiring schools to file exemptions with DOH is a FERPA violation.

The current religious exemption policy is fine as it is, there is no need for a form to be provided by DOH, with extra requirements, infringing on our religious rights. We do NOT need to prove our religious beliefs. It is unconstitutional. IF however, a DOH form is required for religious exemption please include "The religious exception stated need not be directed by the tenets of an established religious organization."

"In May 2017, Del Bigtree & Robert F. Kennedy, Jr. suspected that HHS was not fulfilling its critical vaccine safety obligations as required by Congress in The National Childhood Vaccine Injury Act of 1986 of assuring improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. A lawsuit revealed that HHS had never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety."
<http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

↑↑Our state shouldn't follow ACIP due to lack of safety studies. The general issue of following the ACIP schedule is that there are no studies on the synergistic affect of each vaccine that keeps getting added to the schedule.

"Adding to public concern about vaccines is the fact that immunization is mandated by many state and local school entry requirements. Because of this widespread use, safety problems with vaccines can have a potential impact on large numbers of persons." – CDC

Anti-choice mandates violate civil liberties. Mandated medical procedures degrade modern medicine and destroy the foundations of our health care system. When you give up the power to choose what can be done to your body — in this case what can be injected into you or your child's body — you are no longer a free, autonomous, sovereign individual.

Please have public hearings held on every island concerning these proposed rule changes that will immensely affect our state. Residents need to ask questions and be made aware of such rule changes before they are made.

Sincerely,
Natasha Sky



If there is RISK, there must be choice

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Please OPPOSE HAR 11-157
Date: Thursday, November 01, 2018 11:15:43 AM

Aloha Hawaii Department of Health,

I am writing, as a mother and physician, my deep concern and opposition of HAR 11-157. There are many reasons to oppose this bill. First of all I am deeply concerned about the fact that the current CDC vaccine schedule has never been studied in its entirety for children or adults. In the poor studies that have been done, the control included all the toxic adjuvants and ingredients except the active ingredient. Thus there is no comparison to children who are unvaccinated. Also all vaccine companies hold no legal responsibility since the 1986 vaccine law which shields vaccine manufacturers from liability. Our government pays out for vaccine injured individuals and has paid out about 4 billion dollars. We also fail to give true informed consent on these medical procedures. Rarely do I see patients who have had access or have been offered a look at the vaccine insert. We do not require parents to sign consents for vaccines. This is also unethical.

Another cause for concern is the ingredients in these vaccines which are highly toxic, including:

Formaldehyde/Formalin - Highly toxic systematic poison and carcinogen.

Betapropiolactone - Toxic chemical and carcinogen. May cause death/permanent injury after very short exposure to small quantities. Corrosive chemical.

Hexadecyltrimethylammonium bromide - May cause damage to the liver, cardiovascular system, and central nervous system. May cause reproductive effects and birth defects.

Aluminum hydroxide, aluminum phosphate, and aluminum salts - Neurotoxin. Carries risk for long term brain inflammation/swelling, neurological disorders, autoimmune disease, Alzheimer's, dementia, and autism. It penetrates the brain where it persists indefinitely.

Thimerosal (mercury) - Neurotoxin. Induces cellular damage, reduces oxidation-reduction activity, cellular degeneration, and cell death. Linked to neurological disorders, Alzheimer's, dementia, and autism.

Polysorbate 80 & 20 - Trespasses the Blood-Brain Barrier and carries with it aluminum, thimerosal, and viruses; allowing it to enter the brain.

Glutaraldehyde - Toxic chemical used as a disinfectant for heat sensitive medical equipment.

And these are just a few of the known toxic chemicals. The Supreme court has declared vaccines as "unavoidably unsafe" and yet we continue to subject children to them in order to access public school. It is completely unethical to subject children to vaccines, in the number required already. Increasing the requirement is plain wrong. We know it impairs neurological development and increases the incidence of allergies, asthma and eczema. So while it may seem we are saving money from a public health stand point initially, we are giving children chronic disease.

Please see that there is cause for concern. Please do not pass HAR 11-157.

In Health,

Dr Anne Dericks, ND
Naturopathic Doctor
Midwife
Holistic Pelvic Care™ Specialist



Confidential Communication:

This email message and any attachments are intended only for the addressee. This email and any attachments may be privileged, confidential, and protected from disclosure. If you are not the intended recipient, any dissemination, distribution, or copying is expressly prohibited. If you received this email message in error, please notify the sender immediately by replying to this email message or by telephone

From: [REDACTED]
To: [REDACTED]
Subject: Small world? Or big problem? Against more mandatory vaccines being added to the school schedule.
Date: Thursday, November 01, 2018 11:37:47 AM

I am a native born [REDACTED] girl who recently moved back from [REDACTED].

One strong incentive for my leaving California was the incredibly burdensome and authoritarian rules regarding mandatory vaccinations and school attendance. Many people have fled California because of the mandatory vaccination requirements there.

I am the mother of three children aged 17, 2.5, and 9 months.

My 17 year old was fully vaccinated according to the CDC schedule until aged 12 when he had a severe reaction to the DTAP and Varicella vaccine. Within 4 hours of the shots, he had 2 days of 104 degree fever which was not controllable with fever reducing medications - and vertigo that lasted several days. Luckily for him the reaction did not leave permanent effects/disability, but he will not be receiving another vaccine unless he as an adult decides to do so independently.

My two younger children have not been vaccinated and will only receive a VERY limited number of vaccines if any. This will happen whether or not Hawaii decides to strip my right to choose as a parent.

I have seen FAR too many adverse reactions and read many independent studies that are critical of vaccines and contradictory to the CDC's recommendations to go ahead blindly following their advice to the detriment of my children's health.

Over the last 20 years, I have watched my cousin's husband's health deteriorate after he contracted polio from the vaccine in the early 80's. He received \$1,000,000 from the vaccine court for his injuries - and that does not even begin to cover the quality of life lost due to his disability.

One million dollars seems like a ton of money, but it's nothing compared to the nearly 4 BILLION dollars the vaccine court has already paid out to people who have been permanently maimed or killed by vaccines.

That being said, 4 BILLION dollars in less than the vaccine manufactures make in a year on the schedule currently being administered to our children... and they have ZERO liability. How is this okay? Where is the outrage? Where are the elected officials and public servants acting on the behalf of the people concerned by this?

I know 2 women who have had third trimester losses within 2 weeks of receiving the now recommended DTAP and FLU shot. Two much loved and wanted, viable babies dying before they were born. Coincidence? Maybe. Or maybe it has something to do with these vaccines having ZERO safety studies conducted in regard to pregnant women... except for "passive surveillance". No safety studies, but VAERS reported a 4250% increase in miscarriages within 28 days of receiving the flu shot according to this study: <http://www.cidrap.umn.edu/news-perspective/2017/09/study-signals-association-between-flu-vaccine-miscarriage>

Where is the outrage? Small world, or big problem?

I volunteered as a Sunday school teacher at my church in Los Angeles where more than 50% of all the children had either learning disabilities or SEVERE food allergies... 50%!

This is shocking to me, but apparently it is the new "normal". According to this study, 54% of all insured children suffer from a chronic condition or learning disability:

<https://www.sciencedirect.com/science/article/pii/S1876285910002500>

That seems insane to me, but according to current CDC data 25% of children currently aged 2-8 suffer from a chronic disease:

<https://www.cdc.gov/healthyschools/chronicconditions.htm>

According to this CDC report: 60% of adults in America have a chronic disease, and 40% have two or more:

<https://www.cdc.gov/chronicdisease/resources/infographic/chronic-diseases.htm>

Drug companies have far too much power and too many incentives to continue on with business as usual.

Enough is enough.

The unbiased, un paid for science is there. Vaccines are not safe or effective.

Where there is risk, there must be choice.

Our people are suffering.

Our health situation in this country is in crisis, and it's not due to the threat of Measles, chickenpox, HPV, OR the flu.

Please do the right thing.

Jessica Penner

From: [REDACTED]
To: [REDACTED]
Subject: STRONG OPPOSITION TO HAR-157
Date: Thursday, November 01, 2018 12:39:48 PM

STRONG OPPOSITION TO HAR-157

Aloha,

I am writing to ask that you cancel HAR-157 for the following reasons:

1. It is not right to mandate something that is known to cause harm. If you read any vaccine insert you will see all the harmful ingredients not highlighted by the doctors that administer these vaccines.
2. You are doing much more harm than good with this mandate. There are no studies that prove the safety of the current mandatory vaccine schedule, so as any parent it is natural for us to be wary of injecting these poisons into our children to supposedly protect us from said diseases. By the way, it was recently exposed that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. How can you continue to pass laws that mandate vaccines when this problem exists?
3. HPV is a sexually transmitted disease. Children should not require a vaccine for an STD to attend school. In school, children are attending class and learning -- they are not having sex and spreading this disease. The HPV vaccine happens to be the most controversial vaccine for good reason -- because of the debilitating side effects that have ruined the lives of many across the world. HPV is a very common disease that most people will contract at some point in their lives -- and for many it clears up on their own or with natural, immune-boosting treatment. It rarely turns into cancer and if it does it takes a long time to do so; meanwhile, it can be monitored and treated before it becomes life-threatening.
4. Requiring the flu vaccine for school attendance is also inappropriate. The flu vaccine is contraindicated for people with egg allergies, which is a common allergy. Most people getting the flu shot are not screened for egg allergies, and this can be very dangerous! Moreover, the efficacy rate of the flu vaccine is so low, not to mention studies show that the flu vaccine puts you more at risk for catching other respiratory illnesses. Again, this is yet another vaccine that does more harm than good. There are safe, alternative methods for boosting the immune system to guard against the flu as well as effective treatments for the flu. I myself have never received a single flu shot in my entire life and I've only caught the flu a few times during my childhood and they were not life-threatening or debilitating because my mother believed in natural medicine and so she kept me healthy and treated me with natural medicine. Most people that I know who often catch the flu are people who subscribe to getting the flu shot regularly. If you do your research, most people that die of the flu have received the flu shot, ironically! This is because vaccines break down the immune system; they do not build it. Vaccines

supposedly "induce immunity" by suppressing the immune response to said disease. Is this really "immunization" or just "suppression of disease expression"? What happens when you repeatedly inject viruses into the body and then suppress the body's immune response to them???

The answer is not a good one! In the natural medicine profession we have observed that the disease will exist in the body for a long time in dormancy (latency) and later on when the body is weak for whatever reason the latent disease will manifest as other illnesses.

Vaccination is NOT immunization!

5. Medical Freedom is a basic right. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents. Please help us protect our keiki.

Sincerely,

Mei Li Shikiya

Seconded by Lauren Faye Vierheilig

From: [REDACTED]
To: [REDACTED]
Subject: Written testimony opposing immunizations
Date: Thursday, November 01, 2018 12:58:16 PM

While my family and I have been vaccinated, it has come to my attention that vaccinations are not 100% safe and could be the cause of many illnesses, physical and mental that my family has been through. I do not believe anyone has the right to force anyone to have foreign matter injected or invade a physical body. It should be a choice and leave it at that. Pharmaceutical companies care about every dollar they make from us, NOT about our health and wellness. They are all about profit. Please do not let this pass.

Sincerely, Jayrah Belin

From: [REDACTED]
To: [REDACTED]
Subject: Oppose Mandate of Vaccinations
Date: Thursday, November 01, 2018 2:48:08 PM

Please do not force us and our keiki to take vaccines against our will.

Mahalo!

To: Hawaii State Department of Health
Hearing Date/Time: Thursday, Nov. 1, 2018, 3:00 p.m.
Place: Hawaii Department of Health, Kinau Hale Boardroom, 1st Fl.
Re: Testimony of Planned Parenthood Votes Northwest and Hawaii in support of
Proposed Amendments to H.A.R. Title 11, Chapter 157, Examination and
Immunization

Dear Director Anderson,

Planned Parenthood Votes Northwest and Hawaii (“PPVNH”) writes in support of proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization, which seek to codify the United States Department of Health and Human Services’ Advisory Committee on Immunization Practices’ General Best Practice Guidelines for Immunization.

PPVNH is dedicated to protecting and promoting the sexual and reproductive health of Hawaii’s people and we support the proposed amendments because they will help to prevent HPV and HPV-related cancers. In our health centers, we see firsthand the devastating effects of HPV on our patients.

According to the Center for Disease Control and Prevention, 79 million people in the United States are currently infected with HPV and 14 million new cases are expected each year. HPV is so common that nearly all sexually-active men and women will get at least one type of HPV at some point in their lives. There is no cure for HPV - only treatment for related health problems. Yet, too few adolescents in Hawaii are receiving HPV vaccines.

Adopting the recommendations of the CDC will help to increase the rates of vaccinated individuals and, in turn, reduce the spread of HPV and HPV-related cancers.

While we can’t protect our youth from everything, we can help to protect them from cancer in the future by adopting these regulations now.

Thank you for the opportunity to testify in support of this important effort.

Sincerely,
Laurie Field
Hawaii State Director

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Thursday, November 01, 2018 4:34:38 PM

Dear DOH:

My name is Ryan McMillan; I am a second year student at the [REDACTED]
[REDACTED]. I support the amendments proposed for Title 11, Chapter 157
“Examination and Immunization” as this would help to better the health of our students and
community. Thank you and have a wonderful weekend.

All the best,

Ryan

Ryan McMillan

From: [REDACTED]
To: [REDACTED]
Subject: Public testimony (HAR 11-157)
Date: Thursday, November 01, 2018 10:21:59 PM

I am writing in regard to the proposal (HAR 11-157) to update school vaccination and examination requirements.

I strongly believe that our right to body sovereignty must be respected as the policy on immunization and medical examinations is discussed. I do NOT support mandatory vaccinations and urge the DOH to uphold our constitutional rights to freedom of choice.

For religious and health reasons many cannot vaccinate and should not be left out of consideration is these policies.

Thank you,

Noelle Purvis
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: About mandatory immunization
Date: Thursday, November 01, 2018 5:29:30 PM

This is absolutely absurd and under no circumstance should it be allowed to pass. I can say personally, that no matter what decision you make, we as a family will NOT be participating in these immunizations. If that means we have to take our kids out of school or move, we will. Under no circumstances, whatsoever, will we participate in any mandatory vaccination requirement. It is a violation of our rights as humans and is no better than rape. You are trying to forcibly penetrate us and inject an unwanted substance into our bodies. You do not have our consent, and no means no. If you don't like it, than oh well. We will not be participating, period. All you will successfully be doing is making it more difficult for us to find education, but you will not be succeeding in getting us to agree to any vaccinations.

You may think you are acting in our best interests, and that we just don't know any better. But you are basing your information off of blind trust given to the people who bribe you. They tell you its safe and you believe them. Well we don't, and we should have the right to not have things injected into our bodies.



Virus-free. www.avast.com

Testimony Presented Before the Department of Health
State of Hawai'i
Thursday, November, 1, 2018 at 3:00 pm
Testimony of
May Rose I. Dela Cruz, DrPH

Re: Hawai'i Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization"

Dear Dr. Bruce Anderson,

I am writing to offer my testimony in **strong support of HAR 11-157 proposed rules**. This update of the Administrative Rules would establish immunization and requirements for school, post-secondary school, and child care facility attendance in Hawai'i and to provide for the immunization of indigents and other high-risk individuals.

These immunization updates will bring much needed, up-to-date Advisory Committee on Immunization Practices (ACIP) requirements to our current rules. This update is especially important to require students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels, especially for the HPV vaccine. The HPV vaccine prevents certain cancers and is recommended for both males and females at 11 to 12 years old. The proposed Admin Rules would reinforce this recommendation and increase Hawai'i's HPV vaccine rates.

Recently, there was an outbreak of measles, mumps, and Hepatitis A in our state. These outbreaks stem from unvaccinated individuals who contracted these illnesses and spread them to other unvaccinated individuals. Vaccines can prevent outbreaks and save lives. Newborns and persons with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, these vulnerable groups will stay protected. Vaccinated individuals, such as students, protect those who cannot be immunized.

As a public health researcher, I have researched, educated, seen, and experienced the devastation of vaccine preventable diseases. They are costly and carry a heavy burden to individuals and families. Please support the Admin Rules 11-157 to prevent further hardship to others and to protect our *keiki*.

Mahalo for allowing me to submit testimony.

Affiliations are given for identification purposes only. Opinions presented here are personal views and not the official views of the University of Hawai'i or any other organization or entity.

From: [REDACTED]
To: [REDACTED]
Subject: Administrative Rules (HAR 11-157)
Date: Thursday, November 01, 2018 11:22:19 PM

Aloha,

My name is Candee-Jo Jardine and I am against mandatory vaccinations. That is not to say that I am against any vaccination, but making vaccinations mandatory for any and all is just atrocious. It is a basic human right to govern ones own body. Any other situation where a persons body/self is touched, harmed, or otherwise acted upon without said persons permission is considered a crime. How is this not the same? Yes, some people believe that vaccines are necessary. Others do not. The great thing about America (supposedly) is that we have a choice. That choice should not be taken away. I do not support mandatory vaccinations.

Mahalo,

Candee-Jo Jardine

Sent from my iPhone

Written Testimony Presented to the
Department of Health, State of Hawai'i
For Proposed Amendment of HAR Title 11, Chapter 157
"Examination and Immunization"

Public Hearing, Thursday, November 1, 2018
3:00-4:00 PM
Kinau Hale Boardroom
1250 Punchbowl St.
Honolulu, HI 96813

Submitted by:
Mary Boland, DrPH, RN, FAAN
Dean and Professor
School of Nursing and Dental Hygiene
University of Hawai'i at Mānoa

My name is Mary Boland, and I am the Dean for the University of Hawai'i at Mānoa (UHM) School of Nursing and Dental Hygiene. Thank you for the opportunity to submit testimony to the proposed rules related to H.A.R. Title 11, Chapter 157.

UHM Nursing **supports** the intent of the proposed amendments, updates and clarifications of the immunizations and examination requirements for school, post-secondary school and child-care facility attendance in Hawai'i **with the request to revise section §11-157-5 to include amendments pursuant to Act 45, S.L.H. 2014.**

Vaccinations are an important population health effort which ensures the health and safety of individuals and the community at large by preventing the risk of contaminating infectious disease and protecting against some cancers. The UHM Nursing program teaches safe administration, monitoring, care coordination and patient education to nurses and advance practice nursing population, alike. Both nurses, who may administer vaccines, and nurse practitioners, who may prescribe and administer vaccines, are vital to ensuring that the people of Hawai'i receive timely vaccinations that are appropriate for their age, health, and other factors. In addition, UHM Nursing engages in the Hawai'i Keiki: Healthy and Ready to Learn program with the Department of Education. This program establishes certified school nurses in the DOE system and collaborates with key partners, including the Department of Health, to ensure proper infectious disease prevention and reporting. Providing additional guidance and updating the required vaccinations for school aged children to reflect national best practices have the potential to improve the health and wellbeing of school aged children now, with lasting impacts on their health in the future.

UHM Nursing respectfully requests that the proposed amendments include statute change achieved in Act 45, S.L.H 2014 which found that various sections of the Hawai'i Revised Statutes omit advanced practice registered nurses (APRNs) from the definitions or designations of health care entities who may provide health care, prescribe drugs, or sign forms (Standing Committee Report 1624-14). In Act 45, S.L.H. 2014, §325-34 Exemptions and §302A-1156

Exemptions were amended to add APRNs to the list of qualified providers who may certify exemptions for vaccinations.

In both sections listed above, the recognized providers are licensed physicians, physician assistants, or advanced practice registered nurses. This description matches the term “practitioner” in the Hawai’i Administrative Rules Title 11, Chapter 157 Section 2 which reads, (with proposed amendments):

"Practitioner" means a physician, advanced practice registered nurse, or physician assistant licensed to practice in any of the states or territories of the United States. A physician, advanced practice registered nurse, or physician assistant whose license is on inactive status or who is not actively practicing shall not be deemed to be a practitioner for the purposes of this chapter."

Further, APRNs in Hawai’i have grown 104% from 2005 to 2017, with over half of licensed APRNs in this state practicing in a primary care specialty. While the primary care provider shortage remains a pressing reality, APRNs provide critical services in ensuring high quality access to primary care services for people of all ages and in all geographic locations, including the most rural and remote areas in this state (Hawai’i State Center for Nursing, 2017). Further, APRNs are shown to provide care for a higher proportion of vulnerable patients, including publicly insured, uninsured, women, and people residing in rural areas than other care providers (Buerhaus, 2018). Ensuring that the administrative rules reflect current state law enables APRNs to deliver care for the patients and respond to the state’s health needs.

Therefore, the UHM Nursing respectfully requests that section §11-157-5 Exemptions (a) is revised as follows, to recognize the legislative amendments achieved in Act 45, S.L.H. 2014 relative to HRS §§302A-1156 and 325- 34:

§11-157-5 Exemptions. (a) Medical exemptions from the requirements for specific immunizing agents shall be granted upon certification by a **practitioner [physician]** ~~on the physician's professional stationery~~ in a form or format specified by the department, that an immunization is medically contraindicated due to a stated cause, for a specific period of time~~[-],~~ in conformance with recognized standard medical practices. The ~~original certificate~~ form shall be provided to the exempt person or parent or guardian. ~~[A copy]~~ Copies of the ~~certificate~~ form shall be maintained in the student's school health record~~[-],~~ in the post-secondary school student's record, or in the child care facility child's record. Issuing practitioners [physicians] shall forward a copy of the form to the department. Reports of such ~~certificates~~ forms in a format specified by the department shall also be submitted to the department by each school~~[-],~~ postsecondary school, and child care facility.

Thank you for the opportunity to submit testimony for the proposed amendments of HAR Title 11, Chapter 157. Your favorable consideration of the requested revisions is greatly appreciated.

References:

Buerhaus, P. I. (2018). Nurse practitioners: A solution to America’s primary care crisis. Retrieved October 25, 2018, from <http://www.aei.org/publication/nurse-practitioners-a-solution-to-americas-primary-care-crisis/>

Hawai'i State House of Representatives Committee on Consumer Protection and Commerce. (2014). Standing Committee Report 1624-14 relating to S.B. No. 2492, S.D.1. Retrieved October 24, 2018 from: https://www.capitol.hawaii.gov/session2014/CommReports/SB2492_SD1_HSCR1624-14_.htm

Hawai'i Revised Statutes, 325-34. Exemptions. Retrieved October 24, 2018 from: https://www.capitol.hawaii.gov/hrscurrent/Vol06_Ch0321-0344/HRS0325/HRS_0325-0034.htm

Hawai'i Revised Statutes, 325-34. Exemptions. Retrieved October 24, 2018 from: https://www.capitol.hawaii.gov/hrscurrent/Vol06_Ch0321-0344/HRS0325/HRS_0325-0034.htm

Hawai'i State Center for Nursing. (2017). *Hawai'i's Nursing Workforce 2017*. Retrieved from <http://www.hawaiicenterfornursing.org/wp-content/uploads/2017/11/2017-Hawaii-State-Nursing-Workforce-Supply-Report-Final-2-2.pdf>



Department of Health, State of Hawaii
For Proposed Amendment of HAR Title 11, Chapter 157
“Examination and Immunization”

Public Hearing, Thursday, Nov 1, 2018
Kinau Hale Boardroom
1250 Punchbowl St.
Honolulu, HI 96813

Written Testimony Submitted by:
Carolyn Ma, Pharm D, BCOP
DEAN
UH Hilo - Daniel K. Inouye College of Pharmacy (DKICP)

My name is Carolyn Ma, and I am the Dean for the UH Hilo Daniel K. Inouye College of Pharmacy (DKICP). The college fully supports the proposed amendments, updates and clarifications of the immunizations and examination requirements for school, post-secondary school and child- care facility attendance in Hawaii.

Relative to these amendments and the offer to assist in immunization advocacy, patient education and administration, the DKICP and all other 144 U.S. nationally accredited (ACPE) schools of pharmacy train pharmacy students to administer CDC recommended vaccinations. Most schools utilize the certified American Pharmacists Association (APHA) course. The DKICP provides training in immunization administration in the first professional year curriculum. Over the next three years of the Doctor of Pharmacy

curriculum, student pharmacists are expected to apply these skills in their experiential rotation courses as well as in numerous community health screening and immunization events. With three years of practice, graduated student pharmacists become very skilled with immunization patient education, administration and monitoring of side effects.

In the last 20 years, pharmacists have become the largest body of health professionals who are able to make a significant impact on vaccination uptake. Pharmacists are highly trained in the areas pertinent for immunizations and the diseases associated with vaccines. Didactic and experiential courses teach information in infectious diseases, community health, self-care, pediatrics and geriatrics. Particular to the Human Papilloma Virus (HPV), coursework includes oncology, women's and men's health, contraception and reproductive pharmacology. Education throughout the four-year professional curriculum focuses therapeutics of medication assessment and therapeutic recommendations via related laboratory tests and subjective/objective findings related to disease and drug therapy. A similar curriculum is included in all U.S. accredited (ACPE) colleges of pharmacy.

The DKICP has also provided training to practicing pharmacists through their training program via the Hawai'i Pharmacists Association. Please note that all immunizing pharmacists and student pharmacists must be certified in Basic Life Support (BLS). BLS certification allows for cardiopulmonary resuscitation (CPR) of adults, children and

infants and for other first responder interventions. In addition, immediate access to epinephrine must be available at any vaccination site.

Per Chapter 461-11.4, HRS, pharmacists may administer a vaccine to persons between 11-17 years of age pursuant to a valid prescription. After vaccination, the pharmacist will immediately provide information to the patient regarding name of vaccine administered, date and location of administration. Within 72 hours, the pharmacists shall provide to the medical home and within five business days, to the DOH immunization registry the same information, as well as the details of the administered vaccine, method and site of administration. Pharmacists who administer vaccines to persons in this particular age range shall complete a training program approved by the ACPE.¹

Adverse reaction reporting of vaccinations should be reported to the Vaccine Adverse Events Reporting System (VAERS). However, the Center for Disease Control (CDC) and the Federal Drug Administration (FDA) state several limitations to the VAERS system in that since the system captures only self-reporting, there may be reporting bias, inconsistent data quality and completeness, and that reports of an adverse event does not necessarily attribute causality to the vaccine. The data-base does not have a non-vaccinated portion for comparison.²

Pertinent to the student population at the University of Hawaii is the concern of the declining rate of the HPV vaccine. The HPV virus is associated with several different cancers (cervical, vaginal, vulvar, anal, esophageal) in both males and females. The HPV vaccine is a cancer preventative intervention. In a recent survey of incoming freshmen performed at the UH Manoa and UH Hilo campuses, only 22% and 5%, respectively, of students have been fully vaccinated.³ Students who had not received at least one of three shot series were 69% (UHM) and 78% (UHH), respectively.³ Although with recent efforts, the vaccination rates have improved, there exists a need for catch-up vaccination efforts as well as coverage for ages beyond the recommended 26 year old group. The FDA recently approved (October 2018) the extension of the vaccine administration to men and women in the 27-45 year old age groups.⁴

In summary, on behalf of the DKICP, I strongly support the amendments to HAR Title 11, Chapter 157 “Examination and Immunization” and believe these changes will improve the health and wellness of our community.

References:

¹ Hawaii Revised Statutes Chapter 461, Pharmacists and Pharmacy 461-11.4

² <https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index.html> , Accessed Oct. 6, 2018

³ Corpuz, SA. Assessing Human Papillomavirus (HPV) & Human Papillomavirus Vaccination among University of Hawai’i at Manoa and University of Hawai’i at Hilo Freshmen. Office of Public Studies, University of Hawai’i at Manoa

⁴ <https://www.nytimes.com/2018/10/05/health/hpv-virus-vaccine-cancer.html>, Accessed October 6, 2018

From: [REDACTED]
To: [REDACTED]
Subject: Forced immunization
Date: Thursday, November 01, 2018 6:11:45 AM

I am not for having medical procedures forced on people. Its slavery, if you do not have the choice is it not? I thought we were beyond that now?

Which big pharma is pushing this on the poor people this time?

From: [REDACTED]
To: [REDACTED]
Subject: Fwd: Testimony in Support of HAR 11-157 Proposed Rules
Date: Thursday, November 01, 2018 6:33:28 PM

Aloha,

As a concerned family member with many nieces and nephews as well as a public health professional working in cancer prevention, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

Furthermore, I believe that vaccine access is closely tied to health equity. Often, the poor health outcomes from people who do not have access to vaccine (e.g. liver and cervical cancer) affect marginalized communities.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Thaddeus Pham
[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Thursday, November 01, 2018 5:02:06 PM

I strongly oppose HAR 11-157. Vaccines should NOT be forced upon anyone. The United States of America prides itself on being a “free” country.
We should be “free” to make our own decisions about vaccines, and the government should not decide for us.

Vinessa Carrillo

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Thursday, November 01, 2018 5:19:59 PM

Thank you all for your consideration into this matter. My name is Yana Dashevsky and I am opposed to HAR 11-157.

I am sure that you have received a lot of personal and written testimony today as to a request for more informed consent and studies to be done in a position to the vaccination schedule for our children. Our kids lives on the line.

After all of the information that you have received today I ask you to consider one item:

EMPATHY.

Empathy to me means putting yourself in the "others" shoes. Take for a moment this time to imagine yourself as a baby as a child who is not able to make a decision for themselves and who's parents responsibility it is to care for their welfare. Now, instead of being sympathetic about the situation consider that this child is yourself. Imagine your own face when you were 2,3,4,5 years old.

Now, imagine your face as you're walking into the doctors office and imagine how you would feel about yourself getting an injection full of positive and negative's at the same time. The research is there, do it. I do not have to continue to prove this point that the effects of antigens in vaccines have not been studied enough. Take this moment to close your eyes and ask yourself what am I fighting for if this [IS ME].

Do I personally want my health and safety to come first and foremost in this equation? Do I personally think that enough research has been done to know the repercussions of vaccinations schedules that include 72 vs 3 vaccines in our modern-day system?

Would I personally want to receive 72 mandated vaccine schedule shots by the time I was nine years old and be forced to except his vaccinations in schools rather than my doctors office?

Personally, I wouldn't argue with anyone of you guys if it was only three vaccines on the table. However when you decide whether it is my choice or not to vaccinate my kids for things like HPV I start questioning you. How would you treat your own self?

Given these mandates if by 2020 HPV is a required vaccines for children in our school system and exemptions are only based on personal out reach from the parents rather than leaving it to the hands of doctors and the parents relationship with their doctors and their children's health, I will know longer live in Hawaii. This is how serious I am about my children and their health. I hope you can just be as serious as I am I imagining if this is happening to you.

Empathy.

I oppose HER space 11Dash 157.

If it was you would you promote it knowing everything you know after today's testimonies?

Thank you again for taking the time to read this letter.

To health and prosperity-

Sincerely,
Yana Dashevsky.

From: [REDACTED]
To: [REDACTED]
Subject: Strongly Support HAR 11-157
Date: Thursday, November 01, 2018 10:16:09 AM

Hi, my name is Hannah Smith and I live in [REDACTED]. I support the rules amendment to include new vaccine requirements. This will allow our keiki to live healthier lives and is supported by medical science. We need to be increasingly aware of the dangers that preventable illnesses cause and vaccines are one way to do it.

Thank you for hearing me,

Hannah Smith
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony - Mandatory Vaccination
Date: Thursday, November 01, 2018 5:58:51 PM

Aloha,

I am writing on behalf of the upcoming hearing in regards to proposing mandatory vaccinations. I have experienced first hand the negative side effects of my daughter receiving the MMR vaccine. She had been receiving her vaccines on the normal schedule and at 12 months when she was due for the MMR, she had a severe reaction that caused her to be hospitalized for awhile and she completely changed from that day on. While in the hospital you could completely see the light in eyes gone, like no one was there. She eventually got better but since has not received a vaccination. I had my son a year later and he has not had not 1 vaccination due to the experience with my daughter, and he is the most healthy child I know. He doesn't get as many colds or flu as she does, he's always been in the top percentile for his age in weight and height. He's hit so many milestones before the expected timeline, he's very bright; even his teachers are amazed at his knowledge and potential. We are born with an immune system for a reason, our bodies are made to fight off illnesses; injecting our children with these diseases is just uncalled for and invasive when it's natural for us as humans to fight off. I am 100 percent against mandatory vaccinations, places where it's become mandatory have not seen a change in the rate of children being diagnosed with illnesses, it's actually the opposite. It is against our rights as Americans and as parents to chose what's best for ourselves and our children. Please hear our concerns and rule wisely.

Mahalo,

Erin Edwards

From:

To:

Subject:

Date:

██████████
██████████
Testimony for HAR 11-157

Thursday, November 01, 2018 6:46:22 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



To: Hawaii State Department of Health
Hearing Date/Time: Thursday, Nov. 1, 2018, 3:00 p.m.
Place: Hawaii Department of Health, Kinau Hale Boardroom, 1st Fl.
Re: Testimony of Hawaii Children's Action Network in support of
Proposed Amendments to H.A.R. Title 11, Chapter 157, Examination
and Immunization

Dear Director Anderson,

Hawaii Children's Action Network writes in strong support of proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization, which will bring Hawaii's rules into compliance with United States Department of Health and Human Services' Advisory Committee on Immunization Practices' General Best Practice Guidelines for Immunization.

HCAN is a Hawaii based non-profit committed to building a unified voice advocating for Hawaii's children by improving their safety, health, and education. Vaccines play an important role in community health. While some individuals cannot be vaccinated—newborns and those undergoing chemotherapy—if approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Codifying the CDC's recommendations will prevent the spread of preventable diseases and infections, including HPV.

Thank you for the opportunity to testify,

Mandy Fernandes
Policy Director
Hawaii Children's Action Network

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Thursday, November 01, 2018 10:11:37 AM

To Whom it may concern,

I would like to write on behalf of the bill HAR 11-157, requiring mandatory vaccines in order for children and adults to attend school.

I believe that every human should have the right to choose what medical procedures are done to us, what medications we take, and what vaccines are injected into our bodies.

I am not against vaccines. I believe in the idea of them, however they have a long way to go before they should ever be considered SAFE FOR ALL. The government should have no say over my body. I am vaccine injured (HPV), and if this vaccine were mandated, I wouldn't have been able to recover, instead I would've had to follow up with 2 additional vaccines in order to attend school. Vaccine manufacturers don't take responsibility for vaccine injuries, will Hawaii's government?

I understand vaccines are a hot topic.

There are usually two very extreme sides to the topic of vaccines. There are people like me, who have first hand seen how vaccines can damage some people. I personally know of over 6 vaccine injured children. Children perfectly fine and developmentally on target, and the next day following their vaccines, are permanently changed, some who suffer severe deficits. I feel until vaccines can be truly proven to be safe for ALL people (which needs to reflect so in the vaccine manufacturers insert to each vaccine) it should in no way be forced upon any persons. You can currently read the dangers of vaccines in the vaccine inserts and on the CDC website.

When a doctor offers you suggestions for medications to take, they inform you a few possible side effects, and then you have the option to read the medication insert for all possible side effects. We then have the choice whether or not we want to take the medication. Imagine if your doctor told you there's a chance of paralysis, infertility, cognitive delays, etc. and then told you that you have no choice in the matter and must take the risk and take the medication or give it to your child. It would be wrong. Just as it's wrong to force vaccinations.

I fully believe in bodily autonomy and don't feel like any government should have a say over what goes into my body.

I hope you'll consider this viewpoint and vote against bill HAR 11-15.

Mahalo for taking the time to read my letter.

Aloha,
Brittany Abella

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Vaccinations
Date: Thursday, November 01, 2018 8:16:41 PM

To whom it may concern-

Is it true that the laws are changing regarding forced vaccinations of children? I hope this isn't so and would like information on this and any public hearings that will be upcoming. I myself was not fully vaccinated until I was a teenager. I never got any illness and am proud that my parents did not subject me to all [the vaccines](#) that were recommended. I am a paramedic and have researched vaccinations recently due to being pregnant. My five nieces and one nephew are not vaccinated and they are in ages 6 mos - 8 years. I have never seen them be ill and we are all proud of providing immunity for our children the most natural way that we can.

Abigail Calo
[REDACTED]

Department of Health, State of Hawai'i
For Proposed Amendment of HAR Title 11, Chapter 157

“Examination and Immunization”
Public Hearing, Thursday, Nov 1, 2018
3:00-4:00 PM
Kina'u Hale Boardroom
1250 Punchbowl St.
Honolulu, Hawai'i 96813

Written Testimony Submitted by:
Laura Reichhardt, MS, APRN, NP-C
Director, Hawai'i State Center for Nursing

My name is Laura Reichhardt and I am the Director of the Hawai'i State Center for Nursing (Center). Thank you for the opportunity to submit testimony to the proposed rules related to H.A.R. Title 11, Chapter 157.

The Center recognizes the considerable work to review the existing rules and develop recommendations to improve the clarity of text and recommend additional vaccination requirements for childcare, school, and post-secondary school entry/ attendance. In reviewing the sections receiving an update to requirements for school and post-secondary school attendance, the **Center respectfully requests the Department of Health to consider including revisions achieved related to immunizations pursuant to Act 45, S.L.H. 2014.**

This measure found that various sections of the Hawai'i Revised Statutes omit advanced practice registered nurses (APRNs) from the definitions or designations of health care entities who may provide health care, prescribe drugs, or sign forms (Standing Committee Report 1624-14). In Act 45, S.L.H. 2014, §325-34 Exemptions and §302A-1156 Exemptions were amended to add APRNs to the list of qualified providers who may certify exemptions for vaccinations.

In both sections listed above, the recognized providers are licensed physicians, physician assistants, or advanced practice registered nurses. This description matches the term “practitioner” in the Hawai'i Administrative Rules Title 11, Chapter 157 Section 2 which reads, (with proposed amendments):

““Practitioner” means a physician, advanced practice registered nurse, or physician assistant licensed to practice in any of the states or territories of the United States. A physician, advanced practice registered nurse, or physician assistant whose license is on inactive status or who is not actively practicing shall not be deemed to be a practitioner for the purposes of this chapter.”

In Hawai'i, APRNs have more than doubled, with 104% growth from 2005 to 2017. Over half of licensed APRNs in this state practice in a primary care specialty, providing critical primary care services in the face of our current primary care provider shortage. These APRNs provide critical services in ensuring high quality access to primary care services for people of all ages

and in all geographic locations, including the most rural and remote areas in this state (Hawai'i State Center for Nursing, 2017). Further, APRNs are highly likely to provide care for the population these administrative rules affect. Research shows that APRNs provide care for a higher proportion of vulnerable patients, including publicly insured, uninsured, women, and people residing in rural areas than other care providers (Buerhaus, 2018). Ensuring that the administrative rules reflect current state law enable APRNs to deliver care for the patients and respond to the state's health needs.

With this rationale, the Center respectfully requests that section §11-157-5 Exemptions (a) is revised as follows, to recognize the legislative amendments achieved in Act 45, S.L.H. 2014 relative to HRS §§302A-1156 and 325- 34:

§11-157-5 Exemptions. (a) Medical exemptions from the requirements for specific immunizing agents shall be granted upon certification by a **practitioner [physician]** ~~[on the physician's professional stationery]~~ in a form or format specified by the department, that an immunization is medically contraindicated due to a stated cause, for a specific period of time~~[-]~~, in conformance with recognized standard medical practices. The ~~[original certificate]~~ form shall be provided to the exempt person or parent or guardian. ~~[A copy]~~ Copies of the ~~[certificate]~~ form shall be maintained in the student's school health record~~[-]~~, in the post-secondary school student's record, or in the child care facility child's record. Issuing practitioners [physicians] shall forward a copy of the form to the department. Reports of such ~~[certificates]~~ forms in a format specified by the department shall also be submitted to the department by each school~~[-]~~, postsecondary school, and child care facility.

Thank you for the opportunity to submit testimony for the proposed amendments of HAR Title 11, Chapter 157. Your favorable consideration of the requested revisions is appreciated.

References:

- Buerhaus, P. I. (2018). Nurse practitioners: A solution to America's primary care crisis. Retrieved October 25, 2018, from <http://www.aei.org/publication/nurse-practitioners-a-solution-to-americas-primary-care-crisis/>
- Hawai'i State House of Representatives Committee on Consumer Protection and Commerce. (2014). Standing Committee Report 1624-14 relating to S.B. No. 2492, S.D.1. Retrieved October 24, 2018 from: [https://www.capitol.hawaii.gov/session2014/CommReports/SB2492_SD1_HSCR1624-14 .htm](https://www.capitol.hawaii.gov/session2014/CommReports/SB2492_SD1_HSCR1624-14.htm)
- Hawai'i Revised Statutes, 325-34. Exemptions. Retrieved October 24, 2018 from: https://www.capitol.hawaii.gov/hrscurrent/Vol06_Ch0321-0344/HRS0325/HRS_0325-0034.htm
- Hawai'i Revised Statutes, 325-34. Exemptions. Retrieved October 24, 2018 from: https://www.capitol.hawaii.gov/hrscurrent/Vol06_Ch0321-0344/HRS0325/HRS_0325-0034.htm
- Hawai'i State Center for Nursing. (2017). *Hawai'i's Nursing Workforce 2017*. Retrieved from <http://www.hawaii-center-for-nursing.org/wp-content/uploads/2017/11/2017-Hawaii-State-Nursing-Workforce-Supply-Report-Final-2-2.pdf>

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Written testimony against HAR-157
Date: Thursday, November 01, 2018 11:46:39 AM

STRONG OPPOSITION TO HAR-157

Aloha,

I am writing to ask that you cancel HAR-157 for the following reasons:

1. It is not right to mandate something that is known to cause harm. If you read any vaccine insert you will see all the harmful ingredients not highlighted by the doctors that administer these vaccines.
2. You are doing much more harm than good with this mandate. There are no studies that prove the safety of the current mandatory vaccine schedule, so as any parent it is natural for us to be wary of injecting these poisons into our children to supposedly protect us from said diseases. By the way, it was recently exposed that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. How can you continue to pass laws that mandate vaccines when this problem exists?
3. HPV is a sexually transmitted disease. Children should not require a vaccine for an STD to attend school. In school, children are attending class and learning -- they are not having sex and spreading this disease. The HPV vaccine happens to be the most controversial vaccine for good reason -- because of the debilitating side effects that have ruined the lives of many across the world. HPV is a very common disease that most people will contract at some point in their lives -- and for many it clears up on their own or with natural, immune-boosting treatment. It rarely turns into cancer and if it does it takes a long time to do so; meanwhile, it can be monitored and treated before it becomes life-threatening.
4. Requiring the flu vaccine for school attendance is also inappropriate. The flu vaccine is contraindicated for people with egg allergies, which is a common allergy. Most people getting the flu shot are not screened for egg allergies, and this can be very dangerous! Moreover, the efficacy rate of the flu vaccine is so low, not to mention studies show that the flu vaccine puts you more at risk for catching other respiratory illnesses. Again, this is yet another vaccine that does more harm than good. There are safe, alternative methods for boosting the immune system to guard against the flu as well as effective treatments for the flu. I myself have never received a single flu shot in my entire life and I've only caught the flu a few times during my childhood and they were not life-threatening or debilitating because my mother believed in natural medicine and so she kept me healthy and treated me with natural medicine. Most people that I know who often catch the flu are people who subscribe to getting the flu shot regularly. If you do your research, most people that die of the flu have received the flu shot, ironically! This is because

vaccines break down the immune system; they do not build it. Vaccines supposedly "induce immunity" by suppressing the immune response to said disease. Is this really "immunization" or just "suppression of disease expression"? What happens when you repeatedly inject viruses into the body and then suppress the body's immune response to them???

The answer is not a good one! In the natural medicine profession we have observed that the disease will exist in the body for a long time in dormancy (latency) and later on when the body is weak for whatever reason the latent disease will manifest as other illnesses.

Vaccination is NOT immunization!

5. Medical Freedom is a basic right. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents. Please help us protect our keiki.

Sincerely,

Mei Li Shikiya



UNIVERSITY
of HAWAII®
SYSTEM

Donald O. Straney, Ph.D.
Vice President for Academic Planning and Policy

Testimony Presented Before the

State of Hawai'i Department of Health Disease Outbreak Control Division (DOCD)
November 1, 2018 at 2:00 p.m.

By Donald Straney
Vice President for Academic Planning and Policy
University of Hawai'i System

HEARING DOCKET NO. R-157-18-07

Public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization"

The University of Hawai'i (UH) appreciates the opportunity to comment on the proposed revisions to Hawai'i Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunizations." The Department of Health (DOH) is an important partner with the UH on many fronts, and UH acknowledges its contribution to public health for our students, faculty, staff and the community. In the interest of public health and promoting educational and human capital in the state, UH offers revisions to the proposed HAR.

First, §11-157-5 (d) provides an exemption from requirements of this chapter for exclusively online learning. UH supports the intent but requests revision of the exemption to clarify the language to exempt students who participate in online courses or programs exclusively or the programs or courses which are exclusively online. UH offers both in person and online or distance learning classes (1,428 sections in Fall 2018), and UH is preparing to increase its offering of exclusively online programs. Therefore, the exemption should apply to the student, program or course, rather than the institution.

Recommended revisions to new sub-section on exemptions:

§11-157-5 Exemptions (d) After-school programs, family child care homes, parent cooperatives, play groups, respite programs, group child care homes, and drop-in child care centers are excluded from the requirements of this chapter. All schools and ~~post-secondary schools~~ that conduct classes and activities exclusively on-line or electronically via remote learning are excluded from the requirements of this chapter. All post-secondary students who attend classes exclusively on-line or electronically via remote learning are excluded from requirements of this chapter.

Second, the proposed HAR §11-157-6.2 allows a postsecondary student to attend on provisional basis for 45 days upon submitting written evidence that the student is in process of receiving required immunizations. UH recommends that the provisional attendance period be

Telephone: [REDACTED]
Fax: [REDACTED]

extended to the last day of the first academic term of attendance. This period is typically 16 weeks (Fall and Spring terms). The current 45 day provisional attendance period (which is continued in the proposed HAR) is implemented by UH campuses as a prohibition of attendance because students who fail to comply after 45 days would exclude a student in the middle of a term leaving students without financial recourse for tuition and fees that have been paid for the term and unable to complete the term academically due to the immunization-related exclusion.

UH offers that the public health risks are limited as commuting students' exposure to other students is similar to other daily interactions such as on an airplane, in a movie theater, or at employment. In fact, many students take both in person and online classes; this Fall, there are 28,000 student registrations for online classes, which reduces students' contact with one another.

Recommended revisions to proposed sub-section on exemptions:

§11-157-6.2. Provisional Attendance (b) The provisional attendance period shall be no longer than three calendar months after the date of provisional attendance to a school or child care facility and ~~no longer than forty-five calendar days after~~ not to extend beyond the last day of the academic term following the date of provisional attendance to a post-secondary school.

Third, the proposed HAR §11-157-6.2 allows a post-secondary student to attend on provisional basis upon submitting written evidence that the student is in process of receiving required immunizations. UH requests that provisional attendance also be granted to all students of a post-secondary school when the post-secondary school has a plan to offer students immunizations within the provisional attendance period. UH believes that the public health purpose can be served when it can provide attending students with health services rather than exclude prospective students who have not accessed health services.

Recommended revisions to proposed sub-section on exemptions:

§11-157-6.2. Provisional Attendance (a) A student or child who does not have evidence of all of the required immunizations may:

- (1) Attend school, ~~post-secondary school~~ or a child care facility provisionally upon submitting written evidence from a practitioner or the department stating that the student or child is in the process of receiving required immunizations; or
- (2) Attend post-secondary school provisionally upon submitting written evidence from a practitioner or the department stating that the student is in the process of receiving required immunizations or if the post-secondary school has submitted a written plan that will ensure the required immunization of students within the provisional attendance period.

Thank you for your consideration.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Friday, November 02, 2018 8:09:55 AM

Aloha,

I am writing to you to let you know that as a parent of three children who attend public school In Hawai'i, I strongly oppose HAR 11-157. Being forced to vaccinate my children is against my rights and freedom. The HPV vaccine is the worst of them all and I refuse to be forced to give my children this or any of the vaccines.

My 10 year old was vaccinated for mumps and still ended up getting them last summer when the outbreak occurred, and many people I know that got them were also vaccinated. That just goes to show you that they don't always work. The reasons behind this new bill doesn't make sense. Parents deserve the right to choose what is put into our children's bodies not any government or state office.

I am asking you to consider my testimony when making your decision. Please oppose this.

Mahalo Nui,

Malia Vasallo
[REDACTED]

[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157
Date: Friday, November 02, 2018 2:43:29 PM

Hi my name is Cherry Wigglesworth,

I'm writing this email in opposition to HAR 11-157.

I strongly feel that my rights as a parent are being threatened. Where there is a risk, there MUST be a choice for us parents.

Let parents decide which vaccines are important for our kids! It is our right as parents, please hear us out and let the parents have the choice for this option.

Thank you so much.

From: [REDACTED]
To: [REDACTED]
Subject: Immunization Ban
Date: Friday, November 02, 2018 9:11:47 AM

Aloha All,

I am writing this email because I am against Mandatory Vaccines . It has been brought to my immediate attention that a law is trying to be passed making it mandatory for all children going to public school to be vaccinated. We have a right as Americans to choose and a right to choose against Vaccinations or not. We shall not be forced into , this it seems very wrong.

Do not pass this bill.

I am against this 1000%

Mahalo

Cassie Sargent
[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: immunization options
Date: Friday, November 02, 2018 9:26:49 AM

i am writing on behalf of my children that attend public schools of hawaii. we do not immunize our children and would like to keep that option a legal right.

please keep hawaii's laws democratic in protecting the rights of your beloved people.

with the present way of the world, this is all the more important for the safety in freedom.

let hawaii'i nei become a leader in holding steadfast to these constitutional protection of citizens.

mahalo nui from our hearts to yours..

alison chuang

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: immunizations in Hawaii
Date: Friday, November 02, 2018 6:59:51 PM

Aloha to whom it may concern,

I want to state that I am very opposed to MANDATORY vaccinations for the residents of the state of Hawaii. We, as Americans, should have the right to choose whether or not we want to vaccinate our children or ourselves. At this time, vaccinations include many toxic ingredients that can be harmful in many ways to human beings. I ask you to take a moment to read the leaflet that comes with the vaccinations and see what all is included in these vaccinations. Should they be cleaned up and these toxic ingredients be removed and also if the law is changed that we can sue the corporations that make and distribute these vaccinations if they damage us or our children, then I think we can then revisit this suggestion. Just in case it is not clear, I **STRONGLY OPPOSE** mandatory vaccinations!!!

Thank you,
Acacia Morrison
[REDACTED] Resident

From: [REDACTED]
To: [REDACTED]
Subject: Vaccine Testimony
Date: Friday, November 02, 2018 10:15:01 AM

I am writing to state how I feel on the situation and I feel the people should have the right to choose if they want to vaccinate their child or not. My children are vaccinated & haven't had any bad reactions but some children do get bad reactions or become disabled or have even died. So I believe people/parents should have a right to choose for themselves and their family.

Mahalo for hearing my Testimony

From: [REDACTED]
To: [REDACTED]
Subject: Testimony of vaccines
Date: Friday, November 02, 2018 12:14:13 PM

To whom it may concern:

My health suffered enormously after having one flu vaccine in 2013. It was the first and only time I consented to have this poison in my body after encouragement from my doctor to do so, since we were going on a trip that included 'third world' countries.

After taking the shot, I felt exhausted and then feverish within 48 hours. After three days, severe nausea and vomiting followed, and I couldn't even keep water down. The vomiting was relentless; I became so dehydrated that my husband called an ambulance since I couldn't even move without gagging and spitting. The team immediately put an IV in to get fluid into me because of my jaundiced face and cracked skin. I went to the Er and was treated with anti-nausea medicine with continued IV for four hours. I never want to repeat this scenario and would not wish that experience on anyone.

By making vaccines mandatory, children and babies will be subjected to this type of possibly fatal reaction. There are over 50 viral strains in each vaccine administered to kids. If even one of them affects the CNS adversely, the child could have damaging seizures, which could result in autism, muscular dystrophy, or other cerebral-related lifelong affliction. Please don't force anyone to put these toxins in their system. It doesn't end well for those around them either, who can experience the virus shedding and become infected upon contact. This puts everyone at risk.

Thank you for reading my testimony and for taking it into consideration when voting. It should be a no-brainer to not poison our kids with live viruses at such a high magnitude.

Aloha Ke Akua,
L. George

[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [REDACTED]
Subject: Proposed Changes to HAR 11-157
Date: Friday, November 02, 2018 1:06:12 PM

Aloha,

For the health of our communities, I am writing to strongly support the proposed changes to HAR 11-157.

Mahalo,
John Ishoda

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Re: HAR 11-157 - strongly oppose
Date: Friday, November 02, 2018 1:43:35 PM

Aloha

My name is Jennifer Carman
and I'm writing on strong opposition to
HAR 11 - 157.

I feel that my rights as a parent are being
threatened.

I'm sending this on behalf of myself not a group
but my opinion represents the thousands
of others who are not even aware of their
rights or the truth about vaccines.

Human beings are created in balance
To fight off disease. Our immune systems
Get stronger by doing this. Vaccines contain
Dangerous and lethal toxins and this is a fact,
Not an opinion.

Here's one of many official, professional,
Organizations and their website link -
<https://www.nvic.org/>

Jennifer Carman
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: FW: OPPOSE HAR 11-157
Date: Friday, November 02, 2018 4:53:45 PM

FYI – not sure if you received this one already. Thanks.

From: DOH webmaster
Sent: Friday, November 02, 2018 4:34 PM
To: Balajadia, Ronald [REDACTED] Ungos-Markham, Jocelyn
[REDACTED]
Subject: FW: OPPOSE HAR 11-157

Hi ~

Forwarding inquiry below.

Thank you,
DOH Web Mail (vc)

NOTICE: Individuals should always review or confer with their supervisors about the request and composed responses to ensure it conforms with current DOH position on various policy areas. If a question and or response is current on potential “hot topic” or a “controversial” issue review and approval from the appropriate deputy may be required.

From: Anita and John Fernie [REDACTED]
Sent: Friday, November 02, 2018 4:26 PM
To: DOH webmaster [REDACTED]
Subject: OPPOSE HAR 11-157

I am writing because I am concerned about certain populations who have a higher risk for adverse vaccine reactions receiving some of these vaccines, as most influenza vaccines for both children & adults still contain thimerisol (mercury), and the HPV vaccine is a newer vaccine with no long term studies of safety and has a higher reported incidence of adverse reactions than other vaccines. Some medical conditions recognized in research studies as increasing the risk for adverse vaccine reactions do not qualify for CDC medical vaccine exemptions. I am also concerned that the reporting requirements to the Dept of Health may violate individual's rights to privacy of their health information.

Thank you for your consideration.

Anita Fernie

[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: School vaccination policy
Date: Friday, November 02, 2018 4:03:49 PM

Hi , my name is Lindsey Bronkhorst and I am writing our senators to let them know that I oppose the new bill HAR 11-157. I don't feel it is right that any vaccines should be considered mandatory for our children to get a good education . My daughter luckily has a medical exemption because she is one of the many that was vaccine injured as a child, she had a seizure and went into anaphylactic shock and quit breathing as a tiny infant after her vaccines. I continued with these vaccines per her Dr. who stated to me that there was no way the vaccines caused this. She continued to have seizures after each vaccine received before I finally found a new Dr. who had me stop then immediately and tested her for the MTFHR genetic mutation. She tested positive for this as did the rest of my family. It is becoming more understood now that having this genetic mutation can highly increase your risk for adverse side effects with vaccinations. I strongly disagree that the public school system should require all students to get vaccines without first being tested for this mutation. It is a violation of our rights as a parent to not be able to choose to make a medical choice for OUR children. My daughter is so smart, always at the top of her class and I just can't imagine her not being able to be able to participate in school because of this vaccine requirement. And I know there are many other families that are in a similar situation as me. Please be the voice we need in government and help stand up for our rights as parents. This is why we voted for you, because we trust you to be on our side. Vaccines should be the parents choice, plain and simple. Thank you for your time.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: STRONG OPPOSITION TO HAR 11-157
Date: Friday, November 02, 2018 1:46:54 PM

STRONG OPPOSITION TO HAR 11-157

Aloha,

I am writing to ask that you cancel HAR 11-157 for the following reasons:

1. It is not right to mandate something that is known to cause harm. If you read any vaccine insert you will see all the harmful ingredients not highlighted by the doctors that administer these vaccines.
2. You are doing much more harm than good with this mandate. There are no studies that prove the safety of the current mandatory vaccine schedule, so as any parent it is natural for us to be wary of injecting these poisons into our children to supposedly protect us from said diseases. By the way, it was recently exposed that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. How can you continue to pass laws that mandate vaccines when this problem exists?
3. HPV is a sexually transmitted disease. Children should not require a vaccine for an STD to attend school. In school, children are attending class and learning -- they are not having sex and spreading this disease. The HPV vaccine happens to be the most controversial vaccine for good reason -- because of the debilitating side effects that have ruined the lives of many across the world. HPV is a very common disease that most people will contract at some point in their lives -- and for many it clears up on their own or with natural, immune-boosting treatment. It rarely turns into cancer and if it does it takes a long time to do so; meanwhile, it can be monitored and treated before it becomes life-threatening.
4. Requiring the flu vaccine for school attendance is also inappropriate. The flu vaccine is contraindicated for people with egg allergies, which is a common allergy. Most people getting the flu shot are not screened for egg allergies, and this can be very dangerous! Moreover, the efficacy rate of the flu vaccine is so low, not to mention studies show that the flu vaccine puts you more at risk for catching other respiratory illnesses. Again, this is yet another vaccine that does more harm than good. There are safe, alternative methods for boosting the immune system to guard against the flu as well as effective treatments for the flu. I myself have never received a single flu shot in my entire life and I've only caught the flu a few times during my childhood and they were not life-threatening or debilitating. Most people that I know who often catch the flu are people who subscribe to getting the flu shot regularly. If you do your research, most people that die of the flu have received the flu shot, ironically! This is because

vaccines break down the immune system; they do not build it. Vaccines supposedly "induce immunity" by suppressing the immune response to said disease. Is this really "immunization" or just "suppression of disease expression"? What happens when you repeatedly inject viruses into the body and then suppress the body's immune response to them???

The answer is not a good one! In the natural medicine profession we have observed that the disease will exist in the body for a long time in dormancy (latency) and later on when the body is weak for whatever reason the latent disease will manifest as other illnesses.

Vaccination is NOT immunization!

5. Medical Freedom is a basic right. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents. Please help us protect our keiki.

Sincerely,

Leslie Ho'opai
Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Strongly Oppose madated vax
Date: Friday, November 02, 2018 5:55:26 PM

I have a family history of severe vaccine reaction. I chose not to vaccinate my child as an infant due to serious health risk. I am strongly opposed to government mandated vaccines as I should be able to make informed consent as to the need vs risk to the health of my family. It should be a basic human right as individuals to determine our own health choices especially when severe or fatal consequences can result. The Pharmaceutical industry as the largest lobbying group cannot be trusted to disclose health risks therefore the State should not dictate my right to accept or decline immunizations. This proposal is about economics not public health.

Morgan Hawk

--

Morgan M Hawk
Director of Youth Programs
Fundraising and Events Coordinator
The Lavender Clinic
...everyone deserves a little T.L.C.

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Friday, November 02, 2018 4:10:47 PM

Jacquelyn Born
[REDACTED]

I strongly oppose this bill as Hawaii Keiki have no need to add these extra vaccines. We have no disease outbreaks and no history of disease outbreaks. The only ones these benefit are the manufacturers who make more money when we poison our children. We should focus on nutrition education and sanitation.

Jacquelyn Born

From: [REDACTED]
To: [REDACTED]
Subject: Testimony - Mandatory Vaccination
Date: Thursday, November 01, 2018 5:58:51 PM

Aloha,

I am writing on behalf of the upcoming hearing in regards to proposing mandatory vaccinations. I have experienced first hand the negative side effects of my daughter receiving the MMR vaccine. She had been receiving her vaccines on the normal schedule and at 12 months when she was due for the MMR, she had a severe reaction that caused her to be hospitalized for awhile and she completely changed from that day on. While in the hospital you could completely see the light in eyes gone, like no one was there. She eventually got better but since has not received a vaccination. I had my son a year later and he has not had not 1 vaccination due to the experience with my daughter, and he is the most healthy child I know. He doesn't get as many colds or flu as she does, he's always been in the top percentile for his age in weight and height. He's hit so many milestones before the expected timeline, he's very bright; even his teachers are amazed at his knowledge and potential. We are born with an immune system for a reason, our bodies are made to fight off illnesses; injecting our children with these diseases is just uncalled for and invasive when it's natural for us as humans to fight off. I am 100 percent against mandatory vaccinations, places where it's become mandatory have not seen a change in the rate of children being diagnosed with illnesses, it's actually the opposite. It is against our rights as Americans and as parents to chose what's best for ourselves and our children. Please hear our concerns and rule wisely.

Mahalo,

Erin Edwards

From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157
Date: Saturday, November 03, 2018 8:53:00 AM

My name is Neal Uehara. I am writing in opposition to HAR 11-157. I feel that my rights as a parent are being threatened. Where there is risk, there must be a choice. Let parents decide which vaccines are important.

I appreciate you consider it very carefully. Because it might affect your children and your children's children.

Sincerely, Neal Uehara

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: HPV vaccine
Date: Saturday, November 03, 2018 7:52:25 PM

To whom it may concern,

My name is Lacey Maxey and I am writing in opposition to HAR 11-157. I feel that my rights as a parent are being threatened. Where there is risk, there must be choice. Let parents decide which vaccines are important, especially when it comes to vaccines for sexually transmitted infections. It is not up to the government to decide what injections my child(ren) receive.

From: [REDACTED]
To: [REDACTED]
Subject: Opposition to HAR 11-157
Date: Saturday, November 03, 2018 6:07:19 AM

Aloha,

My name is Summer Yadao, my address is [REDACTED]. Phone
- [REDACTED].

I am writing in opposition of any proposed mandate of vaccinations for my or any children.

The pharmaceutical industry is already a billion dollar industry, making money off of us as science experiments as they push out all kinds of so called 'remedies' for all kinds of ailments. Only for them to be recalled and/or brought to court for causing harm or death as side effects of their drugs.

Parents are and should be the only ones who make decisions about what goes into our children's bodies, period.

Mahalo,
Summer

From: [REDACTED]
To: [REDACTED]
Subject: Re: Mandatory Vaccinations
Date: Saturday, November 03, 2018 9:20:54 AM

Please uphold our right to choose which vaccines and what time table to use (if any) for our own children. We must be able to keep our Right for Religious/Philosophical objection to vaccines.

My son had a reaction (brain swelling) to the multiple vaccines he received at 1 year old... it is not recommended that my other children receive the same vaccines doses at the same time, as they may also have a reaction and the outcome may be more severe.

I retain the democratic Right to make informed decisions for my children based on what is best for my family... that is why we are Americans and proud to uphold our strong American Rights.

Thank you,
Catherine (Lightfoot) Martin, CPM
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Aloha and NO
Date: Saturday, November 03, 2018 10:01:55 AM

This bill will impose upon my body sovereignty, freedom to choose what is right and healthy for my body or my child's bodies. I strongly disagree with mandatory vaccinations. It is no other person's right to impose themselves or their beliefs on another human being by forcing them to put poison into their bodies for their profit. This is not Nazi Germany!

Erin Weathersby

From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157
Date: Sunday, November 04, 2018 8:04:42 AM

Aloha,

My name is Jacklyn Marfil and I am writing to let you know that myself and my ohana
STRONGLY OPPOSE

HAR 11-157. Where there is a risk, there must be a choice. I feel it is our choice as
parents to make these decisions, especially when it comes to vaccinations. Please let the
makua decide what is important for THEIR keiki!

Mahalo nui loa.

Get [Outlook for Android](#)

From: [REDACTED]
To: [REDACTED]
Subject: Oppose mandatory vaccinations
Date: Sunday, November 04, 2018 11:30:25 AM

To whom it may concern,

I am writing to voice my opposition to any and all legislature that would make vaccinations in any way mandatory for both children and adults alike in any situation. I believe it is a personal and parental right to make decisions regarding vaccination, not the right of our local or federal government to mandate them.

Sincerely,

Briana Ansley
Hawaii, citizen, parent & teacher.

Sent from my iPhone

From: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]
Subject: Re: HAR 11-157 - strongly oppose
Date: Sunday, November 04, 2018 12:24:12 PM

Aloha

My name is Richard Solari
and I'm writing on strong opposition to
HAR 11 - 157.

I feel that my rights as a parent are being
threatened.

I'm sending this on behalf of myself not a group
but my opinion represents the thousands
of others who are not even aware of their
rights or the truth about vaccines.

Human beings are created in balance
To fight off disease. Our immune systems
Get stronger by doing this. Vaccines contain
Dangerous and lethal toxins and this is a fact,
Not an opinion.

Here's one of many official, professional,
Organizations and their website link -

<https://www.nvic.org/>

Richard Solari
[REDACTED]

On Fri, Nov 2, 2018 at 1:43 PM Jennifer - [REDACTED] wrote:

Aloha

My name is Jennifer Carman
and I'm writing on strong opposition to
HAR 11 - 157.

I feel that my rights as a parent are being
threatened.

I'm sending this on behalf of myself not a group
but my opinion represents the thousands
of others who are not even aware of their
rights or the truth about vaccines.

Human beings are created in balance
To fight off disease. Our immune systems
Get stronger by doing this. Vaccines contain
Dangerous and lethal toxins and this is a fact,
Not an opinion.

Here's one of many official, professional,
Organizations and their website link -

<https://www.nvic.org/>

Jennifer Carman



Gut Doctor "I Beg Americans To Throw Out This Vegetable Now"

food-frauds.com

<http://thirdpartyoffers.netzero.net/TGL3231/5bdce0ebf11360ea1e93st03vuc>

From: [REDACTED]
To: [REDACTED]
Subject: vaccine testimony
Date: Sunday, November 04, 2018 1:16:45 PM

I plead of you to not move forward on this proposed new vaccine schedule. Both of my children have had all their vaccines on schedule. However, no one in our family have ever had the flu shot (even when the H1N1 scare occurred) and none of us have ever had the flu due to strong immunities and frequent hand washing. Totally unnecessary, and this vaccine should remain a choice for those who feel they benefit from it.

The HPV vaccine gave my son months of adverse reactions. Spaciness, extreme fatigue, his vision decreased from 20/20 to 20/80 after vision testing in a 3 month period. He complained of daily bouts of dizziness. No illnesses or other life changes in this time period other than this vaccine. I absolutely attribute his symptoms to the Gardasil vaccine.

Hep A? Perhaps. But HPV and the flu mandatory..no way!

Hawaii has always been a melting pot for people with different belief systems. It is my strong belief that not only are these proposed vaccines unnecessary, in some cases they are downright dangerous. Please listen to the people. This is not North Korea.

Mahalo, Angela Slatinsky

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Urgent! Attack on our medical freedom. Forced medicine = No liberty.
Date: Sunday, November 04, 2018 5:21:10 PM

Aloha!

My name is Martina and I am mom of two perfectly healthy unvaccinated children on [REDACTED]. Thank you for this opportunity to provide testimony. As a community member here in Hawaii and a health medical freedom advocate, I am writing to strongly oppose HAR-11-157. I also request hearings on all islands.

I almost died from a vaccine years ago. My children can not receive vaccines because of that family history.

This proposal violates many sections of the United Declaration of human rights. Mandatory laws that threatens a child's education are unjust laws because they disproportionately target those in society without the family, community, or monetary support that would allow for home schooling their children. For what good reason will a perfectly healthy unvaccinated child not have the opportunity to get an education?

By allowing these proposals to go through we will see an outrage from the public. People would rather home school or move out of state then to vaccinate their keiki with a proven extremely dangerous vaccine, as the HPV vaccine.

Our keiki will NOT be your test subjects. It's time to separate pharma and state. The ACIP meeting at the CDC Oct. 24th this year, pharmaceutical lobbyists outnumbered legislators. Our public health agencies and departments all have public-private partnerships with pharmaceutical companies.

Giving under influence to choose who stand in profit in the billions-liability free of adequate safety data. Then sits back to wait for "after-marketing" reporting.

WE, the public are the test subjects in aftermarket reporting. UNACCEPTABLE.

Why did state epidemiologist Dr. Sarah Park testify against a bill this year to provide patients/parents full informed consent prior vaccination. Hence read a real insert and be told ALL adverse events that can follow after injection, such as death, seizures, brain swelling and paralysis.

She testified it could hurt her flu shot school program. Why is that? Conflicts of interests? Should she be investigated?

Also who sponsors Hawaii immunization coalition? You will see many written testimonies from this group. Their arguments to support this rule change is weak and unjust.

They say they want mandates in school for certain vaccines to get high vaccination rates, and in return lower rates of vaccine-preventable diseases.

That statement is a lie. HPV vaccine has NEVER once been proven to prevent cervical cancer. New studies show that cervical cancer has INCREASED in the age group vaccinated for. HPV is NOT a public health threat. Why would we vaccinate ALL Hawaii's keiki with a vaccine that has injured over 59,000 children reported to VAERS and 326 deaths. FDA admits that only 1 to 10% of adverse events even get reported. So what numbers are we really looking at here. There are criminal charges in many countries against the maker Merck(see link), same company that killed 60,000 Americans with viox. Why on earth would parents give their trust to this extremely dangerous product, with their children's lives?

Their argument that vaccines protect the elderly, newborns and immuno-compromised can easily be dismissed. None of those attend school settings. Also they all DO get vaccinated. Including pregnant women. The only immuno-compromised that do not receive vaccines are cancer patients attending chemo. They are therefore also not in a school setting. Also this statement does not make any sense since recently vaccinated individuals can shed live virus. Hence recently vaccinated can not give blood for six weeks after live virus injection, nor are they allowed to visit cancer patients during that time.

Another argument is the theory of herd immunity. Another lie. 94% of the adult population is not up to date with their vaccines. Therefore completely unvaccinated since vaccines IF they even work, wane about 2 to 5 years. Should adults not be able to attend work then if not fully up to date with the adult schedule of 120 doses of vaccines. Anyone can spread disease. There are thousands of infectious diseases but somehow people fear only the 13 we have vaccines for. Why is that? It is called propaganda that is pushed in every direction. I get bribed with a \$5 giftcard at Walmart to go get a free flu shot for the clerk to reach their quota for bonus. That is NOT for health. Please stop this madness.

Also all recent outbreaks have been in fully vaccinated individuals. Syracuse mumps outbreak was in 100% fully vaccinated individuals. Their faulty dangerous products should NOT be forced upon anyone.

When a product injures and kills thousands of people it gets taken off the market. Except when it's a vaccine. It's get mandated.

NCVIA of 1986 is passed by Congress and provides total liability protection to the vaccine maker. Same year the vaccine schedule tripled. Coincidence?

U.S citizens are no longer able to sue a vaccine maker if they are injured compensation are now paid out of taxes, not by the vaccine makers. Only signed into law because they no longer found it profitable if they had to be responsible for all injuries and death.

By passing proposed changes you are opening a door for catastrophic proportions. Parents will refuse to bring their children to school under such oppressing and criminal laws.

Medical freedom is our basic human right. Where there is a risk there must be a choice.

Parents responsibilities are for their children not the false propaganda marketing gimmick "for the herd".

I respectfully request that proposed changes be thrown out due to the fact it is based on profit over our children's health, and that we as parents decide what goes in our children's bodies. If we lose that right. We lose all our freedom and that should upset every single citizen of this country.

I am begging you to look at all the facts and science. Not only the one that protects profit.

Pono, do what is right.

Do not support this unjust, medical tyranny proposal.

We all deserve more freedom, not less.

Oppose HAR-11-157.

Warmly,
Martina, [REDACTED] resident.

"In your previous meeting you advocated for less independent testing, considered 'redundant',

in order to speed up the supply of products.⁷ The recent administration of 250,000 defective vaccines in China⁸, the tragedy of the oral polio campaign in India with over 450,000 cases of paralysis and death⁹, the damage caused by the Dengue vaccine in the Philippines¹⁰, reports from all over the world of chronic pain and paralysis after administration of the HPV vaccine^{11, 12}, show that vaccine safety and efficacy are being tragically disregarded in this drive for fast-tracking approval and easy certification."

<https://www.efvv.eu/open-letter-to-the-who-from-international-organisations/>?

fbclid=IwAR00wrJQLI9NaP4mj_EGMVs9KdF_5haN41pK_kbNJxyT6YRXQ2ypMNatm0g

<https://changingtimes.media/2018/09/13/the-gardasil-controversy-as-reports-of-adverse-effects-increase-cervical-cancer-rates-rise-in-hpv-vaccinated-age-groups/>

From: [REDACTED]
To: [REDACTED]
Subject: Vaccination Proposal
Date: Sunday, November 04, 2018 8:58:03 PM

To whom it may concern:

I am a mother of four unvaccinated children and very concerned how Hawaii State mandatory vaccinations would effect our family. We have chosen not to vaccinate for personal and religious reasons and I believe it is our right as parents to make that decision for our children. If it was to become mandatory, we would be forced to pull our children out of public schools and enroll them into an alternative option. I urge the state to really investigate and study the chemicals and additives put into the vaccinations, which can cause more harm than the actual illness itself.

Mahalo for your time,

Andrea Kaleiohi

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Reasons to oppose HAR 11-157
Date: Sunday, November 04, 2018 10:14:03 PM

To whom it may concern,

The risk of vaccination is not insignificant. To view the risk of vaccine injury, as documented by the Federal Health Resources and Services Administration, please see the following url:
<https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-oct-2018.pdf>. Compensated injuries represented here are injuries that are permanent or fatal. The document represents a gross under reporting of vaccine injuries since it documents only those vaccine injuries filed in a federal court and represents only permanent, fatal and near fatal injuries. Vaccine injuries are real and they are much more common than published data suggest.

Any decision regarding a medical procedure that involves risk should be based upon an informed consent between the doctor and patient that involves assessment of the individualized benefits verses risk for any procedure. Mandatory vaccines in any form, as proposed by HAR-11-147 violate the basic right to make informed healthcare choices and place the citizens of Hawaii at increased risk for iatrogenic illness by enforcing a one sized fits all medical procedure. Medical interventions can be put in place to help protect from vaccine injury, but only if patients are properly informed of the risks and have a choice in the matter.

Let it be known I oppose HAR-11-157.

Mahalo,

Kim Marzetta

In the Grace of Love, I AM Guided

From:

To:

Subject:

Date:

strongly oppose Hawaii Administrative Rules/HAR 11-157

Sunday, November 04, 2018 2:59:15 PM

Dear Hawaii State Department of Health,

I **strongly oppose** Hawaii Administrative Rules/HAR 11-157 to add more mandatory vaccines including HPV and Meningococcal vaccine for all seventh graders, Influenza vaccine for all young children, Hepatitis A vaccine for all children, and an additional dose of MMR for post-secondary school attendance and Meningococcal vaccine for all first-year students living in on-campus housing. Enhanced reporting requirements for health practitioners and schools and enhanced reporting requirements for medical and religious exemptions.

I am a wife, a mother, and a 3rd generation military family. I am pro-vaccine as long as it can be pro-clean green vaccine, and with the way vaccines are made, they do not fit under clean and green because of the toxic chemicals. But what I am not is pro-mandate vaccine. I'm pro medical freedom, for people to have a choice in what they want or do not want in their body.

Disclaimer! Before I start I want to make sure you are aware that I am using the same sources you all do. I always refer to the CDC, FDA, and vaccine manufactures (Merck, GSK, Pfizer, etc.) so that we are all on the same page as far as our knowledge is based off of the information that is provided from these sources that **I hope is consistent, credible, and current.**

You see how I made a disclaimer right in the beginning so we are all on the same page?

Something I know should be done for all parents before administering vaccines, given full disclosure of what is about to happen before it happens, what could happen after it happens, all the good and bad, so they can make the best informed decision.

But, it's a little too late since the bill for informed consent was opposed. That informed consent by giving the parents the package insert to read over during or before the appointment would be an "undue burden", "waste of time", and would be too "time consuming" for both parents and physician (based off of the oppositions submitted for HB 2622) .

But guess what? Anyone who chooses to be a *good* parent knows that when you become a parent, everything we do is time consuming, what we do for our children is never a waste of time, and they are absolutely **not** an undue burden.

We are willing to take the time necessary to have all the information even if it is alarming. Because in the end, the blame will not be on the CDC, FDA, or vaccine manufacturers because as the parent our children are our responsibility. From the day we conceive, that precious small life to us is everything. We grow, nurture, and love them with love we have never experienced. We teach them that lying is bad, and withholding truth is one in the same, so let's all be clear that my focus here is **truth.**

I want to uncover the truth for the sake of time to just focus on one of the vaccines from the list of what is proposed to be added.

The HPV Vaccine also called Gardisal, if this is passed will be required of 7th graders, both boys and girls the age of 12-13. These boys and girls who are capable of reading and understanding, so let's let both parents and the children aware of some of the facts from the Gardisal package insert.

First, let's look at the intended purpose of this HPV vaccine. The indications and usage on FDA.gov states that it is, "...for the prevention of the following diseases caused by Human Papillomavirus (HPV) types included in the vaccine...Cervical, vulvar, vaginal, and anal cancer caused by HPV types 16 and 18...Genital warts (condyloma acuminata) caused by HPV types 6 and 11...And the following

precancerous or dysplastic lesions caused by HPV..."

(<https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm111263.pdf>)

Reason #1 Why I don't support mandating more vaccines:

My following question after the purpose of anything is what does it consist of, and in this case, what's in it? Just like I read a menu or packaging for ingredients; I want to know what's in it before I decide to consume it or not.

"What are the ingredients in GARDASIL?"

The ingredients are proteins of HPV Types 6, 11, 16, and 18, amorphous aluminum hydroxyphosphate sulfate, yeast protein, sodium chloride, L-histidine, polysorbate 80, sodium borate, and water for injection."

(https://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_ppi.pdf)

I have this rule of thumb that I apply to my life... If I can't pronounce it, and if I don't know what it is, I probably shouldn't be eating it. Keep it simple. I know the contents of an organic apple, the ingredients would say: Apple. I will eat that apple. But, if it was a package of sliced conventionally grown apples grown with pesticides and added chemicals to preserve the apples, I would avoid eating those apples.

This logic applies the same to vaccines. We should know what these ingredients are and what they are capable of before putting it into our children's bodies.

So let's just look at one of the ingredients listed above: amorphous aluminum hydroxyphosphate sulfate

I found this study "*Insight into the cellular fate and toxicity of aluminium adjuvants used in clinically approved human vaccinations*" by [Mold M1](#), [Shardlow E1](#), [Exley C1](#). and in their conclusion they found that "Through *in vitro* cellular modelling, our results further shed light on the capacity of ABA (aluminium based adjuvants) to deposit at sites distant to the injection site as has been suggested in macrophagic myofasciitis (MMF), whereby aluminium is proposed to translocate through draining lymph nodes to distant organs" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981857/>).

Aluminum is one of the most commonly used ingredient in most vaccines. So this ingredient has the ability to move throughout the body to lymph nodes and distant organs. Let's say, it travels to the brain and causes inflammation, which is called **encephalitis**.

Is this possible? **Yes**. How do I know? **It lists it as one of the adverse events on Postmarketing Experience on the Gardisal package insert as encephalomyelitis** which according to the dictionary is "**inflammation of the brain and spinal cord, typically due to acute viral infection.**" You will see more later on my reason #4.

So again to my apple analogy. If I read the ingredients on my apple that stated there was amorphous aluminum hydroxyphosphate sulfate, and I knew it can travel through my lymphnodes and to my organs like my brain and cause inflammation and potential damage. I would DEFINITELY stay away from that poisoned apple like the one from the old witch on Snow White.

I encourage you to learn more about ingesting aluminum vs. injecting aluminum in this well written objective view on it <http://vaccinepapers.org/vaccine-aluminum-travels-to-the-brain/>

Reason #2 Why I don't support mandating more vaccines:

So can we all agree that the goal is to prevent cancer caused by certain types of HPV. But, and this is a big but, the package insert states, "**GARDASIL has not been evaluated for the potential to**

cause carcinogenicity or genotoxicity."

Let me get out my handy dandy dictionary so I can understand this correctly in laywomen terms.

Carcinogen is "a substance capable of causing cancer in living tissue." (dictionary.com)

"A genotoxin is a chemical or agent that can cause DNA or chromosomal damage. Such damage in a germ cell has the potential to cause a heritable altered trait (germline mutation). DNA damage in a somatic cell may result in a somatic mutation, which may lead to malignant transformation (cancer). (<https://www.ncbi.nlm.nih.gov/pubmed/19157059>)

Let's let that sink in for a moment...

You are going to require boys and girls entering 7th grade to get the HPV vaccine that is supposed to prevent certain types of cancer with a substance that hasn't been tested for the potential of causing cancer. So, potentially preventing cancer with something that could potentially cause cancer? Is anyone else confused by this? Do our children not deserve better options?

Preventing cancer doesn't come from a syringe of something that may contain cancer causing ingredients. Maybe instead we should teach our children how to prevent illness and cancer by eating nutrient dense foods, drinking plenty of water, getting enough sunshine and exercise, practicing safe sex and good hygiene. Shouldn't we put more emphasis on these simple yet important aspects of preventing cancer?

Reason #3 Why I don't support mandating more vaccines:

Now let's continue with warning and precautions, just like when you are preparing to ride a roller coaster, they have a short video or explanation of the precautionary measures like wearing the safety harness, keeping all limbs inside the cart, and look forward to avoid injury.

Here is the **Gardasil warning and precaution.**

"Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position" (fda.gov)

I copied that straight from the FDA Gardasil Package Insert website, and no your eyes aren't misleading you, I purposely left the part that vaccines is spelled incorrectly on the insert. If they are careless enough to miss a spelling error, makes me wonder, what else are they careless about...

So again as a laywoman, I wanted to make sure I understood what that warning and precaution was stating so I searched, **"What is tonic-clonic movements?" and this was the result, "A type of seizure that involves a loss of consciousness and violent muscle contractions." (Mayo Clinic)**

So if you were about to ride a roller coaster and they indicated that you will need to be monitored for 15 minutes after the ride to make sure you do not lose consciousness or have violent muscle contractions, I don't know about you, but I would not be lining up for that ride.

Reason #4 Why I don't support mandating more vaccines:

Just in case the potential for cancer, mutations, and seizures weren't enough...

"The following adverse events have been spontaneously reported during post-approval use of GARDASIL."

"Blood and lymphatic system disorders: Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, lymphadenopathy.

Respiratory, thoracic and mediastinal disorders: Pulmonary embolus.

Gastrointestinal disorders: Nausea, pancreatitis, vomiting.

General disorders and administration site conditions: Asthenia, chills, death, fatigue, malaise.

Immune system disorders: Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

Musculoskeletal and connective tissue disorders: Arthralgia, myalgia.

Nervous system disorders: Acute disseminated encephalomyelitis, dizziness, Guillain-Barré syndrome,

headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonicclonic

movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis.

Infections and infestations: cellulitis.

Vascular disorders: Deep venous thrombosis."

Now, I am definitely not lining up for that ride.

So to bring my point home, and to be very clear, I **strongly oppose** adding more vaccines like this one above, the HPV vaccine to be mandated for our children. Our children who until they are old enough to have personal autonomy, it is our responsibility to speak up for them, stand up when things don't seem right, and protect them from potential dangers.

I support the theory behind vaccines, that's why I said I am pro-vaccine as long as those vaccines are clean and green. We need for vaccines to be better tested for safety of the ingredients whether they are cancer causing, capable of DNA mutations and damage, and impairment of fertility for our children's future. They deserve better, we as parents deserve better information so that we are aware of the risks vs. benefit.

No matter what side you stand on, we all want to do what's right for our children and protect them, that is our main goal, but at what cost? Do we have to risk all of those above mentioned reasons? The toxic substances like aluminum entering their bodies, the unknown about if the vaccine will cause cancer, DNA mutations, impairments to their fertility, seizures, paralysis, or worse case scenario a blood clot that could lead to a parents worst nightmare?

Please, I urge you to do better for our children and their futures. Don't mandate vaccines, give people the opportunity to be educated on this topic. I took my time to read the package inserts, to look up public medical studies, yes it included medical jargon I didn't understand, but nothing a search couldn't clarify for me.

Was it an "undue burden"? NO, because our children are not a burden.

Was it a "waste of time"? NO, because our children deserve our time.

Was it "time consuming"? Yes, but worth every single moment.

Thank you if you made it this far to reading, it really means a lot to me.

Adriessa Goodman

From: [REDACTED]
To: [REDACTED]
Subject: Strongly Opposed to Forced Vaccinations!
Date: Sunday, November 04, 2018 12:04:10 AM

Dear Honorable Department of Health Public Servant,

Please consider what Hawaii County has already passed in 2009 concerning mandatory vaccinations:

“WHEREAS, there is insufficient scientific evidence proving that vaccines are safe or effective, therefore it is not in the best interest of public health to impose mandatory vaccinations without exemptions; and

WHEREAS, swine flu and the flu vaccines both contain Thimerosal, a preservative for vaccines composed of mercury, one microgram of mercury is considered toxic and flu shots contain 25 micrograms. By age two, most United States children have received around 237 micrograms of mercury through vaccines; and

WHEREAS, the fast tracked government vaccines contain a substance called squalene that is suspected of causing serious long-term damage to the body; and

WHEREAS, in the wake of potential harm to the individual and the public from vaccinations, and the vacillating interpretation of “vaccine science,” it is in the public’s best interest to amend the vaccine laws, to include the right of medical, religious, and philosophical exemptions from mandated vaccination programs; now, therefore,

BE IT RESOLVED BY the COUNCIL OF THE COUNTY OF Hawai’i, that it recommends that state and federal elected officials who represent the people of the State of Hawai’i amend vaccine laws to include medical, religious, and philosophical exemptions from mandatory vaccine programs that contain thimerasol or squalene.

BE IT FURTHER RESOLVED, that any vaccine known to contain harmful viruses or any materials known to prompt autoimmune diseases or cancer risks shall provide cause for exemption for any person in the State of Hawai’i who so desires such exemption.”

As a member of the Wai'anae Coast Neighborhood Board, I have heard from many of my

constituents who are opposed to "mandatory" vaccines. It's shameful that "bully tactics" of coercion are being resorted to to promote special financial pharmaceutical interests taking advantage of their fear-mongering among our policy makers and public officials. Auwe!

It is ethically abhorrent for any government official(s) to assume dictatorial caesar-like powers to command their subjects to do mandatory vaccinations. Are we public servants or the masters? Must I remind you of Ke Akua's justice to everyone who is not pono?

Good intentions can no longer be used to commit crimes against the public trust. Respect, educate, and recommend, but DO NOT COERCE NOR FORCE my community to do what you think is best for us...we can decided that perfectly on our own, thank you!

Blessings to you,

W. Ken Koike

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Oppose mandatory vaccinations
Date: Sunday, November 04, 2018 11:30:25 AM

To whom it may concern,

I am writing to voice my opposition to any and all legislature that would make vaccinations in any way mandatory for both children and adults alike in any situation. I believe it is a personal and parental right to make decisions regarding vaccination, not the right of our local or federal government to mandate them.

Sincerely,

Briana Ansley
Hawaii, citizen, parent & teacher.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose amendment HAR 11-157
Date: Monday, November 05, 2018 1:37:36 PM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. The State SHOULD not have the right to decide for any parents about vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A CHOICE !!! And there are many risks involved with proof !

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify !!! I ask that you delay your decision on this important issue.

Sincerely,

Jennifer Edmonds
[REDACTED] resident

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Hawaii mandatory vaccinations
Date: Monday, November 05, 2018 5:33:53 PM

My name is Christene Reale and I oppose making vaccinations mandatory. As parents and humans we have the right to choose whether we want to have our children or ourselves injected with vaccinations !

Thank you

Christene Reale

[REDACTED] resident
[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Immunization
Date: Monday, November 05, 2018 3:50:32 AM

I am completely against mandatory immunizations for children and adults.
David Shapiro

From: [REDACTED]
To: [REDACTED]
Subject: Letter
Date: Monday, November 05, 2018 2:01:26 PM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. The State SHOULD NOT have the right to decide for any parents about vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A CHOICE!!! There are many risks involved with proof.

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify. I ask that you delay your decision on this important issue.

Sincerely,

Heather Chandler

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines at school
Date: Monday, November 05, 2018 9:05:15 AM

Aloha,

I am not going to belabor the point of how dangerous vaccines are. We both know, its all over the vaccines safety inserts. You have read at least one, I hope. I have read most of them. In the end it just begs the question who is telling you to poison your own fellow man? How do you sleep at night? How much do they pay you to ruin the lives of innocent children, for their whole life, and the lives of their parents, extended family, friends and acquaintences? Wow, the list gets pretty long pretty quick doesn't it? That means more and more people are coming to terms with what is really happening to us as a society and to mankind in general. It is not "if" but "when" the tipping point is reached which side of the line do you want to be on? Vaccine court will not be able to save you. It is on its way out. Professing ignorance will not save you. You know. History will record this moment as a particularly insidious time when man saw greed as more meaningful than the lives of innocent children being ruined all around him, bringing society to the brink of self destruction. A time that was on a par with the Nazi Holocaust. When the bell tolls many people are going to jail, for the rest of their lives. The whole affair will make the Tobacco Settlements seem like a small blip on the radar. In the time it has taken you to read this note one or two more new kids have been added to the autism list. Time is running short, for everyone. People are waking up. Think carefully before you act, it could be your life on the line before you know it.

With utmost sincerity and humility,

Tom Woolf

Father of a 12 y.o. on the spectrum

--

Every generation needs a new REVOLUTION!

Thomas Jefferson

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157, I OPPOSE
Date: Monday, November 05, 2018 10:56:26 AM

I, Kimberly Carter, **STRONGLY OPPOSE** the NEW VACCINE REQUIREMENTS FOR HAWAII STUDENTS.

Medical freedom is our basic human right. Where there is a risk there must be a choice! As a community member here in Hawaii and a health medical freedom advocate, I am writing to strongly oppose HAR-11-157.

This proposal violates many sections of the United Declaration of human rights. Mandatory laws that threatens a child's education are unjust laws because they disproportionately target those in society without the family, community, or monetary support that would allow for home schooling their children. By allowing these proposals to go through we will see an outrage from the public. People would rather home school or move out of state then to vaccinate their keiki with a **proven** extremely dangerous vaccine, as the HPV vaccine. HPV vaccine has NEVER once been proven to prevent cervical cancer. New studies show that cervical cancer has INCREASED in the age group vaccinated for. HPV is NOT a public health threat. Why would we vaccinate ALL Hawaii's keiki with a vaccine that has injured over 59.000 children reported to VAERS and 326 deaths. FDA admits that only 1 to 10% of adverse events even get reported. So what numbers are we really looking at here.

There are criminal charges in many countries against the maker Merck. , same company that killed 60.000 Americans with vioxx. Why on earth would parents give their trust to this extremely dangerous product, with their children's lives?

When a product injures and kills thousands of people it gets taken off the market. Except when it's a vaccine. It's get mandated.

NCVIA of 1986 is passed by Congress and provides total liability protection to the vaccine maker. Same year the vaccine schedule trippled. Coincidence?

U.S citizens are no longer able to sue a vaccine maker if they are injured compensation are now paid out of taxes, not by the vaccine makers. Only signed into law because they no longer found it profitable if they had to be responsible for all injuries and death.

I respectfully request that proposed changes to be thrown out due to the fact it is based on profit over our childrens health, and that we as parents decide what goes in our children's bodies. If we loose that right. What true rights do we truly have, that should upset every single citizen of this country.

I am begging you to look at all the facts and science.

Pono, do what is right, Oppose HAR-11-157. Where there is a risk there must be a choice!

Warmly,
Kimberly, [REDACTED].

From: [REDACTED]
To: [REDACTED]
Subject: Updated immunization requirements
Date: Monday, November 05, 2018 9:08:09 PM

Good evening. As a public health nurse, I strongly support the addition of CDC and American Academy of Pediatrics recommended vaccines to the requirements for school entry in Hawaii. These vaccines are safe and effective in preventing the spread of these serious and sometimes deadly illnesses. Prevention is the cheapest and most effective way to keep people healthy and prevent illnesses. We need to provide information to the public so they get more information on the vaccines and the illnesses they prevent. Thank you. Jean McDermott [REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Opposition to HAR 11-157
Date: Monday, November 05, 2018 10:17:22 PM

My name is Kristin Stanley and I am writing in opposition to HAR 11-157. I feel that my rights as a parent are being threatened and I should have the CHOICE as to what goes into my children's bodies. I have known several people Injured from certain vaccines and it should be our decision on which ones are right for our children.

Kristin Stanley

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Added links to Martina Dodsons testimony opposing HAR-11-157
Date: Monday, November 05, 2018 12:58:06 PM

Aloha again.

I am adding links to my testimony as they didn't show up on my original one I sent yesterday.
Regarding opposing HAR-11-157
Martina Dodson Maui.

As you can see the evidence that this HPV vaccine is extremely dangerous should be enough for you to kindly stop proposed changes. Also why parents are so upset is that **OUR ONLY FREEDOM LEFT IS OUR RELIGIOUS EXEMPTIONS TO AVOID VACCINATIONS.** That will be taken over by a small group of people at the DOH that should not be in charge of our exemptions, since they obviously will follow the criminal ways California took away parents rights to choose. They will also get the ultimate power to just with the strike of a pen to **TAKE THEM COMPLETELY AWAY** with basically **NO** oversight.

Statement from my friend Kathleen Berrett. Her son died this year following the HPV vaccine.

"Colton was a happy healthy very active boy until he became paralyzed from the neck down and ventilator dependent for 4 yrs due to the gardasil vaccine that was administered to him Feb 2014.

He worked hard and strived to get full rehabilitation. He regained function in his legs however He never was able to use his right arm or neck again. His diaphragm remained paralyzed Making him need a ventilator to Breathe and many cares that go along with being trached and paralyzed. He Only regained a portion of his left arm and hand.

He passed away Jan 5 2018 due to subsequent consequences of his vaccine injury. The damages caused by gardasil are horrific and incomprehensible for many to understand when they looked at my sweet son's smiling face. I will never get to see him smile at me anymore. (Sarcasm alert:

I'm so grateful that he didn't get cervical cancer though, nor have the opportunity to spread it to his wife... that he also got cheated from having)

Gardasil kills, it maimes and damages innocent children so wealthy men can make a huge profit.

It's disgusting!

Thanks for sharing his story"

This is a open letter written to the WHO from hundreds of international organisations representing health freedom. Questioning the vaccine safety. Please read.

https://www.efvv.eu/open-letter-to-the-who-from-international-organisations/?fbclid=IwAR00wrJQLI9NaP4mj_EGMVs9KdF_5haN41pK_kbNJxyT6YRXQ2ypMNatm0g

This book has evidence of the danger of the HPV vaccine. Released last month.

“This book reveals the tragedy of the HPV vaccine scandal.”

—Dr. Luc Montagnier, Nobel Prize Winner for Discovery of HIV

The HPV Vaccine on Trial: Seeking Justice for a Generation Betrayed paints a devastating picture of corporate and government conflicts of interest, negligence, and malfeasance in approving and promoting human papillomavirus (HPV) vaccines, touted to prevent cervical and other cancers. Coming out on the heels of recent New York Times revelations about astounding financial conflicts of interest at Memorial Sloan-Kettering Cancer Center, this groundbreaking book highlights the lack of transparency, manipulated science, and abuse of state power to market this medical juggernaut, already raking in over \$2.5 billion per year.

Authors Holland, Rosenberg, and Iorio uncover:

- HPV vaccines have never been proven to prevent cancer of any kind.
- HPV vaccine inventor Ian Frazer acknowledges that “[C]ervical cancer screening if used and promoted effectively would be almost entirely able to prevent” cervical cancer deaths in countries like the US and Australia, without HPV vaccines.
- No participants in the original HPV clinical trials received true saline placebos.
- The clinical trials never investigated the vaccine’s possible effects on human fertility or potential to cause cancer.
- The clinical trials show that the vaccines can backfire and contribute to HPV lesions, and potentially cancer, in some women. Despite this, neither the manufacturers nor government agencies recommend prescreening to eliminate those with clear risk factors.
- Although the vaccine is targeted for 11-12-year-old children, only a small fraction of clinical trial subjects was in this age range.
- Lawsuits against HPV vaccine manufacturers and government health agencies are progressing around the world, including the US, India, Japan, Colombia, Spain, and France.
- The US government earns millions in royalties from Merck and GSK, the vaccine manufacturers, for its role in the invention of HPV vaccine technology.
- Although the US government proclaims HPV vaccines safe and effective, it has paid out millions of dollars to compensate families for death, brain injury, multiple sclerosis, ulcerative colitis, and other severe, debilitating conditions.

With praise from some of the world’s leading scientists on aluminum, autoimmunity, and vaccines, this book fills a critical void, giving people information they need to make commonsense decisions about this vaccine.

Written in plain language, The HPV Vaccine on Trial ultimately is about how industry, government, and medical authorities may be putting children in harm’s way.

About the Authors

Mary Holland, M.A., J.D., is on the faculty at NYU School of Law, directs its Graduate Lawyering Program, and lives in New York City.

Interview with neurosurgeon Dr. Blaylock
about HPV vaccine.

Merck and its lackeys have made all sorts of wild claims about how Gardasil prevents HPV, as well as cervical cancer, despite the fact that neither of these claims have ever been proven to be true.

"It has never been shown that [Gardasil] prevents cervical cancer," explains Dr. Blaylock to Adams, noting that Merck's widely-aired "One Less" television and internet campaign, which insinuates that Gardasil prevents cervical cancer in young girls, is a complete fraud. "They don't even have scientific evidence of any kind to back up the assertion that this vaccine prevents cervical cancer."

Gardasil has injured, killed far more children than ever would have developed cervical cancer without the vaccine
And yet young girls, young boys, and all young children for that matter, including those that do not even engage in sexual behavior of any kind, are being told that they need Gardasil to protect against a cancer that kills fewer people every year than the vaccine itself. According to the available data, which is under-reported by up to 98 percent, Gardasil has permanently injured and killed far more girls than ever would have developed cervical cancer apart from the vaccine.

Since full side effects are almost never disclosed, Gardasil and many other vaccines are being illegally administered to millions without informed consent

Perhaps most disturbing about Gardasil is the fact that the vaccine was fast-tracked in its development and approval, and is now being administered to millions of people without informed consent. Because the full list of side effects, including the lack of science proving Gardasil's efficacy, is not being disclosed to parents, doctors, pharmacists, and vaccine-administers at grocery store booths are breaking the law by failing to provide informed consent.

Young children and their parents are also not being told that yearly pap smears alone can prevent 80 percent or more of all cervical cancers, or that a young girl's risk of developing cervical cancer apart from the Gardasil vaccine is less than .00002 percent, or less than two-thousandths of a percent, if she gets pap smears.

In essence, parents are being told that Gardasil does all sorts of things that it has never been proven to do, when in reality it has no medical benefits whatsoever, but plenty of serious risk. Meanwhile, the general public is woefully unaware of the fact that vitamin B12, folic acid, vitamin C, curcumin (turmeric), quercetin, and many other nutrients and vitamins naturally prevent HPV and cervical cancer without a vaccine.

Gardasil . . . Here are just a few studies and facts about this vaccine. Like all vaccines one size does not fit all.

You can read the package inserts- there were no true controlled studies. The actual vaccine was tested against amorphous aluminium hydroxyphosphate sulfate, which can't be considered a true placebo as it is not just saline, but an adjuvant used in vaccines. How can

you measure side effects with any accuracy when you're injecting vaccine ingredients in both the control and the test groups?

PEER-REVIEWED LINKS

Primary ovarian failure

<http://www.ncbi.nlm.nih.gov/m/pubmed/23902317/>

Ovarian insufficiency

<http://www.ncbi.nlm.nih.gov/m/pubmed/26125978/>

Autoimmune adverse events

<https://www.ncbi.nlm.nih.gov/pubmed/24468416/>

Quadrivalent human papillomavirus vaccine and autoimmune adverse events: a case-control assessment of the vaccine adverse event reporting system (VAERS) database.

<https://www.ncbi.nlm.nih.gov/pubmed/27406735>

Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature

<https://www.ncbi.nlm.nih.gov/pubmed/27503625>

Human papillomavirus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants.

<https://www.ncbi.nlm.nih.gov/pubmed/23902317>

Vaccine Injury Court Cases of Death caused by HPV vaccine

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

150+ deaths reported to VAERS as of June 2017

<https://wonder.cdc.gov/controller/saved/D8/D17F338>

PACKAGE INSERTS and TRIALS

Here's the broad FDA Package insert

<https://www.fda.gov/.../ApprovedProducts/ucm172678.htm>

Here's Merck's Gardasil 9 <https://www.fda.gov/.../%20ApprovedProducts/UCM426457.pdf>

Trial endpoints

“The outcome of most interest, prevention of cervical or other anogenital cancers, was not a reasonable endpoint for these trials. Trial size and duration would be unmanageable, since cancer is a rare outcome of persistent oncogenic HPV infection, and it usually takes more than a decade for cancers to develop fr

Award winning documentary on dangers of HPV vaccine.

In March 2018, a three-part documentary called “Sacrificial Virgins” was **honored with two awards** at Brisbane, Australia's Watchdog Film Festival – one for the being the festival's best film and the other in recognition of its investigation “in search of truth and justice.” In short, writer, director and filmmaker Joan Shenton released this documentary in order to shed much-needed light on the growing global concerns around popular HPV vaccines' safety: Gardasil and Cervarix.

Link to study confirming rise in cervical cancer of targeted vaccinated age group.
<https://changingtimes.media/2018/09/13/the-gardasil-controversy-as-reports-of-adverse-effects-increase-cervical-cancer-rates-rise-in-hpv-vaccinated-age-groups/>

Peer reviewed studies on dangers of HPV vaccine.
<https://www.learntherisk.org/hpv-studies/>

https://www.healthy-holistic-living.com/7-horrifying-facts-hpv-vaccine.html?utm_source=JV&utm_content=37224-SoJD

Mahalo for your time,
Martina K Dodson

Leonard G. Horowitz



DrLenHorowitz.com

Editor-in-Chief, [REDACTED]

Telephone [REDACTED]

November 5, 2018

RE: DECLARATION OF OPPOSITION TO HAWAII ADMINISTRATIVE RULES CHANGES TO TITLE 11, CHAPTER 157, "EXAMINATION AND IMMUNIZATION."

State of Hawaii
Department of Health, Disease Outbreak Control Division (DOCD),
1250 Punchbowl Street, Room 443, Honolulu, Hawaii 96813
Service by e-mail at: immunization@doh.hawaii.gov

Dear DOH Official(s):

I, LEONARD G. HOROWITZ, the Declarant, under pain of perjury of law, do hereby state and declare as follows:

- 1) I am an individual over the age of twenty-one (21) years, a former resident of Hawaii, current residing in the State of Nevada.
- 2) I represent myself here as an expert in public health, emerging diseases, cancer virology, vaccinology, medical history, and health science intelligence research and analysis.
- 3) I verify that the facts set forth in the attached manuscript titled, "New Evidence from Government Records Vets Fraud Tainting Vaccine Mandates, Two Nobel Prizes, and Three Virus "Discoveries," are true and correct to the best of my knowledge, and that the exhibits contained therein are true and correct copies of the originals in my possession.
- 4) I further declare that I am competent to testify as to the truth of the statements contained herein, and in the attached manuscript.
- 5) This sworn Declaration by e-filing serves you with Constructive Notice the neglect of which violates local and federal laws, your official duties, and places you at risk of liability and prosecution for torts and felonies detailed in the attachment, including but not limited to criminally negligent manslaughter.

FURTHER DECLARANT SAYETH NAUGHT

DATED: [REDACTED]

/s/ Leonard G. Horowitz

Leonard G. Horowitz,
Editor-in-Chief, Medical Veritas International, Inc.



New Evidence from Government Records Vets Fraud Tainting Vaccine Mandates, Two Nobel Prizes, and Three Virus "Discoveries"

by

Leonard G. Horowitz, DMD, MA, MPH, DNM (hon.), DMM (hon.)

Summary

New laws mandating viral vaccines for school children prompted this review of government records pursuant to the 2008 Nobel Prizes in Medicine given two researchers for their "discoveries" of two "novel" "sexually-transmitted" viruses reported to "cause" AIDS and cervical cancers. Both diseases emerged clinically during the mid-to-late 1970s at the same time herpes was exploding. These viruses, HIV/AIDS and HPV, the cervical cancer microbe, along with the sexually-transmitted hepatitis B virus ("HBV") also exploded simultaneously prompting dramatic changes in society and healthcare leading to current efforts to mandate vaccinations for school children for HPV, polio, hepatitis viruses, and more. New evidence of scientific fraud and fraudulent concealment of risks evidenced by government records, however, challenge these Nobel "discoveries," public health measures, vaccination mandates, and controvert false claims of safety tainting vaccines in general. New compelling, neglected, and concealed evidence from government-recorded lab virus experiments identifies a bio-medical virus-production racket influencing the media and sex industry that raises serious questions regarding the "General Acceptance" of vaccines as trustworthy. This paper critically examines this medical intelligence and serves constructive notice to officials pursuant to facts and evidence required for their dutiful administration of health policies to avoid liabilities and damage to citizens.

Background

In October 2018, this author, who has written extensively about government involvements in the vaccine industry, was asked to testify before the Hawaii Department of Public Health regarding [changes](#) to vaccination laws affecting school children and enrollments that includes a new "List of Required Vaccinations." Added therein for "required" "Kindergarten – 12th Grade Attendance" was the Hepatitis A and B vaccines and HPV vaccine. The later two are widely known to be "sexually transmitted diseases" not risking the lives of young children. A quick review of the package insert for Gardasil, (1) the HPV vaccine made by Merck, showed the mixing-up of two control groups, one receiving saline and the other amorphous aluminum hydroxyphosphate sulfate ("AAHS") adjuvant. The AAHS "can have a profound influence on the magnitude and quality of the immune response to HPV vaccine." (2) Combining the two control groups confounded the true assessment of risk. These two substantial discrepancies prompted this author to conduct the following retrospective study of HPV and its vaccine now on the government's mandatory list for "[vaccine preventable diseases](#)."

According to U.S. Government records published during the 1970s, the National Institutes of Health ("NIH") and National Cancer Institute ("NCI") assembled an international coalition to study cancer viruses for vaccine developments during the 1960s. The unprecedented collaboration was titled the Special Virus Cancer Program ("SVCP"). (3) This comprehensive international research group sought "candidate viruses" that "caused" cancers amendable to "preventative vaccines." This effort predated President Nixon's "War on Cancer" by a decade.

In 2008, the [Nobel Prize in Medicine](#) went to German virologist, Harald zur Hausen, for reportedly "discovering" the "*cause* of cervical cancer" in 1976--the "oncogenic human papilloma virus." (4) That "discovery" was made during the time the SVCP was administered by the NCI. So a review of its science pursuant to the emergence of HPV was reasonable. In 1983, zur Hausen reportedly "isolated" the new "tumorigenic HPV16 and 18 strains." The following year, In 1984, zur Hausen is reported to have "cloned HPV16 and 18 from patients with cervical cancer. These HPV types were found in about 70% of cervical cancer biopsies throughout the world," according to the press release issued by the Karolinska Institute--home to the esteemed Nobel Prize Committee. (4)

Public relations press officers for the KI and Nobel judges claimed zur Hausen's "discovery" and "theory" of cancer causation by a single "tumorigenic agent" flew in the face of "dogma." (4) Previously, the SVCP-NCI coalition held that "co-factors" for "co-carcinogenesis" involved multiple "risk factors." At the time, there was "General Acceptance" in science that this co-factor model was accurate. During the 1960s and 70s, there was General Acceptance that cancers were caused by myriad factors such as stress, risky lifestyles, biological and/or chemical agents, or their cumulative damage to human immunity resulting in cancers. This "immuno-suppression" model was the working premise of the SVCP and NCI's efforts. Chemicals, environmental factors including radiation, and biological agents such as viruses were known to cause genetic damage prompting cancers. Cells mutated forming tumors and malignancies from the overwhelming assaults to DNA/RNA and cell repair.

That was the "dogma" in medicine and science before zur Hausen postulated that there were certain types of *herpes viruses* that "caused" malignancies. (5) These DNA viruses, KI officials reported, "could exist in a non-productive state in the tumours." Zur Hausen's "specific searches for viral DNA" sourced his "discovery" that "led to characterization of the natural history of HPV infection, an understanding of mechanisms of HPV-induced carcinogenesis and the development of prophylactic vaccines against HPV acquisition." (4)

Simultaneously, Françoise Barré-Sinoussi and Luc Montagnier were likewise credited for having "discovered" the single "cause of AIDS--the human immunodeficiency virus ("HIV"). Virus production, the KI press reported, "was identified in lymphocytes from patients with enlarged lymph nodes in early stages of acquired immunodeficiency, and in blood from patients with late stage disease." (4) The KI's press release added, "They characterized this retrovirus as the first known human lentivirus [i.e., slow acting virus] based on its morphological, biochemical and immunological properties. HIV impaired the immune system because of massive virus replication and cell damage to lymphocytes. The discovery was one prerequisite for the current understanding of the biology of the disease and its antiretroviral treatment." (4)

KI's promotions neglected, however, this institute's important role in advancing these "discoveries" more than a decade earlier as a collaborator in the SVCP. It also neglected the reasons the Nobel awards committee [rejected Dr. Robert Gallo's](#) nomination. It had come to public knowledge that Montagnier, collaborating with Gallo in the SVCP, was defrauded by Gallo who had renamed the "French virus" "a couple of times," wrote one of Gallo's colleagues. (5) Apparently, Gallo acted to fraudulently conceal his use of Montagnier's virus to justify Gallo's claim of having discovered the AIDS virus before Montagnier.

Solid evidence has emerged since then from the Supreme Court's ruling on the "Daubert standard" concerning the trustworthiness of so-called "experts," and society's "General Acceptance" of science that is often untrustworthy. "General Acceptance" has evolved as a legal "term of art" that holds special meaning in this review. According to the "Daubert standard" established by the U.S. Supreme Court in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), previously-concealed facts are admissible as evidence against the General Acceptance standard.

SVCP records (3) evidence officials at the esteemed Nobel Prize committee's Karolinska Institute ("KI") in Sweden did fraudulently conceal their own agency's conflicting interests in zur Hausen's award. At the same time, the KI promoted and commercialized their cancer enterprise's investments in "single cause etiology virology," neglecting their own past efforts in early gene cloning, virus mutation experiments, pioneering lab technologies, vaccine research and developments, and subscription to the multi-factorial model of cancer.

In addition, the telling government records from the 1970s shown below detail the KI's involvements with the National Cancer Institute ("NCI") in recombining strains of DNA herpesvirus with strains of RNA tumor viruses isolated from patients worldwide with malignancies. The SVCP collaborators "transformed" benign or "latent" herpes viruses into model cancer triggers. These studies were well-justified in science's search for the causes and cures for cancer. (3)

But it is unreasonable and irresponsible that the General Acceptance in medicine, science, and society, heavily influenced by KI's esteemed Nobel Prize Committee, would be deprived of honest information affecting public health, consumer safety, and informed choice-making under these potentially catastrophic circumstances risking world health. Such silence imposed upon intelligence for concealed commercial interests begs redress. Science is presumed to be honest. The medical-legal community holds dishonesty as actionable and such fraudulent concealment or silence as obstructive to justice. The sequestering of the SVCP Progress Reports (3) is akin to "evidence tampering" in law. Denying due process in medical discovery risking and impacting millions of lives is arguably treasonous and genocidal.

These wrongdoings and "impressions of impropriety" are compounded by superficial dismissals of SVCP's questionable methods, materials, and outcomes.(6) The United States General Accounting Office ("USGAO") did this in an alleged "whitewashing" of this subject in 2002.(6) Rather than thank honorable colleagues, citizens and politicians who bravely encourage transparency, discovery, and open debate over these matters of vaccine safety and the cancer industry, the suspects have discouraged such dialogue. Vaccine industrialists argue in favor of censorship, and produce diversionary propaganda, in light of the risk to public confidence in the vaccine industry and corporate profits. (7)(8) Vaccine advocates argue open dialogue will undermine compliance with increasingly "mandated" vaccinations, and place the general population at risk. General Acceptance of vaccination policies is largely based on these dangerous positions evading critical facts. (7-9)

Equally troubling, to sustain the silence and combat opponents, certain vaccine industrialists have commissioned public relations firms, social media "trolls," and Internet "pseudo skeptics" to issue propaganda to protect the global enterprise. Like protection racketeers, these propagandists smear whistleblowers and authors who raise such debate. (10)(11)

The following facts evidence the seriousness of the science being concealed, following this author's 2001 report in *Medical Hypotheses*.(12) This new evidence from old records begs for scientific scrutiny and public discourse. These findings of facts show powerful conflicting interests have imposed the General Acceptance upon which government officials choose to act in advancing mandatory vaccinations. (13) A multinational corporate conspiracy to defraud the public and fraudulently conceal the laboratory creation of cancer-linked viruses HPV, HBV, and HIV is vetted by the public records examined below. (14) The impact on policy makers and the public gaining this medical-legal intelligence is considerable.

FACTS

1. Shown below are photocopies from the 1971 and 1972 SVCP, Progress Reports 8 and 9. These government records prove the program's initiation in 1962, the year Sarah Stewart and Bernice Eddy discovered the "SE [Stewart Eddy] polyoma virus" that was contaminating the Merck drug company's polio vaccines found associated with cancers.(3) These SVCP documents were published exclusively for internal review by collaborators in this program governed by the U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Division of Cancer Cause and Prevention, National Cancer Institute. (14) These documents were rarely found in medical libraries prior to this author's publication in 1996 of

Emerging Viruses: AIDS & Ebola--Nature, Accident or Intentional? wherein related documents are reprinted and analyzed. (15)

CONTRACTOR : Johns Hopkins University (71-2109)
ADDRESS : Charles and 34th Streets, Baltimore, Maryland 21218
PHONE : AC-301, Phone 955-3300
CNTRCT TITLE: Anti-tumor Reactivity in Patients With Leukemia/Lymphoma
DATES : 5/1/72 - 5/30/73
PRINC INVEST: Dr. George W. Santos, Department of Medicine
PROJ OFFICER: Dr. Ronald Herberman, Bldg. 10, Room 5B49, x-61366
Dr. Dan Rubin, Bldg. 37, Room 1B19, x-62760
SEGMENT : Immuno-Epidemiology
SEG CHAIRMAN: Dr. Paul Levine, Federal Bldg., Room 5A12, x-66085
CNTRCT SPEC : Mr. Fred Shaw, Federal Bldg., Room 11C03, x-61521

CONTRACTOR : Johns Hopkins University (71-2121)
ADDRESS : Charles and 34th Streets, Baltimore, Maryland 21218
PHONE : AC-301, Phone 955-3273
CNTRCT TITLE: Studies on Herpes Virus Antigens and Virions in Neoplastic Cells
From Cervical Carcinoma
DATES : 5/5/72 - 5/4/73
PRINC INVEST: Dr. Laure Aurelian, Division of Laboratory Animal Medicine
PROJ OFFICER: Dr. Charles Boone, Bldg. 37, Room 1C08, x-65141
Dr. Robert Manaker, Bldg. 37, Room 1B16, x-63323
SEGMENT : Developmental Research
SEG CHAIRMAN: Dr. Robert Manaker, Bldg. 37, Room 1B16, x-63323
CNTRCT SPEC : Mr. J. Thomas Lewin, Bldg. 37, Room 1A03, x-65025

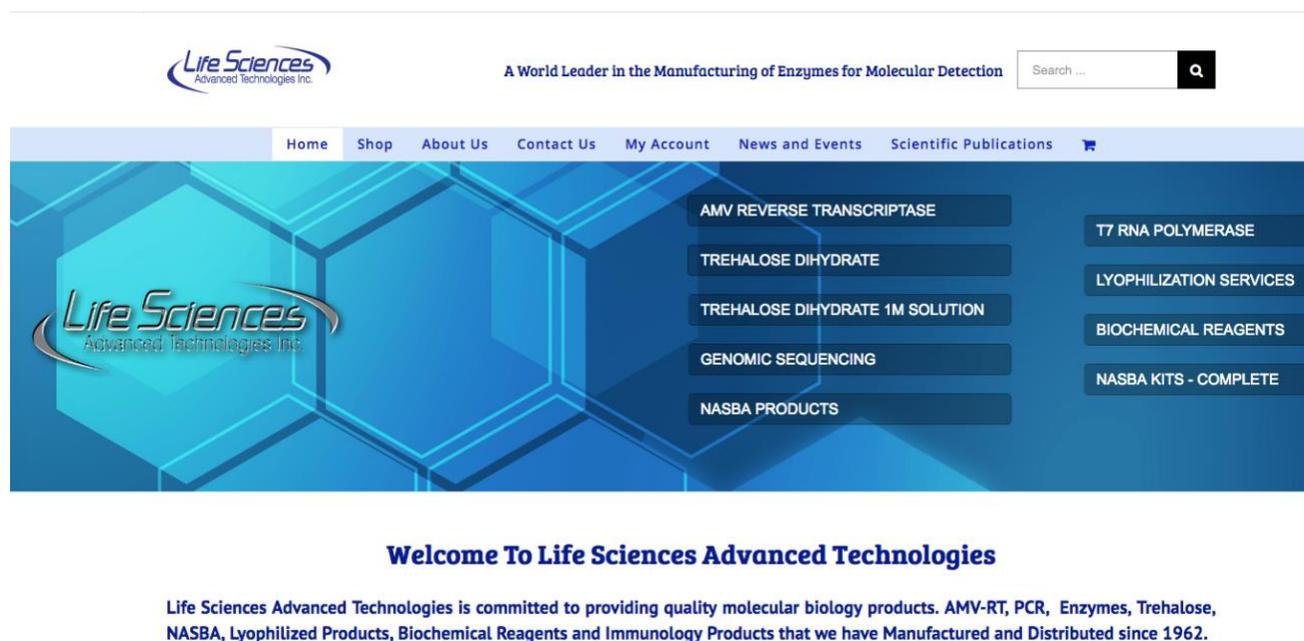
CONTRACTOR : Karolinska Institutet (69-2005)
ADDRESS : S-104 01, Stockholm 60, Sweden
PHONE : 235-480
CNTRCT TITLE: Studies of The Significance of Herpes-Type Virus in The Etiology of
Some Human Cancers
DATES : 4/9/72 - 4/8/73
PRINC INVEST: Dr. George Klein, Department of Tumor Biology
PROJ OFFICER: Dr. Charles Boone, Bldg. 37, Room 1C08, x-65141
Dr. Gary Pearson, Bldg. 37, Room 1B05, x-62600
SEGMENT : Developmental Research
SEG CHAIRMAN: Dr. Robert Manaker, Bldg. 37, Room 1B16, x-63323
CNTRCT SPEC : Mr. J. Thomas Lewin, Bldg. 37, Room 1A03, x-65025

CONTRACTOR : Life Sciences, Inc. (68-711)
ADDRESS : 2950 72nd Street, North, St. Petersburg, Florida 33710
PHONE : AC-813, Phone 345-9371
CNTRCT TITLE: Production and Maintenance of Germfree and Selected Reagent Grade
SPF Animals
DATES : 8/1/71 - 7/31/72
PRINC INVEST: Dr. Wendall Farrow
PROJ OFFICER: Mr. John Kvedar, Bldg. 41, VTPL, x-65341
Dr. David M. Howell, Bldg. 37, Room 1D21, x-61718
SEGMENT : Program Resources and Logistics
SEG CHAIRMAN: Dr. Jack Gruber, Bldg. 37, Room 1D15, x-61718
CNTRCT SPEC : Mr. Charles Fafard, Bldg. 37, Room 1A03, x-65025

CONTRACTOR : Life Sciences, Inc. (69-63)
ADDRESS : 2950 72nd Street, North, St. Petersburg, Florida 33710
PHONE : AC-813, Phone, 347-6191
CNTRCT TITLE: Studies on Marek's Disease as A Model For Herpesvirus-Associated
Oncogenesis
DATES : 8/1/71 - 7/31/72
PRINC INVEST: Dr. Jack W. Frankel
PROJ OFFICER: Dr. Gary Pearson, Bldg. 37, Room 1B05, x-62600
Dr. Michael Chirigos, Bldg. 37, Room 1D19, x-61478
SEGMENT : Developmental Research
SEG CHAIRMAN: Dr. Robert Manaker, Bldg. 37, Room 1B16, x-63323
CNTRCT SPEC : Mr. J. Thomas Lewin, Bldg. 37, Room 1A03, x-65025

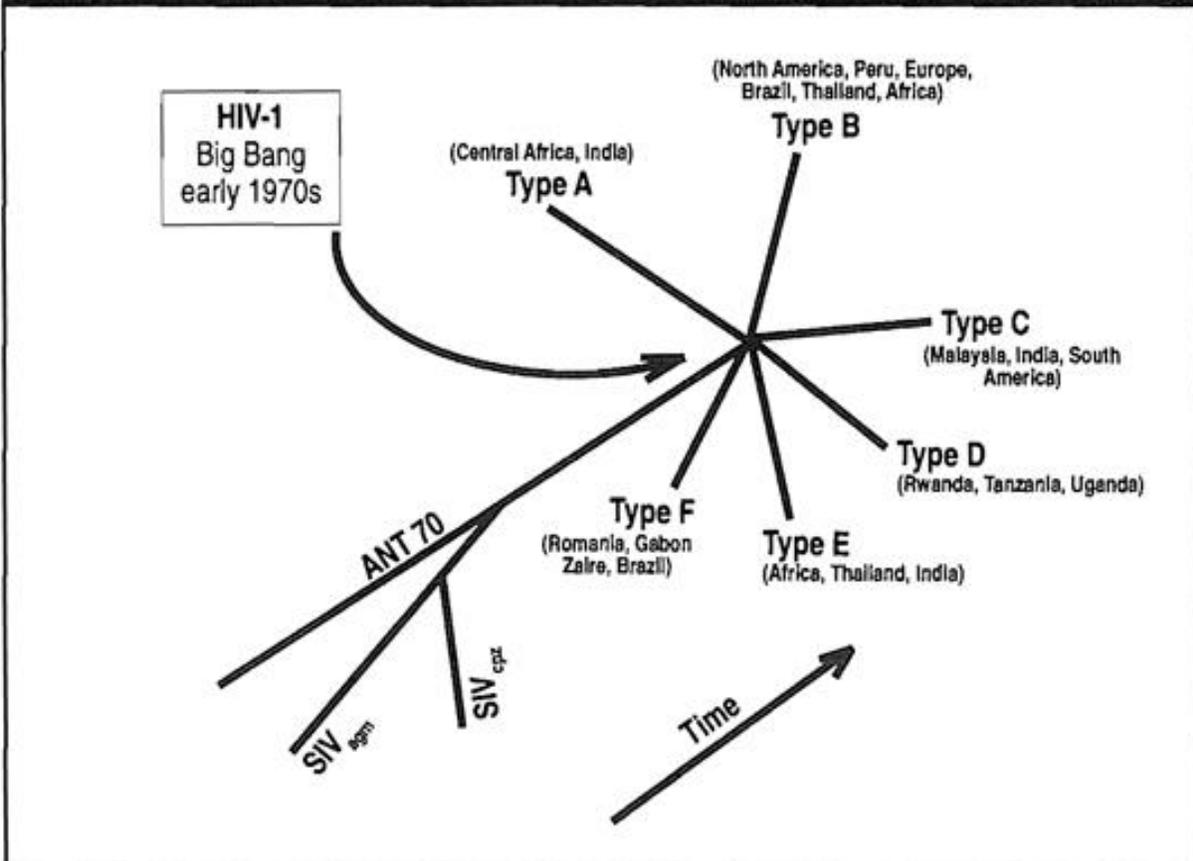
2. Page 410 of the SVCP-NCI Record #9 identifies the KI, below Johns Hopkins University (America's leading hepatitis B research enterprise). Above the KI listing is "Life Sciences, Inc"-- a private company that no longer exists after changing its name to Life Sciences Advanced Technologies, Inc. The "[Life Sciences Industry](#)" is the premier drug and vaccine (i.e., pharmaceutical and biotechnology) enterprise commonly called "Big Pharma." The Life Sciences company began in 1962. As stated above, this date coincides with the year the SVCP-NCI program began, immediately following the discovery of SE polyoma virus, renamed by Merck Drug Company's chief vaccine developer, Dr. Maurice Hilleman, the "SV40" virus.

There is General Acceptance today that SV40 contaminated the early polio vaccines and spread cancers worldwide.(3) From 1962 forward, Life Sciences evolved to become Big Pharma's leading provider of molecular biology products and services as proven by the screenshot below. It is also known that the Life Sciences Building at Los Alamos Laboratory is where Dr. Gerald Myers et. al. published his "Big Bang" theory of HIV/AIDS's emergence in the "early 1970s", based on the use of "genomic sequencing" products and services provided by this company. (15)



3. Shown below is Dr. Gerald Myers's "Big Bang Theory" of HIV/AIDS's emergence in the "early 1970s."(15) "The 'Patient Zero' theory smearing the gay community was determined to be false, largely due to Myers's discoveries. The alleged "hoax" of Randy Shiltz's "Patient Zero" diverted from the laboratory-origin vaccine-transmission theory corroborated by Myers's publications. Picked up by the mainstream press, the Patient Zero falsehood also diverted from Dr. Robert Gallo's NCI SVCP involvements that Gallo deceptively denied in 1996 at the XI International Conference on AIDS in Vancouver, WA. (The interchange between this author and Dr. Gallo is seen on the Internet [HERE](#). It has been viewed by more than 6 million concerned citizens).

Fig. 8.4. The Evolution of AIDS-like Viruses Based on Gene Typing and Molecular Epidemiology Theory as Presented By Dr. Gerald Myers



Chief of the special HIV Sequence Database AIDS Project at the Los Alamos National Laboratory, Myers stated "the preponderance of evidence still argues for an explosive event in the mid-1970s." Regarding the origin of AIDS, he insisted, HIV-1 evolved fairly recently from SIV_{agm}. SV40, the monkey virus Gallo and Bionetics researchers genetically altered in a series of steps and then cultured in human WBCs to alter its outer membrane characteristics, may have been a building block for HIV-2 and HIV-1. Additional evidence suggests that SIV_{agm} may have been man-made as well. Source: See chapter 6, and Myers, G, MacInnes K, and Myers L. "Phenogenetic Moments in the AIDS Epidemic," Chapter 12 in S. S. Morse, ed., *Emerging Viruses* (Oxford, Eng.: Oxford University Press, 1993).

4. The same year that zur Hausen first published his "discovery" of HPV, 1976, the first Gay Related Immunodeficiency Disease ("GRID") patient was "discovered" in New York City. (4) Curiously, those events also coincide with the 2-to-5 year "incubation period" for HIV to express itself in AIDS-related leukemia, lymphoma, and sarcoma lesions following system-wide immunosuppression. Accordingly, the first GRID/AIDS cases would have acquired their infections between 1971 and 1975. This too is consistent with Myers's determinations. (12)

5. Under "Major Findings" of the University of Pennsylvania's Wister group, the SVCP-NCI published in 1972 what was accomplished in 1971: "Rescue attempts have been initiated

employing human sarcomas and leukemias in a variety of combinations designed to activate latent viral genomes." (14)

6. The next SCVP-NCI Report #9 photocopy shown below, contains Johns Hopkins University's contract description. This, like the Hopkins "contact page" reprinted above, appears immediately above KI's contact page, and likewise, their contract description. The Hopkins' description states, "The contractor will compare antigens in cervical carcinoma cells with those induced in Hep[atitis-2 (B-type)] by Herpes simplex virus type I and II." From this it is clear that the Hopkins group triggered hepatitis B infections using Herpes simplex viruses. Then they compared these viral antigens from Herpes type I and II with the antigens found in cervical cancers.

7. The hepatitis B vaccine theory on HIV/AIDS's emergence, precisely as Myers's lab showed exploding in North America and Africa in the "early 1970s," derives from documented studies on gay men in NYC and central African sex workers, conducted between 1972-1974 by the Merck Drug Company--the maker of both the hepatitis B vaccine and the HPV vaccine (i.e., Gardasil) (12)

8. The National Institutes of Health Contract 71-2059 to Merck and Company, Inc. (shown below from Report #8) is titled "Study of Viruses in Human and Animal Neoplasia (i.e., cancer). Directed by Dr. Maurice R. Hilleman, and Robert Gallo's bosses at the NCI, Robert Manaker and Jack Gruber, the Objectives included developing "vaccines or other agents effective for the prophylaxis and therapy of human neoplasia of suspected viral etiology." In that contract, it states: "At the present time, investigations will be focused upon herpes-type (DNA) viruses and "B" and "C" type (RNA) particles. Parallel studies to evolve live attenuated and killed viral vaccines in appropriate animal model systems will be conducted." (14)

Merck and Company, Inc. (NIH-71-2059)

Title: Study of Viruses in Human and Animal Neoplasia.

Contractor's Project Director: Dr. Maurice R. Hilleman

Project Officers (NCI): Dr. Robert A. Manaker
Dr. Jack Gruber

Objectives: To perform investigations designed to develop vaccines or other agents effective for the prophylaxis and therapy of human neoplasia of suspected viral etiology.

Major Findings: This is a new contract.

Significance to Biomedical Research and the Program of the Institute:
Current data support the concept that a virus or viruses are the essential element in most animal tumors studied and that viruses are probably the necessary etiological component in human neoplasia, though expression may be greatly influenced and modified by host and environmental factors. If viruses are the essential element in human cancer, then prophylaxis by vaccines to prevent or minimize infection should provide a rational approach to cancer prevention. This could be accomplished by utilization of live or killed virus vaccines or possibly by vaccines of purified virion subunits.

Vaccines would obviously provide their greatest benefit in preventing infection with oncogenic viruses transmitted horizontally after birth. However, even the possible vertical transmission of hypothetical neoplastic agents does not rule out a potential benefit from vaccines. Nononcogenic viruses may function as essential cofactors in expression of neoplasia, and immunity against such secondary agents might prevent expression of the neoplastic state. Additionally, antibody or cellular immunity may be enhanced by vaccination with homologous virus in virus-dependent cancer. Obviously this research investigation is of fundamental importance to the goals of SVCP and can make unique contributions to the total program.

Proposed Course: The investigators will devote initial efforts to developing methods for propagation, purification, concentration and specific quantitation of candidate viruses suspected or shown to cause cancer in man. At the present time, investigations will be focused upon herpes-type (DNA) viruses and "B" and "C" type (RNA) particles. Parallel studies to evolve live attenuated and killed virus vaccines in appropriate animal model systems will be conducted. Particular attention will be given to developing and applying optimal methods for viral attenuation, viral inactivation, viral quantitation, vaccine safety assessment, and vaccine potency assay.

Date Contract Initiated: March 1, 1971

9. Furthermore, the SVCP contract NIH-71-2025 (from 1971 Report #8) shows Project Officer Dr. Robert Gallo officiating for the NCI. His collaborators explained their Objective of "Evaluation of long-term oncogenic effects of human and animal viral inocula in primates of various species. . . " Progress was reported on "An RNA-dependent DNA polymerase [reverse-transcriptase enzyme that characterizes HIV/AIDS and other "lentiviruses"] similar to that associated with RNA tumor viruses." Gallo's associates detected these enzymes "in human leukemic cells but not in normal cells. . . . The [reverse transcriptase] enzyme was isolated, purified and concentrated 200-fold, making possible its further characterization and study in relation to the leukemic process in man." (14)

Mind you, this was published in 1971, in Project Report #8. Accordingly, this research was done in 1970. And by 1972, vaccines to presumably prevent the AIDS-like viruses were tested in humans. This date corresponds perfectly with the 1972-74 hepatitis b vaccine trials conducted on the gay men in NYC as discussed below. (3) It also corresponds perfectly with Myers's "Big Bang in the early 1970s" implicating vaccine vectors. (12)(15)

BIONETICS RESEARCH LABORATORIES, INC. (NIH-71-2025)

Title: Investigations of Viral Carcinogenesis in Primates

Contractor's Project Directors: Dr. John Landon
Dr. David Valerio
Dr. Robert Ting

Project Officers (NCI): Dr. Roy Kinard
Dr. Jack Gruber
Dr. Robert Gallo

Objectives: (1) Evaluation of long-term oncogenic effects of human and animal viral inocula in primates of various species, especially newborn macaques; (2) maintenance of monkey breeding colonies and laboratories necessary for inoculation, care and monitoring of monkeys; and (3) biochemical studies of transfer RNA under conditions of neoplastic transformation and studies on the significance of RNA-dependent DNA polymerase in human leukemic tissues.

Major Findings: This contractor continues to produce over 300 excellent newborn monkeys per year. This is made possible by diligent attention to reproductive physiological states of female and male breeders. Semen evaluation, artificial insemination, vaginal cytology and ovulatory drugs are used or tried as needed.

Inoculated and control infants are hand-fed and kept in modified germ-free isolators. They are removed from isolators at about 8 weeks of age and placed in filtered air cages for months or years of observation. The holding area now contains approximately 1200 animals up to 5 years old. Approximately 300 are culled every year at a rate of about 25 per month. This is necessary to make room for young animals inoculated with new or improved virus preparations.

During the past year macaques were inoculated at birth or in utero with the Mason-Pfizer monkey mammary virus, Epstein-Barr virus, Herpesvirus saimiri, and Marek's disease virus. EB virus was given with immunostimulation and immunosuppression (ALS, prednisone, imuran). Australia antigen was given to newborn African green monkeys.

The breeding and holding colonies were surveyed for antibody to EBV. All breeders were positive and their offspring contain maternal antibody for several months. Colony-born offspring that have lost maternal antibody and are sero-negative will be surveyed periodically for conversion to the EB positive state.

An RNA-dependent DNA polymerase similar to that associated with RNA tumor viruses was detected in human leukemic cells but not in normal cells stimulated by phytohemagglutinin. The enzyme was isolated, purified and concentrated 200-fold, making possible its further characterization and study in relation to the leukemic process in man.

Significance to Biomedical Research and to the Program of the Institute:
Inasmuch as tests for the biological activity of candidate human viruses will not be tested in the human species, it is imperative that another system be developed for these determinations and, subsequently for the evaluation of vaccines or other measures of control. The close phylogenetic relationship of the lower primates to man justifies utilization of these animals for these purposes. Further study of altered transfer RNA and polymerase enzymes would determine their significance in neoplastic change and provide a basis for selection of therapeutic agents.

Proposed Course: Continuation with increased emphasis on monitoring and intensive care of inoculated animals to determine if active infection occurs, effects of infection, and degree of immunosuppression when used. Further studies of human neoplasms at a molecular level will continue.

10. Complicating matters is the 1969 Department of Defense Appropriations for 1970, Hearings Before a Subcommittee of the Committee on Appropriations House of Representatives, Ninety-First Congress, Part 5, Research, Development, Test and Evaluation, Dept of the Army. Tuesday, July 1, 1969, pg. 79, Washington: U.S. Government Printing Office record that states under the caption "SYNTHETIC BIOLOGICAL AGENTS":

Within the next 5 to 10 years, it would probably be possible to make a new infective microorganism which could differ in certain important aspects from any known disease-causing organism.s. Most important of these is that it might be refractory to the immunological and therapeutic processes upon which we depend to maintain our relative freedom from infectious disease. A research program to explore the feasibility of this could be completed in approximately 5 years at a total cost of \$10 million. (7) [i.e., \$2 million per year over 5 years.] (15)

11. The SVCP was administered by the Litton Bionetics company on behalf of the NCI and Life Sciences industry. (12)(15) This group was overseen by NCI Project Officer Robert Gallo during the early 1970s. During those years, Litton was contracted (under NIH 69-2060) to administer "Support Services for the Special Virus Cancer Program") Under that contract, Litton supplied the experimental viruses, monkeys, chimpanzees and vaccine reagents to SVCP collaborators, including the Merck Drug Company under Merck's contract (NIH 71-2059, titled "Oncogenic Research and Vaccine Development." (Copies of these contracts are downloadable by clicking: [Litton Bionetics and Merck Drug Co SVCP Contracts in 1971](#)). (14)

12. Litton received in the neighborhood of \$2 million per year over "5 years at a total cost of \$10 million" beginning in 1969, the year U.S. Government appropriations for "SYNTHETIC BIOLOGICAL AGENTS" descriptively and functionally identical to HIV/AIDS were authorized by Congress. The screenshot below excerpted from the *Congressional Record*, correlates with the express provisions described in Litton contracts. (See: Project Reports 8 and 9.)

SYNTHETIC BIOLOGICAL AGENTS

There are two things about the biological agent field I would like to mention. One is the possibility of technological surprise. Molecular biology is a field that is advancing very rapidly and eminent biologists believe that within a period of 5 to 10 years it would be possible to produce a synthetic biological agent, an agent that does not naturally exist and for which no natural immunity could have been acquired.

The dramatic progress being made in the field of molecular biology led us to investigate the relevance of this field of science to biological warfare. A small group of experts considered this matter and provided the following observations:

1. All biological agents up to the present time are representatives of naturally occurring disease, and are thus known by scientists throughout the world. They are easily available to qualified scientists for research, either for offensive or defensive purposes.

2. Within the next 5 to 10 years, it would probably be possible to make a new infective microorganism which could differ in certain important aspects from any known disease-causing organisms. Most important of these is that it might be refractory to the immunological and therapeutic processes upon which we depend to maintain our relative freedom from infectious disease.

3. A research program to explore the feasibility of this could be completed in approximately 5 years at a total cost of \$10 million.

4. It would be very difficult to establish such a program. Molecular biology is a relatively new science. There are not many highly competent scientists in the field, almost all are in university laboratories, and they are generally adequately supported from sources other than DOD. However, it was considered possible to initiate an adequate program through the National Academy of Sciences-National Research Council (NAS-NRC).

Source: Department of Defense Appropriations for 1970.

Hearings Before a Subcommittee of the Committee on Appropriations House of Representatives, Ninety-First Congress, Part 5 Research, Development, Test, and Evaluation, Dept. of the Army. Tuesday, July 1, 1969, page 79. Washington: U.S. Government Printing Office, 1969.

Standards of Review

A. "General Acceptance" of "Vaccine Preventable Disease," Safety & Efficacy Concerns

In the case of *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 US 579 (1993) the Supreme Court ruled that "'General acceptance' is not a necessary precondition to the admissibility of

scientific evidence under the Federal Rules of Evidence," (13) Furthermore, "Pertinent evidence based on scientifically valid principles will satisfy those demands." This decision, directed by the Court that was challenged by the defendant's falsification of evidence, encouraged judges, like members of the public and scientific community, to consider scientific intelligence "not generally-accepted." The Supreme Court made this decision based on determining that "reliable" scientific publications were not "reliable" due to their tainting by commercial interests.

B. Silence and Sequestering Science Presents a Pattern of "Most Persuasive" Evidence

The Supreme Court also ruled in the case of *United States ex rel. Bilokumsky v. Tod*, 263 US 149, 154 - Supreme Court 1923 that "Conduct which forms a basis for inference is evidence. [And s]ilence is often evidence of the most persuasive character." This is applicable to the "silence" of health officials and vaccine administrators regarding the risks, and the media's similar silence and censorship regarding risks of vaccine injuries, including autism and cancers commonly associated with herpes-type cancer virus contaminations in vaccinations, including herpes-B, simian cytomegalo virus, and the Epstein-Barr virus ("EBV") linked to cancers, including leukemias and lymphomas commonly produced by Gallo et. al. at Litton Bionetics during the SVCP between 1969 and 1973 as the above contract proves.

C. Criminally negligent manslaughter and assault with a deadly immunization practice

Under New York law, [PEN § 125.10](#) "A person is guilty of criminally negligent homicide when, with criminal negligence, he causes the death of another person. Criminally negligent homicide is a class E felony." Unlike Hawaii, any "vehicle" in New York, including a syringe, satisfies the element.

With respect to mandating vaccinations knowing harm often results, under [HI Rev Stat § 707-710 \(2013\)](#) (1) A person commits the offense of assault in the first degree if the person intentionally or knowingly causes serious bodily injury to another person. (2) Assault in the first degree is a class B felony. [L 1972, c 9, pt of §1; ree L 1986, c 314, §51; gen ch 1993]

In Hawaii, "negligence" is defined by Hawaii HRS §702-206(4). The actor should be aware of a "substantial and unjustifiable risk" with respect to the actor's conduct, the attendant circumstances, and the result of the actor's conduct. The actor's failure to perceive the risk must constitute a "gross deviation" from the standard of care that a law-abiding person would observe in the same situation. (See §702-206(4).) The offense is a class C felony. Negligence is indicated here, given knowledge that official justifications for administering risky vaccines are flawed and proven false by the aforementioned facts as further discussed below.

D. Fraud and Fraudulent Concealment in Virology and Vaccinology

Under Hawaii case law, the elements of *fraud* include: "(1) false representations were made by defendants, (2) with knowledge of their falsity (or without knowledge of their truth or falsity), (3) in contemplation of plaintiff's reliance upon these false representations, and (4) plaintiff did rely upon them." [Shoppe v. Gucci America, Inc.](#), 14 P. 3d 1049 – Haw: Supreme Court 2000.

And **fraudulent concealment** has been defined as “employment of artifice, planned to prevent inquiry or escape investigation, and misled or hinder acquirement of information disclosing a right of action. The acts relied on must be of an affirmative character and **fraudulent.**” [Lemson v. General Motors Corp., 66 Mich. App. 94, 97, 238 N.W.2d 414, 415 \(1975\)](#) quoting [De Haan v. Winter, 258 Mich. 293, 296, 241 N.W. 923, 924 \(1932\)](#). See also: *Au v. Au*, 626 P. 2d 173 – Haw: Supreme Court 1981.

E. Relevant federal standards

Title 18, U.S.C., § 241-Conspiracy Against Rights. “If two or more persons conspire to injure, oppress, threaten, or intimidate any person in any State, Territory, Commonwealth, Possession, or District in the free exercise or enjoyment of any right or privilege secured to him by the Constitution or laws of the United States, or because of his having so exercised the same they shall be fined under this title or imprisoned not more than ten years, or both.”

Title 18 USC § 1349 - Attempt and conspiracy. “Any person who attempts or conspires to commit any offense under this chapter shall be subject to the same penalties as those prescribed for the offense, the commission of which was the object of the attempt or conspiracy.”

Title 18 USC § 4 - Misprision of felony. “Whoever, having knowledge of the actual commission of a felony cognizable by a court of the United States, conceals and does not as soon as possible make known the same to some judge or other person in civil or military authority under the United States, shall be fined under this title or imprisoned not more than three years, or both.”

Title 18 Part I Chapter 96 § 1961 - “racketeering activity” means "(A) any act or threat involving . . . bribery [and/or] extortion, . . . or dealing in a controlled substance or listed chemical (as defined in section 102 of the Controlled Substances Act), which is chargeable under State law and punishable by imprisonment for more than one year; (B) any act which is indictable under any of the [many] provisions of title 18, United States Code. . . "

Discussion

It has come to the public's attention through respected science journals that the field of medicine has been substantially damaged by fraud committed by special interest groups benefiting "Big Pharma" or the "Life Sciences" industry. "(11)(

"Something has gone fundamentally wrong with one of our greatest human creations, "wrote Richard Horton, the editor of the esteemed *Lancet* wrote in 2015. (16) "The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness. As one participant put it, “poor methods get results”. The Academy of Medical Sciences, Medical Research Council, and Biotechnology and Biological Sciences Research Council have now put their reputational weight behind an investigation into these questionable research practices. The apparent endemicity of bad research

behaviour is alarming. In their quest for telling a compelling story, scientists too often sculpt data to fit their preferred theory of the world. . . ."

CONTRACTOR : Wistar Institute of Anatomy and Biology (71-2092)
ADDRESS : 36th Street at Spruce, Philadelphia, Pennsylvania 19104
PHONE : AC-215, Phone 222-6700, x-226
CNTRCT TITLE: Extraction and Characterization of Virus-Induced Transplantation
Antigen From Sarcomas and Leukemia
DATES : 2/1/72 - 1/31/73
PRINC INVEST: Dr. Anthony Girardi
PROJ OFFICER: Dr. James T. Duff, Bldg. 37, Room 1B22, x-65967

SEGMENT : Solid Tumor-Virus
SEG CHAIRMAN: Dr. Robert Huebner, Bldg. 37, Room 2D24, x-63301
CNTRCT SPEC : Mr. Thomas Porter, Bldg. 37, Room 1A03, x-65025

Dr. Horton concluded his heroic editorial stating, "The bad news is that nobody is ready to take the first step to clean up the system."

The aforementioned facts corroborate Dr. Horton's indictment of science and the forces undermining its legitimacy.

This author shares the honorable *Lancet* editor's sentiments, but disagrees with his conclusion. As this paper proves, there are many of us in science and medicine who have taken "the first step" only to be smeared and ostracized by the same enterprise mostly responsible for the fraud in science--the Life Sciences industry. (8, 11) I took that "first step" in 1996 with the publication of *Emerging Viruses: AIDS & Ebola--Nature, Accident or Intentional?* (15) Subsequently, I added a peer-reviewed scientific summary in *Medical Hypothesis* bravely financed and administered by the late unjustly smeared editor, David Horroban. (11) It is that "unclean system" that imposes illegitimacy in science along with "General Acceptance" of its falsehoods. (13) Abuse of the media, including "peer reviewed" publications by propagandists, incorporates the most well-studied science of all--behavioral science. This social engineering of General Acceptance imposes deadly consequences. In this instance, "mandatory vaccinations" foreshadows side-effects from the vaccines for HPV, hepatitis, polio, and other GMO-laced injections. This poisons bloodstreams, damaging brains, and induces cancers according to empirical evidence witnessed worldwide. In the United States, for instance, an explosion of need for special educators now burdens the economy attributable to skyrocketing rates of autism among mercury-poisoning victims. All while health officials excuse the association as "unproven" and "debunked" "conspiracy theory." (17)

A. The Facts Controvert Earlier AIDS-Origin Theories: HIV, HPV and HBV are Lab Viruses Engineered for Vaccine Research and Developments According to the NCI and NIH's Neglected SVCP Records

Confusion over Koprowsky's and the Wistar Institute's alleged role in the AIDS outbreak exemplifies the problem with earlier AIDS-origin theories. Koprowsky was falsely accused by *Rolling Stone* magazine for causing the AIDS outbreak. That indictment was later retracted. But

the scandal rocked medicine. It indicted the Salk vaccine's transmission of SV40 cancer virus and polio.

Sabin's OPV was also confirmed to have spread SV40-related cancers. These transmissions occurred during the 1950s during Koprowsky's watch.(3) That evidence, compounded here, corroborates Bernice Eddy's warning that pandemic cancers would certainly come following SV40's widespread transmission through Merck's tainted polio vaccines produced by both Salk and Sabin.

Accordingly, author Edward Hooper was not far off the mark in *The River: A Journey to the Source of HIV and AIDS*. He conjectured that the Wistar Institute's research had contaminated Albert Sabin's oral polio vaccine ("OPV") carrying chimpanzee simian immunodeficiency virus ("SIVcpz") that is the closest relative to HIV in the primate world. But Hooper's critics, many "pseudo-skeptics" paid to protect the status quo by muddling media, promptly "debunked" Hooper's claimed association after confirming that "monkey cells—not chimpanzee cells" were used by Koprowsky.(9) The "smoking gun"--the *chimpanzee* vector--in the origin of HIV/IDS mystery was still missing. It is no longer. It is vetted below.

The facts seriously implicate the Litton/SVCP cohort for the 1976 clinical emergence of GRID/AIDS ("HIV"), the contemporaneous creation of the liver cancer virus hepatitis B ("HBV"), and the cervical cancer virus--human papilloma virus ("HPV"). These strains and types of viruses were commonly mutated and tested by the Litton/SVCP NCI-NIH contractors years before their announced discoveries by men who concealed their knowledge of these most substantive facts.

This widespread neglect of Litton's actions, like this author's publications, (3; 8) evidences a vaccine racket and reckless concealment of medical history. The press today, biased by conflicting interests more than ever, has obscured the General acceptance among cancer virologists that vaccines have been vectors for communicable diseases. But this doesn't sell vaccines, advertising space *WIRED*, or inspire public confidence.

Dr. zur Hausen too, like Koprowsky, worked at the Wistar Institute in Philadelphia. Wistar, along with the Karolinska Institute, is equally suspect as SVCP collaborators, as is Montagnier's 1970s work in collaboration with Dr. Robert Gallo. These historic associations are grounds for reconsidering these researchers' 1980s "discoveries."

Otherwise, It is unreasonable to neglect or excuse Montagnier's and Gallo's aversion to discussing their roles in the SVCP. To date there is only *silence* and *censorship* concerning the high probability that the "French specimen" sourced, like Gallo's HTLVs, from Litton's SVCP-NCI-NIH Contract 71-2025. That contract, shown above, proves these researchers isolated "RNA-dependent DNA polymerase in human leukemic tissues" in the late 1960s or early 1970s. This predates by 13 years Montagnier's "discovery" of this kind of unique, never-before-seen, retrovirus enzyme. (You need the virus to extract its enzyme.) It is unreasonable to believe that no investigator in Litton's lab, allied with Gallo's group at the NCI, would not have isolated similar "lentiviruses"/retroviruses by 1972 as their contract proves they were commissioned to do.

During the past year macaques were inoculated at birth or in utero with the Mason-Pfizer monkey mammary virus, Epstein-Barr virus, Herpesvirus saimiri, and Marek's disease virus. EB virus was given with immunostimulation and immunosuppression (ALS, prednisone, imuran). Australia antigen was given to newborn African green monkeys.

Further evidencing Litton's and Gallo's important roles in the origin of HIV/AIDS from the first hepatitis B vaccine trials is the contracts shown above and below. NIH-71-2025, shown above, states, "Australia antigen was given to newborn African green monkeys. "Australia antigen" ("AuAg") reported in the SVCP publications was the ***first known agent causing hepatitis***. "*AuAg*" was later re-named "*hepatitis B virus*" and "*HBV*." 12)(14)(15) Shown here is Litton's official statement that corroborates Dr. Maurice Hilleman's recorded statement, "We [at Merck] brought in the African greens. We didn't know we were importing AIDS virus at the time." (7)

Litton Bionetics was certainly the supplier of these viruses to Merck and the other SVCP collaborators. Litton exported the test animals, especially monkeys and chimpanzees from their colonies overseas to Merck in New York under contract number NIH-69-2060 --- "Support Services for the Special Virus Cancer Program," as shown below.

This record also proves viral recombination studies using known cancer triggers, including "EBvirus with immunostimulation and immunosuppression" coupled with hepatitis B viral experiments; and in the same lab, the RNA-dependent DNA polymerase (i.e. "reverse-transcriptase AIDS-virus enzyme) was studied with retrovirus recombinations.

BIONETICS RESEARCH LABORATORIES (NIH-69-2160)

Title: Support Services for the Special Virus Cancer Program.

Contractor's Project Director: Dr. Robert C. Y. Ting

Project Officer (NCI): Dr. George Todaro

Objectives: To provide a laboratory that will collect, process and test specimens from human and animal sources suspected of containing virus associated antigens or antibodies, and to provide other virology, immunology or cell culture services as required.

Major Findings: Services and resources provided in close collaboration with NCI investigators during the past year include: (1) biochemical studies of cell growth regulation with Dr. Todaro; (2) attempts to isolate a human cancer virus with Dr. Bassin; (3) tests for EBV antigens for Dr. Levine; (4) immunological tests of leukemia patients, including studies of twins, for Dr. Levine; (5) CF tests for gs antigens for Dr. Hellman; (6) membrane antigen preparation from human tissue for Dr. Herberman; (7) collection of familial cancer sera and histories for Dr. Fraumeni; (8) tissue and serum bank for Dr. Levine et al; (9) American Burkitt registry and follow-up; and (10) data processing with Dr. Waggoner.

When abortively transformed cells containing SV40 genome were re-infected with SV40, they had a lower rate of transformation than cells without the genome; thus, the presence of SV40 did not confer immunity.

Fetal thymus cells of dogs were cocultivated with irradiated human sarcoma cells. The dog cells showed degeneration and transformation (chromosome analysis now being done).

Rhesus cell cultures infected with Mason-Pfizer virus showed evidence of transformation and caused regressing tumors when subsequently inoculated into newborn rhesus monkeys.

Cellular immunity studies of leukemia patients, using lymphocyte cytotoxicity and cytotoxicity inhibition tests, suggest that cells of such patients possess leukemia-associated antigens and that a widespread antigen system may be operative in human and animal tumors.

Significance to Biomedical Research and the Program of the Institute: This contract laboratory provides an opportunity for a systematic, large-scale effort to detect viruses and/or viral antigens in human tumor materials (particularly leukemias and sarcomas), using tissue culture, immunological, biochemical and EM techniques. This is a major objective of the SVCP.

Proposed Course: It is proposed that this contract will continue to supply the necessary supportive services required to meet the needs of the SVCP.

Date Contract Initiated: June 27, 1969

B. Litton Bionetics' Supply Contracts and the Outbreak of HIV, HBV and HPV

Constructive notice is given here to health officials, the scientific community, and corporate-controlled media, regarding the central role of Litton Bionetics's NCI-SVCP supply contracts, especially NIH-69-2160, in the outbreaks of HIV, HPV, and HBV (i.e., hepatitis B virus) and the ongoing risks of inducing cancers through vaccinations presumed "safe."

This author was the first to evidence Litton's *chimpanzees* were used to grow the viruses needed for the first hepatitis B vaccines manufactured by Merck and tested on homosexuals considered at high risk of hepatitis in NYC between 1972 and 1974. (12)(15) Additional groups targeted for this trial were native Americans, kidney dialysis patients, black women (presumably sex workers) in Central West Africa, and Willowbrook State School for the mentally ill on Staten Island in New York. (12)(15) Co-investigators represented the U.S. Army, the New York University Medical Center, and the New York Blood Bank. (12)(15) Financing this commercial enterprise were the real-parties-in-interest in the pharmaceutical and defense industries. Suspects above the rank of "principle investor" included blood-banking officials and leading stockholders in the companies profiting from vaccine manufacturing and blood-banking. Purcell's 1976 grant application shown above makes these facts known.

Most relevant to AIDS and its origin from Litton and SVCP labs, these studies predate by more than a decade the "detection" and "isolation" of the precise cancer complex *pathognomonic* for AIDS. (A *pathognomonic sign* is a particular sign whose presence means that a particular disease is present beyond any doubt.) This sign is also pathognomonic of AIDS's origin from Litton's lab and/or collaborating SVCP labs involved in the suspect hepatitis B vaccine trials. This cause-effect reasonable conclusion is based on the Litton group's contract statement that they isolated and used "viral antigens" from "human tumors" "particularly leukemias and sarcomas" the combination of which is pathognomonic for AIDS. And they did so by 1972, 10-years before Montagnier (and falsely Gallo too) "discovered" the AIDS virus.

Litton Bionetics's early 1970s contracts also show common studies done in cancer vaccineology and molecular biology with Herpes -type viruses. Extracting, cloning, and mutating genetic material from herpes viruses risked transmitting or cross-contaminating subjects involved in Litton and Litton's privies-in-interest's leukemia and sarcoma studies. The SVCP contractors received their supplies of these products from Litton under their contract (NIH-69-2160). Through such collaboration with zur Hausen and his colleagues in Philadelphia, and Montagnier's colleagues in France, it is most likely zur Hausen "discovered" another herpes-type DNA virus that had been mutated during the SVCP that zur Hausen simply named or re-named "HPV".

C. The Common Practice of Renaming Viruses Confusing Who Discovered What

It is public knowledge that SVCP investigators commonly named or renamed viruses for fame and fortune. For example, it is widely known in virology that Dr. Hilleman at Merck renamed the "Stewart-Eddy polyoma virus (SE-polyoma)" to "SV40". The two women discovered SE polyoma in Merck's polio vaccine in 1962. Then there was the Nobel-thirsty Gallo, snubbed by the KI's Nobel Prize committee for doing worse with Montagnier's "discovery."

There is "General Acceptance" that Montagnier supplied Gallo with HIV for Gallo's NCI studies. Serious doubts about this "story" are raised, however, by the aforementioned contractual evidence, including the dates of such viral trafficking. "It was the French virus that Gallo's lab used for their research," the corporate-controlled media alleged.(5) "Gallo's lab notes, obtained by the *Chicago Tribune*, show that the French virus was renamed a couple of times, apparently to hide the fact that it was being used. Gallo later claimed that the French virus didn't grow."(5) Given the general agreement of Gallo's untrustworthiness, it is unreasonable to believe he didn't falsify his lab notes and this entire story "obtained by the *Chicago Tribune*" that is infamous for fabricating stories.(5)

This reasonable objection follows not only the aforementioned contractual evidence, but also the objections raised by Robert Strecker, M.D., Ph.D., published in *Emerging Viruses: AIDS & Ebola--Nature, Accident or Intentional?* Strecker was interviewed by this author in 1996. He was the first American medical scholar who raised the lab virus AIDS-origin theory. Strecker stated that Montagnier, while working with Gallo at the NCI, discovered that "Epstein-Barr-infected T-cells will just churn out AIDS viruses day after day. . . ." Strecker explained this discovery was necessary to overcome Gallo's problem of producing enough HTLV- III viruses (HIVs) "to make enough antibody, " because as the *Chicago Tribute* story stated, "the French virus didn't grow." Regarding this scandal--the French-American AIDS fracas--Strecker opined, "That's all a lot of bull, because they both had the virus, and they both knew what they were doing from day one."

D. Bionetic's Little Known "Classified" History, Fraudulent Concealments, and Red Flags Urging Reconsideration of the SVCP's Origin of Sexually-transmitted Diseases

Major United States Army Biological Weapons Contractors for Fiscal Year 1969

Mr. Mahon. List for the record the major contractors and the sums allocated to them in this program in fiscal year 1969.
(The information follows:)

The following list contains the major contractors and amounts of each contract.

<i>Contractor</i>	<i>Fiscal year 1969</i>
Miami, University, of Coral Gables Fla.....	\$645, 000
Herner and Co., Bethesda, Md.....	518, 000
Missouri, University of, Columbia, Mo.....	250, 000
Chicago, University, of Chicago, Ill.....	216, 000
Aerojet-General Corp., Sacramento, Calif.....	210, 000
Bionetics Research Laboratories, Inc., Falls Church, Va.....	180, 000
West Virginia University, Morgantown, W. Va.....	177, 000
Maryland, University of, College Park, Md.....	170, 000
Dow Chemical Co., Midland, Mich.....	158, 000
Hazelton Laboratories, Inc., Falls Church, Reston, Va.....	145, 000
New York University Medical Center, New York, N.Y.....	142, 000
Midwest Research Institute, Kansas City, Mo.....	134, 000
Stanford University, Palo Alto, Calif.....	125, 000
Stanford Research Institute, Menlo Park, Calif.....	124, 000
Pfizer and Co., Inc., New York, N.Y.....	120, 000
Aldrich Chemical Co., Inc., Milwaukee, Wis.....	117, 000
Computer Usage Development Corp., Washington, D.C.....	110, 000
New England Nuclear Corp., Boston, Mass.....	104, 000

Source: Department of Defense Appropriations For 1970: Hearings Before A Subcommittee of the Committee on Appropriations House of Representatives, Ninety-first Congress, First Session, H.B. 15090, Part 5, Research, Development, Test and Evaluation of Biological Weapons, Dept. of the Army. U.S. Government Printing Office, Washington, D.C., 1969, p. 689.

As shown above, Litton Bionetics was the sixth leading biological weapons contractor in 1969. Robert Gallo served as the NCI's Project Officer overseeing Litton's contract, NIH-71-2025. Gallo also served in the SVCP as the Developmental Research Segment co-director. As mentioned, Litton Bionetics was the main cancer research supplier to the NCI and SVCP contractors. Litton supplied viruses including retroviruses, experimental reagents, and test animals including *chimpanzees*.(12)(15) The SVCP Progress Report #8 makes clear that Gallo's collaborators at Litton Bionetics colonized several species of monkeys, and supplied cancer researchers and vaccine developers worldwide new experimental viruses, and monkey cell lines. Life Science, Inc. supplied enzymes and other supplies needed for vaccine research too.

Litton Bionetics's contract followed closely the Stewart-Eddy 1962 discovery of cancers being spread through Merck's polio vaccines. Nearly a decade later, the NIH and NCI published Progress Report #8 that detailed Gallo's leadership in the 71-2025 contract that began that same year, in 1962. The 1971 contract, titled "Investigations of Viral Carcinogenesis in Primates," was

expanded in 1972 as the first hepatitis B vaccines were injected into the Willowbrook children and gay volunteers in New York. (See also SVCP Progress Report 9, p. 195).(1)

Litton clearly supplied the Merck Drug Company with mutated viruses for vaccine studies in their contract 71-2059. Litton also supplied Merck with the monkeys and chimpanzees used to culture strains of hepatitis B viruses used by Johns Hopkins researchers as well. Through Merck and the SVCP, Litton's investigators were supplying U.S. Army officials too, as well as the New York University Medical Center and Saul Krugman with experimental materials that were used in testing these agents on the mentally-retarded children. Litton's chimps were used to grow the new viruses for this testing, including the new "hep B vaccine" ("AuAg" Australian antigen) viruses as you can read above. The gay men victimized were largely living in Greenwich Village. Merck's advertisements used to attract homosexual volunteers can still be found online.(15)

All the above has been fraudulently concealed and/or recklessly neglected by willfully-blind officials and the complicit "fake news" media.

Genetic engineering at cooperating SVCP-NCI labs of viruses that were functionally identical to HIV and HPV a decade before their alleged discoveries provides adequate evidence for reasonable concern and reconsideration of this entire matter. Add to this evidence of reckless neglect the clinical emergence dates of these two diseases--HIV/AIDS and HPV cervical cancers both in 1976; the common sexually-transmitted disease connotation as with HBV also manufactured and tested at that time; the satisfied incubation period for HIV/AIDS--2-to-5-years between the very first hep B vaccine trials in 1972-74, and zur Hausen's collaboration with the Americans through Wistar and KI in the SVCP, (12)

Now add the red flag of corroborating evidence of Myers's genetic identification of different strains of HIV, Type A and Type E, emerging contemporaneously in Africa and NYC at the precise locations of the HB vaccine experiments. Add further the precise set of cancers studied, including the pathognomic leukemia-lymphoma-sarcoma lab-engineered disease complex synchronously emerging while cervical cancer's from HPV were reported emerging at the height of the herpes fright.

The KI's 1969 contract NIH-69-2005 was titled "Studies of The Significance of Herpes-Type Virus in The Etiology of Some Human Cancers." This SVCP Progress Report #9 covered the "4/9/71 - 4/8/73" period. The Segment Chairman was "Dr. Robert Manaker"--Robert Gallo's supervisor at the NCI. Manaker was key program manager as Chairman of the "Developmental Research Segment" of the SVCP that included several prominent names in developmental virology including Dr. Anthony Girardi and the University of Pennsylvania's Wistar Institute. (See p. 6, of the SVCP, Progress Report #9.) These proven associations tie the relatively small group of suspects together in what appears to be a cancer virology racket. This racketeering enterprise is equally suspect for administering fraudulent concealments for unjust enrichment. The SVCP-KI contract shown below convincingly documents and confirms the statements made by Strecker about the importance of "Montagnier's alleged discovery"--that EBV from Burkitt tumors added to T-lymphocytes will churn out antigens and viruses, such as we see with AIDS.

Proposed Course: The contractor will compare antigens in cervical carcinoma cells with those induced in Hep-2 by Herpes simplex virus type I and II. Work will continue on the characterization of HSV-2 antigens present in exfoliated cancer cells from patients with cervical cancer.

Date Contract Initiated: May 5, 1971

Current Annual Level: \$92,000

KAROLINSKA INSTITUTE (NIH-69-2005)

Title: Studies on the Significance of Herpes-type Virus in the Etiology of Some Human Cancers

Contractor's Project Director: Dr. George Klein

Project Officers (NCI): Dr. Charles W. Boone
Dr. Gary R. Pearson

Objectives: (1) To obtain additional data on EB virus-host interactions. (2) To investigate host immune responses to tumor antigens. (3) To study the regulation of C-type virus expression in defined systems. (4) To investigate cell mediated tumor immune reaction mechanisms in vitro and in vivo.

Major Findings: EBV related research: membrane antigens, early antigens and virus capsid antigens mediated by EBV have been studied in established lymphoblastoid cell lines. Inhibitors such as mitomycin C increase the amount of antigens detected by immunofluorescence. Mouse lymphoblastoid cell hybrids have made it possible to determine whether the presence of EBV DNA is dependent on one or several chromosomes. BUdR labeled cells were super-infected with tritiated thymidine labeled virus and the heavy cell DNA was recovered and examined for associated EBV. No evidence of integrated EBV genome was found. The incubation of tumor cells with serum from patients with lipo-, fibro-, osteo-, and neuro-sarcoma inhibited the stimulation in one autologous lymphocyte-fibrosarcoma combination.

Significance to Biomedical Research and the Program of the Institute: A major effort of the Special Virus Cancer Program has been the study of the viral involvement in the etiology and course of Burkitt's tumor in man. Research on the relationship between EBV infection and the onset of Burkitt tumor, the development of EBV-coded antigens in infected cells, and the analysis of the immune response to Burkitt tumor is therefore highly relevant to total program.

Proposed Course: The contract effort will continue essentially as described above.

Date Contract Initiated: April 9, 1968

Current Annual Level: \$90,000

E. Solid Evidence of a "Conspiracy of Silence" and the "Smoking Gun": Compounding Evidence of a Racketeering Enterprise in Vaccinology

"Conduct which forms a basis for inference is evidence. Silence is often evidence of the most persuasive character," wrote the Honorable Chief Justice Louis Brandies in *United States ex rel. Bilokumsky v. Tod*, 263 US 149, 154 - Supreme Court 1923.

Shall the scientific community neglect the aforementioned red flags, links between the SVCP cooperating labs and zur Hausen's and Montagnier's little-discussed work in the US researching novel virus subtypes profiting private interests in the NCI and Life Science industry? Shall we neglect reconsidering these facts, the cumulative damage from these diseases, and their true causes revealing potential cures? Because if the true causes are being withheld, as Strecker opined, then the true cures may be similarly concealed.

Ethical practice compels reconsidering these matters by a special "independent" investigative committee and/or grand jury.

Diverting from "silence as evidence," the media has offered, muddled, and debunked "conspiracy theories" as defective indictments. This media silence/negligence and counter-intelligence diverts from the facts and evidence published here and previously. (12) This author's proofs have never been "debunked", only ignored, silenced or censored.(12)(15)(18) This author has diagnosed this scheme of mainstream media hashing of facts, including diversions and obfuscations in the corporate-controlled social media. The pattern and practice of such malfeasance serves as a "protection racket" for the multi-trillion-dollar biotechnology and vaccinology industry. Millions of dollars spent to commission "pseudo-skeptics" and "debunkers" to write Op/Ed pieces and online slams is a drop in the bucket for Big Pharma. This allegation is proven by Big Pharma having been caught financing online "trolls" to supplement battalions of propagandists and PR firms issuing "fake news" and false commentaries as documented in the "Best Film-2016" *UN-VAXXED: A Docu-commentary for Robert De Niro*. (19) None of the skeptics address the "smoking gun" or "missing link"--the chimpanzees.

There is "General Acceptance" in the scientific community that *chimpanzees* are the missing link to HIV. Yet, health officials and vaccine proponents have avoided and evaded their duties to examine the scientific evidence presented by this author in 1996 and repeatedly thereafter. The irrefutable evidence proves chimpanzees were used by the New York collaborators to develop the suspect hepatitis B vaccines given to the many victims beginning in 1972. In the follow-up large scale San Francisco study in 1978, according to Dr. Paul O' Malley who headed up the Merck/CDC hepatitis B study, "an inordinate number of GRID victims" received the suspect vaccines. "Of the first twenty-four GRID cases in San Francisco, in fact, eleven were in the hepatitis B cohort." (15)(21)

In 1976, at the time the first GRID cases were emerging in NYC, Robert Purcell, the Head of the Hepatitis Viruses Section of the National Institute for Allergies and Infectious Diseases ("NIAID") published repeatedly on the use of chimpanzees to culture and reproduce the new strains of HBV needed for human testing after the chimpanzees survived the initial injections. Below is a photocopy of Purcell's grant application to extend trials from New York to San Francisco.

The grant application states, "A newly recognized clinical syndrome, type non-A, non-B hepatitis has been further defined and attempts to identify an etiologic agent intensified through transmission studies in chimpanzees." (12)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)		U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 AI 00026-11 LID
PERIOD COVERED October 1, 1977 through September 30, 1978			
TITLE OF PROJECT (80 characters or less) Laboratory and Epidemiologic Studies of Viral Hepatitis Agents			
NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT			
PI: R.H. Purcell		Head, Hepatitis Viruses Section	LID, NIAID
Y. Moritsugu		Visiting Scientist	LID, NIAID
V. McAuliffe		Research Associate	LID, NIAID
Y. Shimizu		Visiting Fellow	LID, NIAID
G. Hess		Guest Worker	LID, NIAID
J. Slusarczyk		Visiting Fellow	LID, NIAID
L. Mathiesen		Guest Worker	LID, NIAID
Other:			
P. Holland, H. Alter (CC, Blood Bank, NIH)		L. Barker, D. Lorenz,	
K. Soike (Delta Primate Center)		E. Tabor, R. Gerety (FDA)	
J.L. Gerin (MAN Laboratory)			
W. London (NINCDS)			
J. Maynard (CDC)			
COOPERATING UNITS (if any) None			
LAB/BRANCH Laboratory of Infectious Diseases			
SECTION Hepatitis Viruses Section			
INSTITUTE AND LOCATION NIAID, NIH, Bethesda, Maryland			
TOTAL MANYEARS: 99/12	PROFESSIONAL: 51/12	OTHER: 36/12	
CHECK APPROPRIATE BOX(ES)			
<input checked="" type="checkbox"/> (a) HUMAN SUBJECTS <input type="checkbox"/> (b) HUMAN TISSUES <input type="checkbox"/> (c) NEITHER			
<input type="checkbox"/> (a1) MINORS <input type="checkbox"/> (a2) INTERVIEWS			
SUMMARY OF WORK (200 words or less - underline keywords)			
This project consists of continuing studies of the <u>chemistry</u> , <u>structure</u> , <u>epidemiology</u> , <u>immunology</u> and <u>pathology</u> of the <u>human hepatitis viruses</u> . The goal of such studies is the control of human viral hepatitis by application of the most appropriate methods, including <u>active and passive immunization</u> , <u>chemotherapy</u> and interdiction of spread of the viruses. Progress: The biophysical and biochemical characterization of hepatitis A viral antigen has begun, and studies of the immunopathology of hepatitis type A in non-human primates, using defined pools of virus, are in progress. An inactivated subunit <u>vaccine</u> for hepatitis type B has been developed and is undergoing extensive tests of safety and efficacy in chimpanzees and man. A third hepatitis B antigen, <u>e</u> antigen, is being characterized and its relationship to infectivity is being explored. Evidence that populations of hepatitis B viruses may contain defective interfering particles has been obtained, and this finding is being utilized in renewed attempts to isolate the virus. A newly recognized clinical syndrome, type non-A, non-B hepatitis has been further defined and attempts to identify an etiologic agent intensified through transmission studies in chimpanzees.			
Source: USDHEW. <i>Virology: Volume 4—Control of Viral Infections. NIAID Task Force Report.</i> Bethesda, MD: Public Health Service, National Institutes of Health (NIH) 79-1834, 1979, p. 20-65.			

[P]reparations of high density and intermediate density HB virions [viruses] are being purified . . . under conditions of high containment in Dr. Gerin's laboratory. [The same Dr. Gerin who prepared the vaccines for experimentation on New York's homosexual population]. These preparations are being aliquoted and titered [fractioned and standardized] for infectivity in chimpanzees; they will be used for attempts to isolate HBV in a number of tissue culture cell lines.

Cell lines that can be certified as being of ["fetal human or chimpanzee"] liver origin will be inoculated with partially purified HBV that is being titered in chimpanzees. These inoculated cultures will be monitored. . . .

Earlier references to the importance of using chimpanzees to culture and test the hepatitis B viral- vaccine-hybrids are equally compelling. At the International symposium on Viral Hepatitis, Milan, December 1974, Saul Krugman reviewed this subject in "Viral hepatitis type B: Prospects for active immunization. (15) He explained his early research citing the use of chimpanzees in preparing the test antigens of HBV for human trials. Krugman discussed the fact that initial trials were conducted on chimpanzees in the late 1960s, and "serosusceptible unimmunized persons [i.e., humans]" between 1970 and 1974 were injected. This matches precisely the suspect hepatitis B vaccine program in NYC and Willowbrook.

8 More Pages! More Reading Material Than Any Other Weekly!

THE NATIONAL TATTLER ★★★★★
WEEKLY SPECIAL 20¢
VOL. 16, NO. 11 TOPICAL FEATURES OF UNUSUAL INTEREST MARCH 12, 1972

...More For Your Money! The World's Most Comprehensive Weekly Newspaper

Secret 'Horrorifying' Experiments Conducted For 10 Years

TESTERS INJECT RETARDED CHILDREN WITH HEPATITIS

Doctors Forced Parents' Consent -- Knew Some Would Die!

The media, both scientific and lay, has remained silent on these confirmed links to the "smoking gun"--the association between the use of chimpanzees in the suspect HBV vaccine trials in New York, and subsequent deaths.

F. *Wikipedia* publishes classic example of fraudulent concealment at Willowbrook

This general censorship, fraudulent concealment, and even obvious misrepresentation of dates and facts is best demonstrated by *Wikipedia*. The Willowbrook school was closed in 1976 due to reports of child abuse. *Wikipedia* falsely claims the date of closing was "[i]n 1983, [when] the state of New York announced plans to close Willowbrook, which had been renamed the Staten Island Developmental Center in 1974." That fraudulent misrepresentation diverts from public knowledge of the facility's closing in 1976. Only the "school's" biological testing center remained active to accommodate Saul Krugman, Robert Purcell, et. al. Their teams' continued covert operations followed the clinical course of the immune-suppressive cancers in the hep B vaccine recipients.

The mainstream media neglected what the little known *National Tattler* heralded in 1972 as shown here by its headline: "Testers Inject Retarded Children with Hepatitis." The hepatitis B injections for novel virus cancer studies were completely omitted from Geraldo Rivera's extensive reporting on the "child abuse" at Willowbrook--a scandal that rocked the nation. Similar omissions are standard fare in subsequent news and documentary film productions.

Wikipedia also concealed from its Willowbrook coverage the fact that the blood of these earliest victims were "pooled" prior to screening methods becoming available for HIV. This resulted in contaminated blood and blood products being distributed. These products are widely known to have caused the outbreak of AIDS in the hemophiliac community and general populations that consumed these tainted blood products derived from the gay men in NYC and victims at Willowbrook.

Wikipedia further defrauded the public by concealing the military-industrial interests in the HB vaccine trails. *Geraldo* and *Wikipedia* neglected to report the names of the leading investigators and agencies, and also the evidence strongly indicating the first AIDS cases were appearing in Willowbrook test subjects in 1976 synchronous with the GRID cases emerging among homosexuals a few miles away.

Instead, *Wikipedia* evidenced its complicity and criminal negligence by quoting Paul Offit--the leading propagandist for the vaccine industry. Offit is quoted in the *Wikipedia* Willowbrook coverage justifying the work of Saul Krugman and unnamed parties at Willowbrook. Offit neglected what the science world is concerned about most--the chimpanzee HIV/AIDS link in the hepatitis B vaccine trails.

None of the aforementioned spin sources mentioned this author's published science. In fact, *Wikipedia* censored this author's entire biography immediately preceding the "Ebola Emergency" of 2014. Before that, between 2008 and 2014, *Wikipedia's* biography smeared this author using fraudulent concealments to discredit his earlier works.

Wikipedia's fraudulent concealments, misrepresentations, and protection racket disparaging whistleblowers has aided-and-abetted by willful blindness the Life Science racket, and pan-genocide.

G. Correlations of Significance: Predicates and Evidence of Racketeering

The aforementioned certain correlations challenge public health and safety. These are compiled in this section, listed, and summarized below:

(1) Common Nobel Prize awards in medicine between two researchers in molecular biology in the same year for reportedly "discovering" two "new viruses" claimed to have emerged contemporaneously.

(2) Common affiliation of the Nobel Prize's Karolinska Institute with the NCI and SVCP through third party suspects, including the Wistar Institute and Litton Bionetics engaged in the precise research and development of leukemia, lymphoma, sarcoma retroviruses and DNA-type herpes viruses.

(3) Correlation between these "special viruses" and the never-before-seen AIDS "cancer complex" featuring these precise leukemia, lymphoma, sarcoma recombinants that were isolated and tested to induce such precise never-before-seen cancers during these trials.(3)(8) This evidence is pathognomonic for AIDS and its laboratory origin in the SVCP.

CONTRACTOR : Wistar Institute of Anatomy and Biology (71-2092)
ADDRESS : 36th Street at Spruce, Philadelphia, Pennsylvania 19104
PHONE : AC-215, Phone 222-6700, x-226
CNTRCT TITLE: Extraction and Characterization of Virus-Induced Transplantation
Antigen From Sarcomas and Leukemia
DATES : 2/1/72 - 1/31/73
PRINC INVEST: Dr. Anthony Girardi
PROJ OFFICER: Dr. James T. Duff, Bldg. 37, Room 1B22, x-65967

SEGMENT : Solid Tumor-Virus
SEG CHAIRMAN: Dr. Robert Huebner, Bldg. 37, Room 2D24, x-63301
CNTRCT SPEC : Mr. Thomas Porter, Bldg. 37, Room 1A03, x-65025

Date Contract Initiated: April 22, 1969

Current Contract Level: \$51,600

WISTAR INSTITUTE OF ANATOMY AND BIOLOGY (NIH-NCI-E-71-2092)

Title: Extraction and Characterization of Virus-induced
Transplantation Antigen and Rescue of Virus from
Sarcomas and Leukemias

Contractor's Project Director: Dr. Anthony J. Girardi

Project Officer (NCI): Dr. Charles W. Boone

Objectives: To extract and characterize tumor-specific
transplantation antigens induced by selected DNA and RNA
tumor viruses.

Major Findings: (1) In cooperation with Dr. Berge Hampar
(NCI), the peroxidase staining technique for localization
of murine gs antigen is being evaluated. The technique
is both more sensitive and more specific than the fluorescent
antibody technique. (2) Examination of early fetal hamster
tissue for antigens shared with SV40-induced tumor cells
has confirmed Coggin's findings that such a common antigen(s)
exists, but does not support the concept that it is the
important transplantation type antigen since it protects
only male animals. His findings have been extended to show
the embryos of primiparous females were effective immunogens
against SV40 tumorigenesis while those from multiparous
females were not. (3) Rescue attempts have been initiated
employing human sarcomas and leukemias in a variety of
combinations designed to activate latent viral genomes.
These include co-cultivation and fusion with either BPL
inactivated Sendai virus or lysolecithin.

Significance to Biomedical Research and the Program of the
Institute: The treatment of cancer by immunologic methods
has been an attractive hypothesis for decades, but it is
only recently that new and fundamental discoveries in
immunobiology have made cancer immunotherapy a real
possibility. Many tumors possess individually distinct
transplantation antigens against which the host mounts an
immune response. The transplantation antigens of most
virus-caused tumors in different animal species are the
same for a given virus. The work being conducted by the
contractor is part of a larger effort of the SVCP to isolate
and test virus-induced tumor-specific transplantation
antigens in animal model systems.

Proposed Course: (1) Improve use of the peroxidase reaction
technique as a routine assay method for gs antigens and for
intracellular localization of reverse transcriptase. (2) Study
of the relationship of fetal antigen to tumor antigens.

(4) Correction between the timely emergence of profound immune-suppressed clinical cases called GRID and later AIDS following the precise incubation period expected of "lentivirus" or retrovirus infections from the suspect hepatitis B vaccines administered between 1972 and 1974. (3)(8)

(5) Correlation between the herpes-type viruses subjected to genetic alterations in the SVCP labs and the emergence of the "new" DNA virus by zur Hausen et. al., involving the Wistar Institute, the KI and the NCI, favoring commercial enrichment by enterprise called the "Life Sciences Industry."

(6) Correlation in the practice of renaming viruses for academic and commercial gain between what Robert Gallo did purportedly with Montagnier's virus, and what zur Hausen appears to have done with the herpes-type DNA viruses "emerging" from the SVCP labs; thus creating a whole new commercially profitable "family" of herpes called HPVs.

(7) Correlation between the emergence of the first clinical cases of AIDS simultaneously on two far removed continents, in New York City and Central West Africa, precisely the locations where the suspect hepatitis B vaccines were tested.(3)(8)

(8) Correlation between the emergence of the first clinical cases of AIDS among the precise populations receiving the suspect hepatitis B vaccine, namely gay men in NYC and blacks in the AIDS belt of Africa (with Willobrook cases being censored). (3)(8)

(9) Correlation of similar behavioral methods used to develop the false "General Acceptance" in medicine and society that science is infallible and newly-discovered viruses exclusively "cause" deadly cancers, replacing the previously accepted "dogma" of multi-factorial risks.

10) Correlation of organized public relations attacks, smearing and libeling of individuals voicing opposition to objectionable practices in science for commerce; and most telling

11) The "conspiracy of silence" and negligence obstructing informed consent, human rights, public duties to safeguard society, and scientific evidence analysis, open discourse, and justice under circumstances that are arguably treasonous and genocidal.

These eleven predicate acts evidencing racketeering activity as defined by 18 U.S.C. § 1962 (as defined in § 1961).

H. Racketeering in Health Science Fraud and Criminally Negligent Manslaughter

As stated under the aforementioned Standards of Review, the elements of *fraud* are satisfied by: "(1) the false representation that vaccines are "safe," or "safe enough" for injection or oral consumption; 2) government officials' and healthcare workers' knowledge of the falsity of these representations of safety and efficacy (or without knowledge of their truth or falsity in willfully blind obedience to the false "General Acceptance"), (3) contemplating society's and individual

consumer's reliance upon these false representations, (4) with society's and consumer's reliance upon these falsehoods;" (5) causing damage, side effects, illnesses, including brain damage, cancers, and deaths. [Shoppe v. Gucci America, Inc.](#), 14 P. 3d 1049 – Haw: Supreme Court 2000.

Similarly, the elements of **fraudulent concealment** are satisfied by the “employment of artifice” (e.g., false representations of safety or reasonable risk) “planned to prevent inquiry or escape investigation, and mislead or hinder acquirement of information disclosing a right of action.” Including the right to abstain from the “assault” as defined by law. The officials' acts relied on are “of an affirmative character and fraudulent.” [Lemson v. General Motors Corp.](#), 66 Mich. App. 94, 97, 238 N.W.2d 414, 415 (1975) quoting [De Haan v. Winter](#), 258 Mich. 293, 296, 241 N.W. 923, 924 (1932). This fraudulent concealment also “involves the actions taken” by government and healthcare workers “to conceal a known cause of action” such as negligence, assault, breach of public duty to prevent injury, and/or death. [Au v. Au](#), 626 P. 2d 173 – Haw: Supreme Court 1981.

The facts presented here, proven by government records and public knowledge evidences racketeering activities as defined by 18 U.S.C. §§ 1961 and 1962. The “predicate acts” of the enterprise include: (1) bribery of public officials and media censors as the reference below involving Hawaii State Senator, Roz Baker demonstrates;(24) (2) extortion of persons to get vaccinated or risk dying from terroristically-threatened cancers or infections; (3) dealing falsely in controlled chemicals added to vaccines as ingredients, sterilizers, or adjuvants; (4) mail fraud and wire fraud in correspondence between officials, the media, and the public; (5) obstructing justice by scientific evidence tampering and corrupt influence over witnesses, whistleblowers, and the media; (6) obstruction of criminal investigations as occurred in 2002 when the Honorable Representative James A. Traficant, Jr. petitioned the U.S. General Accounting Office to investigate the origin of AIDS on behalf of Boyd Ed Graves (See reference 6: [USGAO on SVCP Investigation](#)); (7) tampering with witnesses, victims, and informants to preclude discovery and prosecution, as the USGAO did with this author who supplied credible scientific evidence censored by GAO officials during their whitewashing (6); (8) retaliating against witnesses, victims, and informants who sought relief and remedies as the enterprise did against Rep. Traficant, Robert Strecker's brother, Ted Strecker, resulting in the latter's death. This author too has been retaliated against as evidenced by public corruption and Paul J. Sulla, Jr. having [stolen my property in Hawaii](#); (9) relating to peonage and slavery in the abuse of test subject such as the Willowbrook children; (10) economic espionage and theft of trade secrets, as Dr. Gallo was vetted for doing purportedly damaging France; (11) interference with commerce in the natural healing arts and sciences by subverting the multi-factorial causes and cures for cancer and general immunity, while disparaging natural healthcare practices; (12) trafficking in biological weapons and chemical weapons under the guise of “cancer control” and “public health” involving fraud in the sale of drugs, vaccines, and securities financing the pharmaceutical companies; and (13) manufacturing and selling biological and chemical products under false pretenses.

Criminally negligent manslaughter is referred to as *criminally negligent homicide* in the [United States](#). “It occurs where death results from serious negligence, or, in some jurisdictions, serious recklessness. A high degree of negligence is required to warrant criminal liability. This bar has been exceeded by the aforementioned facts. People are dying everywhere from myriad illnesses and drug side effects all prompted by the aforementioned vaccine contaminations. These are not

"vaccine preventable diseases." These are "vaccine induced illnesses" grossly neglected by ignorant or "evil obedient" officials. *Willful blindness* is related to criminal negligence. It occurs when a defendant intentionally puts himself in a position where the defendant will be unaware of facts which would render them liable." (10) This is the overriding and overwhelming negligence witnessed in "public health" and medicine today.

Criminally negligent manslaughter also occurs where there is an omission to act when there is a duty to do so, or a failure to perform a duty owed, which leads to a death. In public health and medicine, officials and doctors are not only obligated by "public duty doctrine" and 42 U.S.C. § 1986 to prevent damage to citizens, but also by the Hippocratic oath to "above all do no harm." Willful blindness to these two duties is widespread. The cause of this "General acceptance" and willful blindness is behaviorally-engineered by the persuasive media fundamental to the racketeering enterprise. The existence of the duty to save lives imposes criminal liability on the willfully blind who aid-and-abet the racket and its damage to society. Criminally negligent manslaughter is most common among professionals "who are grossly negligent in the course of their employment." (22)

Conclusion

False "General Acceptance" has been socially-engineered in favor of the theories that HIV "causes" AIDS and HPV "causes" cervical cancers disregarding the many co-factors and commercial interests involved. This General Acceptance of "vaccine science" must be also rejected in light of the aforementioned evidence of scientific fraud, fraudulent concealment of the risks vs. benefits of vaccination, and the media persuasion and censorship practices abused to generate such General Acceptance. (13) So too must the fraud, omissions and misrepresentations of facts, scientific evidence tampering, censorship, and retaliation against witnesses and whistleblowers stop to secure public health and safety. This institutionalized criminal activity must be rejected by every official and activist in lieu of the aforementioned risks and widespread damage done by the "Life Sciences" industry. Urgent reconsideration must be given to the Special Virus Cancer Program ("SVCP") as the apparent origin of the "sexually transmitted diseases" and their viruses claimed to be killing millions of people worldwide, and risking the lives of billions more.

Solid evidence reprinted above shows a commercial enterprise focusing on inducing cancers and viral mutations during the 1960s and early 1970s continuing to the present. The DNA herpes-type viruses and the RNA tumor-inducing immune suppressive retroviruses and their cross-hybrids were central to the mission and actions of the KI, Wistar Institute, Litton Bionetics, Johns Hopkins, the NCI, NIH, and the SVCP. Their officials and collaborating institutions and corporations are comparatively liable for the damages the enterprise has caused and continues to cause. The use of co-factors to induce cancers, including chemicals, radiation, and genetic recombinations of viruses isolated from cancers worldwide, is clear and compelling evidence of the earlier accepted "dogma." The previous "Generally Accepted" dogma has been replaced by extending the "germ theory" into biotechnology and vaccinology for corporate profit over the public's interest using fraudulent claims that the virus alone is the single etiological agent. (4)

The evidence presented here controverts the main defense raised by [Dr. Robert Gallo as televised](#), that "gene cloning" and crude methods of recombinant biotechnology used during the 1960s and 1970s could not account for the emergence of HIV, HBV and HPV viruses "discovered" years later. This is clearly false. This "crude science" was the most active practice of the relatively small group of "experts" financed to administer the SVCP, NCI, NIH and co-contractors' viral "discoveries." This group hybridized and recombined the human and animal deadly viruses during this age of crude, albeit exploding, biotechnology leading to the commercial enterprise we have today.

Medically-legally, *In re Winship*, 397 U.S. 358 (1970), established the need for "a standard of proof" concerning the "confidence our society thinks [w]e should have in the correctness of factual conclusions." This "standard of proof" and "degree of confidence our society" places in vaccines, medicine, the cancer industry, hospitals, and public health has been irreparably damaged by the fraud and criminal actions evidenced herein. Big Pharma's criminal enterprise suffers from its own shortcomings and wrongdoings. Consequently, the holding in *Daubert v. Merrell Dow Pharmaceuticals, Inc.* is most relevant. "General acceptance" of the "vaccine preventable disease" marketing ploy must be urgently reconsidered given the "pertinent evidence" showing fraud. The cited fraudulent concealments and criminal negligence results in manslaughter. This is hereby proven by the clear and convincing facts and government records in evidence. "[B]ased on [these] scientifically valid [government records and] principles" the devil-doers must be disciplined. And these facts clearly compel reconsideration of the entire vaccine industry as a public duty.

Given the legal standards by which fact-finders must justly rule, reasonable discretion holds that every vaccination imposes risks that have been generally concealed and misrepresented by officials and the media. Under these circumstances corrupted by fraud the push for "mandatory immunizations" for "vaccine preventable diseases" evidences a racketeering enterprise as defined by Title 18 Part I Chapter 96 § 1961. This racket and its scheme violates (among many other laws) Title 18 U.S.C., § 241-Conspiracy Against Rights.

This report is delivered to public health officials and lawmakers in Hawaii, but is applicable everywhere. A sworn certified service of this constructive notice sends the following message: Who-so-ever acts by neglect or willful blindness of the aforementioned facts and evidence in government records, and disregards the elements of fraud and felonies in the vaccine industry, aids-and-abets the criminal racket. Such offenders shall be liable under Title 18 USC § 4 - for Misprision of felony, among other laws; and any damage resulting from such negligence, recklessness, or malfeasance, is actionable under 42 U.S.C. § 1986.

-- END --

Declaration of Conflicting Interests

The author proudly declares two conflicting commercial interests in the presentation of this information: (1) NASA science was supplemented by this author's pioneering development of *OxySilver*--a [528 Solfeggio-frequency](#)-enhanced oligodynamic silver-hydrosol incorporating [water-structuring](#) and micro-clustering technology to enhance energetic memory and cellular absorption for optimal benefits claimed to "make all vaccinations and antibiotics obsolete;" and (2) the industry-wide commercial replacement of the risky, costly, and monopolistic allopathic medical paradigm by the freeing natural healing arts and sciences featuring 528 frequency discoveries in musical mathematics.

References

- (1) Gardasil package insert is available for download from the FDA at: <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm111263.pdf>
- (2) Caulfield MJ, Shi L, et. al., Effect of alternative aluminum adjuvants on the absorption and immunogenicity of HPV16 L1 VLPs in mice. [Hum Vaccin](#). 2007 Jul-Aug;3(4):139-45. Epub 2007 Apr 5.
- (3) Horowitz LG. Special Virus Cancer Program. *Medical Veritas* online journal and press release. "[Special Virus Cancer Program](#)" ("SVCP") Concealed Contracts Evidencing Man-Made AIDS Pandemic Released in 20-Year Anniversary of Amazing Discovery." December 5, 2016. You can purchase two of these Reports [HERE](#) in pdf file downloads.
- (4) [Press Release](#). Françoise Barré-Sinoussi and Luc Montagnier Win Nobel Prize for Discovery of HIV. From Nobelprize.org. October 6, 2008. [The Nobel Assembly at Karolinska Institutet](#).
- (5) Roberts S. What AIDS Researcher Dr. Robert Gallo Did in Pursuit of the Nobel Prize. [Spy July 1990](#).
- (6) U.S.G.A.O. Origin of the AIDS Virus. Briefing for the Office of the Honorable James A. Traficant, Jr. GAO-02-809R, June 17, 2002.
- (7) Interview of Dr. Maurice Hilleman by medical historian Edward Shorter's discussing Merck's vaccine-making, in which Hilleman stated, "We brought in the African greens . . . We didn't know we were important in AIDS virus at the time."
- (8) Keim B. Did Merck bring AIDS to America? No. *WIRED*, September 19, 2007. This article is another classic example of "Big Pharmaflag." *WIRED* receives the vast majority of its advertising revenue from Big Biotech. This article exemplifies frivolous argument, diversionary focus, and recklessness in news reporting concealing serious risks to public health and safety from vaccines. Keim falsely claims "the off-camera Merck researchers laugh loudly, and

someone quips, 'What Merck won't do to develop a vaccine.' following Hilleman's crucial admission that corroborates the science. (7) In fact, the nervous laughter came from a WGBH crew, recording the interview for public television.

(9) Association of State and Territorial Health Officials. Health Officials Alarmed by Declining U.S. Vaccination Rates, Country Could Face Scenario Like Europe's Measles Outbreak. [Astho](#). October 26, 2018.

(10) Kane S. Healthcare Holy War Waged by Hearst Challenges World Religions. August 30, 2016. [WarOnWeThePeople.com](#).

(11) Horrobin, D.F. 1990. The philosophical basis of peer review and the suppression of innovation. *J. Am. Med. Assoc.* 263:1438–1441. Dr. Horrobin was terribly smeared by critics online, including *Wikipedia*, following his publication of this author's following paper. Dr. Horrobin is heavily smeared by *Wikipedia* that publishes an outrageously deceptive page on Willowbrook, as discussed above.

(12) Horowitz LG. Polio, hepatitis B and AIDS: an integrative theory on a possible vaccine induced pandemic. *Med Hypotheses*. 2001 May; 56(5):677-86.

(13) To summarize the Supreme Court's ruling on the *Daubert standard*, the court wrote: "General acceptance' is not a necessary precondition to the admissibility of scientific evidence under the Federal Rules of Evidence, but the Rules of Evidence— especially Rule 702—do assign to the trial judge the task of ensuring that an expert's testimony both rests on a reliable foundation and is relevant to the task at hand. Pertinent evidence based on scientifically valid principles will satisfy those demands."

(14) NCI staff. *The Special Virus Cancer Program: Progress Report #8*. Office of the Associate Scientific Director for Viral Oncology (OASDVO). J.B. Moloney, Ed., Washington, D.C.: U.S. Government Printing Office, 1971.

(15) Horowitz LG. *Emerging Viruses: AIDS & Ebola--Nature, Accident or Intentional?* Tetrahedron Press, Rockport, MA, 1996, pp. 6-7. , The book is available through the author's sponsors for a nominal fee [HERE](#).

(16) Horton R. Offline: What is medicine'sw 5 Sigma? Commentary in *TheLancet.com* Vol. 385, April 11, 2015, p. 1380.

(17) College of Physicians of Philadelphia. *The History of Vaccines. Debunked: The Polio Vaccine and HIV* Link Online at: <https://www.historyofvaccines.org/content/articles/debunked-polio-vaccine-and-hiv-link>

(18) Department of Land and Natural Resources, State of Hawaii, republication of "UN Censors Dr. Leonard Horowitz's Origin of AIDS Hypothesis. Online at: <https://dlnr.hawaii.gov/mk/files/2017/03/TIO-Ex-C-57.pdf>.

(20) *UN-VAXXED: A Docu-commentary for Robert De Niro*, a Leonard G. Horowitz production in association with Medical Veritas International, Inc. 2016.

(21) Cantwell A. UN to censor Dr. Len Horowitz manmade AIDS research. March 4, 2008. Published on Rense.com.

(22) *Wikipedia*, defining *criminally negligent manslaughter*, at: <https://en.wikipedia.org/wiki/Manslaughter>.

(23) USDHEW. *Virology Vol. 4--Control of Viral Infections. NIAID Task Force Report*, Bethesda, MD: Public Health Service, National Institutes of Health (NIH) 79-1834, 1979, p. 20-65.

(24) Zur Hausen's "discovery" was said to have been made against the prevailing view during the 1970s concerning multi-factorial cancer. He postulated a role for human papilloma virus (HPV) in cervical cancer. He assumed that the tumour cells, if they contained an oncogenic virus, should harbour viral DNA integrated into their genomes. The HPV genes promoting cell proliferation should therefore be detectable by specifically searching tumour cells for such viral DNA. Harald zur Hausen pursued this idea for over 10 years by searching for different HPV types, a search made difficult by the fact that only parts of the viral DNA were integrated into the host genome. He found novel HPV-DNA in cervix cancer biopsies, and thus discovered the new, tumourigenic HPV16 type in 1983. In 1984, he cloned HPV16 and 18 from patients with cervical cancer. The HPV types 16 and 18 were consistently found in about 70% of cervical cancer biopsies throughout the world.

(25) Krugman S. "Viral hepatitis type B: Prospects for active immunization." In: *International Symposium on Viral Hepatitis, Milan, Dec. 1974. Develop. biol. Standard*. Vol. 30, Munich: S. Karger Basel, 1975, pp. VI; 363-367; the General Discussion can be found on pp. 375-379.

(26) Charges against Hawaii State Senator Roz Baker's on evidence of bribery is presented in an [article](#) published on JudicialCorruptionNews.com by authors Sherri Kane, Leonard G. Horowitz, and anonymous attorneys.

(27) Here is hard evidence of the General acceptance of multi-factorial cancer etiology, directly from page 30 of the SVCP 1977 Report No. 14. Notice this record heralds "Co-Carcinogenesis" involving "biological, chemical, or physical" or environmental factors such as radiation in cancer induction studies. These assaults compounded viral damage from mutating, hybridizing, and recombining especially Herpes DNA viruses (similar to HPV "discovered" by zur Hausen humans and moneys).

4. Projections

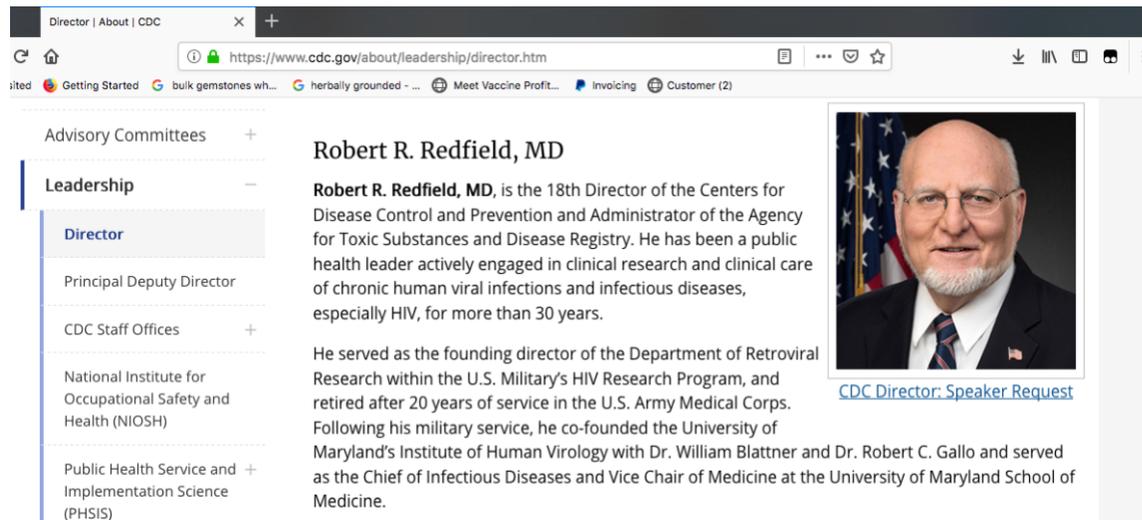
The Viral Oncology Program has set forth a long range research plan to elucidate the role of viruses in human cancers and to exploit any leads that develop for use in the detection, diagnosis, treatment and prevention of cancer. The studies are grouped within the following approaches:

a. Virus Studies

- (1) Basic Studies. Certain basic studies on RNA and DNA viruses in experimental animals and in cell culture will remain an integral part of the Program. The results of these studies have already provided important information about tumor viruses that is applicable to the isolation and identification of human agents.
- (2) Cocarcinogenesis Studies. While it appears that many environmental carcinogens (biological, chemical, or physical) induce cancer, there is evidence that such action is mediated by the activation of latent viruses or viral genes. Cell lines in culture and methods suitable for studying viral-viral, viral-chemical, and viral-physical interactions or cocarcinogenesis are now available and such studies will be considerably expanded:
 - (a) to define the role of endogenous viruses in process of cell transformation;
 - (b) to increase understanding of the relationship of environmental agents as cofactors in carcinogenesis;
 - (c) to extend and develop new methods of inducing tumor virus expression in "normal" cells;
 - (d) to develop reliable, sensitive methods for in vitro carcinogen testing.
- (3) Human Studies. Attempts to isolate RNA or DNA viruses or to detect the presence of viral genetic information and its expression in human tumors will continue. However, considerable emphasis will be placed on developing new probes that can identify viral transforming activity. These efforts will be applied to human cancers:
 - (a) to identify and isolate viruses, virus expression or viral gene products in human leukemias, lymphomas, sarcomas, and carcinomas;
 - (b) to apply specific methods for detecting individuals or groups of individuals at high risk to cancer, i.e., individual susceptibility or predisposition to transformation by viruses.

(27) In the author's opinion, pursuant to the "General acceptance" of vaccines and claims of "safety and efficacy" or "reasonable risk" assurances, the following individuals bear a special burden and should be investigated for conflicting interests, fraud, and treason. This opinion is based on the facts and evidence provided in this article. Such "due process" requires a grand jury to issue indictments, to be advanced by a special "independent" prosecutor free from political and financial interests:

(A) Director of the CDC, Dr. Robert R. Redfield, MD, who co-founded the [University of Maryland's Institute of Human Virology](#) with Dr. William Blattner and Dr. Robert Gallo.



The screenshot shows a web browser window with the URL <https://www.cdc.gov/about/leadership/director.htm>. The page title is "Director | About | CDC". On the left, there is a navigation menu with "Leadership" expanded to show "Director" as the selected item. The main content area features a portrait of Robert R. Redfield, MD, and a text block describing his role as the 18th Director of the CDC. The text states: "Robert R. Redfield, MD, is the 18th Director of the Centers for Disease Control and Prevention and Administrator of the Agency for Toxic Substances and Disease Registry. He has been a public health leader actively engaged in clinical research and clinical care of chronic human viral infections and infectious diseases, especially HIV, for more than 30 years." Below this, it mentions his previous service in the U.S. Army Medical Corps and his role in co-founding the University of Maryland's Institute of Human Virology. A link for "CDC Director: Speaker Request" is visible below the portrait.

B. Director of the HHS, Alex M. Lazar II, was the senior vice president for corporate affairs and communications at Eli Lilly and Co. From 2012 to 2017, he served as president of Eli Lilly USA LLC, the company's largest affiliate. In 2009, Eli Lilly pleaded guilty of defrauding doctors and consumers by promoting Zyprexa for dementia. The \$1.415 billion penalty included an \$800 million civil settlement and a \$515 million criminal fine. The Justice Department said the criminal fine of \$515 million was the largest ever in a healthcare case and the largest criminal fine for an individual corporation ever imposed in a US criminal case.

HHS.gov U.S. Department of Health & Human Services

About HHS Programs & Services Grants & Contracts Laws & Regulations

Leadership -

- HHS Secretary
- Biography
- Priorities
- Blog Posts
- Speeches
- Testimony
- News Releases
- Op-eds
- Videos
- Contact Information

Budget & Performance +

Strategic Plan +

News

Alex M. Azar II



Secretary

HHS Office of the Secretary
E-mail Address: Secretary@HHS.gov
Phone Number: 202-690-7000

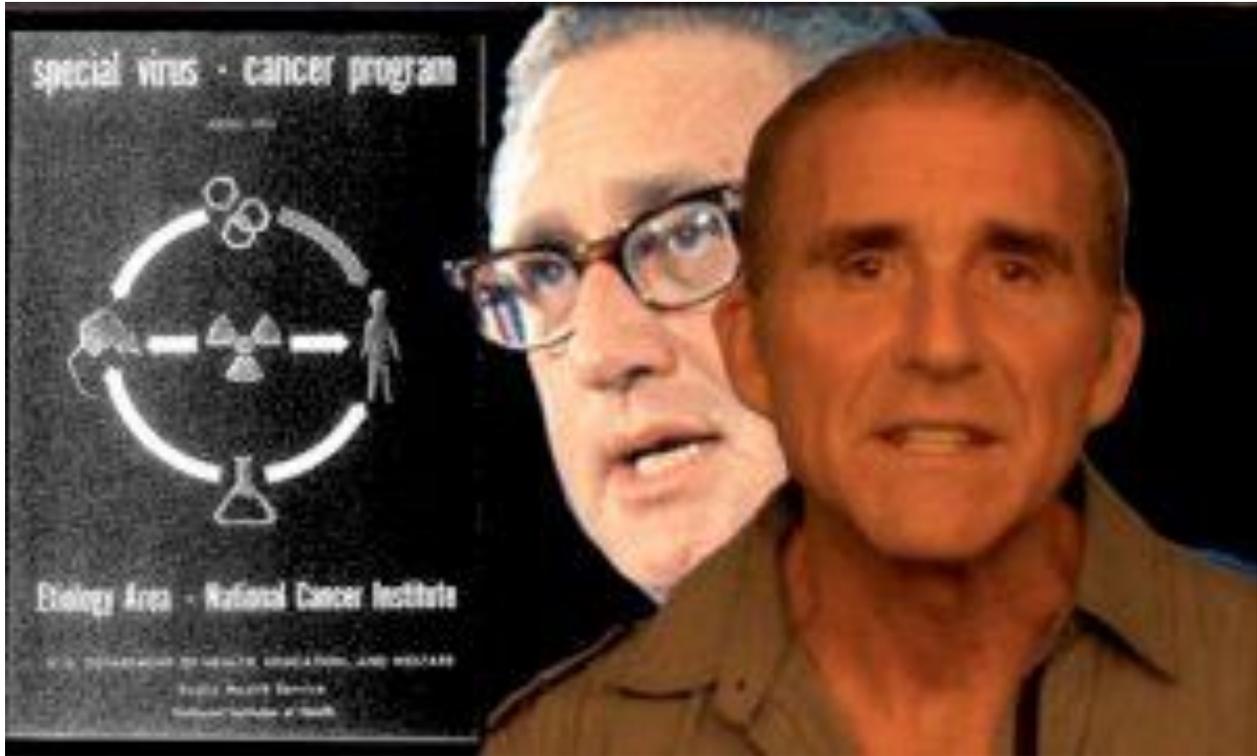
Alex M. Azar II was sworn in as the Secretary of Health and Human Services on Jan. 29, 2018. Azar has spent his career working in both the public and private sectors, as an attorney and in senior leadership roles focused on advancing healthcare reform, research and innovation.

From 2001 to 2007, Azar served at the U.S. Department of Health and Human Services – first as its General Counsel (2001–2005) and then as Deputy Secretary. During his time as Deputy Secretary, Azar was involved in improving the department’s operations; advancing its emergency preparedness and response capabilities as well as its global health affairs activities; and helping oversee the rollout of the Medicare Part D prescription drug program.

In 2007, Azar rejoined the private sector as senior vice president for corporate affairs and communications at Eli Lilly and Co. From 2012 to 2017, he served as president of Lilly USA LLC, the company’s largest affiliate.

It must be known that Eli Lilly produces "Thimerosal"--the mercury preservative used in vaccines linked to autistic spectrum disorder. A provision was fraudulently and untimely inserted into the Homeland Security Act indemnifying vaccine makers against liability at the instruction of [George H.W. Bush who sat on the Board of Directors at Eli Lilly during the 1970's when the SVCP and Litton Bionetics operated.](#) The provision must be repealed in the interest of public health, public safety, and justice.

About the Author



Dr. Leonard G. Horowitz, DMD, MA, MPH, DNM (hon.), DMM (hon.) is considered a "polymath" by his peers. This award-winning medical scholar, author, film-maker, consumer health advocate, drug industry critic, and intelligence industry analyst has published twenty-one books (including three American bestsellers), dozens of peer-reviewed scientific articles, and seven (7) documentary films, including the "Best Film – 2016" at the World International Film Festival in London and Geneva competitions for *UN-VAXXED: A Docu-commentary for Robert De Niro*). Dr. Horowitz's first bestseller, a landmark medical text, *Emerging Viruses: AIDS & Ebola—Nature, Accident or Intention?* is credited by CDC and WHO officials as most influential in establishing vaccination risks opposed by public health activists worldwide. Nonetheless, the United Nations AIDS Secretariat to the UN Theme Group on AIDS [proposed banning the doctor's research](#) in this field.

The doctor's many videos and lectures can be viewed on RevolutionTelevision.net. Dr. Horowitz's second bestseller, *Healing Codes for the Biological Apocalypse*, has prompted a revolution in the music and natural healing arts and sciences. His 2007 decryption of Leonardo da Vinci's most famous drawing revealed the mathematics of *LOVE: The Real da Vinci CODE*; and his follow-up text, the most monumental of his 40-year career, *The Book of 528: Prosperity Key of LOVE*, reveals "God's creative technology," available for revolutionizing every industry, especially music and recording artistry, healthcare and medicine, nutrition, environmental protection, natural resource restoration, along with civilization's transformation as an "enlightened species" choosing peaceful sustainable collaboration versus murderous degenerative competition and lethal consumption.

International acclaim is mounting for the doctor's works revealing Solfeggio frequency physics and metaphysics that has prompted the "[528LOVERevolution](#)" commercialized in the rapidly

growing 528RadioNetwork.com (528Radio.com) that broadcasts “medicinal music” transposed into the “LOVE frequency” of 528Hz the central resonance frequency of chlorophyll, oxygen, and water.

UN-VAXXED
A DOCU-COMMENTARY FOR ROBERT DE NIRO

By Award-winning Author & Filmmaker
Dr. Leonard G. Horowitz

UN-CENSORED VERSION

News Today
De NIRO CANCELS VAXXED FILM DUE TO PRESSURE

TRIBECA
FILM
FESTIVAL

WHISTLEBLOWER EXPOSES CDC VACCINE AUTISM CORRUPTION

VAXXED

DDees.com

WINNER OF FIVE INTERNATIONAL AWARDS INCLUDING

UN-VAXXED:
A Docu-Commentary for Robert De Niro
BEST FILM - 2016
CINEMAGIC LONDON
FILM FESTIVAL
World International
Film Festival

UN-VAXXED:
A Docu-Commentary for Robert De Niro
BEST FILM - 2016
EURO CINEMA
FILM FESTIVAL
GENEVA

Related Articles:

[Free Will and Evil Obedience to Mandatory Vaccinations](#)

[Duty to Warn and A Warning to Wannabe Pro-violence Fascist Tyrants \(and Their Cult Followers\)](#)

Related Videos:

In the video linked [HERE](#), Dr. Robert Gallo is confronted by Dr. Leonard Horowitz at the XI International Conference on AIDS wherein Dr. Gallo was caught lying. Dr. Gallo covered-up his affiliation with Litton Bionetics, the main supplier of genetically-engineered viruses and lab animals from which HIV/AIDS emerged. Today, more than 40 years later, approximately 40 million people have died of AIDS.

Dr. Horowitz's 1996 National best-selling book titled [Emerging Viruses: AIDS and EBOLA: Nature, Accident, or Intentional?](#) was promoted by President Barack Obama's spiritual advisor, Rev. Jeremiah Wright, in 2008. The video linked [HERE](#) records the minister's defense concerning statements he made regarding the AIDS virus being man-made to target people of color.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: DOH Chapter 11-157 Testimony- Oahu
Date: Monday, November 05, 2018 2:40:09 PM

Aloha,

Please see my testimony below opposing the proposed amendment to the DOH's Chapter 11-157.

RE: I STRONGLY OPPOSE the proposed amendment of the Department of Health's Title 11, Chapter 157, Examination and Immunization, HAR (Public Hearing on November 1, 2018).

This proposal limits transparency and public participation while mandating vaccinations via a blanket adoption of the best practices guidance of the federal Advisory Committee on Immunization Practices (ACIP). The DOH cannot have broad-reaching authority with minimal oversight from other branches of government while mandating vaccines for Hawaii's children by gradually whittling away parental consent and involvement.

Further, as a taxpayer, I am requesting a formal response to the following OBJECTIONS to the DOH's proposed Chapter 11-157, HAR, Examination and Immunization. Since my child attends school now and will attend a post-secondary school in Hawaii, I believe this new administrative rule will increase my state taxes.

I would like to see a cost analysis conducted to include the costs associated with implementing Chapter 11-157 and explanations related to the following:

- A) Increased vaccine purchasing costs to the taxpayer.
- B) Increased administrative and operational costs for 292 public schools to implement Chapter 11-157.
- C) Increased costs in Special Education due to new DOH vaccine requirements.

Also, please respond to section D) Questions about the Implementation of Chapter 11-157 which are specific to the proposed amendment itself.

A. Increased Vaccine Purchasing Costs to the Taxpayer:

1. How much will it cost the State of Hawaii to purchase the ACIP recommended vaccines per this proposed rule for children attending daycare, public and private school, and post-secondary schools via the VFC program and the Section 317 Grants on a yearly basis? Some of the recommended costs are represented below:

HPV9 on the CDC's VFC list[1] costs \$168.10 per dose- a 2-3 dose series per child would be \$336.20 or \$504.3

Meningococcal Conjugate on the VFC list is \$73.83 or \$91.81 per dose- 2 doses per child would cost \$147.66 to \$183.62

Hepatitis A on the VFC list is \$19.58 per dose – 2 doses per child would cost \$39.16

If the DOH uses vaccine combinations such as MMR-V (Proquad), the VFC list price is \$125.11 per dose - 2 doses per child would cost \$250.22 (compared to \$21.05 for MMR and \$98.24 for varicella per dose – for 2 doses each would cost \$238.58)

2. What kind sources of funds will be needed to pay for any NEW vaccines that the ACIP recommends after 2020? Will this be a taxpayer expense, if so why?

3. What contingency plans are in place if the VFC and Section 317 funds run out? Will this be an increased taxpayer expense?

4. Does the State of Hawaii use any non-federal sources to pay for our vaccine supplies? If so, what is the average costs incurred purchasing non-contract vaccines. Will this be a taxpayer expense for future shortages?

5. How much will the proposed changes increase vaccine reimbursements and vaccine-related reimbursements such as a vaccine administration fee to Hawaii State Medicaid because of the added ACIP vaccine recommendations? Will this be a taxpayer expense?

6. How many children in Hawaii's state Medicaid, Quest and related programs will receive the newly recommended vaccines and what is the estimated financial costs in these programs? Will this be a taxpayer expense?

B. Department of Education:

According to the DOE's official enrollment count for 2018-2019[2], there is a total of 180,837 children enrolled. The DOH proposal would require DOE personnel from each of the 292 schools to do at minimum the following:

1. Collect, review, maintain and enforce rules related to proof of immunization documents.

2. Monitor and enforce provisional school entry requirements continuously.

3. Monitor and enforce all medical and religious exemption requirements continuously.

4. Submit personally identifiable information to the DOH on a regular basis, either electronically or by copying.

5. Require additional administrative and operational costs per school.
6. Purchase additional equipment, supplies, space and hire personnel.

In 2016, former Superintendent Kathryn Matayoshi submitted testimony opposing SB2316 which required 7th graders to receive 1 dose of the HPV vaccine for school entry citing that the “added administrative and operational workload, school personnel will be tremendously challenged.” Although SB2316 involved only a single vaccine dose for 7th graders compared to three vaccines for 7th graders in the proposed amendment, the message was clear. Mandating any vaccine for school entry would create an additional financial and operational burden to the DOE.

How much would the administrative and operational costs be to the 292 schools in the Department of Education to implement the immunization requirements for 180,837 children under the DOH’s proposed Chapter 11-157? Will this be a taxpayer expense?

C. Cost of Special Education:

In addition there is a total of 1580 children in Pre-K special education and 17,591 children in special education for a total of 19,171[3] children who rely on funding from the Hawaii Department of Education and from the Office of Special Education Programs (OSEP), US Department of Education.

1580	Pre-K
8733	K-6
2926	7-8
5932	9-12

The current autism rate is 1 in 36[4] and has steadily increased over the last 14 years. While the claim is the cause is unknown, there is ample evidence pointing to the number of vaccines administered early in life. In 1962, there were 5 doses of vaccines given. By 1983, 24 doses were administered and by 2017 the number of doses was 72. While the belief that correlation is not causation, the steady increase in the rate of autism has increased in tandem with the number of vaccines added to the vaccine schedule as recommended by the ACIP.

Whether or not the DOH believes autism is related to vaccines, the Department of Education will be responsible for educating children with ADD, ADHD, Asperger’s, Autism, PDD-NOS, Autism, Learning Disabilities, Speech Delay, Multiple disabilities, and the medically fragile in the public schools. This will not be on the Department of Health.

In 2015, the California legislature ignored the pleas of hundreds of testifiers who opposed SB277. This bill eliminated personal and religious exemptions for vaccines while also making it extremely difficult for doctors to write and parents to receive medical exemptions for their child. This sounds like a similar scenario in the Hawaii DOH's Chapter 11-157 -5 Exemptions.

In June 2015, SB277 became California law. The removal of exemptions most likely contributed to the exponential rise in California's autism rates in 2016, to 7 percent and specifically 17 percent in kindergartners in public schools while previously the autism rate had risen basically at the same rate since 2001.[5]

While most parents intuitively know what led to their child's autism, the DOH, CDC, ACIP continue to ignore the increased autism rates. The increased incidence of autism in California is most likely attributed to the increased vaccination rates or the accelerated "catch-up" schedule since many California parents were forced to give their children more than the usual number of doses and in a shorter period of time just in time for school. This same scenario will most likely occur in Hawaii.

How does this relate to the Department of Education? Hawaii's weighted-student formula may be useful in determining the number of "dollars" per child but the special education children are weighted the same as a typical child. Thus, funds for special education services as described under a child's Individualized Educational Program (IEP), and under the Individuals with Disabilities Education Act (IDEA) usually comes from another source of funding such state general funds[6] and federal funds.

The DOH's new proposal under Chapter 11-157 of increasing the number of vaccinations will most likely convert some typically developing children into those needing special education. Without additional funding to properly address the needs of these emerging special education children, they will not be able to receive the fair and proper education they are entitled to under the law. At the same time, taxpayers will be left with funding their increased educational needs and taking care of these children for a lifetime.

The DOH in collaboration with the Department of Education must conduct a financial analysis to determine a baseline for special education costs prior to the adoption of Chapter 11-157.

There must also be an analysis to estimate the potential costs of educating new cases of children in the DOE's special education AFTER the new vaccine requirements are implemented in 2020.

How much does the State of Hawaii expect the taxpayers to pay to fund this DOH vaccine mandate?

D. Questions about the Implementation of Chapter 11-157:

1. In Ch 11-157, the DOH created the definition for

“recognized standard medical practice” to mean “in accordance with the US Dept. of Health and Human Services,’ Advisory Committee on Immunization Practices (ACIP), General Best Practice Guidance for Immunization and future amendments that are adopted by the department” which forces physicians to practice medicine the way the DOH wants them to practice, i.e. following the ACIP guidance.

First, how will the DOH know if a provider is following the ACIP Best Practices Guidance? Will physicians be fined or penalized for not following the ACIP’s Best Practices Guidance, even though it is a ONLY a guidance and a recommendation?

2. Second, the phrase “and future amendments that are adopted by the department” is extremely vague and seems to give the Immunization Branch the authority to adopt ANYTHING in the future, and then force providers to comply, possibly against their own medical judgement. Is this the intent of the DOH?

3. Will parents be fined or penalized if their physicians fail to follow the ACIP recommendations and Best Practices Guidance? Can physicians follow the Guidance based on their own medical judgement? If so, in what way?

4. Under 11-157-3(b) Immunizations, it states “Only those sections of Exhibit B that pertain to the requirements of this chapter, including the specific vaccinations listed in Exhibit A, shall apply.” Since the ACIP guidance is about 197 pages long, please identify the specific sections of the guidance that applies to a corresponding section of the proposed amendment.

Further under 11-157-3(c), it states “if an exhibit conflicts with this chapter, this chapter shall prevail.” Can the DOH provide an example of how such a conflict would occur since the proposed rule supposedly includes information taken directly from the ACIP guidance?

Again, the DOH must specify the exact sections of the ACIP Best Practices Guidance that will be considered part of the DOH’s Ch 11-157, HAR. This is too broad of a reach of authority and too little oversight of the potential changes in the administrative law.

5. Will Table 4.1 Contraindications and precautions in the ACIP guidance (p.52) be the only allowable reasons or “stated cause” i.e. “medically contraindicated due to a stated cause” as per 11-157-5 under medical exemptions? Specifically, if a student has a “severe allergic reaction” as described on (p.53) from a flu vaccine, does that mean the medical exemption will be allowed compared to a student who acquired an autoimmune disease such as GBS or Acute Flaccid myelitis which is not listed as a contraindication?

The Conditions listed in Table 4.2 (p.59) of the ACIP guidance are called “conditions incorrectly perceived as contraindications or precautions to vaccinations.” If a physician, using his own medical judgment for a patient, believes that a particular vaccination would be harmful to his patient and lists one of the misperceived conditions from Table 4.2 as a “stated cause” as per Chapter 11-157-5, would this determination invalidate the Medical Exemption for this patient? How and who makes this determination if

invalidated?

6. Why should a time period be specified for a contraindication such as an autoimmune disease or severe allergic reaction? A peanut allergy lasts a lifetime, thus please justify the need for the time requirement.
7. Does the ACIP guidance trump the physician's best medical judgement when he determines the child's need for a medical exemption?
8. Will someone from the DOH evaluate medical exemptions for "validity" or be able to reject a medical exemption submitted by a physician? With what criteria? If so, who will that be? Please list the criteria to be used for evaluating "validity."
9. If the DOH rules that the religious exemption is not "bona fide," what criteria will be used to make this decision? Who in the DOH or DOE will make this decision? Will the parent receive a written explanation if rejected?
10. Provide a list of religions that are unacceptable for the purposes of a religious exemption.
11. If exemptions can be rejected, will there be an appeal process and would that be an administrative process or in a court of law?
12. If the ACIP best practices guidance changes every 3 to 5 years, will the DOH automatically update its HAR or will it remain the same since the proposed amendment is a blanket adoption of practically the entire document? How will the public and community be informed of these changes?
13. How will the public know which parts of the ACIP best practices guidance have been adopted as law and which have not? How will the DOH inform the community of its decisions and will there be a grace period?
14. How much it will cost state taxpayers for the major overhaul of the updated immunization program? Has the additional training required, communication to providers, and other hidden costs been properly determined? Is this a taxpayer expense?
15. In Ch 11-157, a "Grace Period" is defined as the "four day period prior to minimum required ages or intervals during which an immunization may still be considered valid." In the ACIP Best Practices Guidance, p.13, it also states that "doses of any vaccine administered equal to or greater than 5 days earlier than the minimum interval or age should NOT be counted as valid doses and should be repeated as age appropriate."

The ACIP decisions in this section "Spacing of Multiple Doses of the Same Antigen" under "Timing and Spacing of Immunobiologics" appears to be based on "expert opinion and arrived at consensus" rather than actual clinical trials. This recommendation is not rooted in science but opinion. If physicians do not follow this ACIP guidance exactly,

will the DOH have the authority to dictate how a physician practices medicine related to vaccines?

16. How will the DOH minimize confusion among health care providers when there are substantive changes in the ACIP recommendations versus delays in implementation of these recommendations as allowed in proposed section 11-157-3(d)?

17. The definition of a practitioner includes PA, APRN, or physician licensed to practice in HI. The definition of a physician means a person licensed to practice medicine, including naturopathic and osteopathic medicine. However, the medical exemptions states that only a “physician” is allowed to certify a medical exemption, 11-157-5.

Does this mean that a PA and APRN are not allowed to write medical exemptions or that they can write an exemption but it must be certified by a Physician or Naturopathic physician?

18. What does the DOH mean by “certification by a physician,” on a medical exemption?

19. 11-157-5 states that religious exemptions must be certified to state that a “person’s religious beliefs prohibit the practice of immunization.” What does this mean exactly? If I am an atheist, does this fall under a person’s religious beliefs?

20. The proposed amendment states that a parent must certify that the person’s religious beliefs prohibit the practice of immunization. How does a person go about CERTIFYING their religious beliefs and WHO shall certify this belief?

21. Who will have the authority to deny a religious exemption and on what legal standing?

22. By rejecting a person’s religious beliefs on a religious exemption, whatever they may be, isn’t this religious discrimination, if not, how is it not?

23. In what situations could a Religious Exemption not be acceptable? Provide examples.

24. Please provide sample forms of the proposed Religious Exemption and medical exemption and any other forms, written or electronic, that are proposed by Chapter 11-157 and a list of information that will be required on both forms.

25. Will religious and medical exemption information be stored in the Hawaii Immunization Registry? If so, what other information will be stored in the HIR such as religious and medical exemption information?

26. Can parents refuse to allow their child’s immunization record be copied/sent from the school to the DOH? If not, why not? If so, what is the process?

Can parents refuse to allow their child’s immunization record to be

copied/sent from the physician to the DOH? If not, why not? If so, what is the process?

27. Please provide a sample opting out form to either the school or DOH, if hand-written or electronic. If electronic, what information will be required and who will be submitting an electronic form and to whom in the DOH?

28. To whom does section 11-157-7 Penalties and Remedies apply? – The physician, provider, school personnel, parents, or student? How would this case be decided, in a court of law or by an administrative hearing?

29. 11-157 does not define “vaccine preventable diseases.” However, since Hawaii is in a tropical region where there is a possibility of Zika infections, for example, does this mean that if a Zika vaccine is available, the DOH could mandate it even temporarily due to “unforeseen circumstances”(11-157-3(d))? Realistically, vaccine trials are being conducted at this time for Dengue[7], Ebola[8] and Zika[9] diseases. Also diabetes[10] and breast cancer[11] vaccines are also in clinical trials. If the ACIP recommended these vaccines, could the DOH require all these vaccines as well? Will the people have any say in this matter?

30. What are the estimated overall exemption rates for Hawaii from 2001 to 2018?

31. What are the estimated overall vaccination rates for Hawaii from 2001 to 2018?

32. What is the HPV rate among 7th graders in 2017 or 2018, i.e. cervical cancers, anal warts, genital warts for children in Hawaii?

33. How did the DOH determine the need for the HPV vaccine in Hawaii and was that based on Hawaii statistics or just because it is recommended by ACIP?

34. If a student is vaccinated per a mandatory requirement for school entry and becomes vaccine injured, can the school be held accountable and how will the department of health, immunization branch be held accountable?

35. If the ACIP makes more than one recommendation about a school related vaccine, how will that be communicated by the school to the parents?

36. Is the DOH aware that pediatricians have Incentive Programs[12] that will pay pediatricians a bonus for a certain percentage of children who are fully vaccinated in their pediatric practice? When vaccines are being pushed by pediatricians for monetary gain, is mandating vaccines in the best interests of our children?

37. Will physicians be required to use the Hawaii Immunization Registry (HIR) if Ch 11-157 is adopted?

38. What is the process for parents to acquire information

Member of Hawaii for Informed Consent



-
- [1] <https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html>
- [2] <https://www.hawaiipublicschools.org/VisionForSuccess/SchoolDataAndReports/SchoolReports/Pages/home.aspx>
- [3] <https://www.hawaiipublicschools.org/VisionForSuccess/SchoolDataAndReports/SchoolReports/Pages/home.aspx>
- [4] <https://www.cdc.gov/nchs/data/databriefs/db291.pdf>
- [5] <https://www.sacbee.com/site-services/databases/article90300877.html>
- [6] <https://www.hawaiipublicschools.org/Reports/FY19WSFweights.pdf>
- [7] <https://www.bbc.com/news/world-asia-42929255>
- [8] <https://www.niaid.nih.gov/diseases-conditions/ebola-vaccines>
- [9] <https://www.niaid.nih.gov/diseases-conditions/zika-vaccines>
- [10] <https://www.sciencedirect.com/science/article/pii/S0264410X17307053>
- [11] https://www.hopkinsmedicine.org/kimmel_cancer_center/centers/breast_cancer_program/treatment_and_services/breast_cancer_vaccine.html
- [12] https://thephysicianalliance.org/images/FilesDocuments/2017_BCNCBCSM_PRPBooklet_Final122016.pdf, p.11.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157 - OPPOSE
Date: Monday, November 05, 2018 3:16:04 PM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. As a parent, I should decide the medical interventions appropriate for my own child, not the State. I do believe vaccines are necessary, however I do not agree with the CDC schedule of vaccinations, or the amount of vaccinations required. I support a delayed vaccine schedule, and as a parent it should be my choice.

I do understand the concern about the anti-vax movement putting everyone at risk, and some of the loudest proponents of "no" vaccinations do make the movement sound *crazy*. However, if you listen to the majority of these parents, they are far from crazy. They are deeply concerned about the risks associated with vaccines - both with the toxicity of ingredients as well as the schedule that doesn't take into account the inherent risks of immunizing babies so young. There needs to be studies showing the risks, more information available to the public on every level, before something like this is mandated. Without that information, all parents are hearing is a loud discord of right versus wrong and are unsure of the path to take. Forcing a vaccine mandate doesn't address the issue of parents being (very rightly) worried about the health risks.

There is a vaccine court that doles out money for vaccine injuries. That's because vaccines *can* harm. This is fact. Not all vaccines harm all children. This is also a fact. But because there are two sides, and one side proven to cause harm, this issue should not be taken lightly. Not when our keiki are the ones at risk.

Even more, once vaccinations are mandated, what's to stop pharmaceutical companies from forcing even more vaccinations on children and adults alike? Is the govt taking control in good faith that a billion dollar industry is going to sit by and not create 10-20 more vaccines for every child to be mandated to have? History has shown this will certainly not be the case...

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify. I ask that you delay your decision on this important issue and please please please listen to the people, parents, and concerned citizens of Hawaii nei.

Sincerely,
Katie Edmonds
Nutritional Therapy Practitioner

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157 - OPPOSE VEHEMENTLY
Date: Monday, November 05, 2018 12:58:26 PM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. The State SHOULD not have the right to decide for any parents about vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A CHOICE !!! And there are many risks involved with proof!

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify !!! I ask that you delay your decision on this important issue.

Sincerely,

Harvest Edmonds, RA

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose amendment HAR 11-157
Date: Monday, November 05, 2018 1:37:36 PM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. The State SHOULD not have the right to decide for any parents about vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A CHOICE !!! And there are many risks involved with proof !

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify !!! I ask that you delay your decision on this important issue.

Sincerely,

Jennifer Edmonds
[REDACTED] resident

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157 - Oppose- Public Testimony
Date: Monday, November 05, 2018 3:22:16 PM

To the Department of Health,

**My name is Taylor Kaluahine Reid, I am a mother and Resident on [REDACTED]
[REDACTED] and I strongly oppose amendment HAR 11-157.**

**The State SHOULD NOT have the right to decide for any parents about
vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A
CHOICE !!!**

**There was only a 1 public hearing on Oahu for testimony to be given. We, as
parents and citizens demand that there be other public hearings on each
Island. This is too important of an issue to be rushed and I ask that you
delay your decision on this extremely important issue.**

Sincerely,

Taylor Kaluahine Reid

From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157
Date: Tuesday, November 06, 2018 8:51:05 AM

Dear Department of Health,

My name is Teresa Gochenouer, longtime resident of Honolulu. I attended the hearing last week on this bill and I strongly request that you say an emphatic NO to it. First of all, the Department of Health should never have been allowed to be in this position of changing the law without legislative oversight. I see that this became law in 2013 and I deeply regret not having been a part of that decision by voicing my opinion in opposition to that, as I was unaware this was going on.

This bill is an affront to the American citizen on many levels. First, as an American citizen as provided in the Declaration of Independence, we as citizens of the United States have the right to life, liberty, and the pursuit of happiness. My body and the bodies of my children are protected by law. You cannot force people to be injected with poison under the guise of health. We are protected by law to live with liberty, as individuals, and shall not be forced to comply with your requirements using scare tactics with language that says our choices are at the expense of the community. Second, there is so much corruption in the CDC and the FDA, with collusion by officials and pharmaceutical companies, many who have worked for both, making this a huge conflict of interest, all the while harming children. Thirdly, these drugs have not been tested or been run through trials; the recipients of these vaccines are the trials, how shameful and reprehensible!! Fourthly, since 1986, these pharmaceutical companies have not been held accountable as they are protected by law from being sued by the individuals and families who have been damaged by these vaccines. What a racket! These companies have made billions of dollars and the rate of vaccine injuries has skyrocketed. To think that the Department of Health has the ability to change the vaccine schedule without oversight is horrendous. With the federal suggestion of increases to the vaccine schedule coming at an alarming rate who says when enough is enough!! We the people, the individuals do.

The hearing last week was attended by about 75% against this bill and about 25% for the bill, from my estimation. Of the individuals who testified, the people for the bill were largely people representing entities in the health profession, while the individuals in opposition to the bill were citizens like myself who stand on the principles of our country. The health professionals, while they see the patients with disease in their offices, are talking about the extremes, not the norm of society. Don't let the exception become the rule.

I am extremely against this bill, HAR11-157, because it goes against our God given rights to life, liberty, and the pursuit of happiness. I strongly oppose and it request that you do not pass this bill.

Sincerely,
Teresa Gochenouer
[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157
Date: Tuesday, November 06, 2018 8:59:27 PM

My name is Julie Patry from Lahaina, Hawaii. As a healthcare worker and mother in Hawaii, I am writing to strongly oppose HAR 11-157. I also request that hearings be held on all the outer islands regarding this important decision.

I want to tell you the story of my sister, Laura Meyer. In 1983, my sister Laura was born. I was 8 years old when she was born. My older sister and I were so excited to have a little sister. She was a healthy, beautiful baby. When she was 6 weeks old, my mother took her for her first well baby visit and she received her first immunization, the DPT. Within 12 hours, she had 3 seizures and a period of high-pitched crying. Our family doctor, who gave the immunization, easily diagnosed this as a severe reaction to the DPT shot. From that day on, she had seizures almost daily, and other days she would have many seizures. Our lives were now frequent medical appts and extended hospitalizations. We often had to call an ambulance to begin IV medications while transporting her to the hospital. Many of the important events in all our lives were a balancing act to care for her, often in the hospital, and carry on with life. Because of her reaction to the DPT immunization, Laura had severe brain damage. She never walked....never talked...and, as her doctors noted, was profoundly developmentally disabled. There was no doubt in our minds, or her doctors', that this was a result of the DPT immunization she received at 6 weeks.

Because of the overwhelming evidence in her case, my parents easily found a lawyer confident in our case. However, the National Childhood Vaccine Injury Act of 1986 had recently been passed. My parents chose "Vaccine Court" over a long and protracted court case. My sister was awarded compensation that would fund her care for the rest of her life.

Caring for a profoundly developmentally disabled child was often very difficult for my mother and our family. But Laura also brought our family so much joy and taught us in ways that no one else could have. Laura was a happy, smiling, beautiful child, who didn't know enough to have a care in the world. Despite her disabilities, she was loved by many for her easy-going nature and bright smile. I chose a career as a clinical social worker because of the lessons she taught me.

When Laura was 11 years old, the doctor convinced my parents that her compromised immune system would put her at risk if she did not receive the MMR. The same doctor who gave her the DPT, advised my parents that the risk of those illnesses outweighed the risk of the MMR vaccination. She received the MMR. She fell ill quickly after receiving it and never recovered.

One week later, she had the worst status seizure of her life. We called an ambulance as we had done many times before...within the hour, Laura was pronounced dead from cardiac and respiratory arrest. Her death certificate reads that her death was a result of a status seizure, the DPT reaction, and the MMR vaccine she had received just one week earlier. My sister was gone. This experience tested the strength of our family beyond all measure. It taught us lessons that we will never forget.

My sister would be 35 this year. I wish she was here to share my life with. This story is the legacy of my sister. To tell her story so you know that vaccine reactions do happen. They do exist. Parents are told they must vaccinate their children for the greater good or because the benefits outweigh the risks. For my sister Laura, the risk was the only reality. There was no benefit. For Laura, the benefit was zero and the risk was her life. Where there is this serious of risk, there must be choice.

I have many concerns about the addition of HPV, Hep A, and flu to the schedule of immunizations. I could write pages about my concerns, as you can tell that this is a topic that is near and dear to my heart. However, I will defer to all the other testimony you have received from other well-informed advocates for vaccine choice. My testimony is about my sister, her story. A reminder that vaccine reactions are real and more common than most realize. I now have two beautiful, healthy boys. They have never received a vaccination and it scares me to wonder what might have happened if they did. I could not go through that pain again. We will never know why my sister was so severely damaged by vaccination. I hope that someday our country will care enough to do the real research that is needed to find out, instead of continuing to deny the concerns and allow money and profits to rule the decisions. Until that day, I urge you to remember that vaccination is a medical choice with risks and consequences on both sides. Where there is risk, there must be choice!

Thank you for your time and attention,

Julie Patry



From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Tuesday, November 06, 2018 8:04:42 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Jennifer

Jennifer Di Rocco, D.O., M.Ed.

[REDACTED]
[REDACTED]
[REDACTED]

Confidentiality Notice: This e-mail message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information.

Unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 rule changes for Hawaii vaccine policy
Date: Tuesday, November 06, 2018 1:39:27 PM

The state of Virginia has allowed parents to personally exempt their children from HPV vaccine. Why is it that Hawaii does not allow exemptions for personal beliefs? Religious beliefs are a human and a constitutional right so must be allowed. That in itself is self evident. But, it is an invasion of privacy demanding to know someone's religion. How can you ask one to state their religion as a basis for exemption when even the courts are not allowed to rule on religious interpretation. For example, there are dissenters and idiosyncratic believers among the churches. I may differ in opinion from my religious leader. Yet courts are forbidden to interpret religious beliefs or as to whether a belief is internally consistent. Having one state their religion is of itself absurd because you cannot interpret it. If I differ in opinion from my leaders who is to say who is right? Hep A vaccines from aborted fetuses would be against my belief. Yet, many churches who are against abortion will cave in on the vaccine issue and go along with the government probably for fear of losing their 501c3 status. Disclosing personal information such as one's religion can lead to discrimination. (This has already happened to my family from a DOE employee) Why do you need this information and for what purpose and, who will use this

information wrongly? And what about an atheist and where do they go to get an exemption? How can a vegan get a waiver since vaccines can be of animal or human origin?

Also, there are differences in philosophy in medicine. How does this accommodate someone who believes in oriental medicine? I am an approved NCCAOM candidate which means I am trained in acupuncture and oriental medicine. Personal philosophy, belief or, conscience needs to be accepted for exemptions. If we want to use religion as an exemption, why do we need to state the religious belief? It is not verifiable. There is something sinister about keeping secret lists of people of faith. Can you guarantee to safeguard such information? Our legislators failed us. In many states, legislation goes to many ridiculous lengths to try to circumvent our right to informed consent, even trying to allow teenagers to get the vaccination without their parents consent, though they have not succeeded. This is government overreach and suppression of parental rights.

A family member of mine in her 80's got Lupus after a shingles shot. Similarly, two patients in a care home had the same reaction. No one investigated. If the story was changed to 3 persons ate a restaurant and become ill it would have been investigated. Also, when an incident of a chemical spill which Hazmat responded to and was broadcast on the evening news yet. has to my

knowledge never been reported on the HEER reports. But the offending company was allowed to police themselves and take home the faulty equipment and bury the evidence. This is letting the fox into the hen house to count the eggs. I fear the same here. That those making decisions do not have our best interest in mind. Can we trust those that profit from vaccines to be in charge of policy and research?

We have seen so many vaccines that have been pulled from the market. I don't trust the CDC or the ACIP any other organization to make health decisions for us. They have not proven all vaccines to be safe. We do not like being ordered to play Russian roulette or be their guinea pigs with vaccines. The hearing was clear on this last week and I agree with those who spoke against the bill. Please have hearings for the outer island people.

Thank you,
Linda Manning

From: [REDACTED]
To: [REDACTED]
Subject: I appose mandatory vaccinations!!!
Date: Tuesday, November 06, 2018 10:38:27 AM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. As a parent, I should decide the medical interventions appropriate for my own child, not the State. I do believe vaccines are necessary, however I do not agree with the CDC schedule of vaccinations, or the amount of vaccinations required. I support a delayed vaccine schedule, and as a parent it should be my choice.

I do understand the concern about the anti-vax movement putting everyone at risk, and some of the loudest proponents of "no" vaccinations do make the movement sound crazy. However, if you listen to the majority of these parents, they are far from crazy. They are deeply concerned about the risks associated with vaccines - both with the toxicity of ingredients as well as the schedule that doesn't take into account the inherent risks of immunizing babies so young. There needs to be studies showing the risks, more information available to the public on every level, before something like this is mandated. Without that information, all parents are hearing is a loud discord of right versus wrong and are unsure of the path to take. Forcing a vaccine mandate doesn't address the issue of parents being (very rightly) worried about the health risks.

There is a vaccine court that doles out money for vaccine injuries. That's because vaccines can harm. This is fact. Not all vaccines harm all children. This is also a fact. But because there are two sides, and one side proven to cause harm, this issue should not be taken lightly. Not when our keiki are the ones at risk.

Even more, once vaccinations are mandated, what's to stop pharmaceutical companies from forcing even more vaccinations on children and adults alike? Is the govt taking control in good faith that a billion dollar industry is going to sit by and not create 10-20 more vaccines for every child to be mandated to have? History has shown this will certainly not be the case...

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify. I ask that you delay your decision on this important issue and please please please listen to the people, parents, and concerned citizens of Hawaii nei.

Sincerely,
Ashley Johnson
[REDACTED] born and raised, mother, postpartum care provider.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Immunization Testimony
Date: Tuesday, November 06, 2018 11:08:09 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

--

Vinson Diep, MD, PGY-2
University of Hawaii John A. Burns School of Medicine C/O 2017
University of Hawaii Pediatric Residency Program
Kapiolani Medical Center for Women & Children

November 6, 2018

To: Department of Health
Disease Outbreak Control Division

From: Melinda Ashton, MD
Executive Vice President – Chief Quality Officer

Re: Testimony in Support to suggested amendments HAR 11-157

My name is Melinda Ashton, MD, Executive Vice President & Chief Quality Officer at Hawai'i Pacific Health (HPH). Hawai'i Pacific Health is a not-for-profit health care system committed to providing the highest quality medical care and service to the people of Hawai'i and the Pacific Region through its four hospitals, more than 50 outpatient clinics and service sites, and over 1,600 affiliated physicians. Hawai'i Pacific Health's hospitals are Kapi'olani Medical Center for Women & Children, Pali Momi Medical Center, Straub Clinic & Hospital and Wilcox Memorial Hospital.

HPH is writing in strong support of HAR 11-157 proposed rule update. These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Therefore, limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots due to current low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life. The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you.



Hawaii Chapter Incorporated in Hawaii

November 6, 2018

AAP - Hawaii Chapter

Website: aaphawaii.org

Hawaii Chapter Board

President

Mae S. I. Kyono, MD, FAAP

Phone: [REDACTED]

Email: [REDACTED]

Vice-President

Michael Ching, MD, MPH, FAAP

Phone: [REDACTED]

Email: [REDACTED]

Secretary

Josephine Quensell, MD, FAAP

Phone: [REDACTED]

Email: [REDACTED]

Treasurer

Vince Yamashiroya, MD, FAAP

Phone: [REDACTED]

Email: [REDACTED]

Immediate Past President

R. Michael Hamilton, MD, MS, FAAP

Phone: [REDACTED]

Email: [REDACTED]

Chapter Executive Director

Sharon Hicks

Email: [REDACTED]

To Bruce Anderson, PhD
Director of Health
State of Hawaii

Re: SUPPORT for HAR 11-157 proposed rules update

Dear Dr. Anderson:

Thank you for the opportunity to provide testimony. we are writing in **strong support** for the HAR 11-157 proposed rules update. These changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The updated rules for HPV, meningococcal, and Tdap immunizations are critical for protecting children against these conditions as they grow into adulthood. HPV is just one example of how these vaccines are vital. According the CDC over 43,000 HPV-related cancers are diagnosed in the USA every year. Immunizing boys and girls against this virus will help to reduce these preventable diseases.

We also support the rule for child care facilities to require documentation of physicals and immunizations. These facilities often care for infants and young children who may have incomplete immunity against vaccine preventable diseases. They are also prime locations for transmission of diseases that could be brought home to vulnerable kupuna and immunocompromised family members.

We support strict regulation of medical exemption to immunization. Recent research from California shows that limiting personal belief exemption results in significant improvements in immunization rates. However this has resulted in marked increases in medical exemption. In some schools reportedly 20% of children are medically exempt. This begs belief as medical exemption is typically reserved for situations such as individuals with severe allergic reactions to the specific vaccine. The Department of Health should regulate these exemptions, and physicians who provide unwarranted exemption should be subject to scrutiny.

The Hawaii Chapter of the American Academy of Pediatrics is comprised of over 320 pediatricians and child health professionals in the state of Hawaii. Our Mission is to attain optimal physical, mental and social health and well-being for infants, children, adolescents and young adults. **We respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.**

Sincerely,

Michael S.L. Ching, MD, MPH, FAAP
Vice President, Hawaii AAP

From: [REDACTED]
To: [REDACTED]
Subject: Testimony
Date: Tuesday, November 06, 2018 5:48:40 AM

I was like so say that I have very strong feelings against mandatory vaccinations. Having the right to decide what goes into your own body seems like a minimum freedom that we all should have. Any putting injections into tiny babies is something that parents should have the right to not do or delay. Gardasil is known to have really really bad side affects for some kids. Did you research Colton's story? Please don't let that happen to our kids in Hawaii.

I urge you to ease up on all mandatory vaccines please do not make it more strict. Thank you!!!

Heidi Schemp

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: vaccine
Date: Tuesday, November 06, 2018 10:19:00 AM

vaccinations needed for our safety. mandatory vaccinations needed. keep Hawaii safe

From: [REDACTED]
To: [REDACTED]
Subject: Opposing HAR 11-157
Date: Tuesday, November 06, 2018 10:56:46 AM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. As a parent, one should decide the medical interventions appropriate for their own child, not the State. I do believe vaccines are necessary, however I do not agree with the CDC schedule of vaccinations, or the amount of vaccinations required. I support a delayed vaccine schedule, and as a parent it should be my choice. Considering the CDC schedule has not been tested yet, there is even more concern if it were to pass.

I do understand the concern about the anti-vax movement putting everyone at risk, and some of the loudest proponents of "no" vaccinations do make the movement sound crazy. However, if you listen to the majority of these parents, they are far from crazy. They are deeply concerned about the risks associated with vaccines - both with the toxicity of ingredients as well as the schedule that doesn't take into account the inherent risks of immunizing babies so young. There needs to be studies showing the risks, more information available to the public on every level, before something like this is mandated. Without that information, all parents are hearing is a loud discord of right versus wrong and are unsure of the path to take. Forcing a vaccine mandate doesn't address the issue of parents being (very rightly) worried about the health risks.

There is a vaccine court that doles out money for vaccine injuries. That's because vaccines can harm. This is fact. Not all vaccines harm all children. This is also a fact. But because there are two sides, and one side proven to cause harm, this issue should not be taken lightly. Not when our keiki are the ones at risk.

Even more, once vaccinations are mandated, what's to stop pharmaceutical companies from forcing even more vaccinations on children and adults alike? Is the govt taking control in good faith that a billion dollar industry is going to sit by and not create 10-20 more vaccines for every child to be mandated to have? History has shown this will certainly not be the case...

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify. I ask that you delay your decision on this important issue and please please please listen to the people, parents, and concerned citizens of Hawaii.

Sincerely,
Juliet Simpson
[REDACTED] born and raised and mother of two

From:

To:

Subject:

A public hearing on the proposed Hawaii Administrative Rules (HAR 11-157) to update the school vaccination and examination requirements has been scheduled. Thursday, November 1st at 3:00-4:00pm

Date:

Tuesday, November 06, 2018 10:21:47 AM

I am submitting testimony as a physician and vaccine expert. (Prior medical director of a veterinary vaccine company with patents in viral inactivation and vaccine production and witness in a vaccine injury case)

The move to change the school immunization vaccine requirements is something that deserves great consideration.

I am requesting that you extend hearings to the neighbor islands and will also be requesting an informational briefing for the legislature regarding this issue.

Please realize that a precipitous rule change will negatively affect the uptake and use of vaccines.

Richard Creagan, M.D.
State Representative, District 5

From: [REDACTED]
To: [REDACTED]
Subject: Amendment HAR 11-157
Date: Tuesday, November 06, 2018 10:10:55 AM

To the Department of Health,

I strongly oppose Amendment HAR 11-157. As a parent, I should decide the medical interventions appropriate for my own child, not the State. I do believe vaccines are necessary, however I do not agree with the CDC schedule of vaccinations, or the amount of vaccinations required. I support a delayed vaccine schedule, and as a parent it should be my choice.

I do understand the concern about the anti-vax movement putting everyone at risk, and some of the loudest proponents of "no" vaccinations do make the movement sound *crazy*. However, if you listen to the majority of these parents, they are far from crazy. They are deeply concerned about the risks associated with vaccines - both with the toxicity of ingredients as well as the schedule that doesn't take into account the inherent risks of immunizing babies so young. There needs to be studies showing the risks, more information available to the public on every level, before something like this is mandated. Without that information, all parents are hearing is a loud discord of right versus wrong and are unsure of the path to take. Forcing a vaccine mandate doesn't address the issue of parents being (very rightly) worried about the health risks.

There is a vaccine court that doles out money for vaccine injuries. That's because vaccines *can* harm. This is fact. Not all vaccines harm all children. This is also a fact. But because there are two sides, and one side proven to cause harm, this issue should not be taken lightly. Not when our keiki are the ones at risk.

Even more, once vaccinations are mandated, what's to stop pharmaceutical companies from forcing even more vaccinations on children and adults alike? Is the govt taking control in good faith that a billion dollar industry is going to sit by and not create 10-20 more vaccines for every child to be mandated to have? History has shown this will certainly not be the case...

There was only a 1 hr public hearing on Oahu only for testimony to be given. We, as parents, grandparents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed through without the chance for the public to testify. I ask that you delay your decision on this important issue and please please please listen to the people, parents, and concerned citizens of Hawaii nei.

Sincerely,
Megan Kirkpatrick
Kauai born and raised, mother, botanist.

From: [REDACTED]
To: [REDACTED]
Subject: email testimony to support HAR 11-157 update
Date: Tuesday, November 06, 2018 11:08:17 AM

Thank you for this opportunity to provide testimony. As a Pediatrician and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities. In addition, I would support removal or “Naturopathic Medicine” providers from the definition of “physicians” as they are NOT physicians despite their wishes to be called such. Finally, I would support including “drop-in” child care centers in this as well. Even a brief exposure to someone with pertussis or measles is enough to make a vulnerable child (infant, immunocompromised) extremely ill.

Thank you for your consideration.

Tonya Kratovil, MD, FAAP
Pediatric Hospitalist



From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Tuesday, November 06, 2018 12:55:21 PM

Thank you for this opportunity to provide testimony. As 20 year practicing pediatrician, community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,

Cindy V. Wong, MD

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: support for HAR 11-157
Date: Tuesday, November 06, 2018 11:16:40 AM

Thank you for this opportunity to provide testimony.

As a Pediatrician and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

My specialty is caring for the hospitalized children of Hawaii. Immunizations and the diseases they prevent are not a theoretical or statistical issue in my practice, they are something that I see and deal with every day. The diseases that were prevented for decades and that people think are no longer are a threat, are a very real danger to the children of our community. I have personally cared for children who have died from diseases such as whooping cough (pertussis), influenza and meningococcus (bacterial meningitis). I have had patients who needed to be hospitalized due to complications from rotavirus, Strep pneumoniae, chickenpox and measles. Within the last week I had a patient with issues due to Hepatitis B. This is not a full list but merely a sample of the vaccine preventable illnesses that I see far too frequently. There are so many infections and illnesses that I cannot protect children from because specific vaccines have not been created for them, but we can and should protect children and the larger community from the diseases that we do have safe vaccines for.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Bettina Ackermann, MD

From: [REDACTED]
To: [REDACTED]
Subject: support of HAR 11-157
Date: Tuesday, November 06, 2018 1:18:40 PM

please note and submit my support for HAR 11-157 as it related to immunizations.

as a pediatrician and child psychiatrist i care about the health of all children.

mahalo!

asad ghiasuddin MD, FAAP, FAPA

From: [REDACTED]
To: [REDACTED]
Subject: Support of HAR 11-157
Date: Tuesday, November 06, 2018 5:01:24 PM

Thank you for this opportunity to provide testimony. As a community member, pediatrician and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,

Alicia Turlington, MD
Pediatrician

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in Support of HAR 11-157 on behalf of Hawaii Health & Harm Reduction Center
Date: Tuesday, November 06, 2018 1:15:26 PM
Attachments: [D509B612185F49658F6975479DAB90DF.png](#)
[C32672796F6349C292ED037049C4C280.png](#)
[C6282BC075284FF9A00823B7887897BB.png](#)

Mahalo for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Jasmine Umeno
Executive Assistant
she/her/hers

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

Phone: [REDACTED]

Email: [REDACTED]

Website: [REDACTED]

Follow us on social media



CONFIDENTIALITY NOTICE: This e-mail message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and/or privileged information. Any unauthorized review, use, copying, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender immediately by reply e-mail and destroy the original message and all copies.

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Tuesday, November 06, 2018 2:46:31 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Support for Vaccination
Date: Tuesday, November 06, 2018 2:41:16 PM
Attachments: [image001.png](#)

To Whom It May Concern:

I am old enough that I took care of the gravely ill children who, for example, actually had Hemophilus influenza and Streptococcal pneumonia meningitis/epiglottitis/pneumonia in the 1970's and 1980's. Thanks to vaccines against these dreaded diseases, these diseases are now seen only rarely. I do understand why some in the general public cannot understand why these vaccines are so valuable as they have never seen these illnesses in friends and family—but they do not understand it is because of vaccinations that these diseases are not common. However, if we stop vaccinating, they will come back. Americans need to travel out of the country to countries that do not have well established vaccine programs...such as in 3rd world countries—and then they would “get it”.

Thanks so much for all your efforts to continue vaccinating our population in order to protect the general public.

Geri Young, MD

Chief Medical Officer

[REDACTED]
[REDACTED]

Phone: [REDACTED] | Fax [REDACTED]

Email: [REDACTED]

[REDACTED]

Confidentiality Notice: This e-mail message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 proposed rules update
Date: Wednesday, November 07, 2018 10:32:28 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

I was the previous chair of the Council on School Health at the national American Academy of Pediatrics. Schools rely on children to be healthy in order to learn. Without vaccines, many children would have diseases keeping them from school. I remember being out of school from chickenpox (varicella) and coming back with all of my classmates knowing how to write cursive, which I needed to catch up on.

Vaccines are fundamental to children's health. No state in the nation wants children to be unvaccinated, risking the health of whole groups of students. Vaccine-preventable diseases can spread like wildfire, as evident in communities that don't vaccinate their children.

So I strongly support the update of the HAR 11-157 rules. Do not allow our children to be unprotected.

Thank you for the opportunity to weigh in on this.

Jeffrey Okamoto M.D., FAAP

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 11:41:59 AM

To whom it may concern:

As a practicing pediatrician for 36 years, I strongly support the HAR 11-157 proposed rules update which will make our immunization practices consistent with the recommendations of the ACIP. Vaccines have significantly reduced the frequency and severity of infant, childhood and adolescent infections but are effective only if administered community-wide and at the recommended ages.

Thank you for your consideration.

Keith Matsumoto, MD

Confidentiality Notice: This e-mail message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 11:07:12 AM

To Whom It May Concern.

I oppose any mandatory vaccines for any children in the State of Hawaii students to attend public or private schools. I believe a parent, adult, guardian should have the right to decide what gets injected into their bodies or that of their children. There are many risks to getting vaccines,. In 1988 I lost a son to SIDS after a scheduled vaccine. To this day I will never know if it was vaccine related. Had I known what I know now, I would not have allowed it. Growing up here in Hawaii we had very few vaccine requirements and did just fine. One child lost is Thank You for your time And consideration in this matter.

Aloha,
Sheila Gage

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157 Testimony - One fact that can save thousands of lives
Date: Wednesday, November 07, 2018 11:42:21 AM

Aloha,

Thank you for hearing my testimony. I urge you with all of my heart to oppose HAR 11-157. Here is one fact that will give you the power to save thousands of lives in Hawaii in regard to Gardasil-9 (the HPV Vaccine) -

For every 100,000 people using Gardasil-9 there will be 2,300 serious adverse events. The Cervical Cancer diagnosis rate in the United States is 7.9/100,000. The risk of vaccine damage with Gardasil-9 far outweighs the benefit. This vaccine is not safe, not effective and WILL be pulled off the market eventually. Many Nations have banned it in order to protect the lives of millions of children. What we are about to witness in the State of Hawaii is a crime against humanity if HAR 11-157 passes. How could anyone in their right mind pass this bill? You must oppose it.

PLEASE use your position in office to do what it is right, not what is profitable. HAR 11-157 does not protect our children, it hurts them. Cancer is treatable, death and disability from an unsafe vaccine are not. PLEASE have the courage to stand up to Merck and these ruthless pharmaceutical companies that have zero liability. It is the parents decision whether or not to vaccinate.

There is only one correct answer, and it's to save lives by opposing HAR 11-157.

Mahalo,

Caren Terrell

Registered Voter

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 9:31:30 AM

Good day,

As a physician assistant working in pediatrics, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Regards,

Joel Hamaguchi, PA-C

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 9:23:06 AM

Thank you for this opportunity to provide testimony. As a community member , I am writing to strongly oppose HAR 11-157!

Sincerely

Lisa Wilford

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 rules
Date: Wednesday, November 07, 2018 9:50:40 AM

I am in full support of HAR 11-157 rules!

I used to see Pediatric wards and Pediatric ICUs filled with children and families who were devastated by hemophilus influenza type B infections as well as pneumococcal strep infections. I no longer see these infections to any degree due to the wonderful job these immunizations have done for our community. This is but one example of the incredible success of immunizations.

I have seen a few cases of meningococcal infections in my 30 year career. I never want to see another one of these devastating illnesses. We now have an immunization to help protect against this terrible infection.

I have never seen a child permanently injured by a vaccine in my 30 years of practice where we give 100's of vaccines a week.

Why anyone would not want to provide our keiki with the protection they deserve is beyond my understanding. Immunizations are a corner stone of preventative medicine and care. Thank you for the opportunity to protect the future of Hawaii. Children may only make up a part of our population but they make up all of our future. LET'S PROTECT THEM and our community by having them fully immunized.

Sincerely,

R. Michael Hamilton, MD, MS, FAAP

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 11:54:27 AM

To Whom It May Concern,

I oppose any mandatory medical procedure. I stand for Body Sovereignty. Regardless of your stance towards immunizations it should be your choice whether you do it or not. I personally and professionally, with my education as a Doctor of Chiropractic, have not seen any research about their safety that stands to scrutiny. Please consider people's rights to choose what they put inside their bodies, especially when there is a great and growing body of research that shows the toxicity and the risk that is involved in immunization programs.

Respectfully,

Luis E. Feliu, DC

[REDACTED]
And Father of a 3 year old child who I seeking to protect from such toxins



Student Immunization Initiative
Registered Independent Organization



November 7th, 2018

Re: Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization"

To Whom It May Concern:

The Student Immunization Initiative (SII) is an organization led by graduate students of the University of Hawai'i at Mānoa. SII advocates for the importance of immunization and participates in educational outreach programs with a focus on vaccine-preventable diseases. The majority of SII members participate in biomedical research and have a thorough understanding of the science behind vaccine development and benefits of increased immunization rates in a community. SII was founded in Hawaii in 2016 and has more than one hundred supporters. **SII strongly supports the HAR 11-157 proposed rules.**

The proposed update of the Hawaii Administrative Rules will ensure Hawaii is up-to-date on the most recent recommendations from the Advisory Committee on Immunization Practices (ACIP). The ACIP is comprised of medical and public health experts, including members of the American Academy of Pediatrics and the American Academy of Family Physicians. The ACIP methodically reviews all data regarding a vaccine's safety and efficacy at specific ages to make recommendations for immunization schedules.

The United States Food and Drug Administration's (FDA) approval process ensures vaccines are as safe as possible. FDA clinical trials require three major phases of approval with safety and effectiveness assessed throughout. Due to this stringent safety monitoring, the U.S. has the safest vaccine supply in history. However, the reality is that no vaccine is 100% effective and many individuals, such as newborns and the immunocompromised, cannot be immunized. Therefore, it is imperative to keep vaccination rates high to ensure *community immunity* – protection for those who cannot be vaccinated.

The Centers for Disease Control and Prevention (CDC) makes it abundantly clear that state and local requirements for daycare and school entry, such as the proposed update HAR 11-157, are important tools for maintaining high vaccination rates and thus lowering the rates of vaccine preventable diseases. The proposed update HAR 11-157 will ensure that students entering 7th grade or higher receive the HPV, MCV, and Tdap shots. This requirement is especially important due to low uptake levels and by ensuring protection prior to exposure, especially for the HPV vaccine.

We respectfully request that the Hawaii Administrative Rule 11-157 be supported and passed for the reasons noted above.

Thank you for this opportunity to provide testimony on the proposed rules.

Sincerely,

The Student Immunization Initiative



From: [REDACTED]
To: [REDACTED]
Subject: Hawaii Administrative Rules Testimony
Date: Wednesday, November 07, 2018 8:32:41 AM

November 8, 2018

Bruce Anderson, PH.D.

Director of Health
Hawaii Department of Health

SUBJECT: Hawaii Administrative Rules (HAS) Title 11, Chapter 157,
"Examination and Immunization

Thank you for the opportunity to provide testimony on these proposed rules. I strongly support the rule changes that would establish immunization requirements for school and post secondary students and children enrolled in child care facilities. The Department of Health (DOH), Immunization Branch is charged with monitoring this program.

The Centers for Disease Control and Prevention (CDC) suggests that state and local vaccination requirements for school entry and day care are important for keeping vaccination rates high and as a result lowers rates of vaccine-preventable diseases.

One example of a vaccine-preventable disease is flu. As a former administrator of the Department of Education, I worked with the DOH nurses to develop a coordinated program to provide flu immunizations to all students except those with medical exemptions. It was anticipated that families, often with grandparents living in the home, would also benefit by preventing this disease. Flu could involve visits to a doctor, hospitalizations and even premature death. Parents also could lose time from work. As a result, the flu immunization program has been successful and has continued in Hawaii.

Therefore, I request that the administrative rule changes be supported and

passed to benefit Hawaii's students and families.

Deanna D. Helber, M.S. retired DOE



From: [REDACTED]
To: [REDACTED]
Subject: HPV Vaccine Testimony
Date: Wednesday, November 07, 2018 4:31:20 PM

Dear Director Anderson,

My name is Caroline Stoner, and I am writing to express my support of proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization. The scope of efficient immunization benefits for individuals and the State include, preventing long term healthcare costs and the potential loss of productivity. Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

Specifically, the proposed amendments that address the prevention of HPV and HPV-related cancers. The HPV virus has serious repercussions such as cancer and genital warts, both of which result not only in physical ailments, but also emotional stress.

As a young woman with many dreams and ambitions, I can speak on behalf of the younger generation when I say we deserve to be protected. Proper vaccinations can help ensure I achieve my goals and have the brightest future.

The HPV vaccine is important because it is currently the most common STD virus and has no cure. About one in four—are currently infected in the United States. Every year, individuals in the US are diagnosed with cancer resulting from contracting HPV, and of those diagnosed with cancer, one-third will die from the disease.

If we can protect our youth from the potential of contracting cancer or other harmful symptoms, by adopting these regulations now, we absolutely must.

I urge you to support **HAR 11-157 proposed rules update.** Thank you for the consideration of my testimony.

Mahalo,
Caroline Stoner

--

Public Health Department
Hawaii Pacific University

[REDACTED]
[REDACTED]

(cellphone)

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: I oppose HAR 11-1157 AND my son experienced adverse reactions to vaccines
Date: Wednesday, November 07, 2018 10:14:15 AM

My name is Carolyn Moss and I am writing in opposition to HAR 11-157. I feel that my rights as a parent are being threatened. Where there is risk, there must be choice. Let parents decide which vaccines are important.

My son experienced adverse reactions to vaccines. He now has to live his life combating the effects of these vaccines. If he receives any more vaccines, the effects could be completely devastating to him. Life is difficult enough if you're aren't living with issues.

Please give parents the right to choose the vaccines that are important, those parents who are concerned, actually do their research.

I appreciate your time in considering my testimony.

Thank you,

Carolyn Moss

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Wednesday, November 07, 2018 10:45:00 AM

Dear DOH,

I am a Shane-Earl Kaniela Naeole, second year student pharmacist at the [REDACTED] [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. As a future health professional and resident of Hawai'i, this amendment will help improve our state's health care for future generations.

Mahalo Nui Loa.

Shane-Earl Kaniela Naeole

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Wednesday, November 07, 2018 11:09:57 AM

Dear DOH:

I am a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. With the passing of this amendment, many members of the community who did not fall under the age range for initial vaccination (<26yo) can receive the preventative measures against several of the cancers that the HPV vaccine yields. Thank you for your time and consideration.

Best regards,
Brent Ocker

--

Brent Ocker

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony to OPPOSE HAR 11-157
Date: Wednesday, November 07, 2018 11:26:33 AM

Aloha,

My name is Amber David. I was born and raised here on [REDACTED]. I am a mother of 3 children, all born and are being raised here on [REDACTED].

Thank you for this opportunity to provide testimony. I am writing to you as a mother, that is responsible for the health, safety and well being of my 3 children. I am writing as a concerned community member for all the keiki of Hawaii.

I am writing to strongly oppose HAR 11-157. I also request that there be hearings on all islands.

The amount of vaccines on the CDC suggested vaccine schedule has dramatically increased from 10 doses in 1980, to currently 72 doses for children from birth to age 18.

It greatly concerns me, as it should concern you that there have been no long term studies done showing the safety and effects of the CDC's suggested vaccine schedule. Nor have there been studies done on dosages and large combinations of vaccines given at baby well visits.

The list keeps growing. Again, there have been no safety studies done! To propose to add even more to the already overburdened schedule is irresponsible and a disregard for the safety of our children. Our children are made to be test subjects, and this is unacceptable! If a child does become vaccine injured, the vaccine manufacturers are granted immunity from liability.

If there is even any question about the safety and effectiveness of vaccines, they should not be mandated. If there is a risk, there must be a choice. Parents have the right to informed consent so they can make educated decisions when it comes to vaccines and their own children. Medical freedom is a basic right, and medical freedom should be protected. The future of our keiki depend on it.

The advancement of the proposed mandate could be catastrophic and cause irreversible damage. Please, I urge you to do what is right for the future of our keiki.

Thank you for taking the time to read my testimony.

Aloha, Amber David

[Sent from Yahoo Mail on Android](#)

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Title 11. Chapter 157 Examination and Immunization
Date: Wednesday, November 07, 2018 11:28:37 AM

Dear DOH,

I am a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization" as this would help to increase the health of our students and community. Mandating immunization requirements for school will help us protect our community and students from acquiring diseases that are preventable and educate and spread the awareness of the importance of it.

Thank you,
Jiyoung Min

--

Jiyoung Min

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony
Date: Wednesday, November 07, 2018 11:43:54 AM

Thank you for this opportunity to provide testimony. As a community member and pediatrician, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Kelli-Ann

To: Hawaii State Department of Health
Hearing Date/Time: Wednesday, Nov. 7, 2018, 3:00 p.m.
Place: Hawaii Department of Health, Kinau Hale Boardroom, 1st Fl.
Re: Testimony of Planned Parenthood Votes Northwest and Hawaii in support of
Proposed Amendments to H.A.R. Title 11, Chapter 157, Examination and
Immunization

Dear Director Anderson,

I am a third generation Hawai'i resident, a graduate student at Hawai'i Pacific University, and President of our campus' Generation Action Club. I am writing in support of proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization, which seek to codify the United States Department of Health and Human Services' Advisory Committee on Immunization Practices' General Best Practice Guidelines for Immunization.

The scope of efficient immunization benefits for individuals and the State include, preventing long term healthcare costs and the potential loss of productivity. In the long term, this leads to increased economic productivity and wellbeing for our communities by improving financial security and reducing risk.

Specifically, the proposed amendments that address the prevention of HPV and HPV-related cancers. According to the U.S. Department of Health & Human Services, Hawaii Adolescent Reproductive Health Facts, only 48% of Hawaii's teens reported using condoms during intercourse, compared to national average of 57%. The risk of unprotected sex can lead to contracting STDs including the HPV virus which currently has serious repercussions and currently, no cure.

According to the Center for Disease Control and Prevention, HPV infection can cause, "cancers of the cervix, vagina, and vulva in women; penis in men; anus, back of the throat, including the base of the tongue and tonsils (oropharynx), in both women and men; and can also cause called genital warts." These symptoms cause not only extreme physical ailments, but also cause emotional stress and their treatment can be very uncomfortable.

Sexual and reproductive health of our youth is especially important because the peak time for acquiring infection for both women and men is shortly after becoming sexually active. Ideally females and males will get the vaccine before they become sexually active and exposed to HPV, as outlined in the proposed amendments.

The HPV vaccine is important because it is a very common virus; about one in four—are currently infected in the United States, and about 14 million people, including teens, become infected with HPV each year (CDC). Every year, individuals in the US are diagnosed with cancer resulting from contracting HPV, and of those diagnosed, one-third will die from the disease.

If we can protect our youth from the potential of contracting cancer or other harmful symptoms, by adopting these regulations now, we absolutely must.

Thank you for the opportunity to testify in support of this important effort.

Sincerely,

Maisa Thayer

From:

To:

Date:

Wednesday, November 07, 2018 3:29:48 PM

My stance on this issue as a mother of 4 and grandmother of 6:

My good friends son was born six days before my second child. He went to his doctor for vaccinations and his life was forever changed. That evening he had seizures. They didn't stop. Obviously the poor little guy suffered severe complications due to the vaccines he received. He was normal and just like that his life and his young parents lives were ruined! Needless to say, my son did not show up for his appointment the following week.

Thank god my children and grandchildren are not vaccinated.

I have worked with young children as a teacher and parent all my life and I can honestly say the children raised by alternative, health conscious parents are thriving, strong And healthy.

Government and big pharmaceutical companies do not have the right to discriminate against children who's parents have made the conscious decision to not risk the obvious dangerous consequences of this onslaught of toxic poisons being forced on them in lieu of a public education paid for by their taxes.

Furthermore, the forcing of seventh graders risk their lives by taking the hpv vaccines is ludicrous. This vaccination is obviously dangerous. Please look at the stories of the story suffering endured by these once healthy victims of these vaccines.

Please don't risk our children's safety in exchange for \$ from the evil big pharmaceutical companies.

Don't follow the footsteps of California and other states.

Make Hawaii a trend setter not a weak follower.

Look at the health statistics worldwide.

Respectfully, Nancy Wood. (Rogers)

[Redacted signature block]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony on HAR 11-157
Date: Wednesday, November 07, 2018 4:05:16 PM

To Whom It May Concern:

Please STOP all mandatory vaccinations! There is plenty of evidence that vaccines are not safe. It is our god-given right to live a life free of drugs/vaccines/chemicals if we so choose. Please protect our freedom of choice in all matters of health care.

Thank you,
Allan Reaves

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157 - Oppose- Public Testimony
Date: Wednesday, November 07, 2018 11:37:48 AM

To the Department of Health,

My name is Catherine Posner, I am a mother and Resident on Kaua'I Island and I strongly oppose amendment HAR 11-157.

The State SHOULD NOT have the right to decide for any parents about vaccinating their own children. WHERE THERE IS A RISK THERE MUST BE A CHOICE !!!

There was only a 1 public hearing on Oahu for testimony to be given. We, as parents and citizens demand that there be other public hearings on each Island. This is too important of an issue to be rushed and I ask that you delay your decision on this extremely important issue.

Sincerely,

Catherine Posner

--

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, November 07, 2018 9:15:10 AM

To Whom It May Concern:

As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,

Joseph Gary Dela Cruz MD

From: [REDACTED]
To: [REDACTED]
Subject: STRONGLY OPPOSE HAR 11-157
Date: Wednesday, November 07, 2018 5:16:59 AM

I am submitting my testimony strongly opposing HAR 11-157. The childhood vaccination schedule grows every year and has never been subjected to any testing in its entirety. The vaccine schedule continues to grow and has never been tested for safety. We are not genetic clones and it is well-established in the medical literature that some individuals have genetic make-ups that make them more susceptible to Adverse Events following Vaccination.

Janet Edghill
[REDACTED]

--



Aloha Nui...Janet

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for Proposed Changes to HAR 11-157
Date: Wednesday, November 07, 2018 11:51:31 AM

Thank you for this opportunity to provide testimony. My name is Keanu Wong, I am 26, and as a community member and an uncle to three young nephews, I am writing to strongly support the HAR 11-157 proposed rules update.

The reason why I support the changes to the HAR 11-157 rules come down to the point that there may be certain children and adolescents that don't have the ability to become immunized, such as neonates and children going through chemotherapy; in which case herd immunity, a term used since 1923 and recognized as a naturally occurring phenomenon in the 1930s, helps protect the aforementioned children/adolescents.

As an uncle to an eight month old, a five-year old, and a prenatal child, it worries me that if the immunization requirements don't become more stringent, then my family may be put at risk due to less requirements. There is scientific research that proves that if more vaccine exemptions are in a community, the more that said community is at risk for vaccine-preventable disease outbreaks such as HPV and Meningococcal disease.

I respectfully request that the proposed changes to HAR 11-157 rules be supported and passed for the health of all of our communities.

Thank you for your consideration.

Keanu Wong

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for Title 11, Chapter 157 "Examination and Immunization"
Date: Wednesday, November 07, 2018 11:39:43 AM

Aloha Department of Health,

My name is Karen Pae, and I am a student pharmacist at the [REDACTED]. I support the amendments proposed for Title 11, Chapter 157 "Examination and Immunization." Passing this amendment would help to increase and protect the health of our students and community. By establishing immunization requirements for schools in the State of Hawaii, we would lessen the risk of outbreak of diseases such as the flu, HPV, etc. Immunizations protect future generations as it allows the possibility for eradication of various strains of diseases. Thank you for your time and the opportunity to submit my testimony.

Sincerely,
Karen Pae
--

Karen Pae
Student Pharmacist, Class of 2021

[REDACTED]
Phone: [REDACTED] | Email: [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in support of HAR 11-157
Date: Wednesday, November 07, 2018 9:09:42 AM

Thank you for the opportunity to provide testimony as a pediatrician with 30 years of clinical experience. I strongly support of HAR 11-157 proposed rules update. I have had the personal good fortune during the 1980s to witness the rapid decline over a period of 1-2 years of life-threatening and crippling invasive Hemophilus influenzae disease in children following the nationwide implementation of universal hemophilus influenzae vaccination in children.

The science supporting universal immunization of vaccine-preventable diseases is , for all intents and purposes, irrefutable. It is based upon a wealth of research with vigorous methodology, excellent study design, and adequate population size. There is simply no question that universal vaccination is a substantial public health benefit, preventing both loss of life and limb. Therefore, the burden of proof to discontinue or limit universal vaccination lies with the anti-vaccination coalition.

Demand to see the proof behind the claims of these anti-vaccination groups. Don't settle for less than the careful scrutiny of the science, methodology and study design, and objectivity of the claims these groups wave in front of your faces. Because they will, in the end, come up short. Many of the arguments put forward by anti-vaccination forces are not based on science but temporal associations, the same process that would prove that roosters crowing at dawn cause the sun to rise.

Do not be gulled or lulled by empty rhetoric or dramatic hair-rendering. Truth and reason should not be decided simply by he who shouts the loudest. Passion without substance, or substantiation, after all, is nothing more than hot air.

Thank your for your time, thought, and patience.

Jeffrey Lim, M.D>

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in support of HAR 11-157
Date: Wednesday, November 07, 2018 8:56:25 AM

Immunizations are one of the Top 10 Achievements in Public Health in the 20th Century. Infectious diseases were once very prevalent in the United States and many people died as a result. For example, in 1920 there were 469,924 cases of measles reported in the US and 7,575 died and 147,991 diphtheria cases reported and 13,170 died.

These diseases are NOT gone, they are kept at bay by having a well-vaccinated population. As an example, in April through May of 2017, Minnesota experienced their largest outbreak of measles in 30 years as a result of low vaccination rates among Minnesota's Somali-American community members. Vaccine coverage rates for MMR had dropped from 90% to only 54% at the time of the outbreak as a result of misinformation about the relationship between vaccines and autism. This is the same type of misinformation that opponents to HAR 11-157 are spreading.

Please approve HAR 11-157. Protect our children and our communities.

Thank you,
Michele Nakata

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in support of HAR 11-157 proposed rules update
Date: Wednesday, November 07, 2018 9:05:24 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Benjamin Kilinski
MSN, APRN-Rx, CPNP-PC, NCSN

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in support of HAR 11-157 proposed rules update
Date: Wednesday, November 07, 2018 9:05:24 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Benjamin Kilinski
MSN, APRN-Rx, CPNP-PC, NCSN

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Hawaii Administrative Rules (HAR 11-157)
Date: Thursday, November 08, 2018 5:05:34 AM

To whom it may concern,

My name is Dr. Aki Oshita. I am a father of one son and Doctor of Chiropractic for last 10 years.

I am writing this email to share the concern about school vaccination and examination. Also, since we are Pediatric and Maternity Chiropractic office, we have been similar concerns from the parents.

Based on clinical studies about immunization, anatomy, and physiology, everybody is aware of risk and side effects just like other medication. I am not listing the detailed information since you have heard them all. (However, if you need the scientific evidences from our professions, please let me know.)

As long as we DO know that there are side effects and ricks, we as the human beings SHOULD have OPTIONS, just like nobody forces us to take medications.

Thank you so much for spending time to read this.

--



Dr. Aki Oshita
Foundational Chiropractor [REDACTED]

A [REDACTED]
P [REDACTED] M [REDACTED]
W [REDACTED]



Create your own [email signature](#)

From: [REDACTED]
To: [REDACTED]
Subject: Opposing further required vaccines
Date: Thursday, November 08, 2018 3:20:32 PM

I would like it to be documented that as a resident of Hawaii with children, that I strongly OPPOSE the proposed increased immunizations for school-aged children in the state of Hawai'i. In particular, I oppose the requirements for the flu vaccine and HPV vaccine. I understand and support the science behind vaccinations, have gotten them myself, and have gotten them for my family. However, these two vaccines in particular are very risky for the young to be subjected to. My family has a history of adverse reactions to the flu shot and I plan not to subject my children to be a "lab animal" and have them receive the flu shot and have a potentially fatal reaction simply because it is mandated by law.

Also, I feel compelled to point out that HPV is a sexually transmitted disease and not communicable by any other means. Why would this be required for attendance in a Hawaii school?

We had previously planned to enroll our children in a private school, however we will absolutely resort to homeschooling or moving if these new proposed immunizations become a requirement. I will not risk my family's health and safety so the DOH can pad the pockets of pharmaceutical companies.

Rachel Pierson-Medina

From: [REDACTED]
To: [REDACTED]
Subject: Public time and input
Date: Sunday, November 11, 2018 9:11:47 AM

Do not pass the new immunization rules.

It is my RIGHT to chose for myself and my family how, when or if we vaccinate.

We do not know the long term effects of the flu vaccine and HPV vaccines.

This is inappropriate and I will fight this with every ounce of my being.

You placed the hearing for this for the public on a weekday, before the holidays in the afternoon. That is inconsiderate and unfair. People who have families to support are going to be at work! They'll be working extra hard right before the holidays to maintain the time off they'll need shortly after. You're doing a dis-service to our community by allotting this time frame as the public's opportunity to voice their opinions and you're stripping us of our rights.

Do not pass this!
We should not be forced to vaccinate!

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: HPV
Date: Sunday, November 11, 2018 3:08:10 PM

Aloha, I was reading about this required vaccine for school and I'm totally not comfortable with the HPV & Flu vaccine. I have 3 daughters ages 12,10 & 3. I would never vaccinate my child with these 2. I'm not a anti-Vaccination parent either. My 2 oldest are fully vaccinated except for the 2 listed above. There just is not enough studies done to put this poison on my child especially the HPV. Adults I know who have been vaccinated with HPV (young adults) have tumors and that can't just be a coincidence. If this is a forced procedure done, my kids will not be going to school. My kids go to public school in Lahaina, Maui and I support vaccination but this makes me really not happy to support these 2 particular. STD vaccine is not a illness that can spread like Chicken pox or Measles, it's rediculous that it would be treated like so. Please take this into consideration. Mahalo, April Colpas

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Re: HAR 11-157
Date: Tuesday, November 13, 2018 11:42:46 AM

Good Morning,

Due to a computer screen problem I had while submitting my testimony, I was just able to reread what I wrote and noticed the second to the last sentence was cut off. Please accept my apologies and accept my testimony with the completed sentence.

Thank You...

To Whom It May Concern.

I oppose any mandatory vaccines for any children in the State of Hawaii students to attend public or private schools. I believe a parent, adult, guardian should have the right to decide what gets injected into their bodies or that of their children. There are many risks to getting vaccines,. In 1988 I lost a son to SIDS after a scheduled vaccine. To this day I will never know if it was vaccine related. Had I known what I know now, I would not have allowed it. Growing up here in Hawaii we had very few vaccine requirements and did just fine. One child lost is one too many.

Thank You for your time And consideration in this matter.

Aloha,
Sheila Gage

-----Original Message-----

From: DOH.Immunization [REDACTED]
To: Sheila Gage [REDACTED]
Sent: Wed, Nov 7, 2018 6:18 pm
Subject: RE: HAR 11-157

Aloha Ms. Gage,

Your written testimony has been received. Thank you.

Hawaii Department of Health, Immunization Branch
Tel. (808) 586-8300 Fax (808) 586-8347

From: Sheila Gage [REDACTED]
Sent: Wednesday, November 07, 2018 11:07 AM
To: DOH.Immunization [REDACTED]
Subject: HAR 11-157

To Whom It May Concern.

I oppose any mandatory vaccines for any children in the State of Hawaii students to attend public or private schools. I believe a parent, adult, guardian should have the right to decide what gets injected into their bodies or that of their children. There are many risks to getting vaccines,. In 1988 I lost a son to SIDS after a scheduled vaccine. To this day I will never know if it was vaccine related. Had I known what I know now, I would not have allowed it. Growing up here in Hawaii we had very few vaccine requirements and did just fine. One child lost is Thank You for your time And consideration in this matter.

Aloha,
Sheila Gage

From: [REDACTED]
To: [REDACTED]
Subject: Dec 14th Hearing
Date: Tuesday, November 13, 2018 9:25:41 PM

Hello,

It is my understanding that there is talks to make HPV and the flu vaccine mandatory for school age children. This concerns me GREATLY! I do NOT believe that this should come to pass for a multitude of reasons - the easiest being that a parent should have the right to choose what is best for their child.

Where is the public hearing on this on the 14th? I would like to be in attendance.

Thank you,
Dani

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Friday, December 14, 2018 7:15:07 AM

To whom it may concern,

I am voicing my testimony in vote or favor that this bill does NOT pass. It is my constitutional right that I AM able to CHOOSE what I put into my body and my children's as well as how I govern my own health.

Sincerely,
Jordan Elizabeth Doty

Sent from my iPhone

From: [REDACTED]
To: [REDACTED] [REDACTED] [REDACTED]
Subject: Concerned parent Testimony against vaccine changes
Date: Wednesday, November 14, 2018 1:01:11 PM

Aloha,

As a concerned parent, I am vary worried that the State of Hawaii will be ending the vaccine exception choice for children, as well as, adding two more vaccines to the current schedule. I am concerned about this blanket declaration, because not all people respond well to vaccines. This is also true for medications and food. So, If someone has a food allergy, we do not force them to eat that food. Then why would we mandate across the board vaccinations knowing some children will be compromised and get very sick or have life long illnesses because of it.

As an adult, I am completely up to date on my vaccinations. (Which is rare)However, due to vaccines, I have had to deal with some life altering side effects. These side effects have created a hardship in my overall quality of life and I will be dealing with these side effects for the rest of my days. This has been costly, physically damaging and emotionally draining.

As a parent, who has experienced vaccine side effects and as an informed individual, who knows that all vaccines do have side effects, which sometimes includes death, it is very important to realize that a one size fits all model is not ideal for an entire community. Information on vaccine side effects are available to anyone who asks or researches the topic. This information can be found directly in the vaccine inserts that accompany the vaccines or online. Please, before making any decisions on changing or mandating the vaccine schedule look into the known side effects that do effect some people.

Taking away vaccine exceptions, will cause harm to a certain population of children. We as parents know our children and must do everything to keep them safe. I know some people say, well just home school if you don't like it, but living in Hawaii, our family is in the exact same finacial predicament as so many others. Both my husband and I must work to survive.

Furthermore, to require the hpv vaccine that has done so much damage to so many children around the country and world seems extremely cruel. Beyond my own children, I wouldn't want any parents to be forced to give that vaccine to their children, based on all the bad reactions kids have had. This information is easily attainable through a simple research. I would start with looking at Japan and the information they are learning and publicly sharing about the dangers of the vaccine. Also, hpv is a sexually transmitted disease, not all kids are having unprotected sex or sex at all. So, why in the world would we mandate this completely unnecessary vaccine on them. The risk is absolutely not worth it. We need to trust our children to make good decisions and trust parents to be aware and raise our children responsibly.

So in conclusion, please don't treat all children the same and mandate a vaccine schedule for them that may damage them in the long run.

Please do not add additional dangerous vaccines to the schedule.

Please look into current scientific research that gives a much deeper understanding of how vaccines work.

Think about the children and help us protect the kids who can't handle the toxic load of so many vaccinations.

Sincerely,
A concerned parent

From: [REDACTED]
To: [REDACTED]
Subject: vaccinations
Date: Thursday, November 15, 2018 8:16:08 AM

Aloha,

I oppose mandatory vaccinating of all or any Beings. There is too much evidence that vaccinating children and even adults causes significant injury.

Please do not support this bill mandating vaccinations.

I am a grand mother with a young child in the public school system, we will take our child out of public school if this bill is passed.

Thank you for not supporting this bill,

Caroline Delano

From: [REDACTED]
To: [REDACTED]
Subject: In Support of HAR 11-157
Date: Saturday, November 17, 2018 12:56:29 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Bridget Kinoshita
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Monday, November 19, 2018 9:57:54 PM

Aloha,

My name is Stasia Estep and I am emailing from the island of Kauai in Opposition of HAR 11-157. These proposed changes will make the highly controversial vaccine HPV, as well as Influnza (which every year varies in percentage of effectiveness, and of recent years is anywhere from 10-60% effective - NOT enough to be warrant a mandate) and others, mandatory for public school here in Hawai'i. The first two are under fire in a number of other countries including but not limited to China, Japan and Canada as of recently.

To mandate these, as well as create further restrictions on medical exemptions with no legal liability on the pharmaceutical companies is both irresponsible and inhumane. It is a violation of our human and civil rights to force a medical procedure with stated and reported risks without easily attained refusal options for those unwilling to take the risk. Behind the paid-for rhetoric of "safe and effective" (not to mention conflict of interest regarding CDC recommendations and pharmaceutical studies) history evidences cases of retroviruses, ineffectiveness, brain damage and other extreme medical risks. With risk must come choice. Expanding exemptions, and shrinking mandates should be the measures on the table, NOT the exact opposite which you are proposing: expanding mandates and shrinking qualifications for exemptions.

Also, this is likely in violation of FERPA rules to require schools to report our children's immunization status to a third party, in this case state/local health departments. I encourage you to explain how it doesn't, if that is the case.

Thank you and I strongly OPPOSE HAR 11-157.

Sincerely,
Stasia Estep

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: HAR 11-157
Date: Tuesday, November 20, 2018 12:38:12 PM

Hello,

I am contacting you all to express my concerns in the HAR 11-157. I oppose this bill. I believe the choice to receive these vaccines should be between the parent(s) and the child's doctor. Where there is a risk of injury and death (no matter how small), there must be a choice. Mandatory vaccination violates my rights. HPV and Hep A are not spread by contact. These vaccines shouldn't be mandatory but up to the parent's discretion.

Please do not force a medical procedure on a non consenting individual. This is unethical.

Thank you,
Karine De Lima

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Tuesday, November 20, 2018 8:20:56 PM

Aloha,

My name is Kelly Davis and I am representing myself. I am strongly opposed to HAR 11-157. Many individuals can have serious even deadly reactions to vaccinations. My brother and I both had bad reactions to the MMR shot and screamed for days after the shots. I had learning disabilities afterwards growing up which I eventually outgrew. (I believe I outgrew this because over time my body eliminated the chemicals that were injected). Unfortunately, my brother regressed severely after his vaccinations and he is now diagnosed with Asperger's. No parent should feel forced to give their child a vaccination, or they are not allowed to receive an education. There are many side effects and once the damage is done there is no return. You will be left with a disabled child and cannot even hold anyone liable. Vaccines are not double-blind placebo tested and I believe they should not be forced upon anyone. Health freedom should be a basic human right and no one should be forced to inject something into their body.

Some of the vaccinations required by the DOH are not risks for children at school such as the HPV vaccination which only prevents a sexually transmitted disease. Since children are not having sex at school, I don't see why the school system would feel it needs to be required to attend.

Thank you for taking the time to read this and please do not let HAR 11-157 pass.

Kelly Davis

[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Vaccines
Date: Wednesday, November 21, 2018 9:35:45 AM

This is why vaccines should not be mandatory. This is a published letter. I am in favor of further investigation not only of gardasil but every vaccine.

TO: FDA Commission, Dr. Scott Gottlieb

I fully support this request for investigation. As a co-author of “HPV Vaccine on Trial,” I have spent the past several years investigating Gardasil, Gardasil 9 and Cervarix. What my co-authors and I learned during the research and writing process was deeply unsettling to me. These vaccines have been recommended not only in the US but also in many other nations and now in the US Gardasil 9 is recommended to millions of children and even adults up to age 45. Yet despite recommending these vaccines to millions of children, safety testing was woefully inadequate and should have precluded product approval. Gardasil clinical trials did not include a saline placebo, the gold standard by which to assess new vaccines. Instead, all but a few hundred “control” participants received Gardasil’s aluminum-containing adjuvant AAHS. Aluminum is a known neurotoxin and Merck boasts that AAHS elicits stronger immune responses than older adjuvants. The flip side of this is that it is more reactogenic as well – creating increased risk of injury. Moreover, DNA fragments remaining in the vaccine may be acting as an undisclosed and unapproved adjuvant. The few hundred children who did not receive AAHS as a control received other active and potentially harmful ingredients in a trial protocol that, as our book and the SaneVax letter describe, was fraught with problems. We now know that, from the clinical trials on, people have not been told the truth about this vaccine. In the trials, young women were told the control was saline and that the vaccine already had been shown to be safe. Neither of these things was true. Gardasil 9’s approval hinges on a presumption that Gardasil is safe, a presumption that is inactuate. Thousands and thousands of children and young adults have been injured by these vaccines. Each of their stories merits investigation and attention. Lives have been damaged and children have died far too young. In cases like the Tarsell and Harmon cases, the VICP has recognized that Gardasil vaccination led to death (Tarsell) and devastating and life altering injuries (Harmon). We still don’t know if these vaccines will prevent cancers and, particularly in high resource nations with strong screening programs for cervical cancer, most women are not at risk. According to NCI 0.6% of US women are at risk of cervical cancer in their lifetimes. The incidence of cervical cancer in 15-24 year olds is thankfully very low: 6 in 1,000,000 (Guo et al. 2018). The rate of injuries reported from these vaccines is tragically much higher. Even in the trials, at the time of Gardasil’s approval approximately 50% of participants reported New Medical Condition – many autoimmune. Yet these were largely dismissed as not related to the vaccine with what appears, from publicly available documents and witness accounts, to be little or no investigation, not the rigorous investigation that should have been done. Even if these vaccines are someday proven to prevent some cancers (many of which would have been detected in screening) we must ask, at what cost? The risk side of the risk/benefit analysis has been minimized and “disappeared” through studies poorly designed to detect risk. But in the real world – given the many injuries reported – risk seems to heavily outweigh the as yet unproven benefit. The FDA must immediately investigate to protect the safety of our children and children worldwide as many nations look to the FDA for guidance. Anything less than an immediate, unbiased inquiry is a disservice.

<https://sanevax.org/fda-commissioner-investigate-gardasil-trials/?fbclid=IwAR08I1UPc8gmg-rSp35Leiz0LyKz8WtQI-iYmHw01JZ1wN7XfM-X7QeHv20#comment-82150>

Kimberly Nelli

From: [REDACTED]
To: [REDACTED]
Subject: I support HAR 11-157!
Date: Friday, November 23, 2018 3:38:49 PM

Aloha,

Thank you for this opportunity to provide testimony. As a community member and public health advocate on Kauai, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sincerely,

M. Walters

From: [REDACTED]
To: [REDACTED]
Subject: In support
Date: Friday, November 23, 2018 3:41:37 PM

I support the update of the DOH immunization requirements. Vaccines are safe, effective and good not only for the person receiving them, but for our community as a whole! It is so important not to let a small but vocal proportion of our community (anti-vaxxers) create an unhealthy climate for babies, kupuna and those that are immune-compromised. Please support the update of the bill.

Mahalo, Maile

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Friday, November 23, 2018 5:16:33 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Barbara Kaaumoana

From: [REDACTED]
To: [REDACTED]
Subject: SUPPORT for updating immunization requirement
Date: Friday, November 23, 2018 3:36:45 PM

Aloha,

Thank you for this opportunity to provide testimony. As a community member and public health advocate on [REDACTED], I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Aloha, Maile

From: [REDACTED]
To: [REDACTED]
Subject: Support HAR 11-157 proposed rules update
Date: Friday, November 23, 2018 5:08:16 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate (I am a mother and dentist on the island of [REDACTED]), I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you,

Kaimana Goo-Rahtz, DMD, MPH

From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157 proposed rules update
Date: Monday, December 24, 2018 9:06:18 AM

Thank you for this opportunity to provide testimony. As a family physician in practice in [REDACTED], and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Jeffrey R. Tolan, MD

Board Certified by the American Board of Family Medicine

[REDACTED]

██████████ HI ██████████

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 Update
Date: Saturday, November 24, 2018 2:22:55 AM

To Whom-It-May-Concern,

I am a resident of the island of Kauai and a parent fo a child who has been given immunization shots while growing up.

Anti-vax, sentiment runs deep in the island and is causing harm to our kids. Last year we had an outbreak of mumps on the north shore of Kauai that was easily preventable. The Centers for Disease Control & Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates and in turn lower rates of vaccine-preventable diseases. It also debunks the myth that vaccines cause autism.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Sincerely,

Jeannie Yoshida
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Immunizations are important!
Date: Saturday, November 24, 2018 4:04:09 PM

Aloha Kakou

As a lifelong citizen of Hawaii nei and a kupuna, I am so fortunate to have been born just before but close enough to the time when the polio vaccination was introduced. I remember that it was done in 2 stages and all Kilauea people old and young lined up for immunization. This disease was FEARED and today I am thankful for being spared through immunization! I no longer had to live in fear! As part of the plantation's health care, we received our early infant inoculations for measles mumps and diphtheria. Then at school we got regular shots for tetanus and typhoid. Today both my wife Bebe and I maintain our annual flu immunization and both have hepatitis A, pneumonia, and shingles vaccinations. We believe in them out of personal experience as well as the empirical evidence that backs the science!

We are grateful for the advancements in medical science whereby we personally benefit as well as all our acquaintances and family who will not catch any of the communicable diseases from us.

The CDC GUIDELINES SHOULD BE ADHERED TO AND ADOPTED BY THE STATE OF HAWAII AS OUR MEDICAL POLICY FOR IMMUNIZATION AS WELL!!!

Those people who oppose these guidelines do so at all our peril!!!! Some out of fear purported by pseudo medical science, ignorance or archaic religious beliefs, yet are largely spared these diseases today as unsupportive beneficiaries of CDC's vigilance as well as all of us who are immunized. Go to the website for mothers who have lost children because they chose not to immunize them!! See their pain and regret for not having done so.

Let's not be swayed by the hysteria. Contrary to what our president espouses **WE ARE A NATION OF SCIENCE!!!**

Do not take my word or the word of the vociferous opponents. Let results of **MEDICAL SCIENCE** guide your decision!!!

Mahalo nui
Gary and Bebe Smith

[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Oppose mandated vaccinations
Date: Saturday, November 24, 2018 11:10:35 AM

I am a Maui resident and mother of a one year old.
I strongly oppose any mandatory vaccinations.
I would like to maintain my right and my freedom to choose as a parent, when it comes to the health of my child.
Overall, this is an attack on medical freedoms. If this now, what is next? It is potentially endangering Keiki injecting them with shots for big pharma profits, this is is not pono!
I oppose all and any mandatory vaccinations.

Sincerely,
Michelle Galarza

[REDACTED]

Sent from my iPhone with Love Chelle

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157
Date: Tuesday, December 25, 2018 10:42:30 PM

Aloha,

The Hawai'i State Department of Health (DoH) is urged to abandon and reject the proposed amendments to the Hawai'i State Administrative Rules (HAR) Title 11 Department of Health Chapter 157 Examination and Immunization. If adopted, Hawai'i would attain the dubious distinction of being the most vaccinated state in America.

In regards to the Human Papillomaviru (HPV) vaccination: "... lawsuits have been launched in Japan, France, Ireland, Spain, and Columbia claiming HPV vaccine harm." In fact, "The Vigibase database of the World Health Organization has compiled more than 86,000 serious adverse event reports for Merck's HPV vaccine. They include nervous system disorders (39,092), respiratory, thoracic and mediastinal disorders (6060), vascular disorders (5766), nervous system disorders (39,092), reproductive system and breast disorders (3267), cardiac disorders (2604), and blood and lymphatic system disorders (2035)... The number of AE's (Adverse Events) reported for HPV vaccines, in each country, are overwhelmingly higher than that for other vaccines." Also, a 2012 Canadian study "...suggests that HPV vaccines containing HPV-16L1 antigens pose an inherent risk for triggering potentially fatal autoimmune vasculopathies." Curiously, the US Center for Disease Control (CDC) website seems to omit the aforementioned AE's the CDC HPV Vaccine website despite numerous AE reports on the Vaccine Adverse Event Reporting System (VAERS) Database.

If the HPV vaccine is so safe then why has the "National Vaccine Injury Compensation Program has awarded more than \$5 million to 49 victims in claims made against the HPV vaccine"? In addition, "there is compelling evidence that vaccine manufacturer Merck conducted shoddy, questionable clinical trials; and that a number of individuals around the world have suffered drastic health consequences post HPV vaccination." Suffice it to say, the administration of the HPV vaccine should be halted until further studies on the safety and efficacy of this drug are conducted. Please remember that individuals with both diagnosed and undiagnosed immunodeficiency conditions are at an increased risk of AE's from vaccinations. Thus, increasing the vaccine schedule would further exacerbate the likelihood of more adverse events; and in so doing, imperil the health and lives of this vulnerable population.

Furthermore, why do our Hawai'i students--primarily comprised of underage adults-- need this vaccine? By promoting the HPV vaccines

seems as though the DoH and Hawai'i State Department of Education (DoE) are not only condoning but actually promoting sexual activity among students. If the DoE is genuinely concerned about sexual relations and reproductive health, wouldn't it be far more effective for the DoE to instead focus on sex education?

Before Hawai'i aspires to be the most vaccinated state in the Union, I urge the DoH to step back and contemplate the health of our youth from a holistic viewpoint. Internet technologies (i.e., social media, gaming, etc.) have permeated every facet of our lives. Our children do not have the stamina to withstand the lethal allure of video games such as Fortnite or social media platforms such as Snap Chat. Addiction to video games and social media have adversely affected the young generation. Child predators, sexting, bullying, and other threats are more pervasive than ever. Another urgent matter that the DoH needs to confront immediately is the omnipresence of e-cigarettes in our public schools. Vaping liquid nicotine is a habit that all too often leads to a lifetime of addiction. The DoH must respond to the adverse impact of these technologies upon the well-being of our youth.

In closing, do not increase the vaccine schedule. Do not infringe upon our civil liberties. Please respect the parent's right to make decisions about their children's health. Please reject the amendments to HAR 11-157.

Mahalo.

Most Sincerely,

Amy Halas

Sources:

1). Hawaii Dept. of Health Tries to Force Hazardous Ineffective HPV Vaccine on All Public School Children: Parents Protest Placing Big Pharma Profits Over Public Health

<http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR2nUEOwrpEaQ5oT4JoXmMY0EVEE5EVlgPSV9J33oxmq1QrDM-a9ziFACZY>

2). CDC Human Papillomavirus (HPV) Vaccine Safety

<https://www.cdc.gov/vaccinesafety/vaccines/hpv-vaccine.html#side-effects>

3). Connected Yet Disconnected – Teen Depression and Social Media

<https://www.pinnaclehealth.org/wellness-library/blog-and-healthwise/blog-home/post/connected-yet-disconnected-teen-depression-and-social-media>

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Sunday, November 25, 2018 10:39:40 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

sincerely

Christine A. Cook

AKA Mauli Ola Cook

Christine Anne Cook
AKA: Mauli Ola Cook

October 29, 2018

DOCD, DOH

[REDACTED]

[REDACTED]

Hawaii Department of Health, [REDACTED]

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter157, “Examination and Immunization.”

Strongly **Oppose** Administrative Rules (HAR) Title 11, Chapter157, “Examination and Immunization.” Taking on the ACIP guidelines is not in the best interest of our Keiki’s overall health or best practice of health guidelines for the State of Hawaii.

Dear Hawaii Department of Health,

Thank you for taking the time to read my testimony completely and taking into strong considerations of my testimony. My Name is Dawn Poiani and I am a mother of 3 boys and a health advocate residing in the State of Hawaii. I strongly **oppose** the state of Hawaii taking on the ACIP guidelines as their best practice for immunization. I see serious issues with this proposed rule as there are some inherent flaws in the ACIP vaccine recommendations and . If the state of Hawaii follows the ACIP Vaccine schedule guidelines we are adding multiple new vaccines to our already vaccine burdened schedule. These additional vaccine recommendations have never been tested for safety and synergistic affects of against our current schedule. I have watched hours of multiple different hearings of ACIP and witnessed how new vaccines are approved, and I must say, these hearings are disturbing to watching. I witnessed the ACIP gleefully and irresponsibly approve more vaccines to the pediatric schedule using weak vaccine science and underpowered correlation studies. Every vaccine is approved solely on the safety of the vaccine and if the vaccine will affect the serology of the other vaccines. An example is of the ACIP approval process of approving a new adjuvant in the Hep B vaccine. There are no safety studies done on the new adjuvant given with the currently used adjuvants or the safety of adding it to the schedule as well as there were some risk concerns that the ACIP voted to watch after the Hep B was put on the market. Watch this video and you will get the sense of how

vaccine safety is an after-market concern. https://youtu.be/L_JJMpe00mM. Do we really want to make our children the test subject for the safety of every vaccine that the ACIP recommends adding to our children's vaccine schedule? I don't, these are our children our future! The US Government HHS (Health and Human Services) has never conducted a single safety study as part of the fulfillment of the National Childhood Vaccine Injury Act of 1986 which grants legal immunity to vaccine makers. These safety studies were assigned to HHS in an effort to be the checks and balances over pharmaceutical safety studies and recommendations, because they have no liability for vaccine injuries and death. HHS was also to conduct and report these findings every two years to Congress; these studies have never been done! Exposure to viral particles and adjuvant (aluminum) in vaccines, along with routine exposures to other immune disruptors are '**antigen overload**' for the immune system that could shift the induction of chronic health problems (e.g., increased asthma, ocular or skin allergies, ovarian failure, gastrointestinal conditions or neurological and autoimmune diseases). We are seeing a rapid rise in chronic disease and neurological disorders in the State of Hawaii and across the world. There is only one environmental exposure that can be found in most states as well as most other countries, and that is vaccines. So are vaccines the potential cause of the rise of chronic disease and neurological issues? Are we trading the prevention of a handful of diseases for chronic health issues and neurological problems? We don't know because there has never been an effective study done looking at the vaccine schedule. It is claimed that it is unethical to do a study like that, so the solution is to just put the next new vaccine on the schedule, and see what happens. The ACIP continues to add vaccines to the schedule based on information and studies they receive from vaccine makers that can and do tweak data and find new ways to record reactions and data, in their studies, in an effort to make their vaccines look safer and or more effective (ex. <http://probeinternational.org/library/wp-content/uploads/2014/09/chatom-v-merck.pdf>, <https://www.classaction.com/zostavax/lawsuit/>). Additionally, ACIP calls on VAER to report vaccine injuries as their source of safety once the vaccine is on the market, but VAERS is voluntary and dismally under used for reporting (estimated between 1-10%) yet this is the safety science? There are over 200 vaccines currently being developed, how many more will they add to the schedule without any safety studies against our schedule, how many will be approved gleefully

with poor science? There is only one ingredient and one vaccine adequately studied. From these two studies the mantra has been “the science has been settled that vaccines are safe and effective.” **If the dose makes the poison**, at what point do the trace amounts of aluminum, Antibiotics, Egg protein, Formaldehyde, Monosodium Glutamate, Thimerosal and many many antigens become the tipping point and destroy our children’s health and vitality? I cannot understand how any doctor, immunologist, or virologist can emphatically say that adding to our vaccine schedule is safe. The State of Hawaii should set it’s own schedule based on a **Core Group** of vaccines that are specifically targeted to protect our demographics and geographical tendencies. We have no idea how any vaccine will affect our diverse ethnic population or the affect of our keiki’s overall health by more vaccines to the schedule. It is medically unethical and irresponsible. Are we really going to play a Russian roulette game on our Keiki? The future health of Hawaii deserves better than that. These additional vaccine recommendations do not provide the strength of the benefit to risk ratio to recommend adding further vaccines to the schedule.

By adding the HPV vaccine to the schedule requirements for school entry at 7th grade provides absolutely no benefit to the spread of disease in a school environment. The HPV is a cancer preventative vaccine that may or may not protect the student 20-40 years later from cancer. Additionally, there are serious issues with the way the HPV vaccine studies have been conducted. Manufacturers, did not have to prove that vaccine prevented cancer and were allowed to use precancerous lesions as “surrogate endpoints” in the clinical trials. Scientists do not know if the decline in cases of precancerous lesions will translate into fewer cases of cervical cancer in 20-30 years. None of the participants in the original pre-approval clinical trials received a true saline placebo, an aluminum containing adjuvant was used. Manufacturers never tested HPV vaccines on human fertility (acknowledged in the package insert). Manufacturers never tested HPV vaccine to discover if they might cause cancer (package insert say vaccine has never been tested for “carcinogenicity”). <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>. The original Gardasil clinical trials used a new metric, “**New Medical Conditions**,” as a way to claim that serious health problems after vaccination were unrelated to the vaccine or aluminum-containing placebo.

More than 50 percent of all clinical trial participants reported “new medical conditions,” including infections, reproductive disorders, neurological syndromes, and autoimmune conditions. The FDA never questioned this novel metric. Lawsuits have been filed against Merck, GlaxoSmithKline, and government health agencies around the world, including the US, India, Columbia, Japan, Spain and France. The US government earns royalties from Merck and GSK for licensing HPV vaccine technology (this is an egregious conflict of interest!). Why would the state of Hawaii mandate the HPV vaccine, when the vaccine carries these kinds of flaws in the HPV vaccine safety assurance? As of June 2018, the VICP paid out or settled 126 HPV vaccine claims. A total of 49 people received \$5.8 million after the U.S. Court of Federal Claims found Gardasil injured them <https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-june-2018.pdf>. “The HPV Vaccine On Trial: Seeking Justice for a Generation Betrayed” by Mary Holland. Let the HPV be an optional vaccine and not mandated to the required school entry **Core Vaccines**.

According to the manufacture’s package inserts, the rate of “**serious adverse events**” **from meningitis B vaccine are 2.1% for Bexsero (Novartis)**, <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm431447.pdf> and **1.8% for Trumenba, (Pfizer)**, <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm421139.pdf>. Based on this information, if the roughly 58,000 HI college and undergraduate students receive either of these vaccinations, approximately 1,218 students will experience “severe adverse events,” including death. In 2016, there were 2 cases at Rutgers University, treated with antibiotics and fully recovered. The risk of “**SERIOUS ADVERSE EVENTS**” from the vaccine is much higher than the risk of becoming ill with bacterial meningitis. At a cost of \$100-125 a dose, this is a serious cost to the State of Hawaii. Although Bacterial Meningitis can be a serious disease, it is not common and is very difficult to acquire. The best outcomes in cases of bacterial meningitis occur when the infection is detected early and antibiotics are administered. Public Health initiatives to enhance the awareness of the early symptoms of the infection and the importance of securing appropriate treatment would be impactful. There is no public health situation present that warrants infringing on a person’s right

to decide what medical treatment and intervention is appropriate for him/her and allowing doctors and students to make these decisions for health care is essential.

Hep A cannot become chronic disease and most (70%) of infections in children younger than age 6 are not accompanied by symptoms according to the CDC. To avoid “**antigen overload,**” the Hep A Vaccination should only be recommended for individuals in high-risk settings and not for the requirement of school attendance.

Examples would include people that are at increased risk for acquiring hepatitis A virus (HAV) infection?

- Persons with direct contact with persons who have hepatitis A
- Travelers to countries with high or intermediate endemicity of HAV infection
- Men who have sex with men
- Users of injection and non-injection drugs
- Persons with clotting factor disorders
- Persons working with nonhuman primates
- Household members and other close personal contacts of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity
- People who have chronic liver disease.
- Homeless population.

The cases of Hep A we have seen in Hawaii in the past years have not spread from student to student in schools. Most of our Hep A cases were from food contamination. The healthier approach to preventing the spread of Hep A would be addressing the food importation issues into Hawaii. There is very minimal risk of Hep A spreading from student to student in schools.

The influenza vaccine from year to year is from 10% -60% effective according to the CDC. The flu vaccine, due to the innate natural drift nature of the virus and the absolute guess that the flu vaccine makers must make to pin point the prevalent strain the following year, this vaccine is not affective. The flu vaccine is one of the leading reported vaccines for adverse events according to VAERS. This risk/benefit ratio to require this vaccine for school just doesn't add up. Additionally this vaccine continues to have trace amounts of mercury (Thimerosal),

according to the FDA vaccines with trace amounts of thimerosal contain 1 microgram or less of mercury per dose.: the manufacturers best effort to wash the mercury out is not 100% effective. However mercury in conjunction with aluminum creates a heavier neurotoxic load which comes with risk. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344667/>
<https://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm>
<http://vaccineimpact.com/wp-content/uploads/sites/5/2017/09/DOJ-Report-9.8.17.pdf>

The requirement of a standardized medical exemption is flawed and it is a direct effort to restrict our medical rights. A standardized medical form may intimidate or discouraging a Physician to use their best precautionary principles and medical judgement for each patient. Physicians need to be allowed to write their medical evaluations and exemptions on their own letter head and freely decide if a vaccine is truly appropriate using the best medical judgement for each patient. It is not in the best interest of the patient or the physician to create additional paperwork, road blocks or exemption restrictions to a physicians best medical practice.

The Hawaii Vaccine Coalition is promoting the idea that restricting or even eliminating Religious Exemptions would improve vaccinations rates, which are already higher than the national average. Article I section 4 of the bill of rights “No law shall be enacted respecting an establishment of religion, or prohibiting the free exercise thereof, or abridging the freedom of speech or of the press or the right of the people peaceably to assemble and to petition the government for a redress of grievances. [Ren and am Const Con 1978 and election Nov 7, 1978]. There are inherent constitutional issues of restricting religious exemptions or challenging a persons spiritual beliefs.

Mandatory school reporting of all students with vaccine exemptions may be a violation of FERPA (Federal Educational Rights and Privacy Act) as well create additional financial burden on schools. <https://www.mbm-law.net/newsletter-articles/“ferpa-trumps-hipaa-in-immunization-disclosure”/1020/>

Oppose Administrative Rules (HAR) Title 11, Chapter157

Thank you for the time you took to read my testimony. **I strongly OPPOSE HAR 11-157 rule changes.** These rule changes are not in the best interest of our Keiki's health or the best interest of promoting a healthy child in the State of Hawaii. My uncle is a Surgeon/doctor and he once said "before I prescribe any medication I always ask myself will this drug cause more harm than the disease it is trying to cure?". These rule changes squash our freedom and the fundamental principles of effective and safe medicine - "First Do No Harm." Please host a public hearing statewide to fairly hear all testimony on all islands.

Sincerely,

Dawn Poiani

████████████████████

██

From: [REDACTED]
To: [REDACTED]
Subject: strongly oppose the HAR 11-157 proposed rules update and its exhibits.
Date: Monday, November 26, 2018 4:26:37 PM

strongly oppose the HAR 11-157 proposed rules update and its exhibits.

Thank you for this opportunity to provide testimony. As a community member and human rights advocate, I am writing to **strongly oppose the HAR 11-157 proposed rules update and its exhibits.**

The rule changes conflict with the parents right of medical freedom and to choose with their doctor what it good for their child. There is no one fits all solution, and that its why the personal patient doctor / nurse relationship is so important, to have a trusted communication. This rule will overrule this, and it shows that you have no trust in your own people.

By now I talked to many people (school, nurses, parents of all walks), especially the once that vaccinate and their feedback after they are understanding what this really means for them is opposition. I notice that many people who will be affected are not even aware. Not because we don't believe in vaccines works, but we want our choice for certain vaccines and they have their reasons to do so, so do I. I will keep inspiring these people to be part of this, and to speak up in detail for themselves.

We have already a good basic requirement like most states have. These proposed changes are overboard in my opinion. This rule change will put us in a position that no other state has, we would have to most regulated immunization for school children in all USA. I don't agree that we want or need to be the first experimental state with 12 mandatory vaccines for public education. We need to work with each other and need to resist to dictate each other what to do. Its my way or the highway situation.

There are parts that I agree, but many that I do not agree. This is not acceptable, so I disagree at this point strongly.

I also advice in the name of democracy and true informed consent to make a link between the DOH and DOE to inform everyone that will be affected, all parents and students in the Hawaii public education system about the opportunity to give consent and be part of this decision. Its not fair or good enough to have us informed after the fact.

I am opposing especially forcing the yearly flu vaccine and HPV on our children, these need to be done by informed free consent of the parents for children, teens.

There are other solutions that can help with the HPV epidemic, like a education and free will, spending money on real sexual education on teens and regular free screenings/pap smears/STD checks for young people. There is so much more to say.

I respectfully request that the proposed changes to HAR 11-157 be denied and not passed for holding up the basic right of medical freedom, human

rights and trust.

Thank you for your consideration.

Astrid Drolson, resident of [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Strongly Support HAR 11-157 Proposed Rules Update
Date: Monday, November 26, 2018 10:31:34 AM

Aloha Department of Health,

Thank you for this opportunity to provide testimony. As an advanced practice nurse, long-time employee of the Queen's Medical Center and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Mahalo,

Hob Osterlund, APRN

From: Martina Kalfors
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: Vaccine danger studies added to verbal testimony opppsing HAR 11-157 Martina Kalfors.
Date: Friday, December 21, 2018 7:44:59 PM

Aloha DOH.

After my verbal testimony in [REDACTED]. You stated I could provide more studies. Here you go. Read it all carefully. This will be shared with all legislators to. We the people are NOT ok with this rule change. There was one person in favor of this, she was not a citizen in the U.S. all the other people were affiliated with an organization representing pharmaceutical industry. No individual testimony in favor of HAR-11-157.

But There were over hundred opposing. Why is that? We THE PEOPLE DO NOT WANT THIS. Watch all hearings public on my FB page. Read all the testimonies. Please. Our keiki deserves it.

The added pdf link to the Corvelva study for infrarix hexa contains all contaminates and NO antigens. Came out this week. ALL RISK, NO BENEFIT. This is the trusted science you want us to inject into our keiki. This is absolutely criminal. No question. This should be enough evidence to immediately do a moratorium on vaccines, until all vaccines have been carefully investigated.

Dr. Stephanie Seneff's study pdf. shows traces of Glyphosate in all vaccines. Show us that it is safe to INJECT to our children. Or anyone for that matter.

There are also 60 peer reviewed studies on the danger of hpv vaccine in pdf link.

Thousands of studies on the danger of vaccines on this link. Pick your choice of disease. Many peer reviewed.

<https://medscienceresearch.com/contamination/> <<https://medscienceresearch.com/contamination/>>

<http://www.greenmedinfo.com/blog/200-evidence-based-reasons-not-vaccinate-free-research-pdf-download> <<http://www.greenmedinfo.com/blog/200-evidence-based-reasons-not-vaccinate-free-research-pdf-download>>

New documentary on hpv vaccine danger.

<https://vimeo.com/277078546/7812e25bb1> <<https://vimeo.com/277078546/7812e25bb1>>

<http://vaccinesafetycommission.org/pdfs/Wang%20Yao%202018%20Cytokine%20IL-4%20Hep%20B%20Hippocampus.pdf>
<<http://vaccinesafetycommission.org/pdfs/Wang%20Yao%202018%20Cytokine%20IL-4%20Hep%20B%20Hippocampus.pdf>>

<https://vaccinesafetycommission.org/pdfs/26-2010-Hep-B-Autism.pdf>
<<https://vaccinesafetycommission.org/pdfs/26-2010-Hep-B-Autism.pdf>>

Contaminated vaccines.

<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf> <<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf>>

<https://www.tandfonline.com/doi/abs/10.1080/15287394.2018.1477640?cookieSet=1>
<<https://www.tandfonline.com/doi/abs/10.1080/15287394.2018.1477640?cookieSet=1>>

LIVE VACCINES SHED and spread Infectious Diseases NOT unvaccinated children!

All live virus vaccines contain LIVE viruses. They may be weakened but they can still replicate and infect both the vaccinated, unvaccinated, immunocompromised and "shed" to people around them for weeks after the vaccine is given.

Which vaccines are LIVE?

Chicken Pox- Varivax Section 5.4 (up to 6 weeks):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142812.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142812.pdf>>

MMR- MMRII page 5 (Up to 28 days):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123789.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123789.pdf>>

Shingles- Zostavax Section 5.2:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM285015.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM285015.pdf>>

Rotavirus- Rotateq Section 5:5 (Up to 15 days, fecal shedding):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142288.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142288.pdf>>

Small Pox- ACAM2000 Section 5:10 (Only used in the military but highly contagious):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142572.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142572.pdf>>

But does that REALLY happen? Yes. Yes it can and does as these studies illustrate:

Varicella transfer after vaccine to pregnant mom:

<http://www.ncbi.nlm.nih.gov/pubmed/9255208> <<http://www.ncbi.nlm.nih.gov/pubmed/9255208>>

Pub Med article on Rotavirus shedding:

<http://www.ncbi.nlm.nih.gov/pubmed/18922486> <<http://www.ncbi.nlm.nih.gov/pubmed/18922486>>

Mumps Vaccine sheds:

<http://www.ncbi.nlm.nih.gov/pubmed/24772647> <<http://www.ncbi.nlm.nih.gov/pubmed/24772647>>

Mumps vaccine sheds:

<http://www.ncbi.nlm.nih.gov/pubmed/16266774> <<http://www.ncbi.nlm.nih.gov/pubmed/16266774>>

Measles virus sheds for 1-13 days after vaccination:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC228449/>
<<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC228449/>>

Mumps outbreak in Netherlands linked to those vaccinated twice with MMR:

http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article <http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article>

Measles vaccinated child responsible for outbreak in British Columbia:

<http://www.eurosurveillance.org/images/dynamic/EE/V18N49/art20649.pdf>
<<http://www.eurosurveillance.org/images/dynamic/EE/V18N49/art20649.pdf>>

New York Measles outbreak linked to vaccinated:

<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>
<<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>>

Measles outbreak among the vaccinated:

<http://www.ncbi.nlm.nih.gov/pubmed/8053748> <<http://www.ncbi.nlm.nih.gov/pubmed/8053748>>

We don't know for certain how long shedding occurs because we don't test for it long term or regularly but in rare instances, it has gone on for years:

<http://www.westernmorningnews.co.uk/Vaccinated-man-spread-polio-30-years/story-27693988-detail/story.html> <<http://www.westernmorningnews.co.uk/Vaccinated-man-spread-polio-30-years/story-27693988-detail/story.html>>

Additionally, the Dtap/Tdap and Polio vaccines that are NOT live has been shown to cause the vaccinated to become asymptomatic carriers whenever exposed, thus the vaccinated can be spreading the illness without knowing at any time:

Pertussis carrier:

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376937.htm>
<<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376937.htm>>

Diphtheria carrier:

<http://www.cdc.gov/diphtheria/clinicians.html> <<http://www.cdc.gov/diphtheria/clinicians.html>>

The polio vaccine “does not stop transmission of the virus.” & “when a person immunized with IPV is infected with wild poliovirus, the virus can still multiply inside the intestines and be shed in the feces, risking continued circulation.”

<http://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/>
<<http://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/>>

You can also find that most medical facilities are aware of this. Johns Hopkins and St. Jude hospitals are just a few of many who post precautions for recently vaccinated visitors.

WHY does this matter?

Because society is so deathly afraid of these illnesses that they rush out and load up on vaccines and want to even pass laws forcing others who should never be vaccinated to do the same; but the science shows that it's the vaccinated that are at a higher risk of infections because vaccines heavily suppress the immune system, vaccines are directly linked to spreading illnesses because people are routinely injected with them. Be aware of the infection and carrier risk each vaccine has when making your choice as you will- take cautionary measures being around individuals that are immunocompromised if you have been recently vaccinated or around someone with the illnesses even if you don't show symptoms.

ONE HUNDRED AND FIFTEEN studies on vaccine SHEDDING...

[Www.medscienceresearch.com/shedding/](http://www.medscienceresearch.com/shedding/) <<http://www.medscienceresearch.com/shedding/>>

THE DILEMMA OF VACCINE-INDUCED DISEASE AND UNVACCINATED CHILDREN
VACCINE SHEDDING

It has long been known that vaccines can cause the diseases they were meant to immunise against.

For instance, the live oral polio vaccination can cause polio – a disease named vaccine-associated paralytic polio (VAPP), which is mentioned on the UK dept of health website, immunisation.org.uk
<<http://immunisation.org.uk>>

‘If a baby has had the oral polio vaccine, the live virus can be found in the baby's poop for up to six weeks afterwards.’

It was actually for this reason that the OPV was voted out and injectable polio vaccine re-introduced. The oral vaccine was responsible for the ONLY cases of polio in the developing world. (Committee on Immunization Practices meeting, held 20th June 1996).

According to DRAFT ACIP meeting minutes, February 2001, page 28:

And lastly the myth of herd immunity. A theory that has never been proven to work. Impossible hence booster.

<https://jbhandleyblog.com/home/2018/6/7/herd-immunity-a-dishonest-marketing-gimmick>
<<https://jbhandleyblog.com/home/2018/6/7/herd-immunity-a-dishonest-marketing-gimmick>>

And if you care about the real truth of history. Read Dr. Suzannes book. "Dissolving Illusions".

<https://jbhandleyblog.com/home/2018/5/14/savehumanity>
<<https://jbhandleyblog.com/home/2018/5/14/savehumanity>>

http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR1hPbF_UuhtbtsIMCNp7ukdVWP0bM4Z6eU3XTYriB0-uazolwSXpVd_aQ
<http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR1hPbF_UuhtbtsIMCNp7ukdVWP0bM4Z6eU3XTYriB0-uazolwSXpVd_aQ>

There you go,

Mahalo,
Martina Kalfors.

October 31, 2018

DOCD, DOH immunization@doh.hawaii.gov
[\(808\) 586-8300](tel:8085868300)

Hawaii Department of Health
1250 Punchbowl St.
Honolulu, Hawaii 96813

I **strongly oppose** the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, “Examination and Immunization.”

Dear Hawaii Department of Health,

My name is Kim Haine, I am a Mother and StepMother to 5 children, and was a health care professional for 15 years. I oppose these amendments for several reasons, but primarily because it is not prudent health policy to vastly increase the school vaccine requirements without, acknowledgement and exploration of the **epidemic of chronic disease plaguing America’s children today**.

1. **I oppose the changes to the Medical and Religious Exemption requirements.**

Pertaining to **Religious Exemptions** being “in a format specified by the department” is vague and yet unspecified, therefore leaving room for egregious violations of our Constitutional, First Amendment Rights. It is not up to the government, nor certainly our DOH, to define spirituality or one’s relationship with God.

Medical Exemptions must now be “in a form or format specified by the department, that an immunization is medically contraindicated, due to a stated cause, for a specific period of time, in conformance with recognized standard medical practices”. A physician’s best professional judgement utilizing their intimate patient-specific, as well as family history knowledge, should be the sole determining factor in whether a medical exemption is warranted....period. The “Precautionary Principle of Medicine” must be upheld and not be restricted by bureaucratic oversight.

After evaluating ACIP's most recent General Best Practice Guidelines for Immunization; Section 4 "Contraindications and Precautions", Tables 4-1 and 4-2, it is abundantly clear that ACIP, and any Public Health Department that blindly follows such guidelines, care much more about the judicious uptake and militant adherence to the vaccination schedule, than the prevention of serious, life-long adverse reactions. All conditions listed have been absurdly minimized:

Pertussis Containing Vaccines

- DTaP (Dose 3 – Dose 4) minimum intervals (10/23/2017)
 - Prospective – 6 months
 - Retrospective – 4 months
 - 4 day grace period can be applied to 6 month interval prospectively
 - 4 day grace period can be applied to 4 month interval retrospectively
- Four precautions to DTaP removed
 - Fever $\geq 105^{\circ}$ F within 48 hrs following a dose of DTaP (09/20/18)
 - Persistent, inconsolable crying lasting ≥ 3 hrs within 48 hrs following a dose of DTaP (07/18/18)
 - Collapse or shock-like state with 48 hrs following a dose of DTaP (07/18/18)
 - Seizure within 72 hrs following a dose of DTaP (07/18/18)

See for example table to the left which lists known symptoms of "encephalitis" (brain swelling which can lead to autism), as no longer being a precaution to the DTaP vaccine, let alone a contraindication! There are hundreds of severe adverse reactions listed in ALL vaccine manufacture's package inserts, whether noted during clinical trials

OR post-marketing surveillance, that *should* qualify as a medical exemption, but they do not. **Vaccine Package Inserts** are never given out to patients as **true informed consent**, and most physicians have never even read them. *The Hippocratic Oath* that every American Medical Doctor is sworn in to "**FIRST DO NO HARM**" appears to have been forgotten as it relates to childhood vaccines. Please see a video clip of an actual ACIP vaccine approval meeting in progress here: https://www.youtube.com/watch?v=L_JJMpe00mM

2. I oppose mandatory physician and school reporting to the DOH, the names of children/students whom have not met their immunization requirements, or who have medical or religious exemptions.

The Federal and Educational Rights and Privacy Act (FERPA) and Health Insurance Portability and Accountability Act (HIPPA) standards are in place to protect personal health information and medical records; this would be a grave violation to the intentions of these privacy acts. The reporting of numbers of exemptions may be prudent, however names of students are not necessary, and feels more like a rule approaching communist China.

The only "mandatory reporting" that SHOULD be happening is the reporting by Health Care Professionals of vaccine injuries. We have a failed, passive reporting system in VAERS that, according to a Harvard study funded by our own DHHS, captures an estimated, pathetic 1% of actual vaccine injuries.

3. Finally, I stand in extreme opposition to the requirement of multiple new vaccines to attend daycare and all school institutions in Hawaii.

ACIP recommendations and guidelines are meant to be just that, recommendations, NOT mandates. The new proposed vaccine requirements for Hawaii's children would add approximately 17 doses of 7 new vaccines (including 35+ antigens) for those beginning in daycare. There are no urgent matters in our *school* settings warranting the use/addition of *any* of the proposed vaccines { Influenza; Rotavirus; PCV; Hep A; MCV; TDaP; and especially HPV}. There are also CDC statistics and abundant independent research to back up this claim, as well as facts proving that the risks far outweigh any benefits. HPV (Gardasil) vaccine especially, for a STD not highly communicable in a school setting, is one of the most controversial and dangerous vaccines ever recommended by ACIP. With debilitating autoimmune diseases, paralysis, and even death numbering 60,000 and counting, this vaccine should be pulled from market (as in other countries like Japan), not forced upon schoolchildren.

Important facts pertaining to vaccination:

1. Vaccination is a medical intervention, that carries risk of serious injury, death, and failure to prevent infection or transmission. There are genetic, biological and environmental risk factors rendering some more susceptible to vaccine reactions than others, yet doctors still cannot predict conclusively who will be harmed.
2. Section 13.1 on *every* manufacturer's package insert states that it has "not been evaluated for carcinogenic or mutagenic potentials, or impairment of fertility"
3. In 1986 Congress passed *The National Childhood Vaccine Injury Act* to shield vaccine manufacturers from civil product liability lawsuits for all harm caused by vaccines, including permanent disability and death (Public Law 99-660).
4. Since this 1986 ACT sheltered the vaccine manufacturers from liability, the childhood vaccination schedule has exploded to a current 74+ doses of 17 vaccines (given in pregnancy, on the first day of birth, up to 18 and beyond)
5. **What has also grown concurrently with the vaccination schedule is an epidemic of chronic illness in over half (54%) America's children.**

The gateway period that launched this decline was the late 1980's and early 1990's. Many chronic illnesses have doubled since that time:

- The “4-A” disorders— autism, attention deficit hyperactivity disorder, asthma and allergies—have experienced meteoric growth, affecting children's quality of life and contributing to premature mortality . The spike in autism prevalence has been particularly dramatic, with prevalence as high as 3% (one in 36 children) in some regions . Pediatric autoimmune conditions also are on the rise.
- U.S . children are far more likely to die before their first birthday than infants in other wealthy countries and life expectancy is falling, driven largely by rising death rates in adolescents and younger adults. Suicide is the second leading cause of death in teens, half of whom are reported to have at least one mental, emotional or behavioral disorder.
- The proportion of public school children using special education services is skyrocketing, with estimates ranging from 13% to 25% of school populations .
- The social and economic fallout from these health challenges is hitting home hard—with adverse impacts on intelligence, fertility, household and government finances, employment, productivity, military recruitment and more . The disproportionately high level of neurodevelopmental disability in males versus females is also reshaping society .

Mystifyingly, there is almost no outcry in medical, public health or government circles to find answers and solutions

The potentially dangerous, synergistic and long-term effects of the ever-growing childhood vaccination schedule has never been evaluated properly.

1. A 2013 study by the prestigious Institutes of Medicine (IOM) concluded that:

“ the key elements of the entire (childhood vaccine) schedule: the number, frequency, timing, order, and age of administration of vaccination have not been systematically examined in research studies”

2. In May 2017 Robert F Kennedy Jr.(childrenshealthdefense.org) & Del Bigtree (icandecide.org) filed a lawsuit against our U.S. Department of Health and Human Services suspecting it was not fulfilling its critical vaccine safety obligations.

DHHS is required by Congress as per the NCVIA of 1986, to assure “improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions”. The lawsuit revealed that

DHHS had never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety. <http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

The mission statement of the Hawaii Department of Health as stated is to “protect and improve the health and environment for all people of Hawaii.” Preventing the spread of infectious disease is important, but it appears that we may be trading infectious disease for chronic, life-long illnesses. Cigarettes were once proclaimed safe by the tobacco giants and supposedly did not cause cancer, while antibiotics have been absolute miracle drugs until mutations created resistant super-bugs like MRSA. It appears we may be in need of another great paradigm shift in medicine and public healthcare, or at the very least unbiased, ethical, independent research and regulation. The mantra “Vaccines are Safe & Effective” is losing support quickly in the eyes of astute Americans.

I am an advocate for improved vaccine safety, fully informed consent, and parental choice. These are essential if public confidence is to be restored, not further eroded.

Thank you for your attention to this serious matter,

Dr. Kimberly Haine

Hawaii for Informed Consent (HFIC)



From: [REDACTED]
To: [REDACTED]
Cc:
Subject: Parents against your proposed rules for mandatory immunization changes
Date: Tuesday, November 27, 2018 9:57:21 AM

To Whom It May Concern:

We are writing this as concerned parents who would love to attend the public hearing here on [REDACTED], but due to our work schedule & location, we are unable to. First and foremost, we do vaccinate our child so our concern does not come from a No Vaccine perspective. Our concern is that we feel that your proposed changes takes away a parents right to choose. Currently some of the vaccines that you want to add are optional which means that as a parent we get to decide if we want that vaccine injected into our child or not. We value that option and have actually declined 2 out of the 3 proposed vaccinations you want to add WITH the approval of our son's pediatrician. In one of the vaccines, it had to be given in early infancy and since he's already past that, we don't even know what will happen since he doesn't have it. We don't think that it's right for you to make these currently optional vaccines as mandatory in order for our son to attend school. As parents you should not force us to do something we have already decided WITH the approval of our pediatrician not to do. That is taking away our choices as a parent. In addition, we had heard that if your proposed changes go through, and our child doesn't have the flu shot and there's a flu shot being given at the school, our child will get it even if we don't give consent because it will be a mandatory vaccine. Excuse my language, but HELL NO, that is not right. You cannot stick a needle and inject our child with something we blatantly said no to. There are already so many vaccines that our child has to get, in fact when we were children there was not nearly as much and hey, we're alive and doing fine. As parents, we do get all the mandatory ones for our child, but it's not necessary to add the current optional ones in. Leave that choice up to the parents, we don't want our choices taken away.

Sincerely,
Kimi & Guy Kusumoto

From: [REDACTED]
To: [REDACTED]
Subject: Flu shot spreading 630% more aerosolized flu virus particles
Date: Tuesday, November 27, 2018 2:23:45 PM

Aloha,

I am writing you out of deep concern for the mandatory vaccine laws being considered in our state of Hawaii; and would like to encourage more emphasis on safety, safer vaccines. 32 years of safety studies weren't done and that is deeply concerning. More scientifically-based research and safety studies are needed. Including by reliable independent research scientists who have no financial ties or pressured influences & outcomes placed upon them by the industry. Vaccines are not safe for every person or child — that is widely known already.

Please see the links below. If any of this is true, I vote NO mandatory vaccines in Hawaii and in the US. There are too many vaccine related reactions and deaths. In the news recently there was a Senator who dies after his flu vaccine. When will our health agencies take this seriously?

“Forced vaccinations now can be legally stopped - no quality control for 32 years.” See link:

<https://cairnsnews.org/2018/11/19/u-s-govt-loses-landmark-vaccine-lawsuit/?fbclid=IwAR12fypmkOSi3qtUlglltBSq8OtokrCdVR0dJpbW1CjsDylaLsiAEZ4fvYs>

1.) “Flu vaccine BOMBSHELL: 630% more “aerosolized flu virus particles” emitted by people who received flu shots... flu vaccines actually SPREAD the flu.” See link below.

<https://science.news/2018-01-30-flu-vaccine-bombshell-630-more-aerosolized-flu-virus-particles-emitted-by-people-who-received-flu-shots-flu-vaccines-actually-spread-the-flu.html>

2.) Government document confirms vaccine link to microcephaly. See link below.

<https://www.naturalnews.com/2017-01-19-government-document-confirms-vaccine-link-to-microcephaly.html>

3.) Read “how vaccines increase the risk of pediatric cancer and are being made with genetically-modified cells which mimic cancer cell growth.” See link below.

https://www.naturalhealth365.com/pediatric-cancer-vaccines-2760.html?fbclid=IwAR31kYJomO7LMt8pWzQ1gVkEstkh7gipkDGVFL9HOBiVo62EIHw7_23q75I

4.) “Baby monkeys given standard doses of popular vaccines develop symptoms of autism.” See link below.

<https://www.newstarget.com/2016-07-12-baby-monkeys-given-standard-doses-of-popular-vaccines-develop-symptoms-of-autism.html>

5.) Why wasn't this taken seriously? Retroviruses shouldn't be found deadly viruses in vaccines. A genuine scientist who has strong work, truth & honesty ethics shouldn't be punished for her research.

<https://explainlife.com/scientist-jailed-after-discovering-deadly-viruses-are-delivered-through-vaccines-2841/>

6.) MTHFR gene mutation — vaccines not safe. Autism links MD supported.

<http://www.stopmandatoryvaccination.com/parent/vaccine-injury/vaccines-cause-childs-autism-parents-dont-make-connection-but-new-doctor-does-and-recovers-child/>

7.) ***“The research is hard to ignore, vaccines can trigger autoimmunity with a laundry list of diseases to follow. Vaccines turn our immune systems against us.” See link below.***

<http://www.greenmedinfo.com/blog/attacking-ourselves-top-doctors-reveal-vaccines-turn-our-immune-system-against-us>

8.) “Vaccines are unavoidably unsafe, SUPREME COURT rules!” See link below.

<http://www.hutchnews.com/a1f84eca-2bf8-5839-b94b-d0a0d1c6e7f6.html>

9.) Conscience and Religious Freedom Division and our constitutional rights.

<https://explainlife.com/trump-lays-groundwork-to-ban-mandatory-vaccinations-across-u-s-2730/>

10.) Metals that are particularly detrimental to mitochondrial function include aluminum, arsenic, cesium, tin and thallium. Other toxic metals that many have in their bodies include cadmium, mercury and lead

When you have heavy metal toxicity, you tend to attract EMFs to your body. EMFs in turn impact your body's metabolism and ability to effectively eliminate toxins and heavy metals

<https://articles.mercola.com/sites/articles/archive/2018/04/08/heavy-metal-detox.aspx>

11.) Researchers from the U.S. Centers for Disease Control and Prevention (CDC) conducted a meta-analysis study showing that there is very limited evidence that flu vaccinations for hospital workers provide any benefit for **disease prevention**. The results were published in an early online edition of *Clinical Infectious Diseases* and examined the quality of evidence in studies used to back up the push for vaccinating healthcare workers. What would the benefit for students be then?

12.) Spread the flu, are you crazy?! Here's a CDC funded study showing the vaccinated shed 63 times more flu virus by just breathing!!

<https://thewilddoc.com/cdc-funded-study-shows-the-vaccinated-shed-6-3-times-more-flu->

[virus-just-by-breathing/](#)

13.) Too many beautifully gifted & talented people dying!

Please continue to research deep. We can not afford to overlook the many concerns that are known and those still unknown — without more solid scientifically-based research & safety studies complete.

Mahalo,

Laura Reese


P.S.

Some research shows the nagalase enzyme was added to vaccines. Nagalase prevents Vit production in the body, which is the body's main defense to naturally kill cancer cells.

We can not afford not to do more scientifically- based safety studies / research!

From: [REDACTED]
To: [REDACTED]
Subject: support the HAR 11-157 proposed rules update.
Date: Wednesday, November 28, 2018 1:05:55 PM

Thank you for this opportunity to provide testimony. As a **health care provider** and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you very much!

Emilia C. Suarez M.S. PA-C

From:
To:
Cc:

Subject: vaccines
Date: Saturday, December 01, 2018 9:55:22 AM

Please read & share this information thank you

https://l.facebook.com/l.php?u=http://hawaiiinformedconsent.com/?fbclid=IwAR1sYc5DsCDg4yik9b8hVvN7BR4hro_N9b-7ywHx0Zp4gUG8Oe87aXevsil&h=AT3duBkPzZ7kdd7BNolFeQe5KdqExOIB-woy33Qdqwg1Tep0ksIt1sZ6OiQdivbqLqt3d-TZnrT2LTBLBc1OKsyfW0q_tkasU9DcTZEXd9qPCWnUjmVqw-dVUFdpZM0-9aNpPuTz922n

Call to Action

Call to Action

PLEASE NOTE:

Island-wide hearings have been added by Hawaii Department of Health! Please appear in person if possible AND submit written testimony by **WEDNESDAY, DECEMBER 26th at 4:00pm HST** to immunization@doh.hawaii.gov including your name, address, whom you represent [yourself or a group], and a statement, such as, "Re: HAR 11-157, I OPPOSE" or "STRONGLY OPPOSE" [followed by a sentence stating what it is about the proposed rule(s) you oppose].

NEW VACCINE REQUIREMENTS FOR HAWAII STUDENTS ARE COMING...

unsplash-logoHyttalo Souza

*...from HI Department of Health-Proposed Rule
Changes, bypassing the State Legislature via 2013
Act deferring authority to HI DOH*

Hearing schedule:

Big Island

Hilo Thursday, Dec. 20th 9-11am, Hilo State Office Bldg, 75 Aupuni St.,
Conference Rooms A, B and C

*

Kona Thursday, Dec. 20th 2:30-4:30pm, 74-5044 Ane Keohokalole
Hwy, West Hawaii Civic Center Meeting Hale, Bldg G

Maui

Wailuku Friday, Dec. 14th 2-4pm, Wailuku State Office Bldg, 54 South High Street, Wailuku Video Conference Center, Third Floor

*

Moloka'i (video conferencing from Maui) Friday, Dec. 14th 2-4pm, Moloka'i Dept of Health, 65 Makaena Place, Kaunakakai Video Conference Room 107

Lana'i

Tuesday, Dec. 18th 1-3pm, **Lana'i Public and School Library**, 555 Fraser Avenue, Lana'i City Small Conference Room

Kaua'i

Lihue Friday, Dec. 21st 2-4pm, Kaua'i District Health Office Conference Room, 3040 Umi Street

Basic Info on the Proposed Rule Changes:

The Hawaii Department of Health has announced island-wide hearings on proposed rule changes to include NEW VACCINE REQUIREMENTS for Hawaii's children. (See links at right for official documentation.)

Some of the proposed changes include:

- HPV and Meningococcal vaccine for all seventh graders
- Influenza vaccine for all young children [see Exhibit A, Table 1 in the link]
- Hepatitis A vaccine for all children
- Additional dose of MMR for post-secondary school attendance and Meningococcal vaccine for all first-year students living in on-campus housing
- Enhanced reporting requirements for health practitioners and schools
- Enhanced reporting requirements for medical and religious exemptions
- Blanket adoption of recommendations from Advisory Committee on Immunization Practices [ACIP] as they are approved [see [this video](#) for a shining example of ACIP's abhorrent and negligent decision-making process in action; see also in this [link](#), watch ACIP vote on its new vaccine schedule recommendations, unanimously—immediately after hearing the impassioned comments and criticisms by members of the public at their latest meeting]

Links:

[Amended Hearing Notice with Additional Neighbor Island Hearings in Dec 2018 and Extended Deadline for Written Testimony](#)

[Original Hearing Notice](#)

[Proposed Rule Changes \[Ramseyer Format\]](#)

[Proposed Rule Changes \[Standard Format\]](#)

[Exhibits A and B](#)

CALL TO ACTION

Suggestions for responding to these proposed rule changes to Hawaii Administrative Rules/HAR 11-157:

First, learn about

- your [right to informed consent](#)

- the difference between the inadequate patient information offered on the CDC's "Vaccine Information Statements" [VISs] versus the more complete information provided on the actual vaccine manufacturers' package inserts [not typically viewed by vaccine-administering health care workers and physicians; they can be found published online at the FDA website, [here](#)]
- the **numerous victims of vaccine injury** not acknowledged by the pharmaceutical industry-propagandized medical establishment
- the fact that more and more **physicians and healthcare workers are speaking out** about potentially harmful, one-size-fits-all vaccination policies and the great disparity in claims about "the science" supporting the safety and efficacy of vaccination against communicable diseases
- the fact that there are *hundreds* of new vaccines coming down the manufacturing pipeline—will the mainstream medical community ever recognize any limit to the number of vaccines to be mandated, or are we to be perpetually at the mercy of the pharmaceutical industry to roll up our sleeves to accept their products and contaminants?
- the fact that industry money is interfering in the once-sacred doctor-patient relationship — does your vaccine-pushing healthcare team derive financial gain by vaccinating you and/or your family members? ASK!
- **vaccine contamination** by toxic metals, chemicals and xenobiological agents, like animal- and fetal-derived human DNA—is it *really* so difficult to imagine where the current epidemic of skyrocketing auto-immunity *may* be stemming from?
- the fact that the American Academy of Pediatrics [AAP] has expressed **eagerness to see removed ALL non-medical vaccine exemptions**
- the **nationwide legislative assault on Americans' vaccine exemptions**
- media fear-mongering which quickly blames "unvaccinated" people as the cause for outbreaks of measles, mumps, flu, polio, pertussis, etc. without discussing the phenomena which implicate vaccines themselves in the SPREAD of disease, such as viral shedding from vaccines and strain replacement
- the **2013 Hawaii State legislation** which empowered the Hawaii Department of Health with extensive, excessive latitude to make and alter health policy in the State; decision-making power now resides in very few individuals, if not a single individual, whereas beforehand, there were at least customary checks and balances

Next, prepare written and/or oral testimony and attend the hearing:

- Read the proposed rule changes and consider their potential impact
- Educate friends and family on the issue of these mandates, and urge them to get involved to protect their right to informed consent
- Plan to appear at your nearest hearing, according to the schedule shown above in this post
- Submit written testimony via email to immunization@doh.hawaii.gov, or via post to Disease Outbreak Control Division [DOCD], 1250 Punchbowl Street, Room 443, Honolulu, HI 96813 [officially, must be received no later than Wednesday, December 26, 2018 at 4:00pm, Hawaii Standard Time
- Plan to arrive early to allow for parking
- Oral testimony at the hearing will be limited to *two minutes per person*

Finally,

- **Be alert to future encroachments on medical and religious exemptions, which could be done with the stroke of a pen;** we anticipate impending attempts to curtail our current medical exemption right and to remove our religious exemption. Watch for any future updates to the status of our legal exemptions and any further encroachments on medical freedom and informed consent [[see this PBS Hawaii discussion of religious exemptions](#)]
- Connect with like-minded people in Hawaii and across the US concerned with preserving our right to the traditional definition of informed consent [not to be confused with the World Health Organization's (WHO's) recent attempt to redefine informed consent
- Join our email list for updates on future legislative action, educational events and advocacy
- Remember, this is a marathon—not a sprint; don't get discouraged and apathetic as a result of such encroachments on our medical freedom—get involved!

"The AAP views nonmedical exemptions to school-required immunizations as inappropriate for individual, public health, and ethical reasons and advocates for their elimination."

American Academy of Pediatrics Policy Statement
 Medical Versus Nonmedical Immunization Exemptions for Child Care and School Attendance, Pediatrics September 2016,
 VOLUME 138 / ISSUE 3

When there is risk there must be a choice!



From: [REDACTED]
To: [REDACTED]
Subject: Re: Flu shot spreading 630% more aerosolized flu virus particles
Date: Saturday, December 01, 2018 4:29:57 PM

Aloha,

I am writing out of more deep concern after hearing about the “mandatory vaccine” discussions taking place in Hawaii and in the United States. Americans, scientists, researchers, biochemists, molecular biologists — some independent researchers and more have identified too many RED FLAGS. It’s obvious we need more safety research and safer vaccines NOW. There’s been too much injury and even death. We have to care more and follow up with ACTION. 32 yrs of safety studies weren’t complete by the CDC and that is a MAJOR RED FLAG!

For one, HPV is being linked to infertility, health crisis, paralysis, even death. Beautiful thriving athletic teens in their prime shouldn’t have life-altering outcomes. We should deeply care about that. Why are you having discussions and public hearings about mandatory vaccinations in Hawaii — when 32 yrs of safety studies haven’t been done FIRST?!

There are TOO MANY families in the US and abroad, from our vulnerable population —with a family member disabled, injured, in health crisis, poor health outcomes or dead after receiving the flu shot or other vaccinations. How can we advocate for better safety for ALL families today?

Listen to their stories. Too many fathers, mothers, sisters, brothers, grandparents, and friends including our NY state Senator José Peralta who died — or with poor health outcomes, disabilities, paralysis or dead. Please review any scientific research out there linking vaccines to auto-immune diseases which has impacted our family personally — which can lead to an early demise. All our Fathers... Brothers... Sisters. Friends. Grandparents. Loved ones. They are ALL priceless and irreplaceable!! We have to care more about them too.

Have you considered enough our vulnerable population who are being INJURED from vaccine ingredients and vaccine injections. What can we do to HELP PREVENT injury BEFORE they become a “medical exemption” case? We have life-altering brain & mental health injuries, mass internal injuries, heavy metals crossing the blood-brain barrier, compromised health outcomes, even diseases & cancers spreading. Auto-immune conditions with early demise outcomes. How is this helping our families and communities thrive? Nanoparticles, retroviruses, even nagalase found by independent scientific researchers affecting millions. See previous e-mail for links, please do your own research. More research needed immediately!! Death as the worst outcome. We have to CARE MORE about them too.

See link & testimony below. Retroviruses found in vaccines by experienced PhD biochemist & molecular biologist, her research largely done at National Cancer Institute in Frederick, MD.

<https://m.youtube.com/watch?v=MBEI48og9mM>

* Currently physicians in Oahu are unable to test Hawaii residents for retroviruses.

Auto-immune hits home:

My husband LIVES with a severe auto-immune condition called Ankylosing Spondylitis. At the age of 18 or 20 yrs he was tested for HLS-B27 arthritis blood marker which was negative. After receiving the Hep B vaccine age 28 yrs old he started having severe back pain, he couldn't get a good night's rest or sleep comfortably in bed anymore from the pain, up all hours just trying to find a comfortable position. He was then retested for HLS-B27— and the test came back POSITIVE HLS-B27. Can't say enough how much this has impacted his life and our family — all when in the PRIME of his life. Please prevent this from happening to other fathers, mothers, brothers, sisters, friends in our beautiful state of Hawaii, in the US and abroad.

When scientific research and MD's confirm the highly probable link between Hep B vaccination, inflammation, & auto-immune conditions — these are LIFE-ALTERING reactions and very SERIOUS disabilities we've experienced first-hand and should be taken seriously. Are vaccines safe for everyone? My husbands injury could have been PREVENTED if 32 yrs of safety studies were done!! There is a vulnerable population out there and we need to do a better job protecting them as well!

Vaccination & Auto-Immune

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5607155/>

My husband has faced a life of pain and suffering with Ankylosing Spondylitis or AS — and there are no words to describe how painful it is to watch it take over his body. Simple movements like getting in and out of bed, sitting up from the couch are torture. He's being TORTURED every day by the pain , literally tortured— it's so severe he now can't even take a full breath of air because the inflammation hurts too much. Inflammation is in his chest cavity. Any time he coughs or sneezes it feels like he's being stabbed and he cries out in pain. He has to lift & cross his legs with his hands/arms because it hurts his back too much to lift his leg on its own. And the Humera injections prescribed for 10 yrs... one day he lost half the feeling in his hands, feet, and lips. Long-term side effects are unknown but nerve damage is listed as one. He has nerve damage now and limited use of his extremities.

Our story may hit too close to home for someone else you know — whether it's your own family member or friend. What can we do to prevent this from happening to others? I can't believe how many of our friends and acquaintances have been diagnosed with an auto-immune and Ankylosing Spondylitis as well!! It's becoming a crazy large problem!!

Father blind and paralyzed soon after flu shot. How many more?

See link: <https://news3lv.com/news/local/las-vegas-man-blames-flu-shot-for-triggering-rare-disorder>

Vaccines Revealed, injuries. Watch Dr. Brian S. Hooker PhD testimony. See link below: <https://www.vaccinesrevealed.com/?cookieUUID=7a8ba4a8-baec-492a-b234-cf9e8bff9360>

Colton Berrett, watch video to hear his testimony. Now dead. See link below: <http://www.stopmandatoryvaccination.com/vaccine-injury-2/colton-berrett-another-teen-sacrificed-by-the-hpv-vaccine-dies/>

Soaring Infertility rates with the HPV vaccine. See link below. And you're considering

mandatory HPV vaccination?! Please reconsider.

https://childrenshealthdefense.org/news/vaccine-safety/vaccine-boom-population-bust-study-queries-the-link-between-hpv-vaccine-and-soaring-infertility/?utm_source=mailchimp

Injected aluminum and an increase in cancers. See link below.

<http://www.greenmedinfo.com/blog/cancer-causing-metal-millions-eat-wear-or-have-injected-their-kids>

“A team of scientists from [Zabludowicz Center for Autoimmune Diseases](#) in Tel-Hashomer, Israel, set out to take a deeper look at Shoenfeld’s hypothesis.

“**Vaccines and autoimmunity are linked fields,**” the reviewers state of their data.

Autoimmunity caused by vaccines, they say, can be severe, and even fatal. [So my husband’s condition could be fatal for him? How deeply sad.].

Current research and case studies were reviewed by the team. The ASIA model ultimately explains that adverse vaccine reactions have been occurring since the practice began — and that the adjuvants used to stoke the immune system into action are a major vector for disease. Indeed, in some individuals, adjuvants can set off a wave of immune system reactions that culminates in the onset of any number of autoimmune diseases.” See link below:

<https://www.naturalnews.com/2018-10-16-adjuvants-found-in-vaccines-increase-autoimmune-disease.html>

It is my hope all our health agencies will promote higher SAFETY standards for all. Thank you. *What are we doing to learn about genetic profiles / vulnerabilities? Do we study / follow people’s health long-term before and after vaccination? What do we know about Mitochondrial function or impairment? How does nagalase impact Vit D absorption? Have we studied & compared the health of the vaccinated / to the unvaccinated? Why or why not? Let’s keep asking questions and find the answers.

Kind Regards,
Laura Reese

On Nov 27, 2018, at 2:31 PM, DOH.Immunization <DOH.Immunization@doh.hawaii.gov> wrote:

Your written testimony has been received. Thank you.

Hawaii Department of Health
Immunization Branch
1250 Punchbowl Street, 4th Floor
Honolulu, Hawaii 96813

From: Laura Reese [REDACTED]
Sent: Tuesday, November 27, 2018 2:22 PM
To: DOH.Immunization <DOH.Immunization@doh.hawaii.gov>
Subject: Flu shot spreading 630% more aerosolized flu virus particles

Aloha,

I am writing you out of deep concern for the mandatory vaccine laws being considered in our state of Hawaii; and would like to encourage more emphasis on safety, safer vaccines. 32 years of safety studies weren't done and that is deeply concerning. More scientifically-based research and safety studies are needed. Including by reliable independent research scientists who have no financial ties or pressured influences & outcomes placed upon them by the industry. Vaccines are not safe for every person or child — that is widely known already.

Please see the links below. If any of this is true, I vote NO mandatory vaccines in Hawaii and in the US. There are too many vaccine related reactions and deaths. In the news recently there was a Senator who dies after his flu vaccine. When will our health agencies take this seriously?

“Forced vaccinations now can be legally stopped - no quality control for 32 years.” See link:

<https://cairnsnews.org/2018/11/19/u-s-govt-loses-landmark-vaccine-lawsuit/?fbclid=IwAR12fypkOSi3qtUlglltBSq8OtokrCdVR0dJpbW1CjsDylaLsiAEZ4fvYs>

1.) “Flu vaccine BOMBSHELL: 630% more “aerosolized flu virus particles” emitted by people who received flu shots... flu vaccines actually SPREAD the flu.” See link below.

<https://science.news/2018-01-30-flu-vaccine-bombshell-630-more-aerosolized-flu-virus-particles-emitted-by-people-who-received-flu-shots-flu-vaccines-actually-spread-the-flu.html>

2.) Government document confirms vaccine link to microcephaly. See link below.

<https://www.naturalnews.com/2017-01-19-government-document-confirms-vaccine-link-to-microcephaly.html>

3.) Read “how vaccines increase the risk of pediatric cancer and are being made with genetically-modified cells which mimic cancer cell growth.” See link below.

https://www.naturalhealth365.com/pediatric-cancer-vaccines-2760.html?fbclid=IwAR31kYJomO7LMt8pWzQ1gVkEstkh7gpkDGVFL9HOBiVo62EIHw7_23q75I

4.) “Baby monkeys given standard doses of popular vaccines develop symptoms of autism.” See link below.

<https://www.newstarget.com/2016-07-12-baby-monkeys-given-standard-doses-of-popular-vaccines-develop-symptoms-of-autism.html>

5.) Why wasn’t this taken seriously? Retroviruses shouldn’t be found deadly viruses in vaccines. A genuine scientist who has strong work, truth & honesty ethics shouldn’t be punished for her research.

<https://explainlife.com/scientist-jailed-after-discovering-deadly-viruses-are-delivered-through-vaccines-2841/>

6.) MTHFR gene mutation — vaccines not safe. Autism links MD supported.

<http://www.stopmandatoryvaccination.com/parent/vaccine-injury/vaccines-cause-childs-autism-parents-dont-make-connection-but-new-doctor-does-and-recovers-child/>

7.) ***“The research is hard to ignore, vaccines can trigger autoimmunity with a laundry list of diseases to follow. Vaccines turn our immune systems against us.” See link below.***

<http://www.greenmedinfo.com/blog/attacking-ourselves-top-doctors-reveal-vaccines-turn-our-immune-system-against-us>

8.) “Vaccines are unavoidably unsafe, SUPREME COURT rules!” See link below.

<http://www.hutchnews.com/a1f84eca-2bf8-5839-b94b-d0a0d1c6e7f6.html>

9.) Conscience and Religious Freedom Division and our constitutional rights.

<https://explainlife.com/trump-lays-groundwork-to-ban-mandatory-vaccinations-across->

[u-s-2730/](#)

<!--[if !supportLists]-->• <!--[endif]-->

<!--[if !supportLists]-->• <!--[endif]-->10.) Metals that are particularly detrimental to mitochondrial function include aluminum, arsenic, cesium, tin and thallium. Other toxic metals that many have in their bodies include cadmium, mercury and lead

<!--[if !supportLists]-->• <!--[endif]-->When you have heavy metal toxicity, you tend to attract EMFs to your body. EMFs in turn impact your body's metabolism and ability to effectively eliminate toxins and heavy metals

<https://articles.mercola.com/sites/articles/archive/2018/04/08/heavy-metal-detox.aspx>

11.) Researchers from the U.S. Centers for Disease Control and Prevention (CDC) conducted a meta-analysis study showing that there is very limited evidence that flu vaccinations for hospital workers provide any benefit for [disease prevention](#). The results were published in an early online edition of *Clinical Infectious Diseases* and examined the quality of evidence in studies used to back up the push for vaccinating healthcare workers. What would the benefit for students be then?

12.) Spread the flu, are you crazy?! Here's a CDC funded study showing the vaccinated shed 63 times more flu virus by just breathing!!

<https://thewilddoc.com/cdc-funded-study-shows-the-vaccinated-shed-6-3-times-more-flu-virus-just-by-breathing/>

13.) Too many beautifully gifted & talented people dying!

Please continue to research deep. We can not afford to overlook the many concerns that are known and those still unknown — without more solid scientifically-based research & safety studies complete.

Mahalo,

Laura Reese

██████ resident

P.S.

Some research shows the nagalase enzyme was added to vaccines. Nagalase prevents Vit production in the body, which is the body's main defense to naturally kill cancer cells.

We can not afford not to do more scientifically- based safety studies / research!

From: [REDACTED]
To: [REDACTED]
Subject: STRONGLY OPPOSE HAR 11-157
Date: Saturday, December 01, 2018 10:03:42 AM

Please take my testimony.

I Jesse Spiller-Reiff of [REDACTED] OPPOSE requirements for mandatory vaccines in children. We all should have a choice in life and until my children grow up, it is my responsibility to make these choices. We have many factors why, but one is that my child had a very severe reaction to her vaccination at 2 1/2 years old. I will never forget bringing in a healthy child to her doctor and in return I got a very sick one.

Jesse Spiller-Reiff

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: vaxed
Date: Saturday, December 01, 2018 11:45:19 AM

Dept of health

plz have 3the head authorities at out meeting on the outer islands

plz give me more that 2 min to speak
Oral testimony shall be limited to up to two (2) minutes per testifier.

Plz prove to us the shots are safe or protect us from possible harm

The CDC was found guilty of hiding the truth that immunizations cause Autism and harm
so why would you take your orders from them re our health

Toni Liljengren

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Tuesday, November 20, 2018 8:20:56 PM

Aloha,

My name is Kelly Davis and I am representing myself. I am strongly opposed to HAR 11-157. Many individuals can have serious even deadly reactions to vaccinations. My brother and I both had bad reactions to the MMR shot and screamed for days after the shots. I had learning disabilities afterwards growing up which I eventually outgrew. (I believe I outgrew this because over time my body eliminated the chemicals that were injected). Unfortunately, my brother regressed severely after his vaccinations and he is now diagnosed with Asperger's. No parent should feel forced to give their child a vaccination, or they are not allowed to receive an education. There are many side effects and once the damage is done there is no return. You will be left with a disabled child and cannot even hold anyone liable. Vaccines are not double-blind placebo tested and I believe they should not be forced upon anyone. Health freedom should be a basic human right and no one should be forced to inject something into their body.

Some of the vaccinations required by the DOH are not risks for children at school such as the HPV vaccination which only prevents a sexually transmitted disease. Since children are not having sex at school, I don't see why the school system would feel it needs to be required to attend.

Thank you for taking the time to read this and please do not let HAR 11-157 pass.

Kelly Davis

[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines
Date: Saturday, October 27, 2018 9:34:45 AM

Aloha, My name is Sarah Silva

HAR-157 needs to be taken off the table immediately. Our ohana lives on the island of Kauai and we strongly oppose this proposed rule change for the following reasons:

1. Where there is risk, there must be a choice. Vaccines carry risk. If you don't believe me, read the vaccine insert itself—not the generic “fact sheet” from the doctor, but the actual, lengthy, detailed insert that comes in the vaccine box. It is wrong to mandate a medical procedure that is known to cause harm and carries risk.

2. You are not protecting more children with these rules, you are intentionally putting more children in the way of the risks of vaccines. Parents shouldn't have to set their own child on fire to keep others warm. Have you read the study that shows the effects of the suggested vaccine schedule as a whole? No? Because there isn't one. How dare you try to mandate a medical procedure when there aren't adequate safety studies in place.

It recently came to light that the safety obligations put in place years ago by congress in the National Childhood Vaccine Injury Act were never upheld. This proves that we cannot trust the government to follow through with their promises when it comes to the health and safety of our children—so parents must. Stop making it harder for us to protect our children.

3. HPV is a sexually transmitted disease. It is disgusting and appalling that you are suggesting the HPV vaccine be a requirement for children to attend school. What kind of gatherings are happening that they need supposed protection from an STD? It is also the most controversial vaccine because of the debilitating side effects that have ruined the lives of many across the world.

4. Requiring the flu vaccine is inappropriate. Did you know that the flu vaccine is contraindicated for people with egg allergies? Egg is a common allergy. Most people don't know this nor is the information shared and the basic question “are you allergic to eggs?” asked when the shot is administered. Plus the efficacy rate of the flu vaccine is so low, it's laughable that you'd add it to the list. It shows that you truly do not have the best interest of children in mind.

5. Stop re-defining what a “group” is – Your wording about what a “school” is concerns me. It now defines “school” as a “congregate setting for educational purposes.” That is too general. Even if you listed “exceptions” in a later paragraph, this definition is too vague and I ask that it be changed to “public school.” If you want to have rules for public school, that's one thing, but many, many, many of us have

opted to not send our children to public schools for a wide variety of reasons. Stay out of our options. Stay out of our private schools, stay out of our daycare centers, stay out of our homeschool co-ops, stay out of our playgroups. Stay out. If we wanted our children to be forced into a “one size fits all” mold, we would send them to public school. But we haven’t. We have created our own options because there is no “one size fits all” when it comes to anything—including education and medical decisions.

6. Medical Freedom is a basic right. You don’t know the medical concerns, religious beliefs, or educational background of every individual that you are trying to regulate. Stop pretending you know better. Stop creating blanket rules based on what you believe everyone should believe. Medical freedom should be protected so that INDIVIDUALS can make educated INDIVIDUAL decisions when it comes to their health. Health is personal and varies from individual to individual. Parents have the right to informed consent and making educated decisions when it comes to vaccines. Stop trying to take that away from parents.

Sincerely,

Sarah Silva



Joint Committee on Health and Children

Meeting on Thursday 3rd December 2015

Opening Statement by Ms. Anna Cannon, REGRET

Chairman, Deputies, Senators thank you for hosting us today.

We are representatives of a group of parents who have come together from all over the country to form R.E.G.R.E.T, which stands for Reactions and Effects of Gardasil Resulting in Extreme Trauma. We are a support Group for families with children suffering long term and life changing health issues following the Gardasil HPV vaccination.

Our 130 daughters display a series of debilitating, long term and chronic symptoms, corresponding directly with the Gardasil Patient Information Leaflet (PIL) ¹by the manufacturer. The PIL is the folded leaflet everyone gets included in the medication package when they go into the pharmacy to collect medication.

We are not given this information when signing the consent form for our daughters to get vaccinated with the Gardasil HPV vaccine in first year, secondary school. Instead we are given a marketing leaflet², outlining five mild side effects. Nowhere does it tell us about the risk of long term, chronic life changing side effects.

It doesn't tell us about the daily, severe headaches our girls struggle with for years, the nausea and stomach pains, the debilitating fatigue, the fainting and seizures, and onset of auto immune disorders.

It doesn't tell us that we might regularly end up in the A&E department, watching our teenagers scream in pain, whilst doctors rule out one condition after the other.

It doesn't tell us that our previously healthy, sporty and high achieving girls might never play sports again, never mind socializing with friends, enjoying what should be the most carefree time in their lives.

It doesn't tell us about the impact of these illnesses on our daughters' ability to continue their education, and the resulting psychological impact of having this basic human right taken away.

Parents are not prepared for the emotional strain of watching their child struggle to get out of bed to face another day of pain, fatigue, muscle weakness, dizziness and inability to concentrate. We also worry about how we will manage to raise the funds to meet our daughters many medical needs in years to come.

¹ See Supporting doc: Merck PIL.pdf

http://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_ppi.pdf

² See Supporting doc: Parent Information Leaflet HPV Gardasil Vaccination.pdf

<http://www.hse.ie/eng/health/immunisation/pubinfo/schoolprog/hpv/HPVImmProg.html>

Some of our daughters have contracted potentially life-threatening conditions, rare or unheard of in children their age. And yes, some doctors do admit that they think it is connected with the Gardasil HPV vaccination.

But most medical professionals in GP clinics, A&E departments and Hospitals across Ireland will not acknowledge any connection with this vaccine. Maybe if we as parents had been given the PIL, we could have pointed out the list of possible side effects to these doctors. Instead we struggled, sometimes for years, to understand our previously healthy daughters' range of health issues, before making the connection.

We believe there is significant under-reporting of HPV vaccine adverse reactions to the HPRA (Health Products Regulatory Authority). Before contacting R.E.G.R.E.T., most parents had never heard of the HPRA, or the adverse reaction reporting system. It is also their experience that doctors and consultants failed to report suspicions of side effects even when parents had pointed out the connection.

We all wanted the very best for our children. We trusted that the HSE would act responsibly and respect our right as parents, to be fully and honestly informed before making the decision to sign the consent form. This is a significant decision for parents, considering Ireland is one of the very few countries in the developed world that still do not have a vaccine damage compensation scheme.

Two years ago when the Gardasil vaccination programme was discussed by this Committee, Dr. Colette Bonner from the Department of Health, noted the Committee's concern that there is no vaccine damage compensation scheme. *"There is an expert report which we are considering. I will convey the committee's concerns both to the secretary-general and the Minister on this point,"* she said³.

IN THE INSERT

We now know that Gardasil got CDC fast track approval and underwent a mere six months⁴ of human trial research. Subjects were only followed for 5-15 days⁵ in the safety studies, and only 1200 girls under 16 years of age participated (even though this is the target age for the vaccine). During these clinical safety trials paid for by Merck, 95% of the 'Placebo' injections⁶ contained the same toxic aluminium adjuvant⁷ as the vaccine itself, which resulted in Merck being able to claim that adverse reactions were not significantly higher than those of the Placebo group.

³<http://oireachtasdebates.oireachtas.ie/Debates%20Authoring/DebatesWebPack.nsf/committeetakes/HEJ2012122000010?opendocument>

⁴ & ⁵ In initial trials, participants only followed for 5-15 days from the last dose administered 6 months into trial http://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_pi.pdf

⁶ See section "Clinical Trials Experience": http://www.merck.com/product/usa/pi_circulars/g/gardasil/gardasil_pi.pdf

⁷ <http://www.ncbi.nlm.nih.gov/pubmed/22235057>

What we also now know is that in a later 4-year clinical trial by Merck, 2.5% (1 in 40)⁸ of trial participants reported a serious adverse event* after taking the Gardasil HPV vaccine. In addition, 3.3% (1 in 30)⁹ also reported a new auto-immune condition.

**According to the FDA a serious adverse event must fit one of the following criteria: death, life-threatening, hospitalization, disability or permanent damage, congenital abnormality/birth defect, or the requirement to intervene to prevent permanent impairment¹⁰.*

Given the current rate of incidence of cervical cancer in Ireland is only 13/100,000¹¹, the benefits of this vaccine hardly appear to outweigh the risks.

The benefit, according to politicians and health authorities, is that 50 to 60 lives a year¹² will be saved by the HPV vaccine in Ireland. However Health Technology Assessment Reports from other countries¹³ show that these statistics can only result from the combined effect of screening plus vaccination. However in Ireland these figures are being presented as the effect of vaccination alone.

The truth is that our girls will still require ongoing and regular pap smear tests, as protection from the HPV vaccine has not been shown to last longer than 8 years¹⁴.

Worldwide concerns mounting for the safety of the Gardasil HPV vaccine:

Gardasil has now been dropped from the childhood immunisation schedule in Denmark¹⁵ and replaced with an alternative vaccine. As of September 1st, approximately 1100 girls¹⁶ were being treated (or waiting to be treated) in five Danish regional medical centres for suspected Gardasil related conditions. Japan no longer recommends the HPV vaccine after conducting its own investigation into serious reactions¹⁷.

⁸ See section "*Serious Adverse Events in Clinical Studies*"

http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf

(Note that Gardasil was being used as a placebo in this trial with "Gardasil 9" as the comparison vaccine).

⁹ See section "*Systemic Autoimmune Disorders*"

http://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf

¹⁰ <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm053087.htm>

¹¹ <http://www.ncr.ie/data/incidence-statistics>

¹² These "lives saved" figures have been presented in the Dail as the effect of the vaccine alone but in point of fact can only result from the combined effect of Screening plus vaccination.

¹³ Eg Austria: <http://link.springer.com/article/10.1007%2Fs10389-009-0276-3>

¹⁴ "Loss of 14% of measurable antibodies to HPV 16 after 8.5 years, supporting the belief that Gardasil boosters will be necessary before the 15 year threshold for actual cancer prevention":

<http://www.discoverymedicine.com/Diane-M-Harper/2010/07/03/prophylactic-hpv-vaccines-current-knowledge-of-impact-on-gynecologic-premalignancies/>

¹⁵ Copenhagen Post article: <http://cphpost.dk/news/doctors-question-denmarks-decision-to-switch-hpv-vaccines.html>

¹⁶ Copenhagen Post article: <http://cphpost.dk/news/danish-hpv-centres-flooded-by-ill-girls.html>

¹⁷ http://ajw.asahi.com/article/behind_news/social_affairs/AJ201306150057

This month we have been told that Gardasil's safety has been reaffirmed based on the results of an EMA Review which found no link between Gardasil and two specific medical conditions (CRPS and POTS).

Research Director and Consultant Dr. Jesper Mehlsen from Frederiksberg Hospital has studied many girls with suspected adverse reactions to the HPV vaccine. He has criticised the EMA, for not releasing the evidence of records and data, when submitting their early release conclusion¹⁸. Dr. Mehlsen is now heading an independent investigation into the HPV vaccine, with results due out in April 2016. Speaking in June this year, he said "A realistic estimate is that one in 500 girls experience serious side effects"¹⁹.

Spanish doctor and professor of Public Health, Carlos Alvarez-Dardet from the University of Alicante, has initiated a petition against the HPV vaccine. He is a former President of the European Public Health Association (EUPHA) and was also an advisor at the W.H.O. He is now calling for an immediate stop to the vaccine²⁰.

Last month, researchers announced the results of a Canadian study to show the effect the HPV vaccine had on 170 teenagers who they followed for 4 years. They now question both the safety and benefits of the HPV vaccine, urging Quebec to halt HPV immunization until its alleged dangers have been independently investigated²¹.

French MEP Michele Ravasi has compiled a large petition with hundreds of Physicians signatures calling for a moratorium on the HPV vaccine²².

As parents we feel that the Minister for Health has a duty of care for 130 teenage girls suffering chronic ill health since the Gardasil HPV vaccination. However, he has consistently declined our requests for a meeting to discuss our daughter's situation.

In a Private members Dail question to the Minister for Health in October (PQ: 36264/15), Deputy Maureen o'Sullivan asked for *"the reason parents are not provided a copy of the Patient Information Leaflet (PIL) prior to signing the consent form for the HPV vaccine"*.

The HSE provided a response in the form of a letter from Dr. Kevin Kelleher, Assistant National Director of Public Health, which included this explanation:

¹⁸ <http://nyhederne.tv2.dk/samfund/2015-11-12-hpv-rapport-konklusionen-er-ikke-endelig>

¹⁹ <http://sanevax.org/gardasil-firestorm-in-denmark/>

²⁰ The epidemiologist Carlos Alvarez-Dardet, professor of public health at the University of Alicante and director of the Journal of Epidemiology and Community Health is the author of a manifesto published in the Spanish newspaper El País, giving the reasons why a moratorium on vaccination with Gardasil is imperative http://elpais.com/diario/2007/11/06/salud/1194303609_850215.html

²¹

https://www.academia.edu/16549844/For_a_moratorium_on_the_HPV_vaccine_Pour_un_moratoire_sur_le_vaccin_HPV

<http://www.ledevoir.com/societe/sante/451710/vaccination-contre-les-vph-appel-urgent-a-un-moratoire>

²² <http://sanevax.org/france-are-hpv-vaccines-necessary/>

“All the information provided to parents about vaccination is prepared from the available licensed documentation for each vaccine, the Summary of Products Characteristics (SPC) and Patient Information Leaflet (PIL). The information is presented in clear simple language and approved by the National Adult Literacy Agency so that it can be understood by all adults as the average reading age in Ireland is 12 years of age”.

So the official reason for the HSE withholding the list of known serious, debilitating and long term side effects from the HPV vaccine information literature is because *“the average adult reading age is 12 years old”*, and on that basis the content of these information leaflets is determined. I hope the absurdity of this logic is not lost on the Committee.

As an aside, I note that it was Merck Sharp & Dohme (MSD) who sponsored NALA’s 2007 Irish Health Literacy research project²³.

There are some who would rather dismiss us as ‘Anti-vaccine’ parents, but we all gave our other children their vaccinations, just as we all signed the consent form for this one. We thought we were doing the best for them. Instead we signed away our girls future, and five years later they are still struggling.

Our lives were never the same following the Gardasil HPV vaccination of our daughters, with years taken from them, their parents, siblings and grandparents. We have been given no answers, guidance, or hope.

We live with the guilt of our decision to sign the Gardasil consent form every day, watching our previously healthy young girls struggle to get through their day, with our bags packed 24/7, in case of yet another emergency visit to the hospital.

Read some of our teenage girls stories here; <http://www.regret.ie/victims 2.html>

²³ <https://www.nala.ie/support-us/corporate-sponsorships/msd#.VkyA-OHudKs.facebook>

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines prevent severe diseases
Date: Wednesday, December 05, 2018 12:59:54 PM

Testimony for the need of vaccines:

I, along with other pediatric physicians, hope for the best of health in our patients. I would like to relay a story of a patient who had severe disability due to a vaccine preventable disease. During my residency in Michigan, I saw a case of meningococcal meningitis in a child. This is a severe, fast-spreading disease that affects the covering around the brain (the meninges) and goes through the blood stream to affect the whole body. It is not a disease where a patient can take oral antibiotics and stay home. It requires immediate hospitalization in the ICU (intensive care unit), not just the pediatric ward. The hospital in East Lansing was a regional children's facility so we rapidly had to treat this patient as he came from an outlying area. I saw him in the ICU bed, lying unconscious with central lines and the tell-tale purple purpura rash that we are taught to look for in meningitis. Prior to his illness, he had been a normal boy playing and running around, but would leave the hospital with a leg amputation as well as amputations of many fingers and toes. Over the course of his hospital stay, many of his toes and fingers turned black and necrotic. Despite all of the medical care that we had provided, amputations were necessary to save his life. Some children are not so lucky and die because of this disease. He had to endure weeks of hospitalization and then had to learn to walk with a prosthesis. This is why vaccines are needed to prevent death and severe disability in our children.

Gail Nakaichi, D.O.

From: [REDACTED]
To: [REDACTED]
Subject: Vaccine Requirements Written Testimony
Date: Friday, December 07, 2018 10:34:09 AM

Whitney Herrelson
[REDACTED]

December 7, 2018

Hawaii Department of Health
Disease Outbreak Control Division

To whom it may concern:

As a mother of 2 small children, and a citizen, voter, and taxpayer in the state of Hawai'i, I adamantly oppose the new additions to the recommended vaccine schedule, specifically the influenza and HPV vaccines, as well as any government-mandated vaccines.

Since the introduction of the HPV vaccine, over 25,000 adverse events have been reported to VAERS,, 772 of which were "serious". In addition, 32 recorded deaths have occurred (White, 2014). I strongly believe (from personal experience) that vaccine injuries go largely underreported. *Where there is risk, there must be choice.*

The influenza vaccine is only 40% effective in 2018, but only 10-40% effective for people ages 9-17 (depending on the vaccine type) (CDC, 2018). This vaccine, like all vaccines, does not come without risk.

While I understand that vaccines have and do save lives, I believe it is unethical to force one person to sacrifice his/her health or life via vaccine injury, to protect the masses. The fact is that no vaccine is without risk, and no one can predict who might be negatively affected. Some lives will be lost to vaccines.

Please thoroughly consider the negative impacts from making Hawai'i the most vaccinated state in the US, and well as the ethics surrounding mandated vaccines.

Sincerely,
Whitney Herrelson
[REDACTED]

Reference

Centers for Disease Control. (2018). *Seasonal Influenza Vaccine Effectiveness, 2017-2018*. Retrieved from: <https://www.cdc.gov/flu/professionals/vaccination/effectiveness-year/2017-2018.html>

White M. D. (2014). Pros, cons, and ethics of HPV vaccine in teens-Why such controversy?. *Translational andrology and urology*, 3(4), 429-34.

From: [REDACTED]
To: [REDACTED]
Subject: Testimony for HAR 11-157
Date: Friday, December 07, 2018 10:54:27 AM

To Whom It May Concern:

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life. The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases. As a pediatric hospitalist at [REDACTED], I help to provide care for some of the sickest children in the state and I feel very strongly about vaccinations to keep our keiki healthy. I have seen some terrible outcomes in children who have not been vaccinated with significant life-threatening and life-changing events. No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized. Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders. I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities. Thank you for your consideration.

Sincerely,

Jennifer Di Rocco

Jennifer Di Rocco, D.O., M.Ed.
[REDACTED]
[REDACTED]
[REDACTED]

the intended recipient(s) and may contain confidential and privileged information. Unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in opposition to proposed rule changes
Date: Friday, December 07, 2018 9:50:29 AM

Aloha,

As a mother, public health professional, laau lapa'au, and sovereignty activist, I am appalled by both the proposed rule changes and by the process (the lack of decision-makers at public meetings should immediately invalidate the entire process). Health sovereignty is not a trivial matter for Hawaiian ohana. My dear health research mentor, Dr. Kekuni Blaisdell, proved the link between loss of Ea (manifested through self-determination and body sovereignty) and poor health outcomes for Kanaka Maoli. Interfering with our right of free, informed choice is a direct attack on ea, and it is not okay.

Please halt this entire process immediately. If the State wishes to lower morbidity from contagious diseases, many steps can be taken that will not interfere with health freedoms, nor drive families underground without access to education resources.

Here are some things that can be done:

- mandate SICK LEAVE, including sick child care. Do not allow people who are not well to be forced to continue to work.
- address the housing crisis. Unhealthy, unsanitary conditions are created by both overcrowding and by people feeling they "can't" take off time from work or keep their sick children home. This would have far greater effect on contagious disease containment than mandatory vaccines.
- provide better information on contagious diseases, including containment strategies that can be used in addition to vaccine programs.
- stop pushy, judgmental approaches (like this one) that turn people off to vaccine programs entirely and foster community distrust and polarization.
- for goodness sake, drop the ridiculous idea that if parents choose even one vaccine, they are ineligible for an exemption. That is offensive and dangerous, and by removing the option of partial vaccination, counter to the goal of increasing vaccine rates.

I am available for consultation at any time.

Mahalo nui loa.

Laulani Teale, MPH

[REDACTED]

From: [Yu, Carl MD](#)
To: [DOH.Immunization](#)
Subject: HAR 11-157 Proposed Update
Date: Friday, December 07, 2018 5:56:17 PM
Attachments: [image001.png](#)
Importance: High

Thank you for this opportunity to provide testimony and feedback by email as I will be unable to attend our local meeting on 12/21/2018. As a community member, a father of two children, and a board-certified pediatrician who has been practicing on [REDACTED] for over 6 years, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP), which have also been approved by our professional organization, the American Academy of Pediatrics (AAP), as well as the American Academy of Family Physicians (AAFP), and the American College of Obstetricians and Gynecologists (ACOG).

While this has been disappointingly categorized in some media as "new vaccines," please understand that the proposed changes are to bring Hawai'i in line with what have been recommended as routine vaccines in pediatric and family medicine. In fact, during the 2016 Hepatitis A outbreak in Hawai'i **none** of the 292 affected people were children, which can largely be attributed to the fact that the Hepatitis A vaccine has been a part of the routine vaccination schedule for all children since 2006.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

In fact, this October in my office I was performing physical exams on two of my teenage patients, when with tears in her eyes their mother thanked me for giving them the HPV vaccine. She explained further that this past summer the boys had to witness their father receive treatment for oropharyngeal (throat) cancer due directly to HPV, and was so grateful that her sons would be much less likely to go through the struggle that their father was currently enduring.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I vaccinate my children, but beyond that, I received my MMR booster-- despite showing immunity to mumps in blood testing--as recommended by the Department of Health to protect myself, my other patients, as well as my infant son who is too young to be vaccinated for mumps.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration. Please contact me with any further questions or concerns.

Carl L. Yu, MD FAAP

Pediatrician

[Redacted]

Email:

[Redacted]

[Redacted]

Confidentiality Notice: This e-mail message, including any attachments, is for the sole use of the intended recipient(s) and may contain confidential and privileged information. Unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: HAR- 11 -157 , I oppose
Date: Tuesday, December 11, 2018 8:57:32 PM

Dec 10, 2018

Aloha Hawaii Department of Health,

Thank you for this opportunity to provide testimony.

I STRONGLY OPPOSE THE HAR 11-157 PROPOSED RULES UPDATE.

I OPPOSE INCREASING VACCINE REQUIREMENTS. The risks of adverse reactions include autism, infertility, autoimmune disorders, seizures, paralysis, and death. Increasing vaccine requirements puts are children at greater risks for adverse reactions. There have been no long-term studies done on vaccines proving their safety.

I OPPOSE INCREASING REQUIREMENTS FOR MEDICAL AND RELIGIOUS EXEMPTION. Complicating the exemption process would take away a parent's right to informed consent. Parents must be allowed to refuse the injections of toxic metals, harmful chemicals, allergens, and xeno-biological agents such as animal and fetal derived DNA. Ultimately parents are responsible if anything happens to their child. Doctors and pharmaceutical companies are not held liable for injuries.

The National Childhood Vaccine Injury Act of 1986 ruled that pharmaceutical companies and doctors are not liable for any injuries caused by vaccines. Since then HHS has had the sole responsibility to make and assure improvements in the licensing, manufacturing, adverse reaction reporting, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. Congress required as part of the 1986 act that the secretary of HHS submit a bi-annual reports to Congress detailing the improvements in vaccine safety. In an effort to gain access to these safety reports ICAN and Robert F Kennedy Jr. filed a freedom of information act request in August of 2017 to the HHS only to be blocked from receiving information for over 8 months. ICAN and Kennedy were forced to bring a lawsuit against HHS to provide copies of these reports to Congress or to admit that they never actually filed these reports. The result of the lawsuit was that HHS had to admit that it NEVER filed a single report to Congress detailing the improvements of vaccine safety.

I OPPOSE ADOPTING THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP) RECOMENDATIONS. These recommendations have not been tested and proven safe and pose risks of severe adverse reactions. The FDA admits that only 1-10% of adverse reactions are even reported.

The HAR 11-157 proposed rule changes increase vaccine requirements and complicate the acquiring of vaccine exemptions, which is a complete infringement on our freedom of informed consent. Also none of the vaccines

have ever been tested in a placebo controlled double blind study. The accumulative effects of combined doses have never been studied. If the proposed changes take effect it would allow the CDC to add many more vaccines to the already overwhelming vaccine schedule. According some doctors over 130 more vaccines are in the process of being developed.

In light of this information, parents should be allowed to easily apply for an exemption. Since government agencies are lacking responsibility in holding vaccine manufacturers accountable

By 2018 the US Court of Claims had awarded nearly 4 billion dollars to vaccine victims for their catastrophic vaccine injuries although 2 out of 3 applicants have been denied compensation.

HEALTH FREEDOM AND INFORMED CONSENT ARE BASIC HUMAN RIGHTS!
Everybody must be allowed the right to chose or refuse what to put into their body. Vaccination is a medical intervention that carries a risk of injury or death. The right to informed consent to any medical intervention that can kill or injure you or your child is a human right.

Please consider the health concerns of everyone susceptible to adverse reactions to immunizations.

Thank you again for the opportunity to provide testimony opposing the HAR 11-157 proposed rules update and the adverse consequences it would cause.

Mahalo,

Reka Starr & Zsolt Csillag

Residents

From: [REDACTED]
To: [REDACTED]
Subject: Immunization Update
Date: Wednesday, December 12, 2018 10:45:26 AM

Aloha and thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Erin Baxter, PA-C
Kaiser Pediatric Department

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

12/12/18

State of Hawaii Honorable & Esteemed Congresspersons & Senators,

We are mothers, grandparents, aunts & uncles. We entreat you to listen. You are charged (Obligated) to represent 'the people of Hawaii'. This includes all of us, as Citizens, as Parents, as the Most Vulnerable amongst us, Infants (even in the Womb) and Children.

There are 3 issues at stake here:

1. All our Freedoms.
2. Safety.
3. Responsibility.

1. We are a Democracy. As a State, HI is 100% Democratic, as is most of CA. Are we to understand that Democrats in the State of HI are those who Remove the Most Basic Freedoms of its People? Will It follow the Socialist method of Dividing Families by Removing Personal Freedoms? You will see this as families are separated, overburdened by Damaged Children and left to be further Bullied by the Legislation of their 'elected officials'. Will the State **Be Bullied by Federal threats or Corporate Profits** to Not Only remove our God-given rights to Raise our own Families as we see Safe (& remember the Story of the Wisest Ruler in History-Solomon! Who Demonstrated the True Advocate for their own Child-the one who will watch their child Suffer, but their Mother?). Will HI Legislature Create a Population (Births –of local workers- are Reduced by Vaccines given before or after Birth)*a but critically here, a **Population whose Constant, Dependency Needs for Added Healthcare, Added Educational Services, Added Housing & Caretakers until Well after that of Adults** and will, we believe, Surely, very Soon, Overwhelm HI's Healthcare, Housing, Educational and Welfare System's Budgets! Should such Unwise Legislation be Followed by this State (against Common Sense followed by much of the World re: Vacc.), the 'Democratic HI' will be known as One that Removes its Peoples' Freedoms. One that Places Huge Additional Caretaker Burdens (and Taxes to Pay for Such) on its Population? What has HI's Legislation done to insure our Children's Safety, Can HI Democrats show that they care about Families, that they can Lead our Country by Following the Lead of More Intelligent 1st, 2nd & even 3rd World Countries. Can we Directly have a small part in solving a Bigger Problem by Demanding we Use the "Precautionary Principle" in our Vaccine Legislation to Protect the Health and Welfare of our Citizens, especially those without Voices,our Most Vulnerable?
2. Are these Vaccines PROVEN SAFE? NO. Can this 1986 Legislation be Negated to Remove Unsafe, NeuroToxic Poisons from Vaccines' Ingredients (such as Aluminum, Thimerosal-Mercury-formaldehyde, etc.-need a magnifying glass to Read the Side Effects!); to even List Side Effects in Readable Print, so that Parents are aware of the very Real Risks? The Statistics & History of Vaccines' connection **to just Autism Spectrum alone***b, which has gone from **1/10,000 in 1980's to 1/ 2500 in the 1990's, 1/1000 in the 2000's to 1/88 in 2012, 1/68 in 2016, 1/ 1/59 in 2014, to now 1/44 children? What has Changed?** Is is just Coincidence that the Number of Vaccinations have

been Multiplied, as discussed by others here, has Increased, nearly Proportionately? This FACT means that **Every Person in this Room's "FAMILY" will be Negatively Affected** (in just this One Disorder!) at Least Once in their lifetime. It is the Family (parent, grandparent, siblings) who will watch their child Suffer, never able to live or share their lives to their God-given Potential. Are our 'Representatives' listening? Is the State Ready to Admit Culpability in this, when far more than apprx.1500 (just Autism Spectrum alone) of our Local Kauai Population alone, in the very near future is Affected by AS alone (in '06 1 in 6 'affected' from everything from speech & language impairments to serious developmental ones such as Cerebral Palsy,*e. not Including: MS, Brain Inflammation, paralysis, Epileptic, Blind,Diabetic,Mentally Retarded or Miscarriage Deaths to our Child Population *b&f.). Does the State Know how Difficult and Costly it is for Kauai Schools just to get and retain **even One Special Ed Teacher?** Until there are **Multiple Scientific, Unbiased** (by Gov't or Industry-Funded studies with Proven Conflicts of Interest)* c, **Long-Term Studies that Show Guaranteed Proof of SAFETY** in Vaccinations for Hawaii's Most Vulnerable, Why Can't We Demand to Demand the Use of the Precautionary Principle in the Protection of our Most Vulnerable? Hawaii's Future Citizens? We Have Demanded 'Safety' in our FOODS, with every piece of fruit or vegetable, we can Know where it's Grown, the Ingredients in Packaging & the Pesticides sprayed on it; we Know the manufacturer of the Miniscule Nuts & Bolts of our Autos for 'Our Safety'. Aren't there issues of Constant 'ReCalls' on everything we put into our bodies that Is Not Safe? Isn't it Reasonable, then, to ask for Removal of NeuroToxins from Vaccines? From those 'Corporations' who produce such, who since 1986 are Given a 'Free Ride' from SAFETY REGULATIONS (1986for our Bodies, that of the Defenseless, our Newborn, those in the Womb & our Children? Korea (higher vacc. Rate than US,UK & Australia96.6%=higher AS rate)*d

3. Responsibility, Accountability. Where is this for State of HI? The 'costs/yr.' for ASD in the US ('11) were "estimated at \$11.5 -\$60 Billion"!*e. This significant Economic Burden represents a variety of Direct & InDirect costs from medical care to special Education to Lost Parental Productivity. *e. In '05 av. Annual Medicaid-enrolled costs were 5-6 times higher than normal children w/o ASD. Behavioral interventions (all this for ASD alone) cost \$40-60,000/yr. Who is Responsible for this Damage?

An Educated Parent would Not allow these Poisons into their child's bodies. They are Not Responsible, especially if there IS No Choice given to them. *Are our Legislator's Ready for that blame? From their loved ones, their nieces, nephews, children, grandchildren, for their responsibility as they blame them for their hardships, loss of quality of life and sorrow? Will future legislation remove their retirement funds as a penalty for allowing such?*

There is no 'need' for mandated vaccinations. The US is near tops for 'sanitary conditions' in most places, this is not Africa or a 3rd world island, where just the addition of 'Clean Water' has drastically Reduced Disease (ie. Fiji gov't., 2016). We have No Urgent need for a Plague in 'measles, chicken pox, mumps, even polio right now. Why have we "Shielded Drug Companies from All Liability for Harm" since Congress was Blackmailed in 1982 by Vaccine Corporations (Merck,Wyeth,Lederle &

Connaught) & 2-22-2011? *f *The Vaccines Creators are Not Accountable in a Court of Law by their Peers (the PUBLIC in HAWAII, too) for ANY Damages, even if these Vaccines could Easily have been Made Less Toxic! They are completely IMMUNE from Damages (lawsuits) to Hawaii's Children, Hawaii's Future. The Vaccine Industry, Big Pharma is out of Control. From 23 doses of 7 vaccines 36 years ago to 70 doses of 16 vaccines in the 90's to 130 doses of Government Recommend vaccines until we are 78 years old! Today, there is NO Responsibility from the Drug Companies for To Make 'Safe Vaccines' for Human Children. There is No Accountability for Damages to Families, to Babies, to our Cherished Keiki, our Kapuna from even a Death Sentence!*

*The day after the Supreme Court blocked lawsuits against drug companies for Unsafe Vaccines, the Democratic-Controlled Congress approved 'seatbelt safety.' *f **Civil liability** put pressure on Federal Health Agencies to replace use of a contaminated, neurotoxic polio vaccine that can paralyze people, with one that cannot. On Our Urging, HI Congress & Senators, we Demand that you Stand up to this Corporate "Bully" as other States have. Please, bring Common Sense to Government. Take on the 'Elephants in the Room' with our support, or we the People will soon suffer immensely, see the Results and Vote appropriately-against you.*

b. Autism Science Foundation, 2018

c. Fourteen Studies

d. Korea Herald 7-27-17

e. CDC

f. National Vaccine Information Center.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 Strongly Oppose
Date: Thursday, December 13, 2018 8:43:44 PM

Aloha,

I strongly oppose the proposed rule to mandate vaccinations for all young children.

Where there is risk, there MUST be choice.

I have 2 autistic cousins who were vaccine injured. There is more to the story. It is not a black and white issue.

My children attend public school. Please do not take away our medical freedom.

Thank you,

Natalie Norberg

[REDACTED]



Submitted electronically to: [REDACTED]

December 13, 2018

Bruce Anderson, PhD
Director of Health
Hawaii Department of Health
335 Merchant Street, Rm. 213
Honolulu, Hawaii 96813

RE: Amendments to Title 11, Chapter 157 – “Examination and Immunization”

On behalf of Kaiser Permanente, including the more than 600 physicians and providers of Hawaii Permanente Medical Group, this letter supplements our original testimony submitted on October 29, 2018.

We wholeheartedly endorse evidence-based recommendations to enhance immunization requirements in Hawaii. The proposed rule changes will conform with current national recommendations by the Centers for Disease Control and Prevention and the American Academy of Pediatrics.

There are many unfounded or disproven theories and myths about vaccine dangers. **In truth, vaccinations are extremely safe, and complications are exceedingly rare.** Vaccinations help protect our most vulnerable keiki from terrible diseases that can be debilitating and sometimes deadly.

VACCINATIONS PROTECT OUR KEIKI

No child should suffer from a preventable disease when safe, effective protection is available. Delaying or declining immunizations leaves keiki unprotected when they’re potentially most vulnerable.

Children and adults who are not protected can become very sick and spread illness. We’ve seen this happen most recently in the islands with an extended outbreak of mumps. We must remain vigilant in Hawaii, which has a vast international traveler community. With serious and even deadly diseases circulating globally, we need to protect everyone in the community to keep each other safe and healthy.

VACCINES ARE TESTED FOR SAFETY BEFORE RECOMMENDED

Vaccinations have been falsely associated with various developmental difficulties and conditions. The reason this confusion happens is understandable; vaccinations are given to infants and children during the same time in life when developmental challenges become detectable. When this happens, it’s easy for parents to attribute developmental difficulties or diagnoses to vaccinations a child may have received, even when there’s no scientific or other plausible link.

HOW CAN WE PROTECT OUR KEIKI?

Parents/guardians should complete all well-keiki visits and keep up with recommended immunizations. We do not recommend deviating from the standard schedule:

- Spacing out shots leaves your child unprotected against serious diseases when he or she is most vulnerable.
- Combination shots reduce the total number of injections and provide safe, effective protection.
- Multiple shots during one visit mean fewer trips to the doctor's office and less stress for your child.

Keeping up with the standard schedule is safest so that parents/guardians don't have to worry about leaving gaps in protection.

In conclusion, Kaiser Permanente Hawaii strongly supports the proposed amendments to HAR Title 11, Chapter 157 because they conform and align to the CDC's ACIP recommendations. We believe that the recommended vaccines are a safe, efficient and cost-effective way to protect against vaccine-preventable diseases.

Thank you for your time and consideration. Please do not hesitate to contact Daryl Kurozawa, MD, Associate Medical Director, Government Relations at [REDACTED] or [REDACTED] if you have any questions or require additional information. Alternatively, you may contact Jonathan Ching, Specialist, Government Relations at [REDACTED] or [REDACTED].

From: [REDACTED]
To: [REDACTED]
Subject: Opposition to additional recommended vaccines
Date: Thursday, December 13, 2018 5:42:23 PM

Hawaii Department of Health
Disease Outbreak Control Division

To whom it may concern:

As a mother of 3 small children, and a citizen, voter, and taxpayer in the state of Hawai'i, I adamantly oppose the new additions to the recommended vaccine schedule, specifically the influenza and HPV vaccines, as well as any government-mandated vaccines.

Since the introduction of the HPV vaccine, over 25,000 adverse events have been reported to VAERS,, 772 of which were "serious". In addition, 32 recorded deaths have occurred (White, 2014). I strongly believe (from personal experience) that vaccine injuries go largely underreported. *Where there is risk, there must be choice.*

The influenza vaccine is only 40% effective in 2018, but only 10-40% effective for people ages 9-17 (depending on the vaccine type) (CDC, 2018). This vaccine, like all vaccines, does not come without risk.

While I understand that vaccines have and do save lives, I believe it is unethical to force one person to sacrifice his/her health or life via vaccine injury, to protect the masses. The fact is that no vaccine is without risk, and no one can predict who might be negatively affected. Some lives will be lost to vaccines.

Please thoroughly consider the negative impacts from making Hawai'i the most vaccinated state in the US, and well as ethics surrounding mandated vaccines.

Sincerely,
Noelle Manriquez

Reference

Centers for Disease Control. (2018). *Seasonal Influenza Vaccine Effectiveness, 2017-2018*. Retrieved from: <https://www.cdc.gov/flu/professionals/vaccination/effectiveness-year/2017-2018.html>

White M. D. (2014). Pros, cons, and ethics of HPV vaccine in teens-Why such controversy?. *Translational andrology and urology*, 3(4), 429-34.

From: [REDACTED]
To: [REDACTED]
Subject: Support for HAR 11-157
Date: Thursday, December 13, 2018 8:11:07 PM

This is a message in support of vaccination.

From: [REDACTED]
To: [REDACTED]
Subject: Support of HAR 11-157
Date: Thursday, December 13, 2018 7:02:58 PM

Thank you for this opportunity to provide testimony. As a pediatrician who cares for the keiki of Maui, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

As a pediatrician, I feel that a primary part of my job is to prevent health problems so that our keiki can thrive throughout childhood and continue to do so in adulthood. All of the vaccines that have been added protect against infections that cause serious illness and death, and I hope for a day when no one else dies from these vaccine-preventable illnesses. This rules update can help the community come closer to that goal.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Jodie Toward, MD

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HAR 11-157
Date: Tuesday, December 25, 2018 4:50:57 PM

Thank you for this opportunity to provide testimony.
As a former school teacher for children with severe disabilities, mom and community member,
I OPPOSE THE PROPOSED RULE CHANGES HAR 11-157.

I am opposed to mandatory vaccines and over regulation for school children. I have met many children whose condition was caused or made worse by vaccinations. I believe that it is a parent's right to choose whether or not they want their children to be vaccinated.

I am also concerned that the requirements to report on children who aren't vaccinated does not comply with privacy laws (The Family Educational Rights and Privacy Act (FERPA), *20 U.S.C. § 1232g, requires written parental consent before personally identifiable information from your child's education records is disclosed to the health department.* & HIPPA) in our schools and I miss the draft for new standardized medical & religious exemption forms are not part of this proposal, even so they very important part of the process and need to be discussed with professionals and public.

At this point, there is not enough evidence to prove that vaccines are safe for all children and especially for this population demographic. There is no one fits all solution. Informed consent, medical freedom are very important for this country and its people.

There is a huge list of potential side effects that may come from vaccinations. In fact, there is even a special court known as vaccine court created to handle issues with side effects and damages to children.

Toxic ingredients are allowed to be added to vaccinations without any responsibility on the part of the vaccine companies. The rules for safety in vaccines are almost non-existent.

For these reasons and many more, I strongly oppose bill 11-157 requiring mandatory vaccinations for school children. Parents need choices on what's best for their kids!

Sincerely,
Kamala Knudsen, Kauai

From:
To:
Cc:

[REDACTED]

Subject: Please, Please, Please - HAR 11-157
Date: Friday, December 14, 2018 3:42:43 AM

Hi there,

Choosing to inject/inhale something into your body or child's body should be your choice. No matter what it is.

You may have a strong belief that mandatory vaccination is the right thing to protect people but what if it's not? What if it harms more than helps? Many don't believe it until something happens to their own child or family member.

It's a game of Russian Roulette. The risks outweigh the benefits. Those that do have a bad reaction, that's it for them. It's either permanent and significant damage or death. And we have no idea who will have that reaction until it's too late.

These are our babies. Deciding between a potential illness or a possible bad vaccine reaction are 2 of the worst concepts a parent has to decide on. But at least we have a choice. At least we have some comfort in feeling we are doing what's best for our kids. Without that choice, we all become bad parents because while we strictly measure out our tylenol to be precisely 1 1/2 teaspoons to be sure we don't accidentally "poison" our babies, we just allow vials of confirmed poisons to pump through their veins on a whim.

Please. This is not ok. Please do not vote for mandatory vaccination for public and private schools, and daycares. Ask yourself what you actually know for real? You know you wouldn't want someone injecting heroin or house cleaner into your loved one. That is what it feels like you're asking so many parents to do to their kids. How could moms and dads sleep at night if that's what they feel they're allowing? How can we send our kids to school if that was the only way they could go? What IF mandatory vaccines causes tons of Hawaii residents to move away, pull their kids out of school? What if mandatory vaccination harms or kills tons more of Hawaii kids than you could have projected. What if?

You may be thinking the exact same thought about what if the opposite were true? Well, that's why we need to keep the decision to vaccinate a choice. If you allow mandatory vaccination and something happens to my child, it will be your fault.

This is serious and deserves serious thought about its implications. Do not take this lightly and do not be a follower. Our kids lives and every parents rights to protect their child is in your hands. This means, all Hawaii children are yours. Can you handle that?

Summer Anderson
[REDACTED]



From: [REDACTED]
To: [REDACTED]
Subject: Opposition! HAR-11-157
Date: Friday, December 14, 2018 7:56:26 AM

To whom it my concern,

My name is Marcy Cayton. I live on [REDACTED] at [REDACTED]. I strongly oppose HAR 11-157. I believe this is something you decide in your family for yourself, not through the government.

Thank you,
Marcy

Sent from my iPad

From: [REDACTED]
To: [REDACTED]
Subject: Please look into this research below, and honor a Parent's Choice to vaccinate or not. Mahalo ~
Date: Friday, December 14, 2018 8:24:19 PM

To Whom It May Concern,

My family and I strongly oppose the requirement of vaccinations.
Please honor a parent's right to choose what they feel is best for their child,
not what the government or some bureaucratic organization that may not have the child's best interest at heart.

Since this is the issue at hand, I hope you will be openminded and look into this extensive research below.

Mahalo for your consideration,

A Concerned Parent.

**Here are documentaries proving that:

- a) vaccines aren't safe
 - b) vaccines aren't effective
 - c) vaccines have never been proven to reduce disease or improve immunity in real world populations and
 - d) vaccines are only proven to harm all infants, toddlers, children, adults and seniors.....
- on all measurements of health, no exceptions, straight across the board.

1. Vaccination – The Silent Epidemic – <http://bit.ly/1vvQJ2W>
2. The Greater Good – <https://bit.ly/2HXtM6A>
3. Shots In The Dark – <http://bit.ly/1ObtC8h>
4. Vaccination The Hidden Truth – <http://bit.ly/KEYDUh>
5. Vaccine Nation – <http://bit.ly/2IrdksA>
6. Vaccination – The Truth About Vaccines – <http://bit.ly/1vlpwvU>
7. Lethal Injection – <http://bit.ly/1URN7BJ>
8. Bought – <http://bit.ly/2olaeOm>
9. Deadly Immunity – <http://bit.ly/1KUg64Z>
10. Autism – Made in the USA – <http://bit.ly/1J8WQN5>
11. Beyond Treason – <http://bit.ly/1B7kmvt>
12. Trace Amounts – <http://bit.ly/2ELnUZm>
13. Why We Don't Vaccinate – <http://bit.ly/1KbXhuf>
14. Autism Yesterday – <http://bit.ly/1URU2A7>
15. The Vaccinated Girls - Sick and Betrayed – <https://bit.ly/2y4vlcL>
16. Vaxxed – <https://bit.ly/2O7QjkZ>
17. Man Made Epidemic – <http://bit.ly/1XsOi0R>
18. 50 Cents A Dose – <http://bit.ly/2c0h07P>
19. Direct Orders – <http://bit.ly/1ivShHg>
20. Dtap – Vaccine Roulette <http://bit.ly/2dBnc3u>
21. Truthstream News: About All Those Vaccines – <http://bit.ly/2gCma4o>
22. Hear The Silence – <https://bit.ly/2BW9K9f>
23. Cervical Cancer Vaccine – Is It Safe? – <http://bit.ly/2h3Dvsh>
24. Vaccines Revealed – <https://www.vaccinesrevealed.com/free/>
25. The Truth About Vaccines – <http://bit.ly/2mX4Tyc>
26. Vaccine Syndrome – <https://bit.ly/2O7xU7O>
27. Injecting Aluminum – <http://bit.ly/2qPkFwo>
28. Manufactured Crisis: HPV, Hype & Horror – <https://bit.ly/2pEdULG>
29. Sacrificial Virgins - HPV Vaccine Killing Kids – <http://bit.ly/2xGOmb>

<https://childrenshealthdefense.org/news/cdc-data-reanalysis-shows-strong-statistically-significant-relationship-between-mmr-vaccine-autism/>

[utm_source=mailchimp&fbclid=IwAR26JSoUwQ6BRysKoG-yui7Wri.wifU5XLP-HvG6ocrpPfrwY-f2TcJY4L_k](https://www.facebook.com/utm_medium=social&utm_campaign=sharebar&fbclid=IwAR0sQ77JjHjZbZLchacizEvuKA9Q5s_MF5jSHJ7O20w4OzfchuXIRae19Do)

https://nworeport.me/2018/12/11/dept-of-justice-admits-flu-shot-is-most-dangerous-vaccine-in-us/?fbclid=IwAR0QAz6KIee31of0ZepguSCKUzsRevYmSk_Bcpt8XHkLg62XKQ3mhayng

https://newspunch.com/study-babies-vaccines-die/?fbclid=IwAR03_KaIcjdttbbOkL0_1sILQpKtOBIXoCeW2Q96xIsD-vDa-MGBUgo11Gq8

<https://www.mirror.co.uk/news/uk-news/boy-8-gets-worst-case-13729986?>

[utm_source=facebook.com&utm_medium=social&utm_campaign=sharebar&fbclid=IwAR0sQ77JjHjZbZLchacizEvuKA9Q5s_MF5jSHJ7O20w4OzfchuXIRae19Do](https://www.facebook.com/utm_medium=social&utm_campaign=sharebar&fbclid=IwAR0sQ77JjHjZbZLchacizEvuKA9Q5s_MF5jSHJ7O20w4OzfchuXIRae19Do)

December 14th, 2018 - HAR 11-157 TESTIMONY TO STRONGLY OPPOSE BILL

Location: 54 South High Street, Wailuku, HI, 96793

Room: Video Conference Center (third floor)

Testimony Submitted By: Eric Day, Citizen of the USA and Hawaii

Aloha everyone, my name is Eric Day, I live in Kihei. I am not anti-vaccine, I am not pro-vaccine, I'm vaccine aware. The science is crystal clear, vaccines are unsafe. I am pro-child, pro-family, pro-community, I am pro-science, I am pro-health, pro-wellbeing, pro-safety. I am pro-government transparency. I am pro-pharmaceutical company accountability. I am pro-honesty, I am pro-critical thinking. I am pro-freedom. That's why we're here.

- I'm here today speaking as an individual and the father of a healthy toddler and I strongly oppose this bill, HAR 11-157. I'm also here testifying as a member of Hawaii for Informed Consent, and we strongly oppose the bill as well. HFIC is a non-partisan group advocating for your right to choose or refuse any medical treatment or procedure. HFIC is comprised of ordinary people who have come together with one goal in mind. That goal is the preservation of freedom, more specifically medical freedom. We're a group of doctors, lawyers, engineers, medical practitioners and so on.
- Truthfully? I shouldn't even be here, I should be at the park pushing my little girl on the swings and enjoying life with her, but I'm not. Why? In 2013 SB1138 gave the Department of Health way too much power over the citizens of Hawaii. The DOH has this power without the checks and balances of our government and legislative process. The DOH does not represent the people. They represent the CDC and the pharmaceutical interests that fund them. This bill is NOT about public health, it is about profit. Let's get in to it...

THIS BILL CAN NOT BE MADE A LAW

Promoting mandatory vaccination for entire populations with products that essentially rely on manufacturers' data for their general safety and efficacy is a breach of the precautionary principle, and as such becomes a forced medical experiment. Did you know your babies and children are called "Post-marketing safety surveillance" by the vaccine manufacturers, the CDC and the ACIP (Advisory Committee on Immunization Practices) in regard to adverse events? This is UNACCEPTABLE! It's cheaper to see what Adverse Events happen to the public after vaccination than doing long term premarket trials and studies. Did you know that pre-market trials only use healthy people to determine safety? This is not science! Vaccines are not a one size fits all solution. I'm not a Doctor or a Scientist, but I KNOW THIS! The manufactures have zero liability for any vaccine injuries. They're protected by federal law in the 1986 NCVIA. They don't have to do the research. Since the health risk of vaccination is entirely borne by individuals, the Department of Health and the State of Hawaii must ensure that fully informed consent is left in place and observed. Parents must have

medical decision choice for their children and themselves. When there is risk there must be choice. Humans have many genetic variations, mitochondrial disorders, allergies to various foods and ingredients used in vaccines. Did you know that the above listed people are not included in the premarket trials? They say it would be unethical to include them. Hmm. Unethical? You know what's unethical? A crime against humanity! That is exactly what is being done to our children. Our kids are lab rats! Hawaii Department of Health - I ask this question and demand an answer - How is it ethical and legal to mandate these vaccines for the general public when unbiased premarket trials and studies have NEVER BEEN DONE? Adverse events to vaccines are GUARANTEED because of this lack of doing the science. Did you know Merck is in court right now for fraudulent premarket trials of the HPV Vaccine? Did you know there's been over 59,634 severe adverse events to the HPV Vaccine up to September 14, 2018? And it's estimated that only between 1-10% of adverse events have even reported. We can prevent this cancer with early detection and ZERO side effects. DOH, my child is not your experiment! DOH, you say you're all educated? Really? You're going to mandate the HPV vaccine with the knowledge of this information? I'll tell you this, if you do, you are implicit in a crime against humanity.

THIS BILL IS ILLEGAL ACCORDING TO US LAW

Is everyone here aware that The US Supreme Court acknowledged in the case Bruesewitz vs Wyeth that Congress considers that vaccines are "unavoidably unsafe"? I'm here to let or remind any government employees or department of health officials present that using the term "vaccines are safe" is a false claim according to US Law. THIS IS A FACT! US Law regards vaccines as "unavoidably unsafe." This decision comes from the language of the 1986 National Childhood Vaccine Injury Act (42 USC sec 300aa-22, re manufacturer responsibility.) For this reason ALONE, there must not be any vaccines that are mandated. They are ALL "unavoidably unsafe" according to US Law. In fact in a recent lawsuit against the Department of Health and Human Services, Robert F Kennedy Jr and Del Bigtree proved that not a single required biennial report on the safety and efficacy of vaccines has ever been submitted to congress for over 32 years! THIS is a blatant disregard of US Law, and so is this bill.

Hawaii Department of Health, I ask these questions and we the people of Hawaii demand answers in full and with detail:

1. In regard to the Small Business Regulatory Review Board "Pre-public hearing small business impact statement" dated June 27, 2017, What is the actual increased financial burden to small businesses like daycare centers, preschools and kindergartens for collecting all of the vaccine information from children and their parents and reporting it to the DOH or State? The DOH has not done a cost analysis. Where are the numbers? The DOH answer of "we don't anticipate any increase in financial cost to small businesses" does not work. This is not a cost analysis.
2. What will the increased financial burden be on schools as more and more students require special education? Since 2016 the State of California has

seen an increase of 17% in Autism in Kindergartners since SB277 bill went in to effect mandating vaccines. The Hawaii Department of Education will soon feel this financial burden for funding more Special Education programs.

3. How is it legal for a school to send private student medical records to the DOH or State of Hawaii? This is a FERPA violation. FERPA is Family Educational Rights and Privacy Act. HIPAA does not have authority here. FOR THE RECORD: The law states if there is not a declared communicable disease outbreak in the school, Personally Identifiable Information from student health data can not be sent to the DOH or State of Hawaii. IT IS ILLEGAL!
4. Where is the form and format for Medical Exemption in this bill? This bill contains no details. How long does a medical exemption last? Is it for all vaccines? Is it for each vaccine? Does an adverse event have to happen first? Does the medical exemption require approval of the DOH?

DOH - you must answer all of these questions. We the Citizens of Hawaii demand it.

Thank You,

Eric Day

Member of Hawaii for Informed Consent

December 14, 2018

Public Testimony to Oppose HAR 11-157

54 South High Street, Wailuku, HI, 96793 (Maui County)

Video Conference Center (third floor)

Aloha, I am testifying today as an individual and as a member of Hawaii for Informed Consent to oppose HAR 11-157. The DOH submitted an application to the Small Business Regulatory Review Board (SBRRB) entitled, "Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board" received on June 27, 2017 by Ms. Dori Palcovich, Administrator. There are many problems with this Impact statement which will be presented here at this public hearing as a matter of record. The concerns are as follows:

1. Through a UIPA request to the SBRRB, Ms. Palcovich's records showed that the SBRRB received the DOH's Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board on June 27, 2017. In addition the DOH also submitted at that time, two documents, a version of HAR Chapter 11-157, dated May 26, 2017 and a copy of the ACIP guidance.

On July 19, 2017, the SBRRB voted to send the proposed rules dated May 26, 2017 to a public hearing. However, the version of Chapter 11-157 dated May 26, 2017 is **DIFFERENT** from the version that is currently posted on the DOH website which is dated September 5, 2018. The September 5, 2018 version was also the version that was debated on at the public hearing on Oahu on November 1, 2018 and will be the same version for the remaining hearings on the outer islands.

There are substantive differences in these versions of Ch. 11-157 relating to the tuberculin testing and the process to move these proposed rules to public hearing should have been halted but was not.

QUESTION: Was the DOH legally or ethically required to submit an up-dated Ch. 11-157, at minimum to the SBRRB or at least disclose this information to the SBRRB?

2. Page 2, question 1, basically asks how small businesses may be adversely affected by the proposed rules. The DOH responded "The health care providers should not be adversely affected by the proposed rules. Child care centers, compulsory schools and post-secondary should not be affected by the proposed rules."

QUESTION: What documents, notes, or additional information did the DOH use to support their assertion that these providers "should not be adversely affected?"

QUESTION: What additional written information, testimonies or summaries of information were submitted by health care providers, child care centers, compulsory schools and post-secondary providers that support the DOH's claim that these providers "should not be adversely affected?"

3. Page 2, question 2, asks for dollar amounts of increased direct costs in fees, fines, and indirect costs including reporting, recordkeeping, equipment construction, labor, professional services, revenue loss, or other costs associated with compliance.

The DOH response was "Increased indirect costs associated with enhance screening and recordkeeping maybe be incurred by some schools and post-secondary schools. The Department does not anticipate any increased costs associated with compliance to health care providers." However, no dollar amounts were provided as required.

QUESTION: The DOH admitted that "some schools and post-secondary schools" may incur increased costs. What are these estimated dollar amounts?

QUESTION: What information did the DOH use to assert that health care providers are not anticipated to incur any increased costs?"

4. Page 2, question 3, asks for the probable monetary costs and benefits to the agency or other agencies directly affected.

QUESTION: The DOH stated that it estimates that the additional requirements necessary for implementation have been determined to be \$60,000 for the 1st year and \$5,000 for additional years. Where is the cost analysis showing how the DOH arrived at both of these figures and what is the plan the DOH intends to implement to achieve these goals?

QUESTION: Since the Department of Education is another agency that will be affected by the additional recordkeeping and monitoring as described in the proposed rules, what information did the DOH use to determine the probable monetary costs for the Department of Education to implement these additional requirements?

5. Page 3, question 4, asks for the methods the DOH considered or used to reduce the impact on small business. The DOH's response was that the training provided would assist the providers and affected organizations to understand the changes to the requirements so that they would be able to screen records appropriately.

QUESTION: When small businesses are required to provide the man-power to implement the recommendations proposed by Ch. 11-157, exactly what are the expected duties necessary to properly screen the documents and what are the estimated costs in man-power and supplies needed to satisfy this requirement?

6. On page 3, question 7, the question asks how the DOH involved small business in the development of the proposed rules.

DOH's response was that the 'School and Immunization Requirements Working Group' was made up of representatives from private compulsory and post-secondary institutions, the American Academy of Pediatrics, Hawaii Chapter, the Hawaii Association of Independent Schools, and Kaiser Permanente, Department of Education, the Department of Human Services, and Tuberculosis Control, Public Health Nursing, Disease Investigation, and Immunization Branches of the Department of Health.

However, there are NO small businesses or individuals represented in this working group. Therefore, it is questionable as to whether any small businesses were involved in the development of the proposed Ch.11-157 rules.

7. On Page 3, question 7a, asks if there were any **recommendations** made by small businesses and whether the recommendations were incorporated in the proposed rule. If yes, explain, if no, why not.

Instead of answering "yes" or "no" to this question, the DOH stated that the 'School and Immunization Requirements Working Group' member organizations emphasized the need for delayed effective date to allow training materials and training to take place of the rules' effective date.

QUESTION: Why did the DOH fail to directly answer this question? Is it because they did not appear to have solicited any responses from small businesses such as daycare business owners, individual providers or the like in their working group?

The exclusion of small businesses from the working group implies that small businesses such as daycare centers and individual providers did not provide any recommendations and thus their input were not incorporated into the proposed rule.

Further, the DOH's solution of providing training and training materials was created by LARGE businesses which included Kaiser Permanente, the HAIS for private schools, and post-secondary institutions which include community colleges and universities.

This omission of small businesses from the working group should invalidate this entire application and the DOH should be required to properly solicit input from small businesses such as daycare centers, other child-care facilities, and individual small business owners before the proposed amendment is allowed to move forward.

8. On page 3, question 8, asks whether the proposed rules include provisions that are more stringent than those mandated by a comparable or related federal, state, or county standards, with an explanation of the reason for imposing the more stringent standard.

The DOH's response states that the proposed school examination and immunization regulations are consistent with the United States Centers for Disease Control and Prevention's Advisory

Committee on Immunization Practices (ACIP) recommendations and are comparable to and in some instances less stringent than other states' school and post-secondary school immunization and examination requirements. The proposed rules are not more stringent than any comparable or related federal, state or county standards.

The DOH's statement is false. There are three problems with the DOH response:

- A. The DOH states that their school examination and immunization regulations are consistent with the ACIP recommendations. However, the issue is that the ACIP guidelines are recommendations and are not federal, state, or county standards. The ACIP guidelines are not mandates or laws from the federal or state governments.
- B. The DOH claims that the ACIP recommendations are comparable to and in some instances less stringent than other state immunization requirements. For example, some states have personal exemptions for vaccinations but Hawaii does not. Hawaii's religious exemption is restricted and this proposed rule will also restrict medical exemptions compared to other states with looser restrictions for these exemptions.

In states that only have medical restrictions such as Mississippi,¹ only 9 vaccinations are required for school entry from K to 12th grade and only Tdap is required for 7th grade. West Virginia² only requires 9 vaccines for school entry from K to 12th grade. California³ does not require the Hep A, flu, HPV or meningococcal vaccines compared to the DOH's proposed rules which would require these vaccines.

Further, only 2 states require HPV. Virginia⁴ requires HPV for 6th graders and a total of 11 vaccines for school entry. Rhode Island⁵ requires a total of 14 vaccines for entry in child-care centers which allows for non-restricted religious exemptions. Most states do not require the flu vaccine but it appears that DOH's proposed rules will.

The DOH's proposed rules will increase 9 vaccines to 14 vaccines for children in K-12, and 6 vaccines to 13 vaccines for children in child care centers. These include Tdap, HPV, and MCV for 7th graders, in addition to the Hep A, and flu vaccine.

Therefore, the DOH's Ch. 11-157 appears to be MORE stringent rather than less stringent than any comparable or related federal, state or county standards which contradicts the DOH's written statement.

- C. Most states comply with the Federal Educational Rights to Privacy Act (FERPA) in their state laws and rules which require written parental consent before releasing any educational

¹ http://www.msdh.state.ms.us/msdhsite/_static/resources/2029.pdf

² <https://dhr.wv.gov/oeps/immunization/requirements/Documents/8-31-17%20%20NewSchoolEnterers.pdf>

³ <https://www.shotsforschool.org/k-12/>

⁴ <http://www.vdh.virginia.gov/immunization/requirements/>

⁵ <http://www.health.ri.gov/immunization/for/schools/>

QUESTION: If the DOH will not conduct a cost analysis, can the DOH definitively demonstrate that the DOH's proposed rules are "not more stringent than any comparable or related federal, state or county standards?"

In conclusion, the DOH's "Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board" dated June 27, 2017 has many questionable items and the public deserves answers before Ch11-157 hearings are adopted including the following:

- 6 1. The differences in the Ch. 11-157 versions submitted to the SBRRB which was voted on in July 19, 2017 and moved to public hearing.
2. The vague and non-committal responses provided by the DOH when dollar amounts were specifically asked for.
3. The absence of a daycare provider, or child care center representative, or individual small business representatives on the School Examination and Immunization Requirements Working Group and the inappropriate DOH response provided when recommendations from these small businesses were required.
4. The DOH's claim that their proposed rules are not more stringent than any comparable or related federal, state or county standards when there is evidence to the contrary.
5. The need for a cost analysis if the DOH's their proposed rules are indeed MORE stringent than any comparable or related federal, state or county standards.

Before the DOH's Chapter 11-157 can be adopted, these concerns related to small business must be evaluated and reviewed. Mahalo.

[Dues/Donations](#)
[Blog | Member Login](#)


American College of Pediatricians Best for Children

- [Health Professionals »](#)
- [Parents »](#)
- [The College Speaks »](#)
- [About Us »](#)

You are here: [Home](#) › [The College Speaks](#) › [Position Statements of the College](#) › [Health Issues](#) › [New Concerns](#)

about the Human Papillomavirus Vaccine

New Concerns about the Human Papillomavirus Vaccine

American College of Pediatricians – January 2016

The American College of Pediatricians (The College) is committed to the health and well-being of children, including prevention of disease by vaccines. It has recently come to the attention of the College that one of the recommended vaccines could possibly be associated with the very rare but serious condition of premature ovarian failure (POF), also known as premature menopause. There have been two case report series (3 cases each) published since 2013 in which post-menarcheal adolescent girls developed laboratory documented POF within weeks to several years of receiving Gardasil, a four-strain human papillomavirus vaccine (HPV4).^{1,2} Adverse events that occur after vaccines are frequently not caused by the vaccine and there has not been a noticeable rise in POF cases in the last 9 years since HPV4 vaccine has been widely used.

Nevertheless there are legitimate concerns that should be addressed: (1) long-term ovarian function was not assessed in either the original rat safety studies^{3,4} or in the human vaccine trials, (2) most primary care physicians are probably unaware of a possible association between HPV4 and POF and may not consider reporting POF cases or prolonged amenorrhea (missing menstrual periods) to the Vaccine Adverse Event Reporting System (VAERS), (3) potential mechanisms of action have been postulated based on autoimmune associations with the aluminum adjuvant used¹ and previously documented ovarian toxicity in rats from another component, polysorbate 80,² and (4) since licensure of Gardasil® in 2006, there have been about 213 VAERS reports (per the publicly available CDC WONDER VAERS database) involving amenorrhea, POF or premature menopause, 88% of which have been associated with Gardasil®.⁵ The two-strain HPV2, *Cervarix*TM, was licensed late in 2009 and accounts for 4.7 % of VAERS amenorrhea reports since 2006, and 8.5% of those reports from February 2010 through May 2015. This compares to the pre-HPV vaccine period from 1990 to 2006 during which no cases of POF or premature menopause and 32 cases of amenorrhea were reported to VAERS.

Many adolescent females are vaccinated with influenza, meningococcal, and tetanus vaccines without getting Gardasil®, and yet only 5.6% of reports related to ovarian dysfunction since 2006 are associated with such vaccines in the absence of simultaneous Gardasil® administration. The overwhelming majority (76%) of

VAERS reports since 2006 with ovarian failure, premature menopause, and/or amenorrhea are associated solely with Gardasil®. When VAERS reports since 2006 are restricted to cases in which amenorrhea occurred for at least 4 months and is not associated with other known causes like polycystic ovary syndrome or pregnancy, 86/89 cases are associated with Gardasil®, 3/89 with *Cervarix*TM, and 0/89 with other vaccines administered independently of an HPV vaccine.⁵ Using the same criteria, there are only 7 reports of amenorrhea from 1990 through 2005 and no more than 2 of those associated with any one vaccine type.

Few other vaccines besides Gardasil® that are administered in adolescence contain polysorbate 80.⁶ Pre-licensure safety trials for Gardasil® used placebo that contained polysorbate 80 as well as aluminum adjuvant.^{2,7} Therefore, if such ingredients could cause ovarian dysfunction, an increase in amenorrhea probably would not have been detected in the placebo controlled trials. Furthermore, a large number of girls in the original trials were taking hormonal contraceptives which can mask ovarian dysfunction including amenorrhea and ovarian failure.² Thus a causal relationship between human papillomavirus vaccines (if not Gardasil® specifically) and ovarian dysfunction cannot be ruled out at this time.

Numerous Gardasil safety studies, including one released recently,⁸ have looked at demyelinating and autoimmune diseases and have not found any significant problems. Unfortunately, none of them except clinical safety pre-licensure studies totaling 11,778 vaccinees⁹ specifically addressed post-vaccination ovarian dysfunction. While data from those studies do not indicate an increased rate of amenorrhea after vaccination, the essential lack of saline placebos and the majority of participants taking hormonal contraceptives in those studies preclude meaningful data to rule out an effect on ovarian function.

A Vaccine Safety Datalink POF study is planned to address an association between these vaccines and POF, but it may be years before results will be determined. Plus, POF within a few years of vaccination could be the tip of the iceberg since ovarian dysfunction manifested by months of amenorrhea may later progress to POF. Meanwhile, the author of this statement has contacted the maker of Gardasil, the Advisory Committee on Immunization Practices (ACIP), and the Food and Drug Administration (FDA) to make known the above concerns and request that (1) more rat studies be done to look at long-term ovarian function after HPV4 injections, (2) the 89 VAERS reports identified with at least 4 months amenorrhea be reviewed by the CDC for further clarification since the publicly available WONDER VAERS database only contains initial reports, and (3) primary care providers be notified of a possible association between HPV and amenorrhea. A U.S. Government Representative responded that they “will continue to conduct studies and monitor the safety of HPV vaccines. Should the weight of the evidence from VAERS or VSD and other sources indicate a likely causal association between POF and HPV vaccines, appropriate action will be taken in terms of communication and public health response.”

The College is posting this statement so that individuals considering the use of human papillomavirus vaccines could be made aware of these concerns pending further action by the regulatory agencies and manufacturers. While there is no strong evidence of a causal relationship between HPV4 and ovarian dysfunction, this information should be public knowledge for physicians and patients considering these vaccines.

Primary author: Scott S. Field, MD
January 2016

The American College of Pediatricians is a national medical association of licensed physicians and healthcare professionals who specialize in the care of infants, children, and adolescents. The mission of the College is to enable all children to reach their optimal, physical and emotional health and well-being.

A printable Adobe Acrobat (pdf) copy of this position is available by clicking here: [New Concerns about the Human Papillomavirus Vaccine](#).

References:

1. Colafrancesco S, Perricone C, Tomljenovic L, Shoenfeld Y. Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants. *Am J Reprod*

HAR 11-157 Hearing Testimony

I'm Lori Auldridge. I'm a Maui Mom of 3 and I oppose HAR 11-157.

I'm not anti-vax or pro-vax. And I don't believe that being opposed to HAR 11-157 makes a person anti-vaccine. I think there needs to be less emphasis on the "sides" of an issue and emphasis placed on the issue at hand, which are the proposed vaccine requirement changes by the Department of Health.

Here my questions:

1. Is there anyone in this room who has voting power or who will be making decisions on the outcome of HAR 11-157?
2. If not, how will they hear this testimony? If so, how will the other decision makers hear this testimony?
3. What proof will we be provided that deciding persons will hear our concerns?
4. What proof will we have that our concerns and questions are being genuinely considered? Because honestly at this point, from where I sit, it seems like these hearings are all for show and the decision to pass HAR 11-157 has already been made.

Here are my concerns:

* **I'm concerned about the wording** – it's too vague & inconsistent. It paves the way for our individual choice and medical freedoms to be taken away, starting with vaccine mandates in schools.

Plus the exemption forms that the ACIP recommends are too strict and don't truly give parents choices. There is no choice if our options are vaccinate or get a strict exemption that has to be approved by a secondary individual. That isn't the parent deciding what is best for their individual child, that is literally allowing someone else to make medical decisions for your child. How can a doctor who sees a child for 10 mins every 6 months to know what is best for that individual child? And a religious leader doesn't get to be the expert on what an individual believes. Relationships with God are personal.

That's where the role of the parent is essential. HAR 11-157 word choices pave the way for parents' rights and medical freedoms to be taken out of the equation. Strict medical exemptions are not a choice, it's a restriction of choice. Forcing someone to do something that they don't want to do is bullying.

* **I'm concerned that the Department of Health can make such overreaches.** I don't agree with the 2013 vote to allow the DOH to make changes outside the legislative process. Unfortunately, I was unaware of this motion back in 2013 but am opposed to it

now as it affects me. Which brings up this point: just because something doesn't personally affect you now doesn't mean it won't affect you later. I highly encourage parents of young children or parents-to-be to pay attention. Individual freedom is the core belief and foundation of this country.

This may not personally affect you at the moment, but our individual rights are being whittled away.

* **Why make these changes?** There are no medical problems in our schools that warrant these changes. I have a problem with the term "outbreak" being overused and sensationalized by the media and the DOH to create unnecessary fear. Why make changes just to say you made changes while in a position of power?

I believe the DOE has more pressing matters to address—like budgeting, teacher shortages, and quality education.

The sentiment of "no child left behind" when it comes to education appeals to people because it honors the individual. It implies that every child is important. That same individuality should be given to medical decisions...because every child is important.

For DOT. 12/14/18 Maui Hearing

Aloha my name is Martina Dodson, I am a citizen of United States, live on Maui and I also am a health freedom advocate. Me and my family strongly oppose HAR-11-157.

I almost died from a vaccine. Injury and death is not rare as some people might think. CDC claims one in a million doses. Add that up and its many serious events including death, paralysis, seizure, swelling of the brain etc. What kind of real statistic is that?

If these rule changes go through HI will be the most vaccinated state in the U.S. we also will know WHO TO HOLD RESPONSIBLE FOR THE DEATH AND INJURY THAT WILL happen to Hawaii's keiki. We might not be able to hold them accountable by law for the tragic events that will occur.

BUT MY WORDS HERE IN THIS TESTIMONY, WE WILL GO BACK TO AND LET EVERY SINGLE PERSON IN THIS STATE KNOW, WHO THE CORRUPT PEOPLE ARE THAT SET THIS FORTH IN THE PUBLICS EYES, AND WE WILL HOLD THE PERSONS SUCH AS ROZ BAKER, BRUCE ANDERSON AND DR SARAH PARK AND EVERYONE ELSE INVOLVED ACCOUNTABLE FOR THE ENORMOUS CATASTROPHIC DISASTER to mandate and vaccinate all Hawaii's keiki with the proven dangerous HPV vaccine.

The evidence are overwhelming of the danger of this particular vaccine. If it would have been a regular medication on the market it would have been recalled by now. But because it is labeled a vaccine the can mandate this poison. Only 3 states have this mandated for school it is called medical tyranny. Over 400 deaths have been reported and over 59,000 adverse events to VAERS. Keep in mind FDA admits only 1 to 10% even gets reported.

I urge you to look at proposed rule change. It is a sneaky way to take away parents rights and parents choice. Especially when they want to mandate vaccines for diseases that do not spread in school environment.

Where is the medical justification for 74 doses vaccines before the age of 18. 4 billion has been paid out for injury and death from vaccine court. You cant simply call it science when a vaccine maker have full legal immunity from damage claims. 1986 NCVIA was created and the vaccine schedule tripled. Coincidence?

1 in 40 children with autism. I watched my friends perfectly healthy twin boys go in for a multidose vaccine appointment. Directly after both permanently brain injured later diagnosed with autism. The annual cost for autism is \$268 billion and is expected to be \$1 trillion 2025. These growing costs now fall on families and on tax payers through the cost borne by local school districts, states and medicaid.

53 % of American children with auto immune disorders

Cancer is the leading cause of death in children

U.S has the highest infant mortality rate in a developing country. Also the most vaccinated.

IT CAN ALL BE TRACED BACK TO THE INSANE KIDS SCHEDULE THAT HAS NEVER BEEN TESTED FOR SAFETY IN COMBINED DOSES. NEITHER HAS ANY VACCINE EVER BEEN EVALUATED FOR THE ABILITY TO CREATE CANCER, CAUSING GENE MUTATION NOR THE IMPAIRMENT OF FERTILITY. STATES IN 13.1 IN EVERY SINGLE VACCINE INSERT.

Current Immunization Requirements
(last updated 2001)

Proposed Immunization Requirements
(current CDC recommended vaccines)

give back to Kelly Livanov
or
Laura Hassen

Current Pediatric (all children up to two years of age)	Proposed Pediatric (all children up to two years of age)
DTaP or DTP [Diphtheria, Tetanus, Pertussis]	DTaP
Polio (IPV [Inactivated] or OPV [Oral])	Polio (IPV)
MMR [Measles (Rubeola), Mumps, Rubella]	MMR
Hib [<i>Haemophilus influenzae</i> type b]	Hib
Hepatitis B (Hep B)	Hep B
Varicella (chickenpox)	Varicella
	Hepatitis A (Hep A)
	Pneumococcal Conjugate Vaccine (PCV)
	Rotavirus
	Influenza

Current Preschool/Childcare	Proposed Preschool/Childcare
DTaP or DTP	DTaP
Polio (IPV or OPV)	Polio (IPV)
Hib (1 dose after age 12 months)	Hib (age appropriate)
Hep B	Hep B
MMR	MMR
Varicella	Varicella
	Hep A
	PCV

Current K-12	Proposed K-12
DTaP or DTP	DTaP
Polio (IPV or OPV)	Polio (IPV)
MMR	MMR
Hep B	Hep B
Varicella	Varicella
	Hep A
	Human Papillomavirus (HPV)*
	Meningococcal Conjugate Vaccine (MCV)*
	Tdap [Tetanus, Diphtheria, Pertussis]*
	*for students entering/attending school in grade 7 or higher

Current 7th Grade	Proposed 7th Grade
Hepatitis B	HPV
MMR	MCV
Varicella	Tdap

Current Post-Secondary	Proposed Post-Secondary
Two doses of measles-containing vaccine with at least one of the two being MMR	MCV**
	MMR (2 doses)
	Tdap
	Varicella
	**first-year students living in on-campus housing only



I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Michelle L. Apo	[REDACTED]	96793
2. Raynette K Maxwell	raynette [REDACTED]	96790
3. Simenu Clarke	[REDACTED]	96732
4. MARIA ORBIA FERRACINI	[REDACTED]	96732
5. BULOCAN, ASHLEY	[REDACTED]	96793
6. Shayna Kanuho	[REDACTED]	96793
7. Rodalisa Delacruz	[REDACTED]	96793
8. Allison Takai	[REDACTED]	96793
9. Erin Baxter PA-C	[REDACTED]	96768
10. Desmond Wilstead	[REDACTED]	96753
11. Beth Dressel	[REDACTED]	96779
12. Anne Quijess	[REDACTED]	96708
13. Megha Chondok	[REDACTED]	96773
14. [REDACTED]	[REDACTED]	96732
15. Mitchell [REDACTED]	[REDACTED]	
16. David Bacchus [REDACTED]	[REDACTED]	96793
17. Janah Visitation	[REDACTED]	96732
18. Shirley Hidalgo	[REDACTED]	96732
19. Laura Hasser [REDACTED]	[REDACTED]	96793
20. Kaelyn Lewis	[REDACTED]	96793

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. George Talbot MD	[REDACTED]	96968
2. Vona Diener, MD	[REDACTED]	96768
3. Megan Wright, DO	[REDACTED]	76790
4. Roberto Kona, DO	[REDACTED]	96779
5. Bien Lazatin, Jr MD Bin Lazatin	[REDACTED]	96793
6. Jay Park, [REDACTED] RN	[REDACTED]	96768
7. JOHN MERSEL	[REDACTED]	96793
8. Leona Arenberg Coffin	[REDACTED]	96768
9. Nicole Fernandez	[REDACTED]	94753
10. Julie Enos	[REDACTED]	96793
11. Valerie Thumacher	[REDACTED]	96732
12. Sally Bowler	[REDACTED]	96768
13. Guy S V G MD	[REDACTED]	96793
14. Kevin Riglas	[REDACTED]	96793
15. Cheeneth Dela Cruz	[REDACTED]	96793
16. Roman Valle	[REDACTED]	96793
17. Victoria Yahiky	[REDACTED]	96732
18. Shelby Yanos	[REDACTED]	96793
19. Stella Mae Ong	[REDACTED]	96732
20. Zyra, delacruz	[REDACTED]	96732

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Mawelyn Edmalin	[REDACTED]	96732
2. Gemma Lapitan	[REDACTED]	96732
3. Melanre Salvador	[REDACTED]	96753
4. DESIREE CORPUZ	[REDACTED]	96753
5. Honey Dean Edmalin	[REDACTED]	96732
6. Alexander Lapitan	[REDACTED]	96732
7. CESTR CORPUZ JR		96753
8. CLATRE CALLOS		96753
9. LORETO CALLOS JR		
10. AIZA ALEJO		96753
11. GAIL MATEUI		96732
12. MARITES CADANAS GANCENA		96732
13. CLARITA CACHO		96753
14. PHILIP CACHO		96753
15. EDITH EDMALIN		96732
16. ANGIE IDELLA		96753
17. VALENTIN IDELLA		
18. CONCHITA JARAMILLO		96764
19.		
20.		

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

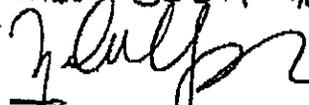
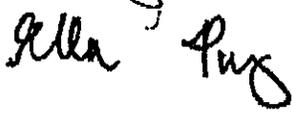
Name	Email	Zip Code
1. Stephanie Rosario	[REDACTED]	96753
2. RYAN Manzella	[REDACTED]	96753
3. ERROL BUNTYAN	[REDACTED]	96793
4. Jodie Toward	[REDACTED]	96793
5. Rennia Cabal	[REDACTED]	96793
6. Jay Ferris	[REDACTED]	96768
7. Beth ^{Quetta}	[REDACTED]	96793
8. Maria Termulo	[REDACTED]	96793
9. Lisa Stearns	[REDACTED]	96768
10. Michelle Senamonthy	[REDACTED]	96768
11. Sophia Rohr	[REDACTED]	96753
12. Ivan Komola	[REDACTED]	96790
13. Rey LICUDAN	[REDACTED]	96761
14.		
15.		
16.		
17.		
18.		
19.		
20.		

I support the CDC, AAP and FAAP Recommendations for the Childhood Vaccine Schedule for the Hawaii DOE.

Name/Signature

Email

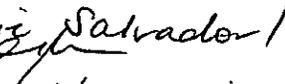
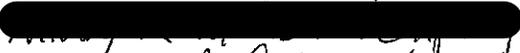
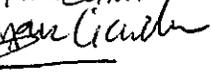
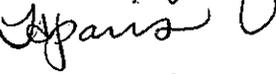
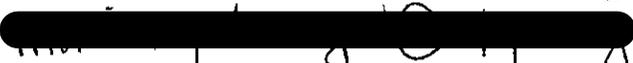
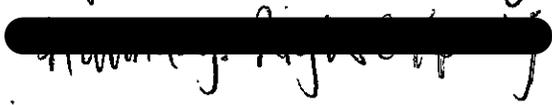
Zip Code

- 1. Lisa Sodekai,   96732
- 2.   96753
- 3.   96732
- 4.   96793
- 5.
- 6.
- 7.
- 8.
- 9.
- 10.
- 11.
- 12.
- 13.
- 14.
- 15.
- 16.
- 17.
- 18.
- 19.
- 20.

PLEASE Return to by 12/13 (Hearing 12/14/18)

(01/14/18)

I support the CDC, AAP and FAAP Recommendations for the Childhood Vaccine Schedule for the Hawaii DOE.

Name/Signature	Email	Zip Code
1. Arenith Ventura / 		96732
2. Melanie Salvador / 		96753
3. Minny Morizumi		96761
4. Lillian 		
5. REIBY CALMA		96761
6. Kyle Murray except HPV 2 		96761
7. Grace Murray / 		96793
8. 		96761
9. Erme Wang		96779
		96732
10. DAKREN KASH		
11. Scott Corderman		96732
12. Tyler Locks		96793
13. Jamar Gueens		96792
14. Kato Juees		96793
15. Monica Borge		96732
16. Maile Alan		96730
17. Shauna Riggs		96793
18. Jennifer Rici		96707
19. Denise Fujiyama		96744
20. Dana Medeiros		96744
21. Charie Torres		96816

PLEASE Return to by 12/13 (Hearing 12/14/18)
 Felcy Waudais  or Laura Hassen (MLN Clin

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Kim Ginoza	[REDACTED]	96793
2. Kim Kawakami	[REDACTED]	96732
3. Chanel Akahi	[REDACTED]	96793
4. Ernewang	[REDACTED]	96779
5. Sherri Visaya	[REDACTED]	96732
6. Healani DeMello	[REDACTED]	96793
7. Sherry Anne Orquiza	[REDACTED]	96732
8. Lana Aganos	[REDACTED]	96732
9. Joann Gam	[REDACTED]	96732
10. Tracy Aituro	[REDACTED]	96753
11. Brett Shapiro	[REDACTED]	96753
12. Elizabeth Hoku	[REDACTED]	96708
13. CYRIL DALMON	[REDACTED]	96753
14. Samantha Heintz	[REDACTED]	96753
15. Marlaina Reyes	[REDACTED]	96753
16. Gail Matson	[REDACTED]	96732
17. Wynne Andron	[REDACTED]	96793
18. Kathy Ortiz Tom	[REDACTED]	96706
19. Chris Kellman	[REDACTED]	96793
20. Janet McCary	[REDACTED]	96793
21. Domingo B. Gumpal	[REDACTED]	96732
22. Jenelyn Ornanagan	[REDACTED]	[REDACTED]
23. Desiree-Janel Reyes	[REDACTED]	96708
24. Beatrice Kaohi-Prothero	[REDACTED]	[REDACTED]
25. (TALINE) Han	[REDACTED]	[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157 I OPPOSE
Date: Friday, December 14, 2018 4:24:23 PM

Aloha Hawaii DOH

Thank you for the opportunity to provide testimony. I STRONGLY OPPOSE THE HAR 11-157 PROPOSED RULES UPDATE!

My why:

1 - Making this mandatory TAKES AWAY our FREEDOM

2 - Plenty of parents will choose TO vaccinate & if a vaccine is supposed to protect a child then there should be no fear of unvaccinated people being around them because the vaccinated people are (supposedly) protected by the vaccine!

3 - Making this mandatory, the DOE will notice a huge numbers loss as families (who have made the EDUCATED decision not to vaccinate) will choose to homeschool their child

4 - Those who vote for HAR 11-157 will be staying they don't care about our freedoms & we will not vote for them in the next election

Summer Dillberg

[REDACTED]
concerned parent, citizen, & registered voter

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Friday, December 14, 2018 7:15:07 AM

To whom it may concern,

I am voicing my testimony in vote or favor that this bill does NOT pass. It is my constitutional right that I AM able to CHOOSE what I put into my body and my children's as well as how I govern my own health.

Sincerely,
Jordan Elizabeth Doty

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: Fwd: Vaccine vs. Disease Trade-offs: Cheating Children's Immune Systems • Children's Health Defense
Date: Friday, December 14, 2018 11:16:57 AM

Aloha again,
Please do your diligence and read up what about what is really going on when children are injected with these vaccines.
Mahalo,
Barbara Barry
[REDACTED]

<https://childrenshealthdefense.org/news/vaccine-vs-disease-trade-offs-cheating-childrens-immune-systems/>

Vaccine vs. Disease Trade-offs: Cheating Children's Immune Systems

December 13, 2018



By the Children's Health Defense Team

These days, one policy-maker after another seems to be promoting no-exceptions vaccination policies—hawking an incessant and growing barrage of childhood vaccines that begins prenatally and continues throughout childhood. Despite these efforts, the narrative that vaccines are keeping children healthy is rapidly crumbling.

Rates of chronic and autoimmune illness in American children have climbed to obscene levels ([54%](#) at last count), concurrently with rising vaccination rates—while U.S. life expectancy is [falling](#).

None of the individuals who present vaccination as an unquestioned good ever discusses the trade-offs involved in tampering with the exquisitely sophisticated human immune system, especially during a child's earliest developmental stages, nor do they acknowledge that two of vaccination's basic premises are patently false:

1. It has become clear that the short-lived antibody production that vaccines seek to induce is nothing like the comprehensive lifelong immunity that results from a natural infection;
2. An honest look at health statistics shows that vaccines exact a high cost when they re-engineer children's immune systems; rather than entering adulthood in robust health, many children are paying the piper via some form of immune dysfunction at some point down the road.

Creating an imbalanced immune system

Scientists admire the [immune system](#) as “the most complex system that the human body has.” It is also a “model of [versatility](#),” carrying out an impressive range of essential functions. These include differentiating between “harmless self” and harmful invaders (e.g., bacteria, viruses, fungi or toxins); amplifying the immune response; excreting cellular debris (through mechanisms such as fever, sweating, rash and expectorations); engaging in tissue repair; interacting with the gut microbiome; and more.

This “incredibly [precise](#)” system has two coordinated arms. The cell-mediated immune system is characterized by the activity of white blood cells that travel to the area(s) of infection to eliminate the infected cells. The humoral immune system prompts the formation of

antibodies that target invader-specific proteins (antigens) for destruction.

Interfering with such a precise immune response (the result of millions of years of evolutionary fine-tuning) carries with it massive risk of unintended consequence[s]—and those consequences are now manifesting in the form of an autoimmunity crisis.

The hallmark of vaccination is that it bypasses the cell-mediated response in favor of a “[mock infection](#),” while encouraging a disproportionate humoral response. According to an elegant new [book](#) by Dr. Thomas Cowan (*Vaccines, Autoimmunity, and the Changing Nature of Childhood Illness*), this “reckless” suppression of the cell-mediated response is a very bad idea: “Interfering with such a precise immune response” (the result of “millions of years of evolutionary fine-tuning”) carries with it “massive risk of unintended consequence[s]”—and those consequences are now manifesting in the form of an autoimmunity crisis. Cowan states:

“The deliberate provocation of antibodies without prior cell-mediated activity produces an imbalance in our immune system and a state of excessive antibody production. This excessive antibody production actually *defines* autoimmune disease. ... With millions of people suffering from autoimmune disease, at a number unheard of before the introduction of mass vaccination programs, how can this connection be deemed controversial?”
[Emphasis in original]

Forfeiting protections

Immunologic dysregulation—including dysfunction of the type brought about by vaccination—is associated not just with autoimmunity but also with [cancer](#), and childhood cancers are

[skyrocketing](#). In contrast, many of the once-universal childhood illnesses were, in fact, protective against various cancers. Stated another way, acute infections, and especially those that caused fever, were historically “[antagonistic to cancer](#).” For example:

- Naturally acquired [mumps](#) engendered immunity to **ovarian cancer** through antibodies against a cancer-associated antigen.
- Individuals who experienced fever-inducing infectious illnesses in childhood (such as [rubella and chickenpox](#)) had a lower risk of **non-breast cancers**, including [melanoma and ovarian cancer](#).
- Acute childhood infections protected against Hodgkin’s lymphoma, and [measles](#), in particular, protected against **non-Hodgkin’s lymphoma**.

...children who successfully go through measles...have less heart disease, arthritis, allergies, autoimmune diseases, and overall better health than those who never get measles.

Frenzied media stories about “measles outbreaks” notwithstanding, there are multiple reasons to view natural measles infection in childhood as beneficial. As summarized in Cowan’s book, “children who successfully go through measles...have less heart disease, arthritis, allergies, autoimmune diseases, and overall better health than those who never get measles.” Children’s Health Defense has noted previously how the benefits of measles used to be [taken for granted](#)—until, says Cowan, the vaccine came along “and changed the way we think about measles.”

Ironically, viruses’ potential to serve as “possible agents of tumor destruction” attracted interest as long as a century ago, when clinical experiences showed that, “given the right set of conditions, cancers would sometimes regress during [naturally acquired virus infections](#).” In the current era, the use of viruses as an anti-cancer treatment has

morphed into the “[respectable field](#)” of oncolytic virotherapy, even leading to clinical trials—and “[measles virus](#) still represents a highly interesting candidate for such an approach.”

Genetically engineered viral interventions also promise the pharmaceutical industry profits, whereas simply allowing children to get the measles and acquire their cancer protection naturally cannot be monetized.

Unfortunately, enthusiasm for viruses as “serious contenders in cancer treatment” has further entrenched scientists’ reliance on [vaccine strains of measles virus](#) (which are, after all, “[amenable to genetic modification](#) in the laboratory”)—fostering zeal for a “new age of [engineering immunity](#)” and more of the misplaced faith in “rational manipulation of the immune system” that gave rise to vaccines in the first place. (If anyone has concerns about the potential for these genetically engineered viruses to prompt further unintended consequences, they are keeping their concerns to themselves.) Genetically engineered viral interventions also promise the pharmaceutical industry [profits](#), whereas simply allowing children to get the measles and acquire their cancer protection naturally cannot be monetized.

Circling the wagons

Increasingly, vaccine bullies are employing strategies that would have been unthinkable even five years ago. For example, a children’s hospital in Florida that is [under investigation](#) for medical errors and an unexpectedly high mortality rate in its young heart surgery patients recently announced that it will [deny services](#) to unvaccinated or partially vaccinated children; the hospital is also taking a “[hard line](#)” on flu shots, requiring not just employees but also “non-employee physicians, medical students in training, drug and medical

device representatives and volunteers” to get a shot or (in the case of employees) run the risk of being fired. The reason cited for these unnuanced policies is “patient safety.”

...vaccines are disrupting normal immune system function and leaving both children and adults vulnerable to far more serious chronic diseases.

As these hard-line tactics multiply, it is vital to keep the failure of the U.S. vaccine program in the public eye. The far-from-uncommon phenomenon of [vaccine failure](#) in vaccinated individuals has made it abundantly clear that a vaccine-induced antibody response—the typical indicator of vaccine “protection”—is essentially worthless as a guarantor of real immunity. Even worse, vaccines are disrupting normal immune system function and leaving both children and adults vulnerable to far more serious chronic diseases. The vaccine establishment may not be willing to admit that the vaccination paradigm is fatally flawed, but it is sadly apparent that, in Dr. Cowan’s words, “our communities, hospitals, and schools are filled to the brim with sick and injured children—often suffering from illnesses that barely existed a hundred years ago.”

[Sign up](#) for free news and updates from Robert F. Kennedy, Jr. and the Children’s Health Defense. CHD is planning many strategies, including legal, in an effort to defend the health of our children and obtain justice for those already injured. Your [support](#) is essential to CHD’s successful mission.

From: [REDACTED]
To: [REDACTED]
Subject: Copy of pages presented at recent hearing on 12/14/18
Date: Saturday, December 15, 2018 2:23:08 PM

To whom it may concern:

I am sending a copy of names and email addresses which were presented to the moderator during my testimony at the Maui hearing on 12/14/18 in support of proposed updates to the vaccine schedule for schools. I wanted to be sure this packet was received by you.

Thank you,
Laura K. Hassen, MD

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Michelle L. Apo	[REDACTED]	96793
2. Raynette K Maxwell	[REDACTED]	96790
3. Simona Clarke	[REDACTED]	96732
4. MARCO ANTONI TORRES	[REDACTED]	96702
5. BULOGAN, ASHLEY	[REDACTED]	96790
6. Shayne Kanuho	[REDACTED]	96793
7. Rodalisa Oela Cruz	[REDACTED]	96793
8. Allison Takai	[REDACTED]	96793
9. Erin Baxter PA-C	[REDACTED]	96746
10. Desmond Winstead	[REDACTED]	96753
11. Beth Dressel	[REDACTED]	96779
12. Anne Quinlan	[REDACTED]	96788
13. Megha Chondke	[REDACTED]	96773
14. [REDACTED]	[REDACTED]	96772
15. Mitchell [REDACTED]	[REDACTED]	
16. David Barchus [REDACTED]	[REDACTED]	96793
17. Janah Visitation	[REDACTED]	96732
18. Shirley Hidalgo	[REDACTED]	96732
19. Laura Hassen [REDACTED]	[REDACTED]	96793
20. Kaenya Lewis	[REDACTED]	96793

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. George Talbot MD	[REDACTED]	96968
2. Vona Diener, MD	[REDACTED]	96768
3. Megan Wright, DO	[REDACTED]	76790
4. Roger Kava, DO	[REDACTED]	96779
5. Brian Lazarus, Jr MD	bin.lazarus@[REDACTED]	96793
6. Jay Forns	[REDACTED]	96768
7. John MEXEL	[REDACTED]	96793
8. Leona Arenberg Coffin	[REDACTED]	96768
9. Nicole Fernandez	[REDACTED]	94753
10. Julie Enos	[REDACTED]	96793
11. Valerie Thumader	[REDACTED]	96732
12. Sally Bowler	[REDACTED]	96768
13. Guy SVOINOV	[REDACTED]	96793
14. Kevin Riglos	[REDACTED]	96793
15. Cheeneth Dela Cruz	[REDACTED]	96793
16. Roman Valle	[REDACTED]	96793
17. Victoria Yahiku	[REDACTED]	96732
18. Shelby Yanos	[REDACTED]	96793
19. Stella Mae Ong	[REDACTED]	96732
20. Zyla delacruz	[REDACTED]	96732

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Mawelyn Edmalin	[REDACTED]	96732
2. Gemma Lapitan	[REDACTED]	96732
3. Melanre Salvador	[REDACTED]	96753
4. DESIREE CORPUZ	[REDACTED]	96753
5. Honey Dean Edmalin	[REDACTED]	96732
6. Alexander Lapitan	[REDACTED]	96732
7. CESTAR CORPUZ JR		96753
8. CLATRE CILLOS		96753
9. LORETO CILLOS JR		
10. AIZA ALEJO		96753 96732
11. GAIL MATSUI		96732
12. MARITES CADANAS GANCENA		96753
13. CLARITA CACHO		96753
14. PHELIP CACHO		96753
15. EDITH EDMALIN		96732
16. ANGIE BELLA		96753
17. VALENTIN BELLA		96764
18. CONCHITA JAFAMILLO		
19.		
20.		

I support the CDC and AAP Recommendations for Childhood Vaccine Schedule for the DOE.

Name	Email	Zip Code
1. Stephanie Rosario	[REDACTED]	96753
2. RYAN Manzella	[REDACTED]	96753
3. ERROL BANTUAN	[REDACTED]	96793
4. Jodie Toward	[REDACTED]	96793
5. RENNIA Cabal	[REDACTED]	96793 96768
6. Jay Fans	[REDACTED]	
7. Brian [REDACTED]	[REDACTED]	96793
8. Maria Termulo	[REDACTED]	96793
9. Lisa Stacey	[REDACTED]	96768
10. Michelle Senamonthy	[REDACTED]	96768 96753
11. Sophia Rohr	[REDACTED]	
12. Ivan Kausle	[REDACTED]	96790
13. ROY LICUDAN	[REDACTED]	96761
14.		
15.		
16.		
17.		
18.		
19.		
20.		

I support the CDC, AAP and FAAP Recommendations for the Childhood Vaccine Schedule for the Hawaii DOE.

Name/Signature	Email	Zip Code
1. Lisa Soderstrom	[REDACTED]	96732
2. [REDACTED]	[REDACTED]	96753
3. [REDACTED]	[REDACTED]	96732
4. Alla Pug	[REDACTED]	96743
5.		
6.		
7.		
8.		
9.		
10.		
11.		
12.		
13.		
14.		
15.		
16.		
17.		
18.		
19.		
20.		

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Children's Health Defense - please read
Date: Sunday, December 16, 2018 10:11:25 AM
Attachments: [generation-sick-ebook.pdf](#)

Aloha,

Please read the Children's Health Defense e-book. Thank you!

<https://childrenshealthdefense.org/wp-content/uploads/generation-sick-ebook.pdf>

Regards,
Laura Reese

From: [REDACTED]
To: [REDACTED]
Subject: Children's Health Defense - please read
Date: Sunday, December 16, 2018 10:11:25 AM
Attachments: [generation-sick-ebook.pdf](#)

Aloha,

Please read the Children's Health Defense e-book. Thank you!

<https://childrenshealthdefense.org/wp-content/uploads/generation-sick-ebook.pdf>

Regards,
Laura Reese

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Read 157 Research Papers Supporting the Vaccine
Date: Sunday, December 16, 2018 9:43:01 PM

I'm reading 157 Research Papers Supporting the Vaccine / Autism Link
ck out there web site and then plz submit it for testimony from me

<https://www.scribd.com/saved>

Thanks Toni Liljengren

12/17/18

Disease Outbreak Control Division (DOCD)
1250 Punchbowl Street, Room 443
Honolulu, Hawaii 96813

My name is Cynthia Henry Keener, my son Makana Keener was born on April 07, 2009. A perfectly healthy infant w/ no complications at birth nor I during pregnancy.

Makana was growing & thriving like my other two children at the same age. He was hitting all his milestones w/ ease. On April 15, 2010 I took Makana in for his routine 12 mos vaccines. He had been ill w/ an alleged respiratory infection and had been on antibiotics one two weeks prior and still had a runny nose. So, I being his mother and having had worked in a Neonatal, Peds, & Newborn Nursery for a total of twelve years questioned his compromised immune system after being on antibiotics. Stating that I didn't feel it was good to give him the MMR, Varicella & Hep A vaccine all at once it'd be too much for him.

Kauai Medical clinic's Dr. Ross exclaimed he'd be fine, I still questioned vaccinating, and he went into drawing a diagram on paper covering lying on patient table. Explaining the statistics & logistics of not vaccinating. My now twenty-six yr old daughter was there and witnessed him talking me into doing something I didn't really want to. He talked me into it and we gave all five vaccines.

Two days later my little boy had a seizure. I took him into the Kauai Medical Clinic after this seizure episode and Dr. Weiner asked me if I was sure he wasn't having a tantrum! I was insulted by her to say the least. I knew what a seizure looked like. Makana began to regress in his walking and talking.

My son continued for two mos to have seizures that Dr. Ross said were not related to the vaccines and it was just a coincidence. They referred us to Ped. Neuro on Oahu @ Kapiolani, Dr. Abe. Who of course put Makana on AEDs. This anti-seizure med made Makana have more seizures as they didn't properly diagnose him. Took him back various times after he was continually having more seizures to our Ped. Dr. Ross at Kauai Med. Clinic & he said to trust Dr. Abe he graduated from Stanford.

For almost one year I fought against the treatment of Makana as he was lethargic, not talking, & barely walking. I began to call hospitals in the mainland, UCLA Epilepsy research Ctr. in Los Angeles. They were able to properly diagnose Makana's seizures that they were unable to in the state of Hawaii. They did 24 hr EEG. Low and behold his seizures were stemming from another part of the brain that required a different med. Could not do a 2 EEG in the whole state of Hawaii, nor did they do the proper genetic testing.

Makana has been on 4 different medications, had three dif pediatric neurologist here in Hawaii. Three different pediatricians, & two Epileptologists care for him in California. The last nationally renowned physician at UCSF Benioff Children's Hospital in San Francisco where we discovered that Hawaii didn't do the extremely important genetic testing to figure out if he is epileptic or not. I was told they had at UCLA where they exclaimed, he had IS Infantile Spasm syndrome. By this time, I had done plenty research & I let them know I didn't agree.

After extensive genetic testing for an anomalies Makana came back with nothing. NO genetic markers for epilepsy, anomalies, retardation nothing! UCSF doctor stated that he seemed to be vaccine damaged & had brain damage from AEDS.

The whole time I was telling all doctors involved with my son that this was from his vaccines all but one denied this. She wouldn't even put it into writing, her hospital had state of the art everything that I am positive was funded partially by pharmaceutical co's of course.

Per the CDC a severe reaction to the MMR is jerking seizures. Well to this date my son still has these jerking seizures which are categorized under Nocturnal seizure disorder, upon waking. Nocturnal seizure disorder stems from brain injury or infection.

My son has developmental delays, ADHD which brain damage goes hand in hand with. Per MRI / CT Scan no obvious brain damage is seen. My son has many cognitive delays & behavioral issues, he is on the Autism Spectrum and struggles w/ daily living.

The Dr. Ross the pediatrician that coerced me into vaccinating my child up until very recently wouldn't even look me in the eye. Nor did he report to VAERS the seizure activity that commenced two days after vaccinating my son. Another physician did who quit working at Kauai Med Clinic as a pediatrician for reasons he wouldn't disclose, he reported it!

How many unreported adverse reactions have gone unidentified at Kauai Medical Clinic? Statistically reactions from low grade fever which is now what docs deem normal all the way to deaths go unreported. CDC does not have true statistics across the nation that is fact.

Dr. Ross of Kauai Med. Clinic years ago was interning w/another pediatrician there who **did report** an adverse reaction to a vaccine. That very pediatrician was let go a month later and that was 25 years ago. I know the MO of these doctors on this small island.

I OPPOSE ANY ADDING OR MANDATING OF MORE VACCINES ON AN ALREADY OVERLOADED & DANGEROUS CHILDHOOD VACCINE SCHEDULE!

I OPPOSE ON THE BASIS THAT WE ARE PERFECTLY MADE IN GOD'S IMAGE TO NOT PUT CONTAMINATES INTO OUR BODIES.

I OPPOSE ON THE BASIS OF HUMAN RIGHTS, DO NOT USE THE DOE SYSTEM TO BULLY PARENTS INTO NOT HAVING CHOICE ABOUT VACCINATION.

I AM PROCHOICE!

I OPPOSE on the basis that there is a full awareness by federal government & the medical industry that there IS a Vaccine Injury Court set in place for those who are injured and die due to vaccines that aren't properly safety tested.

The American Association of Pediatrics recommends that a newborn infant receive the Hep B right after birth because it's an opportune time (PBS) but the FDA states that a two month old infant should only have 25 micrograms of aluminum and no more than that BUT AT BIRTH A NEWBORN GETS IN THE HEP B VACCINE 250 micrograms.

How is this logical?

WHERE THERE IS RISK THERE MUST BE CHOICE!

From: [REDACTED]
To: [REDACTED]
Subject: Anti Vacc testimony
Date: Monday, December 17, 2018 7:25:22 PM

I grew up with a belief against immunizations, I know it helps the world but some of the Ingredients & outcomes are something I wouldn't do to me or my children. There is a HUGE community of people who haven't been immunized or didn't immunize their own children. It should be a choice & right WE PEOPLE have to do to our own body & still deserve to be treated like human beings & attend normal schools! please don't take away our basic human rights.

Mahalo & Aloha

From: [REDACTED]
To: [REDACTED]
Subject: Anti vaccinations
Date: Monday, December 17, 2018 7:45:00 PM

I am sending my anti-mandatory vaccination testimony. I believe that it is a basic human right to choose. Our country alone is based off of our freedom. They are taking that away when they take away our choice. I think that it is OK to choose if you want to vaccinate or if you don't but it is wrong to tell someone they must. The vaccinations are pumped full of preservatives, poisons, and also the sickness itself, There's so many risks there must be a choice. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: Submitted evidence to DOH meeting on Kausal on the 21st please read
Date: Monday, December 17, 2018 9:34:26 AM
Attachments: header-logo_bronze-resized-5-2.png



THE UNITED STATES
DEPARTMENT OF JUSTICE

[HOME](#) [ABOUT](#) [AGENCIES](#) [RESOURCES](#) [NEWS](#) [CAREERS](#) [CONTACT](#)

[Home](#) » [Office of Public Affairs](#) » [News](#)

SHARE

JUSTICE NEWS

Department of Justice

Office of Public Affairs

FOR IMMEDIATE RELEASE

Monday, July 2, 2012

GlaxoSmithKline to Plead Guilty and Pay \$3 Billion to Resolve Fraud Allegations and Failure to Report Safety Data

Largest Health Care Fraud Settlement in U.S. History

Global health care giant GlaxoSmithKline LLC (GSK) agreed to plead guilty and to pay \$3 billion to resolve its criminal and civil liability arising from the company's unlawful promotion of certain prescription drugs, its failure to report certain safety data, and its civil liability for alleged false price reporting practices, the Justice Department announced today. The resolution is the largest health care fraud settlement in U.S. history and the largest payment ever by a drug company.

GSK agreed to plead guilty to a three-count criminal information, including two counts of introducing misbranded drugs, Paxil and Wellbutrin, into interstate commerce and one count of failing to report safety data about the drug Avandia to the Food and Drug Administration (FDA). Under the terms of the plea agreement, GSK will pay a total of \$1 billion, including a criminal fine of \$956,814,400 and forfeiture in the amount of \$43,185,600. The criminal plea agreement also includes certain non-monetary compliance commitments and certifications by GSK's U.S. president and board of directors. GSK's guilty plea and sentence is not final until accepted by the U.S. District Court.

GSK will also pay \$2 billion to resolve its civil liabilities with the federal government under the False Claims Act, as well as the states. The civil settlement resolves claims relating to Paxil, Wellbutrin and Avandia, as well as additional drugs, and also resolves pricing fraud allegations.

"Today's multi-billion dollar settlement is unprecedented in both size and scope. It underscores the Administration's firm commitment to protecting the American people and holding accountable those who commit health care fraud," said James M. Cole, Deputy Attorney General. "At every level, we are determined to stop practices that jeopardize patients' health, harm taxpayers, and violate the public trust – and this historic action is a clear warning to any company that chooses to break the law."

"Today's historic settlement is a major milestone in our efforts to stamp out health care fraud," said Bill Corr, Deputy Secretary of the Department of Health and Human Services (HHS). "For a long time, our health care system had been a target for cheaters who thought they could make an easy profit at the expense of public safety, taxpayers, and the millions of Americans who depend on programs like Medicare and Medicaid. But thanks to strong enforcement actions like those we have announced today, that equation is rapidly changing."

This resolution marks the culmination of an extensive investigation by special agents from HHS-OIG, FDA and FBI, along with law enforcement partners across the federal government. Moving forward, GSK will be subject to stringent requirements under its corporate integrity agreement with HHS-OIG; this agreement is designed to increase accountability and transparency and prevent future fraud and abuse. Effective law enforcement partnerships and fraud prevention are hallmarks of the Health Care Fraud Prevention and Enforcement Action Team (HEAT) initiative, which fosters government collaboration to fight fraud.

Criminal Plea Agreement

Under the provisions of the Food, Drug and Cosmetic Act, a company in its application to the FDA must specify each intended use of a drug. After the FDA approves the product as safe and effective for a specified use, a company's promotional activities must be limited to the intended uses that FDA approved. In fact, promotion by the manufacturer for other uses – known as "off-label uses" – renders the product "misbranded."

Paxil: In the criminal information, the government alleges that, from April 1998 to August 2003, GSK unlawfully promoted Paxil for treating depression in patients under age 18, even though the FDA has never approved it for pediatric use. The United States alleges that, among other things, GSK participated in preparing, publishing and distributing a misleading medical journal article that misrepresented that a clinical trial of Paxil demonstrated efficacy in the treatment of depression in patients under age 18, when the study failed to demonstrate efficacy. At the same time, the United States alleges, GSK did not make available data from two other studies in which Paxil also failed to demonstrate efficacy in treating depression in patients under 18. The United States further alleges that GSK sponsored dinner programs, lunch programs, spa programs and similar activities to promote the use of Paxil in children and adolescents. GSK paid a speaker to talk to an audience of doctors and paid for the meal or spa treatment for the doctors who attended. Since 2004, Paxil, like other antidepressants, included on its label a "black box warning" stating that antidepressants may increase the risk of suicidal thinking and behavior in short-term studies in patients under age 18. GSK agreed to plead guilty to misbranding Paxil in that its labeling was false and misleading regarding the use of Paxil for patients under 18.

Wellbutrin: The United States also alleges that, from January 1999 to December 2003, GSK promoted Wellbutrin, approved at that time only for Major Depressive Disorder, for weight loss, the treatment of sexual dysfunction, substance addictions and Attention Deficit Hyperactivity Disorder, among other off-label uses. The United States contends that GSK paid millions of dollars to doctors to speak at and attend meetings, sometimes at lavish resorts, at which the off-label uses of

Wellbutrin were routinely promoted and also used sales representatives, sham advisory boards, and supposedly independent Continuing Medical Education (CME) programs to promote Wellbutrin for these unapproved uses. GSK has agreed to plead guilty to misbranding Wellbutrin in that its labeling did not bear adequate directions for these off-label uses. For the Paxil and Wellbutrin misbranding offenses, GSK has agreed to pay a criminal fine and forfeiture of \$757,387,200.

Avandia: The United States alleges that, between 2001 and 2007, GSK failed to include certain safety data about Avandia, a diabetes drug, in reports to the FDA that are meant to allow the FDA to determine if a drug continues to be safe for its approved indications and to spot drug safety trends. The missing information included data regarding certain post-marketing studies, as well as data regarding two studies undertaken in response to European regulators' concerns about the cardiovascular safety of Avandia. Since 2007, the FDA has added two black box warnings to the Avandia label to alert physicians about the potential increased risk of (1) congestive heart failure, and (2) myocardial infarction (heart attack). GSK has agreed to plead guilty to failing to report data to the FDA and has agreed to pay a criminal fine in the amount of \$242,612,800 for its unlawful conduct concerning Avandia.

"This case demonstrates our continuing commitment to ensuring that the messages provided by drug manufacturers to physicians and patients are true and accurate and that decisions as to what drugs are prescribed to sick patients are based on best medical judgments, not false and misleading claims or improper financial inducements," said Carmen Ortiz, U.S. Attorney for the District of Massachusetts.

"Patients rely on their physicians to prescribe the drugs they need," said John Walsh, U.S. Attorney for Colorado. "The pharmaceutical industries' drive for profits can distort the information provided to physicians concerning drugs. This case will help to ensure that your physician will make prescribing decisions based on good science and not on misinformation, money or favors provided by the pharmaceutical industry."

Civil Settlement Agreement

As part of this global resolution, GSK has agreed to resolve its civil liability for the following alleged conduct: (1) promoting the drugs Paxil, Wellbutrin, Advair, Lamictal and Zofran for off-label, non-covered uses and paying kickbacks to physicians to prescribe those drugs as well as the drugs Imitrex, Lotronex, Flovent and Valtrex; (2) making false and misleading statements concerning the safety of Avandia; and (3) reporting false best prices and underpaying rebates owed under the Medicaid Drug Rebate Program.

Off-Label Promotion and Kickbacks: The civil settlement resolves claims set forth in a complaint filed by the United States alleging that, in addition to promoting the drugs Paxil and Wellbutrin for unapproved, non-covered uses, GSK also promoted its asthma drug, Advair, for first-line therapy for mild asthma patients even though it was not approved or medically appropriate under these circumstances. GSK also promoted Advair for chronic obstructive pulmonary disease with misleading claims as to the relevant treatment guidelines. The civil settlement also resolves allegations that GSK promoted Lamictal, an anti-epileptic medication, for off-label, non-covered psychiatric uses, neuropathic pain and pain management. It further resolves allegations that GSK promoted certain forms of Zofran, approved only for post-operative nausea, for the treatment of morning sickness in pregnant women. It also includes allegations that GSK paid kickbacks to health care professionals to induce them to promote and prescribe these drugs as well as the drugs Imitrex, Lotronex, Flovent and Valtrex. The United States alleges that this conduct caused false claims to be submitted to federal health care programs.

GSK has agreed to pay \$1.043 billion relating to false claims arising from this alleged conduct. The federal share of this settlement is \$832 million and the state share is \$210 million.

This off-label civil settlement resolves four lawsuits pending in federal court in the District of Massachusetts under the *qui tam*, or whistleblower, provisions of the False Claims Act, which allow private citizens to bring civil actions on behalf of the United States and share in any recovery.

Avandia: In its civil settlement agreement, the United States alleges that GSK promoted Avandia to physicians and other health care providers with false and misleading representations about Avandia's safety profile, causing false claims to be submitted to federal health care programs. Specifically, the United States alleges that GSK stated that Avandia had a positive cholesterol profile despite having no well-controlled studies to support that message. The United States also alleges that the company sponsored programs suggesting cardiovascular benefits from Avandia therapy despite warnings on the FDA-approved label regarding cardiovascular risks. GSK has agreed to pay \$657 million relating to false claims arising from misrepresentations about Avandia. The federal share of this settlement is \$508 million and the state share is \$149 million.

Price Reporting: GSK is also resolving allegations that, between 1994 and 2003, GSK and its corporate predecessors reported false drug prices, which resulted in GSK's underpaying rebates owed under the Medicaid Drug Rebate Program. By law, GSK was required to report the lowest, or "best" price that it charged its customers and to pay quarterly rebates to the states based on those reported prices. When drugs are sold to purchasers in contingent arrangements known as "bundles," the discounts offered for the bundled drugs must be reallocated across all products in the bundle proportionate to the dollar value of the units sold. The United States alleges that GSK had bundled sales arrangements that included steep discounts known as "nominal" pricing and yet failed to take such contingent arrangements into account when calculating and reporting its best prices to the Department of Health and Human Services. Had it done so, the effective prices on certain drugs would have been different, and, in some instances, triggered a new, lower best price than what GSK reported. As a result, GSK underpaid rebates due to Medicaid and overcharged certain Public Health Service entities for its drugs, the United States contends. GSK has agreed to pay \$300 million to resolve these allegations, including \$160,972,069 to the federal government, \$118,792,931 to the states, and \$20,235,000 to certain Public Health Service entities who paid inflated prices for the drugs at issue.

Except to the extent that GSK has agreed to plead guilty to the three-count criminal information, the claims settled by these agreements are allegations only, and there has been no determination of liability.

"This landmark settlement demonstrates the Department's commitment to protecting the American public against illegal conduct and fraud by pharmaceutical companies," said Stuart F. Delery, Acting Assistant Attorney General for the Justice Department's Civil Division. "Doctors need truthful, fair, balanced information when deciding whether the benefits of a drug outweigh its safety risks. By the same token, the FDA needs all necessary safety-related information to identify safety trends and to determine whether a drug is safe and effective. Unlawful promotion of drugs for unapproved uses and failing to report adverse drug experiences to the FDA can tip the balance of those important decisions, and the Justice Department will not tolerate attempts by those who seek to corrupt our health care system in this way."

Non-monetary Provisions and Corporate Integrity Agreement

In addition to the criminal and civil resolutions, GSK has executed a five-year Corporate Integrity Agreement (CIA) with the Department of Health and Human Services, Office of Inspector General (HHS-OIG). The plea agreement and CIA include novel provisions that require that GSK implement and/or maintain major changes to the way it does business, including changing the way its sales force is compensated to remove compensation based on sales goals for territories, one of the driving forces behind much of the conduct at issue in this matter. Under the CIA, GSK is required to change its executive compensation program to permit the company to recoup annual bonuses and long-term incentives from covered executives if they, or their subordinates, engage in significant misconduct. GSK may recoup monies from executives who are current employees and those who have left the company. Among other things, the CIA also requires GSK to implement and maintain transparency in its research practices and publication policies and to follow specified policies in its contracts with various health care payors.

"Our five-year integrity agreement with GlaxoSmithKline requires individual accountability of its board and executives," said Daniel R. Levinson, Inspector General of the U.S. Department of Health and Human Services. "For example, company executives may have to forfeit annual bonuses if they or their subordinates engage in significant misconduct, and sales agents are now being paid based on quality of service rather than sales targets."

"The FDA Office of Criminal Investigations will aggressively pursue pharmaceutical companies that choose to put profits before the public's health," said Deborah M. Autor, Esq., Deputy Commissioner for Global Regulatory Operations and Policy, U.S. Food and Drug Administration. "We will continue to work with the Justice Department and our law enforcement counterparts to target companies that disregard the protections of the drug approval process by promoting drugs for uses when they have not been proven to be safe and effective for those uses, and that fail to report required drug safety information to the FDA."

"The record settlement obtained by the multi-agency investigative team shows not only the importance of working with our partners, but also the importance of the public providing their knowledge of suspect schemes to the government," said Kevin Perkins, Acting Executive Assistant Director of the FBI's Criminal, Cyber, Response and Services Branch. "Together, we will continue to bring to justice those engaged in illegal schemes that threaten the safety of prescription drugs and other critical elements of our nation's healthcare system."

"Federal employees deserve health care providers and suppliers, including drug manufacturers, that meet the highest standards of ethical and professional behavior," said Patrick E. McFarland, Inspector General of the U.S. Office of Personnel Management. "Today's settlement reminds the pharmaceutical industry that they must observe those standards and reflects the commitment of Federal law enforcement organizations to pursue improper and illegal conduct that places health care consumers at risk."

"Today's announcement illustrates the efforts of VA OIG and its law enforcement partners in ensuring the integrity of the medical care provided our nation's veterans by the Department of Veterans Affairs," said George J. Opfer, Inspector General of the Department of Veterans Affairs. "The monetary recoveries realized by VA in this settlement will directly benefit VA healthcare programs that provide for veterans' continued care."

"This settlement sends a clear message that taking advantage of federal health care programs has substantial consequences for those who try," said Rafael A. Medina, Special Agent in Charge of the Northeast Area Office of Inspector General for the U.S. Postal Service. "The U.S. Postal Service pays more than one billion dollars a year in workers' compensation benefits and our office is committed to pursuing those individuals or entities whose fraudulent acts continue to unfairly add to that cost."

A Multilateral Effort

The criminal case is being prosecuted by the U.S. Attorney's Office for the District of Massachusetts and the Civil Division's Consumer Protection Branch. The civil settlement was reached by the U.S. Attorney's Office for the District of Massachusetts, the U.S. Attorney's Office for the District of Colorado and the Civil Division's Commercial Litigation Branch. Assistance was provided by the HHS Office of Counsel to the Inspector General, Office of the General Counsel-CMS Division and FDA's Office of Chief Counsel as well as the National Association of Medicaid Fraud Control Units.

This matter was investigated by agents from the HHS-OIG; the FDA's Office of Criminal Investigations; the Defense Criminal Investigative Service of the Department of Defense; the Office of the Inspector General for the Office of Personnel Management; the Department of Veterans Affairs; the Department of Labor; TRICARE Program Integrity; the Office of Inspector General for the U.S. Postal Service and the FBI.

This resolution is part of the government's emphasis on combating health care fraud and another step for the Health Care Fraud Prevention and Enforcement Action Team (HEAT) initiative, which was announced in May 2009 by Attorney General Eric Holder and Kathleen Sebelius, Secretary of HHS. The partnership between the two departments has focused efforts to reduce and prevent Medicare and Medicaid financial fraud through enhanced cooperation. Over the last three years, the department has recovered a total of more than \$10.2 billion in settlements, judgments, fines, restitution, and forfeiture in health care fraud matters pursued under the False Claims Act and the Food, Drug and Cosmetic Act.

Court documents related to today's settlement can be viewed online at www.justice.gov/opa/gsk-docs.html.

Related Materials:

Remarks by the Deputy Attorney General James M. Cole at the GSK Press Conference
Remarks by Acting Assistant Attorney General for the Civil Division Stuart F. Delery at the GSK Press Conference

Topic(s):
Consumer Protection

Component(s):
Civil Division

Press Release Number:

12/17/18

Disease Outbreak Control Division (DOCD)
1250 Punchbowl Street, Room 443
Honolulu, Hawaii 96813

My name is Cynthia Henry Keener, my son Makana Keener was born on April 07, 2009. A perfectly healthy infant w/ no complications at birth nor I during pregnancy.

Makana was growing & thriving like my other two children at the same age. He was hitting all his milestones w/ ease. On April 15, 2010 I took Makana in for his routine 12 mos vaccines. He had been ill w/ an alleged respiratory infection and had been on antibiotics one two weeks prior and still had a runny nose. So, I being his mother and having had worked in a Neonatal, Peds, & Newborn Nursery for a total of twelve years questioned his compromised immune system after being on antibiotics. Stating that I didn't feel it was good to give him the MMR, Varicella & Hep A vaccine all at once it'd be too much for him.

Kauai Medical clinic's Dr. Ross exclaimed he'd be fine, I still questioned vaccinating, and he went into drawing a diagram on paper covering lying on patient table. Explaining the statistics & logistics of not vaccinating. My now twenty-six yr old daughter was there and witnessed him talking me into doing something I didn't really want to. He talked me into it and we gave all five vaccines.

Two days later my little boy had a seizure. I took him into the Kauai Medical Clinic after this seizure episode and Dr. Weiner asked me if I was sure he wasn't having a tantrum! I was insulted by her to say the least. I knew what a seizure looked like. Makana began to regress in his walking and talking.

My son continued for two mos to have seizures that Dr. Ross said were not related to the vaccines and it was just a coincidence. They referred us to Ped. Neuro on Oahu @ Kapiolani, Dr. Abe. Who of course put Makana on AEDs. This anti-seizure med made Makana have more seizures as they didn't properly diagnose him. Took him back various times after he was continually having more seizures to our Ped. Dr. Ross at Kauai Med. Clinic & he said to trust Dr. Abe he graduated from Stanford.

For almost one year I fought against the treatment of Makana as he was lethargic, not talking, & barely walking. I began to call hospitals in the mainland, UCLA Epilepsy research Ctr. in Los Angeles. They were able to properly diagnose Makana's seizures that they were unable to in the state of Hawaii. They did 24 hr EEG. Low and behold his seizures were stemming from another part of the brain that required a different med. Could not do a 2 EEG in the whole state of Hawaii, nor did they do the proper genetic testing.

Makana has been on 4 different medications, had three dif pediatric neurologist here in Hawaii. Three different pediatricians, & two Epileptologists care for him in California. The last nationally renowned physician at UCSF Benioff Children's Hospital in San Francisco where we discovered that Hawaii didn't do the extremely important genetic testing to figure out if he is epileptic or not. I was told they had at UCLA where they exclaimed, he had IS Infantile Spasm syndrome. By this time, I had done plenty research & I let them know I didn't agree.

After extensive genetic testing for an anomalies Makana came back with nothing. NO genetic markers for epilepsy, anomalies, retardation nothing! UCSF doctor stated that he seemed to be vaccine damaged & had brain damage from AEDS.

The whole time I was telling all doctors involved with my son that this was from his vaccines all but one denied this. She wouldn't even put it into writing, her hospital had state of the art everything that I am positive was funded partially by pharmaceutical co's of course.

Per the CDC a severe reaction to the MMR is jerking seizures. Well to this date my son still has these jerking seizures which are categorized under Nocturnal seizure disorder, upon waking. Nocturnal seizure disorder stems from brain injury or infection.

My son has developmental delays, ADHD which brain damage goes hand in hand with. Per MRI / CT Scan no obvious brain damage is seen. My son has many cognitive delays & behavioral issues, he is on the Autism Spectrum and struggles w/ daily living.

The Dr. Ross the pediatrician that coerced me into vaccinating my child up until very recently wouldn't even look me in the eye. Nor did he report to VAERS the seizure activity that commenced two days after vaccinating my son. Another physician did who quit working at Kauai Med Clinic as a pediatrician for reasons he wouldn't disclose, he reported it!

How many unreported adverse reactions have gone unidentified at Kauai Medical Clinic? Statistically reactions from low grade fever which is now what docs deem normal all the way to deaths go unreported. CDC does not have true statistics across the nation that is fact.

Dr. Ross of Kauai Med. Clinic years ago was interning w/another pediatrician there who **did report** an adverse reaction to a vaccine. That very pediatrician was let go a month later and that was 25 years ago. I know the MO of these doctors on this small island.

I OPPOSE ANY ADDING OR MANDATING OF MORE VACCINES ON AN ALREADY OVERLOADED & DANGEROUS CHILDHOOD VACCINE SCHEDULE!

I OPPOSE ON THE BASIS THAT WE ARE PERFECTLY MADE IN GOD'S IMAGE TO NOT PUT CONTAMINATES INTO OUR BODIES.

I OPPOSE ON THE BASIS OF HUMAN RIGHTS, DO NOT USE THE DOE SYSTEM TO BULLY PARENTS INTO NOT HAVING CHOICE ABOUT VACCINATION.

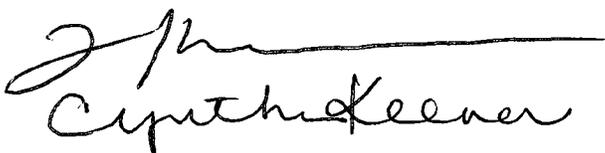
I AM PROCHOICE!

I OPPOSE on the basis that there is a full awareness by federal government & the medical industry that there IS a Vaccine Injury Court set in place for those who are injured and die due to vaccines that aren't properly safety tested.

The American Association of Pediatrics recommends that a newborn infant receive the Hep B right after birth because it's an opportune time (PBS) but the FDA states that a two month old infant should only have 25 micrograms of aluminum and no more than that BUT AT BIRTH A NEWBORN GETS IN THE HEP B VACCINE 250 micrograms.

How is this logical?

WHERE THERE IS RISK THERE MUST BE CHOICE!



Cynthia Keener

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]
Subject: Written Testimony Opposing HAR 11-157
Date: Tuesday, December 18, 2018 7:20:26 PM

Richelle Paoli
Written Testimony Opposing HAR 11-157
To Be Presented at Hearing in [REDACTED] on
12.20.2018

To Whom It May Concern at the Department of Health:

Thank you for providing the opportunity to provide written and oral testimony. I hope that this testimony reaches the proper parties and that you will thoughtfully consider the public opinion and the voices of the parents as you make decisions on this crucial issue which affects our children and our future so greatly. I am a mother of four and a Registered Nurse. I currently hold active license in two states. We have lived in [REDACTED] for three years. I was employed at the Kona Community Hospital Emergency Room until leaving to have my son last year.

First, I think it is imperative to always keep in mind that we all share the same goals here, and that is to make the safest, healthiest choices for our youth. That being the case, it is only natural that this topic would become an extremely sensitive and heated one as we hold conflicting opinions of how to reach these goals. The desire to protect our children is innate and we will do so at all costs. This also makes us liable to make irresponsible choices in the face of blatant and pervasive misinformation(1). My personal and professional experience and deep research to find the truth has led me to the sad realization that the people are being systematically lied to.

This is happening in ways that are not only morally wrong, but also definitively illegal. This is evidenced by our healthcare providers' failure to provide true informed consent (as required by the HI revised Statutes 671-3)(2). Patients are receiving false information as well as important information being omitted when it comes to vaccines. We are assured that vaccines are 'safe and effective,' that we need them, that the diseases they protect against are dangerous and deadly, and that if we don't vaccinate we will compromise 'herd immunity' and endanger others. I have found these all to be lies. In fact, a patient who should be able to trust their doctor to guide them in such choices is not really given any express choice in the matter at all, these procedures are performed as a matter of course, and anyone who has educated themselves and objects will be subjected to intense ridicule, discrimination, and guilt and shame tactics in attempt to pressure the patient into compliance. The negative term "anti-vaxxers" and their demonization by faulting them for any disease outbreak by the media is evidence of this. So is the decision of many doctors to exclude patients from their practice who refuse vaccinations (which can be attributable to financial incentives for practices with high vaccination compliance rates).

Of course, if vaccines are really the answer to protecting public health, then aren't these actions justified? I am sure that medical professionals and individuals alike are convinced that this is so, and are only doing what they think is best and right. But we can NEVER neglect to examine the facts and the interests that are controlling the public thought. As you will remember, there have been many claims made by the medical community which were later found to be false and dangerous (tobacco was claimed to be safe, and Thalidomide, Fenfluramine, Baycol, and DES were just a few drugs recalled due to devastating side effects). If vaccines are indeed the great advancement that many believe, wouldn't we all be lining up? Why is force necessary? Why are the people objecting? Many would love to chock this up to frenzy created by fraudulent scientists, Russian trolls spreading discord, and misinformed parents. But when the pharmaceutical companies are the second most profitable industry in the world, with vaccines being their most profitable sector, it would be NEGLIGENT TO OVERLOOK how this affects public information and therefore decision making. Corporate interest owns 90% or more of the news media, and has crept into

our university systems, which train our medical professionals, and publish most of our research(3). Medical doctors receive an average of 2 hours TOTAL education on diet THROUGHOUT their education, yet diet is the foundation of health. The medical community credits vaccines with eliminating Polio and smallpox. I urge you all to do your own research into the history of vaccines, so that you can see that most vaccine programs were in fact initiated AFTER the diseases which they take all credit for eradicating were on the decline due to other interventions(4).

When a health professional tells you that vaccines are "proven safe and effective," and that "the science is settled," while he or she may indeed believe this to be the case, the fact is, it is not. Anyone who understands science understands that science is theory which should always be open to further questioning and testing, and which can be "proven" and disproven again and again. To place all faith in specific "science" and to simply stop questioning is to take on a more religious stance, which is dangerous and negligent in matters involving human rights and the public health. In order to provide TRULY informed consent, the medical professional should review with the patient the informational insert that comes with the vaccine. The fact is, most medical professionals have never seen this insert, parents certainly never see them, and are instead given a biased handout with very limited information(5). The fact is, no vaccine is or can be proven completely safe, and their components have not been tested for safety. ZERO studies on long term health effects have been conducted, and very few studies involving completely unvaccinated controls have been performed, due to ethical reservations. Many researchers can testify to the difficulty in getting their work published when it does not agree with the mainstream model, and many have been discredited, slandered, and lost their practice when they simply QUESTIONED the safety and efficacy of vaccines. This should concern us all to the core.

The severity and frequency of vaccine injury is simply not disclosed to parents. Much of the reason for this is that the statistics are completely unknown. This is due to the fact that (according to the FDA) only 1% of adverse events associated with vaccines end up reported to VAERS (the Vaccine Adverse Event Reporting System). The reason for this is that most doctors are not even aware of the system's existence, while others refuse to use it due to their training. So it follows that most parents have no way of knowing about VAERS. (It is important to note here that VAERS and the Vaccine Court were developed as a result of the 1986 National Childhood Vaccine Injury Act (NCVIA), which was passed after vaccine companies threatened to remove DTP from the market after being inundated with lawsuits involving death and serious injury due to the vaccine. This act then removed liability from the vaccine companies, with the government assuming responsibility instead. Meaning the companies that produce the vaccines have ZERO liability when their products hurt people, a concept unheard of in the pharmaceutical industry. Out of the cases that are reported to VAERS, very few of those meet the criteria to be heard in vaccine court, which according to parents that have been through the entire process, is a biased and cruel system, not one built to support the bereaving family. However, 3.9 billion dollars has been paid out to vaccine injured families since the court's establishment.) This is all information NOT disclosed to parents. Wouldn't you want to know this pertinent information before making an INFORMED decision?

Parents are instead routinely told that vaccines are 'safe and effective'. This open letter to the WHO(6) adequately sums up many of the safety concerns of the global community, which the medical community has thus far failed to address. As a nurse and a concerned citizen, I have personally spoken with many parents who have witnessed firsthand some of the devastating effects of vaccines. None of the many parents I have spoken with in the community had doctors who even believed their stories, let alone being reported to VAERS because they were unaware of its existence. Just start asking around, and you will see for yourself. Why aren't these parents' voices being heard? Why aren't their children being counted? Why would the DOH blanket adopt recommendations from the Advisory Committee on Immunization Practices (ACIP), an organization which we have all seen has no regard for the completely rational and justified public outcry against mandatory vaccination practice? To do so is to ignore and dismiss the call for justice by the people.

In response to safety concerns, many are responding with the idea that although it carries some risk, the benefit of mass compulsory vaccination outweighs the risk, both for the individual and the community. This is based on the assumption that vaccines are effective, and the ignorance of the benefits of natural wild type immunity. Thankfully, some independent researchers are continuing to put out non-biased information, which can still (for now) be found, although it requires significant effort and the general

population will not find it. We now know that some vaccines are never effective from the beginning in low-responders (Obukhanych, 2012(7)), which there is currently no way to determine if you or your child will be. Most other vaccines have efficacy that wanes over time, with few lasting beyond ten years, which is one reason more and more keep being added to the schedule. At what point will we say, enough is enough? We are requiring our children to get vaccines which we don't have. And claiming that if they don't, they endanger the herd. What about us?

On the concept of herd immunity (a term coined by Hedrich in the 1930s pertaining to natural immunity in measles which has since been redefined by the medical community to apply to vaccines based on the assumption that they provide immunity akin to the wild-type), the medical community and media continues to blame "anti-vaxxers" whenever there is an outbreak of a vaccine preventable disease, hyper-focusing on these 16 vaccine preventable diseases because they feed into the sensationalism. They paint previously common and rarely complicated childhood diseases as life-threatening and terrifying (measles, mumps, rubella, varicella). The medical community continues to up the percent of vaccinated people we must attain in order to achieve this version of vaccine acquired "herd immunity". The problem is, this is an illusion. Even in countries with 95-99% vaccination compliance (Quebec, Canada and China) measles outbreaks still occur because even vaccinated people can contract and carry measles(7), as we have seen. This is because even in high responders, vaccine induced antibodies wane over time. Whereas natural exposure created the lifelong immunity which up until 1989 (when second dose MMR was added to the schedule) doctors were taught that one dose of MMR would provide. We can vaccinate everyone, and there will still be measles. Other facts of concern on measles/MMR:

-55% of Americans are out of compliance with today's schedule, with most born before 1985 having only 1 dose of MMR. Yet our kids will be required to have 3? What about all the adults?

-Efficacy wanes quickly. By age 20, only 13% have measles antibodies after 2 doses and the second dose gives only a 6 month titer bump(7)

-Mass vaccination efforts have pushed measles into more vulnerable populations (young infants and older adults) where it does more damage. Pre-vaccine, it was a common childhood illness with rare complications (see old cartoons and media), most commonly affecting children aged 1-15 years who handle the disease much better and then acquire lifelong immunity which mothers would pass to their breastfed infants (protecting them in this vulnerable stage). Mass vaccination has eliminated this maternal immunity, resulting in the the vulnerability of young infants to the disease(7)

-Mumps was also a routine childhood disease with rare complications seen. Mumps vaccine induced immunity is also quickly waning, as evidenced by outbreaks in fully vaccinated 15 year olds

-Rubella, a disease so often mild that half of people did not realize they were infected, was reportedly eliminated from the US in 2004. The WHO reports that Rubella vaccine induced protection does not last past 15 years

-Many parents have witnessed their children regress into autism (and other neurological and behavioral disorders) before their very eyes after receiving their MMR. Their experiences and concerns are currently being defiantly ignored by the mainstream medical community, whose stance continues to be, definitively, "vaccines do not cause autism." Despite the fact that many studies have indeed pointed to a link(8,9).

Another vaccine which is being proposed as mandatory by the HAR 11-157 legislation is Gardasil, or the HPV vaccine. The concerns surrounding this vaccine are abundant and extremely serious. First of all, this is another vaccine most adults do not have and are not required to receive. It protects against SOME specific strains of HPV indicated in cervical cancer (a disease which takes 10-20 years to develop and is fully preventable by others means such as routine pap smears). The vaccine contains both aluminum and polysorbate 80, neither of which have been adequately tested for human safety, and which the medical community will insist are safe because the levels are minuscule compared to safely INGESTED levels, a route of ingestion which allows the body to respond in a completely different way. The vaccine's convoluted safety trials, fast-tracking despite zero threat of dangerous outbreak, and intentionally excluded side effects (including causing ovarian failure and infertility in young teen girls, seizures,

depression, and death) have left 300 girls around the world dead, and caused 46,000 very serious reactions in others(10). All that in the name of possibly protecting a much smaller number of girls from cervical cancers that could have been prevented by other safer means. According to Peter Gotzsche, MD and head of the Cochrane Institute in Copenhagen, Denmark, "the general public is not receiving honest information (about Gardasil)."10

-Cervical cancer one of the rarest and most preventable cancers

-Studies DO NOT support the claim that the vaccine has lowered cancer rates

-The Japanese government now refuses to recommend or pay for Gardasil due to its devastating side effects

-Yet despite all this, you want to mandate it for our young children?

When it comes to Flu vaccine, a recently published study (Yan, 2018(11)) funded by the CDC showed that contagious mist was 6.3 times more prevalent in individuals vaccinated for the flu in both the current and previous years than in unvaccinated individuals. Meaning that these vaccinated persons were actually MORE contagious and more likely to spread flu virus to others. Vaccinated individuals get sick with the flu and die, like 6 year old Emma Splan from Connecticut just this month. Reports of injury from flu vaccine are commonplace. There are zero laws in place which prevent kids or adults with active infectious diseases from attending school. Yet we want to legally mandate our kids get shots that their teachers don't even have to get?

These are just a few of the reservations and concerns which NEED to be addressed. It is wholly unreasonable to mandate that our children receive these vaccines WITHOUT even providing complete, true and accurate disclosure to us as parents. Where there is risk, there must be a choice, as with any other medical procedure. Isn't that reasonable? Many parents are not even aware that they have a choice, they don't know about exemptions, they cannot homeschool their kids, and they are simply not being told the truth in order to make an INFORMED decision. We the parents are the ones who must make the decisions we feel are best for our babies, and we and our kids are the ones who have to live with the consequences of those choices. Not government, not DOH, not CDC and not ACIP. Our keiki are not healthy. That much is CLEAR. Chronic childhood illness has skyrocketed and continues to rise. It is obvious that what we ARE doing is NOT working. Time to take a new approach, one that removes corporate dollars from the equation, because that is the ONLY way we can remove conflict of interest and TRULY put the health of our people FIRST. It is UNETHICAL to force children and families to undergo a procedure when there are so many unanswered questions, so much financial interest swaying the truth, and SO MUCH AT STAKE.

Thank You,

Richelle Paoli, RN

Feel free to contact me with further questions:

[REDACTED]

References

1 Vaccines and Other Conditions, Vaccine Education Center. Children's Hospital of Philadelphia. Retrieved From <https://www.chop.edu/centers-programs/vaccine-education-center/vaccines-and-other-conditions>

2 Hawaii Revised Statutes 671-3, Informed Consent Law. Retrieved From https://www.capitol.hawaii.gov/hrscurrent/Vol13_Ch0601-0676/HRS0671/HRS_0671-0003.htm

3 Ioannidis, John P.A. (2005). Why Most Published Research Findings are False. PLoS Med. Retrieved From [Why Most Published Research Findings Are False](#)

4 Humphries, Suzanne MD and Bystrianykn, Roman. (2013). Dissolving Illusions: Disease, Vaccines, and the Forgotten History. CreateSpace Independent Publishing Platform.

5 CDC. (2018).Vaccine information Handout, MMR. Retrieved From [Vaccine Information Statements -](#)

[VISs - CDC information sheets for patients](#) versus: FDA. Package Insert, MMR. Retrieved From <https://www.fda.gov/downloads/BiologicsBloodVaccines/UCM123789.pdf>

6 Open Letter to the WHO from International Organisations on the Issue of Vaccine Safety. (2018). Retrieved From https://www.efvv.eu/open-letter-to-the-who-from-international-organisations/?fbclid=IwAR3_rXU-SiDuGW3aPzZfSfbSc0FURVabRJRXwiTa8zH6gyxxtRcQOu3y1u4

7 Obukhanych, Tetyana. (2012). Vaccine Illusion: How Vaccination Compromises Our Natural Immunity and What We Can Do To Regain Our Health [E-Reader Version].

8 157 Research Papers Supporting the Vaccine/Autism Link. Retrieved From [157 Research Papers Supporting the Vaccine/Autism Link | Autism Spectrum | Autism](#)

9 CDC's Own Data Support Link Between MMR Vaccine and Autism. (2018). Retrieved From [CDC's Own Data Support Link Between MMR Vaccine and Autism](#)

10 The Alliance for Natural Health. (2018). Manufactured Crisis. Retrieved From <https://vimeo.com/277078546/7812e25bb1?fbclid=IwAR04VKK4yKdfyGW43bnVWyLYAIKZKhtzNNW9C9gCQiGVgj0LHJUMVtukBk>

11 Yan, Jing, multiple others. (2018). Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. PNAS. Retrieved From [Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community](#)

Martina Dodson

Lanai 117K-11-157
Hearing.

12/18/18

Aloha my name is Martina Dodson, I am a citizen of United States, live on Maui and I also am a health freedom advocate. Me and my family strongly oppose HAR-11-157.

I almost died from a vaccine. Injury and death is not rare as some people might think. CDC claims one in a million doses. Add that up and its many serious events including death, paralysis, seizure, swelling of the brain etc. What kind of real statistic is that?

If these rule changes goes through HI will be the most vaccinated state in the U.S. we also will know WHO TO HOLD RESPONSIBLE FOR THE DEATH AND INJURY THAT WILL happen to Hawaii's keiki. We might not be able to hold them accountable by law for the tragic events that will occur.

BUT MY WORDS HERE IN THIS TESTIMONY, WE WILL GO BACK TO AND LET EVERY SINGLE PERSON IN THIS STATE KNOW, WHO THE CORRUPT PEOPLE ARE THAT SET THIS FORTH IN THE PUBLICS EYES, AND WE WILL HOLD THE PERSONS SUCH AS ROZ BAKER, BRUCE ANDERSON AND DR SARAH PARK AND EVERYONE ELSE INVLOVED ACCOUNTABLE FORT HE ENOURMOUS CATHASTROPICH DISASTER to mandate and vaccinate all Hawaii's keiki with the proven dangerous HPV vaccine.

The evidence are overwhelming of the danger of this particular vaccine. If it would have been a regular medication on the market it would have been recalled by now. But because it is labeled a vaccine the can madate this poison. Only 3 states have this mandated for school it is called medical tyranny. Over 400 deaths have been reported and over 59,000 adverse events to VAERS. Keep in mind FDA admits only 1 to 10% even gets reported.

I urge you to look at proposed rule change. It is a sneaky way to take away parents rights and parents choice. Especially when they want to mandate vaccines for diseases that do not spread in school enviroment.

Where is the medical justification for 74 doses vaccines before the age of 18. 4 billion has been paid out for injury and death from vaccine court. You cant simply call it science when a vaccine maker have full legal immunity from damage claims. 1986 NCVIA was created and the vaccine schedule tripled. Coincidence?

1 in 40 children with autism. I watched my friends perfectly healthy twin boys go infora multidose vaccine appointment. Directly after both permanently braininjured laater diagnosed with autism. The annual cost for autism is \$268 billion and is expected to be \$1 trillion 2025. These growing costs now fall on families and on tax payers through the cost borne by local school districts, states and medicaid.

53 % of American children with auto immune disorders

Cancer is the leading cause of death in children

U.S has the highest infant mortality rate in a developing country. Also the most vaccinated.

IT CAN ALL BE TRACED BACK TO THE INSANE KIDS SCHEDULE THAT HAS NEVER BEEN TESTED FOR SAFETY IN COMBINED DOSES. NEITHER HAS ANY VACCINE EVER BEEN EVALUATED FOR THE ABILITY TO CREATE CANCER, CAUSING GENE MUTATION NOR THE IMAIRMENT OF FERTILITY. STATES IN 13.1 IN EVERY SINGLE VACCINE INSERT.

Children's Health Defense



From the desk of Robert F. Kennedy, Jr., Chairman
Children's Health Defense

The Honorable Richard Pan
State Capitol
Room 5114
1303 Tenth Street
Sacramento, CA 95814-4900

October 12, 2018

Dear Senator Pan:

I encourage you to read the enclosed book, *How to End the Autism Epidemic*. It provides a complete and accurate account of how vaccine manufacturers and the Centers for Disease Control have worked together to hide an epidemic of autism caused by giving too many vaccines to American children without any regard for the vulnerable subset of children who are at grave risk from vaccine reactions.

I want you to know that just a few weeks ago, I petitioned the Inspector General of the Department of Justice and both Congressional Judiciary Committees to investigate two key Justice Department lawyers' actions during the 2009 "Vaccine Court" Omnibus Autism Proceedings (OAP). Systematic acts of fraud by these two officials caused the OAP to deny compensation to over 5000 families whose children developed autism as the result of vaccination. I provided the Inspector General and Congress with evidence that HHS and two DOJ officials lied to the court, the victim's families and the public to conceal the fact that the government's lead expert had informed them that vaccines could, in fact, cause autism in some children. In order to hide his opinion, the DOJ hurriedly dismissed their expert from providing oral testimony in the OAP. But that was just the start of the cover up. This is a complex story involving intentionally malicious acts, and Chapter 6 of the enclosed book does an excellent job of laying out the entire series of events.

Since this miscarriage of justice, roughly one million children have been diagnosed with autism. According to parents, a significant number of these cases resulted from vaccine injuries. As of 2015, the projected annual cost for autism was \$268 billion and is expected to reach \$1 trillion by 2025. These growing costs now fall on families and on taxpayers through the costs borne by local school districts, states and Medicaid.

Vaccine manufacturers and the CDC have worked hand-in-hand to create a bloated vaccine schedule never properly tested for real side-effects. Every state is now facing skyrocketing special education costs and dramatic increases in chronic health problems amongst its children. I hope you will share this information at once with your State's Attorney General to investigate this matter more fully. We can and must protect our children's health. Please do not hesitate to contact me for more information:

.. @childrenshealthdefense.org

Yours Sincerely,

Robert F. Kennedy, Jr., Chairman
Children's Health Defense

VACCINES DOSES for U.S. CHILDREN

1962

1983

2018

TOTAL DOSES: 5

TOTAL DOSES: 24

TOTAL DOSES: 72

Polio
Smallpox
DTP

DTP (2 months)
OPV (2 months)
DTP (4 months)
OPV (4 months)
DTP (6 months)
MMR (15 months)
DTP (18 months)
OPV (18 months)
DTP (4 years)
OPV (4 years)
Td (15 years)

Influenza (pregnancy)
DTaP (pregnancy)
Hep B (birth)
Hep B (2 months)
Rotavirus (2 months)
DTaP (2 months)
HIB (2 months)
PCV (2 months)
IPV (2 months)
Rotavirus (4 months)
DTaP (4 months)
HIB (4 months)
PCV (4 months)
IPV (4 months)
Hep B (6 months)
Rotavirus (6 months)
DTaP (6 months)
HIB (6 months)
PCV (6 months)
IPV (6 months)
Influenza (6 months)
Influenza (7 months)
HIB (12 months)
PCV (12 months)
MMR (12 months)
Varicella (12 months)
Hep A (12 months)
DTaP (18 months)

Influenza (18 months)
Hep A (18 months)
Influenza (30 months)
Influenza (42 months)
DTaP (4 years)
IPV (4 years)
MMR (4 years)
Varicella (4 years)
Influenza (5 years)
Influenza (6 years)
Influenza (7 years)
Influenza (8 years)
Influenza (9 years)
HPV (9 years)
Influenza (10 years)
HPV (10 years)
Influenza (11 years)
HPV (11 years)
DTaP (12 years)
Influenza (12 years)
Meningococcal (12 years)
Influenza (13 years)
Influenza (14 years)
Influenza (15 years)
Influenza (16 years)
Meningococcal (16 years)
Influenza (17 years)
Influenza (18 years)

*In 1986, pharmaceutical companies producing vaccines were given full federal protection from lawsuits resulting from vaccine injury or death via the Childhood Vaccine Injury Act passed by Congress. If vaccines are so safe, why did they need a law to protect from liability?

After this law, vaccines became HIGHLY profitable. There are almost 300 vaccines in development, and mandatory vaccine laws for children — and ADULTS — being pushed in most states.

The US gives 2-3x more vaccines to children than most developed countries, yet we have skyrocketing rates of childhood issues that are NOT seen in other countries. Things like asthma, childhood diabetes, food allergies, childhood leukemia, developmental delays, tics, ADHD, autism, lupus, arthritis, eczema, epilepsy, Alzheimers, brain damage, etc... It's NOT a coincidence.

Vaccines contain toxic chemicals that do NOT belong in our bodies, such as aluminum (known to cause brain and developmental damage even in small doses), polysorbate 80, MSG and formaldehyde (known to cause cancer in humans).

**LEARN
THE
RISK[®]**

Knowledge • Action • Health

Know the Facts

Mercury in Flu Vaccines

- The Food and Drug Administration (FDA) warns pregnant women and young children not to eat fish containing high levels of methylmercury. Yet the Centers for Disease Control and Prevention (CDC) recommends pregnant women and infants get influenza vaccines, many of which contain mercury from the preservative thimerosal.
- According to Environmental Protection Agency (EPA) guidelines one would have to weigh 550 lbs to safely process the 25mcg of mercury in a flu vaccine. Mercury is known to be highly toxic to brain tissue and can impact critical stages of brain development in a fetus in utero, an infant or a child.
- In 2004, the Environmental Protection Agency (EPA) estimated that one in every six women has mercury blood levels that could pose a risk to an unborn child. Two studies in 2012 showed that a mother's mercury exposure is linked to attention problems in her children.
- Scientific studies have documented that mercury rapidly crosses the placenta and accumulates in the fetus at higher levels than in the mother. Ethyl mercury used in vaccines resulted in more than double the amount of mercury deposited into primate infant brains than equal amounts of ingested methylmercury.
- In 2001, the prestigious Institute of Medicine recommended that pregnant women, infants and children NOT receive vaccines preserved with mercury but the CDC Advisory Committee that makes vaccine recommendations chose not to follow their advice.
- It is inconsistent and dangerous to recommend vaccines containing ethylmercury when also counseling pregnant women to avoid seafood high in methylmercury due to the known harmful effects mercury can have on the developing fetus.
- Thimerosal-containing flu vaccines contain 250 times the mercury level the EPA uses to classify hazardous waste. Unused thimerosal-containing flu vaccine should be returned to the manufacturer for appropriate disposal.

For complete references, please visit our website at www.childrenshealthdefense.org/flufacts

OUR MISSION about us



Children's Health Defense

Mission

Our mission is to end the childhood health epidemics by working aggressively to eliminate harmful exposures, hold those responsible accountable, and establish safeguards so this never happens again.

How to Get Involved

Sign up for free updates at www.childrenshealthdefense.org

Become a lifelong member of Children's Health Defense for just \$10.00. Use social media to help us to get the word out regarding the childhood health epidemics and what can be done to stop them.

Support our efforts through a generous tax deductible donation

Children's Health Defense

1227 North Peachtree Pkwy, Suite 202
Peachtree City, GA 30269
Phone: 202-854-1310

Contact us to volunteer or for additional information

Follow us on Facebook and Twitter

www.facebook.com

@childrenshd



FLU VACCINES what you need to know

You want to do *everything* right for your health, you would never knowingly allow someone to inject something into you or your children that wasn't completely safe. Before getting a flu vaccine, you need to know this:

The Supreme Court ruled that vaccines are

unavoidably
UNSAFE

146741nc 00006n

Know the Facts: Flu Vaccines During Pregnancy

According to influenza vaccine package inserts, "Available data on influenza vaccines administered to pregnant women are insufficient to inform vaccine-associated risks in pregnant women."

A 2017 CDC study links miscarriage to flu vaccines, particularly in the first trimester. Pregnant women vaccinated in the 2010/2011 and 2011/2012 flu seasons had two times greater odds of having a miscarriage within 28 days of receiving the vaccine. In women who had received the H1N1 vaccine in the previous flu season, the odds of having a miscarriage within 28 days were 7.7 times greater than in women who did not receive a flu shot during their pregnancy.

A study published in 2016 that looked at the safety of flu vaccines found a moderately elevated risk for major birth defects in infants born to women who had received a flu vaccine during the first trimester of pregnancy. A study published in 2017 found an elevated risk of autism spectrum disorders in children whose mothers had a first trimester flu shot. Flu vaccine administration is documented to cause an inflammatory response in pregnant women. Recent research found inflammation during pregnancy is associated with the development of autism spectrum disorders.

A large study in approximately 50,000 pregnant women over five flu seasons found no difference in the risk for developing influenza or similar illnesses between those who received the influenza vaccine during pregnancy and those who did not.

An independent 2014 review found no randomized controlled trials assessing vaccination in pregnant women. It states, "The only evidence available comes from observational studies with modest methodological quality. On this basis, vaccination shows very limited effects."

Know the Facts: Flu Vaccines for Infants and Children

A review in the medical journal The Lancet found a lack of health benefits from influenza vaccine in children under two along with significantly increased rates of vaccine-related adverse events.

A study that compared children who received flu vaccine to those who did not found no significant difference in the rate of influenza between the active and placebo groups. It also found that the group of children who received the flu vaccine had a 4.4 times relative risk of non-influenza respiratory tract infections.

An Australian study found one in every 110 children under the age of five had convulsions following vaccination with the FLUVAX H1N1 vaccine in 2009. Additional research found a spike in cases of narcolepsy in children associated with the H1N1 vaccine.

2018 - 2019 Flu Vaccines

Influenza vaccines — United States, 2018–19 influenza season*

Trade name Manufacturer	Presentation	Age Indication	Mercury (from thimerosal, µg/0.5 mL)
Inactivated Influenza Vaccines (IIVs) and Recombinant Influenza Vaccine (RIV4)†			
Afluria Seqirus	0.5 mL, prefilled syringe	≥5 yrs	NR
	5.0 mL, multi-dose vial	≥5 yrs (needle/syringe) 18 through 64 yrs (jet injector)	24.5
Fluzix Quadrivalent GlaxoSmithKline	0.5 mL, prefilled syringe	≥6 months	NR
FluLaval Quadrivalent ID Biomedical Corp. of Quebec	0.5 mL, prefilled syringe	≥6 months	NR
	5.0 mL, multi-dose vial	≥6 months	<25
Flucelvax Quadrivalent Seqirus (ccIV4)	0.5 mL, prefilled syringe	≥4 yrs	NR
	5.0 mL, multi-dose vial	≥4 yrs	<25
Fluzone Quadrivalent Sanofi Pasteur	0.25 mL, prefilled syringe	6 through 35 months	NR
	0.5 mL, prefilled syringe	≥3 years	NR
	0.5 mL, single-dose vial	≥3 years	NR
	5.0 mL, multi-dose vial	≥6 months	25
Trivalent IIV (IIV3s)			
Afluria Seqirus	0.5 mL, prefilled syringe	≥5 years	NR
	5.0 mL, multi-dose vial	≥5 yrs (needle/syringe) 18 through 64 yrs (jet injector)	24.5
Fluad Seqirus (aIV3)	0.5 mL, prefilled syringe	≥65 yrs	NR
Fluzone High-Dose Sanofi Pasteur (HD-IIV3)	0.5 mL, prefilled syringe	≥65 yrs	NR
Quadrivalent RIV (RIV4)			
FluBlok Quadrivalent Sanofi Pasteur	0.5 mL, prefilled syringe	≥18 years	NR
Live Attenuated Influenza Vaccine (LAIV4)			
FluMist Quadrivalent Astrazenca	0.2 prefilled intranasal sprayer	2 through 49 yrs	NR

Abbreviations: IIV=inactivated influenza vaccine; RIV=recombinant influenza vaccine; HA=hemagglutinin; LAIV=live attenuated influenza vaccine; mos=months; yrs=years.

More Vaccine Facts to Know

Every year, the Centers for Disease Control and Prevention (CDC) and pharmaceutical companies mount an aggressive campaign in the mainstream media to persuade Americans to get their flu shots. Flu shots are big business: industry analysts estimate that within the next five years, the U.S. flu vaccine market will be worth almost \$3 billion annually.

The CDC has advised the industry to hike demand through the use of a "recipe" of messaging to get your flu shot now through advertisements that include "...statements of alarm by public health authorities...prediction of dire outcomes from influenza...continued reports that influenza is causing severe illness affecting lots of people...repeated urging of influenza vaccination..." that bombard consumers.

From 2014 to 2015, the NVICP flu shot settlements increased from \$4.9 million to \$61 million—an 1100% increase. As the Vaccine Adverse Event Reporting System (VAERS), a voluntary surveillance system, is acknowledged by the government to capture as little as one percent of actual adverse events, the flu vaccine injuries and deaths are substantially underreported.

According to the CDC, over the past 14 seasons, the effectiveness of the influenza vaccine has varied from 10% to 60%.

When offered a flu vaccine

Vaccine decisions should not be made without doing your research first and deciding if the influenza virus is a significant concern for you and your family.

Be sure to find out the manufacturer and avoid vaccines from multi-dose vials that contain the preservative thimerosal.

Review the evidence regarding the effectiveness of the flu vaccine in actually preventing influenza. For information visit www.summaries.cochrane.org

Do not let yourself be pressured into receiving a vaccine that you don't want; should you choose to vaccinate, insist that your doctor or pharmacist find you a mercury-free vaccine.

Tips for Preventing the Flu

Simple techniques such as avoiding those with flu-like illnesses, eating a healthy diet and good hand washing can prevent many cases of flu. If you do contract influenza, optimizing vitamin D levels, fluid intake and rest can boost immune function.

Martina Dasun

From: [REDACTED]
To: [REDACTED]
Subject: Fwd:
Date: Tuesday, December 18, 2018 3:13:06 PM

Sent from my iPhone

Begin forwarded message:

From: Javannah Andrade [REDACTED]
Date: December 18, 2018 at 5:07:04 PM PST
To: [REDACTED]

Aloha,

I'm writing on behalf of the immunization shots bill regarding student to be vaccinated to attend schools in Hawaii. I hope you take consideration on the procedures of your actions and actually look into what you are considering. I am an Hawaiian woman and a mother of 3, who all aren't vaccinated whom also rarely ever get sick they're very active and strong smart kids whom I am trying to raise correctly. Besides the fact that all the "shoots" vaccines diseases what ever form of name of your preference is synthetic lines of diseases more than 1 in each shoot which proves that the old diseases are no longer in existence their for we are spreading synthetic lines of diseases that man created by taking the dead bodies of abortions/babies and making more filthy diseases because you need filth very dirty conditions to even catch a virus and that's how people got sick back hundreds of years ago we are way advanced with access to clean water to drink, bathe etc electric. Which already advances us to a more sustainable living. If it's hard to be clean that's proof of how lazy you want to be sorry to say. However a human is born with an immune body system that has the capacity of 100% of function to keep you healthy. Your body is strong whenever you get sick without being vaccinated your body uses the equivalent of 3-17 percent to fight off any viruses diseases cold what ever it may be. However after being vaccinated your body immune system goes weak their for needing to use more out of its 100% so instead of using the 3-17 percent per symptom it raises to 30-70 percent leaving you vulnerable to getting more sick. Ex: say you have a cold stomach ache say that was 45% out of the 30-70 however shortly after you got a sore throat so you use 50% you already are using 95% with only 5 left now your vomiting but you only have 5 percent you have nothing left leaving you sick for a longer duration of time, now you need medicines to help cause your body is to weak to fight for you. Besides all the cases on trial right now in California for this exact reasonings also all the cases that proved vaccines causes autism. Besides the fact that it's a risk of death cause it states effects if dying get to the hospital immediately why is that even an option?! Some people are okay with playing with children's lives I refuse to this is not a game and you should look at the facts before mandating such life impactful decisions on our children's future. I could go on and state more also other ingredients like inbombing fluid and other harmful chemicals however if what I said didn't scare you already than it doesn't bother

you. However at least let parents who do care to have a choice because as a parent I can't see myself volunteering my children's health because a man or woman said so the guilt would kill me knowing I would have to harm them because of someone's greed. We already were stolen given sickness now more sickness and harm when will it be enough what else will be taken from us all of us. Please take my words into consideration on your actions thank you and mahalo

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Wednesday, December 19, 2018 1:42:34 PM

Aloha,

As a concerned parent, I am writing you to let you know that I oppose HAR 11-157. Some of the vaccines listed are dangerous. The risk does not outweigh the "protection" given by said vaccines.

Gardasil, for one has been linked to the deaths of over 400 girls. 400! That is heartbreaking.

To make this a mandatory vaccine is not a smart move.

I could go on and on and provide you with much research, but I will keep this short and sweet.

Thank you for hearing me out.

Sincerely,

Laura Roberts

From: [REDACTED]
To: [REDACTED]
Subject: Informed Consent for Hawaii
Date: Wednesday, December 19, 2018 10:25:57 PM

Aloha DOH of Hawaii

Informed Consent is the only prudent choice

The following letter with references and expert council sums up my thoughts after years of research.

https://www.efvv.eu/open-letter-to-the-who-from-international-organisations/?fbclid=IwAR1cTVa_pj1Yji5W3Hf4ex3bBMI3Yu5QWSyiMbLkVuSwAGUILe3DVxCAcog

From a Mother, Moriah Smith

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Aloha/Please NO Mandatory Vaccines
Date: Wednesday, December 19, 2018 3:37:18 PM

Aloha Honorable Hawaii Department of Health,

I am writing to please request that you not continue forward with mandatory vaccinations. This would be an egregious action for you to press forward as a tool for big pHARMA by requiring this from the people and children of Hawaii. We, the people you are entrusted to serve, have resoundingly stated we do not want this, so it is styming that faced with so much data against vaccines, which you have been sent and are hearing, plus the fact that there is not really data of any long term substance to support such an action and blind support of forcing people to submit like prisoners to your will and desire because you have this power.

It is full-hearted at best or corrupt at worst to push forward with an agenda striping the Freedom of Choice and Body Sovereignty, as well as the rights of Informed Consent and it will not bode well in the long run for your Department, so I highly recommend you hear the will of the people and STOP this agenda now. You have been presented with not just impassioned pleas, but outright facts and figures proving that vaccines and their effectiveness are still not really well tested nor proven safe, especially in regards to multiple doses given at one time or in one injection.

The FDA requires far less testing of vaccines than by-mouth pharmaceuticals; hence, the proliferation of them. The timeline from concept to profit is faster, but not safer. Do you realize that in the few clinical trials even done, if a required test is five days, but the baby dies on the six day, it's not noted?

Please do not push forward with this agenda. Stay the honorable and do the right thing here, by NOT pushing forward with this Orwellian Agenda.

Thank you for considering my request.

Mahalo,

Susan Bambara
Kurtistown

From:

Subject:

Date:

[REDACTED]
[REDACTED]
Anti vaccine

Wednesday, December 19, 2018 11:19:03 PM

Aloha, sending my Anti mandatory vaccine thoughts. My family and I have a strong belief in natural healing and medicine, BUT we do reach out for a doctors help when needed OR wanted with personal preference. I think it should be the same with immunizations. It should be a want/need that the family as a unit gets to CHOOSE as a whole. - Not one that should be forced on family. We ourselves and our family's know us better than any doctor that might see us 1-4 times a year, so to think that you want to FORCE us to vaccinate when you know close to nothing about our health/living or dietary habits seems like insanity to me, also a form of abuse of authority to take away not only a basic human right to have a choice but also taking away the choice that America is supposed to give us, "freedom" right? I oppose the need for mandatory vaccinations, we should choose if that's something we want. Mahalo.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Comment about the HPV vaccine
Date: Wednesday, December 19, 2018 11:29:49 AM

Dear Sir or Madam,

I am appalled that the Hawaii Department of Health is considering mandatory vaccinations for children for the human papilloma virus. How can anyone who oversees the health of Hawaii's children seek to force a vaccination which may potential have serious side effects. Is the department so in bed with the pharmaceutical industry that it is ignoring safety issues?

While U.S. citizens are prohibited from suing vaccine manufacturers, lawsuits have been launched in Japan, France, Ireland, Spain, and Columbia claiming HPV vaccine harm.

It is beyond question that some children are permanently disabled or die from their vaccine exposures. A broad spectrum of suspected and confirmed adverse vaccine events has grown in the decades from the beginning of mass vaccination. (U.S. Dep't of Health Res. & Human Servs. Admin., National Vaccine Injury Compensation Program Monthly Statistics Report (2017)).

In the U.S. the NVICP has paid affected families approximately \$3.7 billion since it began taking claims in 1989.
<http://law.emory.edu/elj/content/volume-67/issue-3/articles/liability-vaccine-injury-united-european-world.html>.

The Vigibase database of the World Health Organization has compiled more than 86,000 serious adverse event reports for Merck's HPV vaccine. They include nervous system disorders (39,092), respiratory, thoracic and mediastinal disorders (6060), vascular disorders (5766), nervous system disorders (39,092), reproductive system and breast disorders (3267), cardiac disorders (2604), and blood and lymphatic system disorders (2035). <http://www.vigiaccess.org/>

Among 12 - 17 year olds, 45,000 adverse events have been reported.

The number of AE's reported for HPV vaccines, in each country, are overwhelmingly higher than that for other vaccines. But national health authorities and medical professionals continue to deny any causal relationship between HPV vaccines and AE's.

Under the Freedom of Information Act, in 2013 Judicial Watch received documents from the Department of Health and Human Services (HHS) revealing that its National Vaccine Injury Compensation Program has awarded more than \$5 million to 49 victims in claims made against the HPV vaccine. <https://www.judicialwatch.org/press-room/press-releases/hpv-vaccine-injuries-and-deaths-is-the-government-compensating/>

Judicial Watch also received documents, under the Freedom of Information Act, from the U.S. Food and Drug Administration (FDA) detailing reports of adverse reactions to Gardasil. The adverse reaction reports detail 26 deaths reported between September 1, 2010

and September 15, 2011 as well as incidents of seizures, paralysis, blindness, pancreatitis, speech problems, short term memory loss and Guillain-Barré Syndrome.

The conservative watchdog points out, “Merck has waged an aggressive lobbying campaign with state governments to mandate this HPV vaccine for young girls.”

It’s fascinating that Dr. Julie Gerberding, who approved Gardasil when she was director of the C.D.C., was subsequently hired by Merck in 2010 as president of Merck Vaccines. In 2015 she made more than \$2 million selling Merck shares.

https://en.wikipedia.org/wiki/Julie_Gerberding

While the CDC and international government bodies promote the vaccine’s safety, there is compelling evidence that Merck conducted shoddy, questionable clinical trials; and that a number of individuals around the world have suffered drastic health consequences post vaccination.

According to a 2015 Atlantic magazine article, Merck’s top selling vaccine is Gardasil, which brings in \$1.7 billion in sales. With such massive sales is it any wonder any attempts to raise safety issues are routinely dismissed, contrary to evidence.

<https://www.theatlantic.com/business/archive/2015/02/vaccines-are-profitable-so-what/385214/>

There is widespread concern about adverse effects caused by the Gardasil vaccination. They include paralysis, narcolepsy, respiratory dysfunction, cognitive impairment, involuntary movements, blood clots, and a rapid heartbeat.

A 2016 Canadian study looked at over 195,000 girls who had received HPV vaccines. Within forty-two days of HPV vaccination, the girls experienced over 20,000 emergency room visits or hospitalizations. But only 198 adverse events were reported. Liu XC, Bell CA, Simmonds KA, Svenson LW, Russell ML. Adverse events following HPV vaccination, Alberta 2006–2014. *Vaccine* 2016;34(15):1800-1805.

In 2012 Canadian researchers looked at whether or not some serious autoimmune and neurological ADRs followed HPV vaccinations are causal or merely coincidental. They analyzed post-mortem brain tissue specimens from two young women who suffered from cerebral vasculitistype symptoms following vaccination with Gardasil. They conceded “our study suggests that HPV vaccines containing HPV-16L1 antigens pose an inherent risk for triggering potentially fatal autoimmune vasculopathies.”

“The fact that many of the symptoms reported to vaccine safety surveillance databases following HPV vaccination are indicative of cerebral vasculitis, but are unrecognized as such (i.e., intense persistent migraines, syncope, seizures, tremors and tingling, myalgia, locomotor abnormalities, psychotic symptoms and cognitive deficits), is a serious concern.”

“It thus appears that in some cases vaccination may be the triggering factor of fatal autoimmune/neurological events.”

<https://www.omicsonline.org/open-access/death-after-quadrivalent-human-papillomavirus-hpv-vaccination-causal->

or-coincidental-2167-7689.S12-001.php?aid=9036

The basis for HPV vaccination is its ability to prevent precancerous lesions related to HPV type 16 and 18 infections and the idea that preventing those lesions would prevent cervical cancer. According to University of Louisville researcher Dr. Diane Harper who led clinical trials of HPV vaccination, HPV infection can take years to result in cervical cancer. That leaves plenty of time for screening, treatment and prevention. Furthermore, 90% of HPV infections are removed from the body by its own immune system and related processes without medical or other consequences within three years. Only a tiny minority leads to cancer.

The FDA licensed Merck's vaccine as a result of trials that were just three years long.

Dr. Kelly Brogan notes: "In the marketing and licensure of the HPV vaccine, changes to cervical cells have been equated with death. This is called using a "surrogate marker" and in vaccine research, this is considered acceptable because we can't otherwise prove a non-event is attributable to an intervention. There are leaps in logic and in science inherent in this practice that render conclusions nothing more than false marketing." <https://kellybroganmd.com/new-gardasil/>

Former neurosurgeon Dr. Russell Blaylock claimed in 2013: "It has never been proven that the HPV vaccine prevents cervical cancer."

A study by researchers at the University of Texas looked at HPV vaccination data from 2007–2012. The results showed that young women 20 to 26 years of age who received the four-strain Gardasil vaccine were actually more likely than non-HPV-vaccinated women to be infected with high-risk nonvaccine strains of HPV ten years later. Guo F, Hirth JM, Berenson AB. Comparison of HPV prevalence between HPV-vaccinated and non-vaccinated young adult women (20-26 years). *Hum Vaccin Immunother* 2015;11(10):2337-2344.

A review published in 2014 in *Autoimmunity Reviews*, "On the relationship between human papilloma virus vaccine and autoimmune disease," pointed out: "Along with the introduction of the HPV vaccines, several cases of onset or exacerbations of autoimmune diseases following the vaccine shot have been reported in the literature and pharmacovigilance databases, triggering concerns about its safety."

The authors caution that, "the decision to vaccinate with HPV vaccine is a personal decision, not one that must be made for public health. HPV is not a lethal disease in 95% of the infections; and the other 5% are detectable and treatable in the precancerous stage."

<http://www.ncbi.nlm.nih.gov/pubmed/24468416>

In a July 2016 lawsuit against Gardasil's manufacture Merck, in the Superior Court of the State of California, Los Angeles County, evidence was presented questioning the safety of adjuvants in vaccines that can produce autoimmune disorders, such as the addition of aluminum salts.

<http://www.greenmedinfo.com/blog/merck-accused-fraud-deceit-and-negligence-us-gardasil-case>

“It is medically and scientifically accepted that aluminum salts are toxic to and damage the human cells at the injection site. In addition, the aluminum salts cause inflammation at the site. These aluminum salts may bind with the free DNA released from the damaged and dying cells at the injection site. The combination of the Aluminum salt bound by the human DNA is effective in activating Toll Like Receptors (“TLR”), whose function in the immune system is highly complex.”

Lawsuits internationally include one against the French manufacturer of Gardasil in 2013, where the court found 50% of the blame for a teenager’s subsequent multiple sclerosis on Gardasil. Two weeks after the first injection, she experienced sensory and motor problems in the upper limbs. Three months after the second injection she was hospitalized. <https://www.reuters.com/article/us-sanofi-lawsuit/sanofi-sued-in-france-over-gardasil-vaccine-idUSBRE9AN0FX20131124>

In Japan, an injury lawsuit in 2017 against the state and the HPV vaccine drug makers prompted the Japanese health ministry to withdraw their official recommendation for the HPV vaccination.

Twenty eight girls and women suffering what they say are side effects from cervical cancer vaccines that were recommended by the government, demanded compensation from the state and drug makers at the Tokyo District Court. <https://www.japantimes.co.jp/news/2017/02/13/national/crime-legal/suit-opens-tokyo-court-cervical-cancer-vaccine-side-effects/#.XBg7OCx7ILM>

The plaintiffs, ranging in age from 15 to 22, said they have experienced a wide range of health problems, including pain all over their bodies and impaired mobility, after receiving HPV vaccines between 2010 and 2013.

Erina Sonoda, a 20-year-old college student, reported she started to suffer strong menstrual pain after receiving the second of three recommended shots of the Cervarix vaccine, and the pain spread to other parts of her body after the third vaccination. Due to agonizing pain, Sonoda said she has difficulty walking without a cane and often must use a wheelchair.

According to the health ministry, 2,945 people out of the 3.39 million women who had received the shots by the end of April 2017 reported side effects.

In Columbia anthropological researcher Mario Lamo-Jiménez, has raised concerns about the side effects of Gardasil, and is assisting attorneys prosecuting the collective action lawsuit filed by 700 women in that country demanding some \$160 million in compensation from Merck. <https://hetq.am/en/article/84400>

She reported Columbian girls suffering from ASIA syndrome after vaccination, as well as onset of early menopause, where there is a premature ovarian failure and they become sterile, as well as Guillain Barré Syndrome.

In Ireland around 650 girls reported requiring medical intervention or treatment after receiving the HPV vaccine, according to data collected

by the State's medicines watchdog. Ireland accounts for one in five of all reports of suspected adverse reactions against Gardasil in Europe. At this time there are eight cases filed in Ireland's High Court that relate to the HPV vaccine.

At least 6 Danish women have report they developed chronic health problems during an HPV clinical trial. At Aalborg University Hospital, one of the trial sites in Denmark, Miam Donslund began to experience persistent flu-like symptoms as well as two infections, one of which required hospitalization, shortly after immunization. Stine Sørensen began to experience general discomfort, headaches, and a profound fatigue that often made her miss school after she got her first shot of Gardasil. All the women have one or more agonistic autoantibodies in their bodies.

German scientist Gerd Wallukat noted about the autoantibodies, they reveal "the classical pattern I've seen in patients after vaccination."

In Spain in 2017, the High Court of Justice of Asturias condemned the Asturian Health System for the death of Andrea, a young Spanish girl who died in September 2012 after getting the second shot of the HPV vaccine. The Court admonished the hospitals of Jove and Cabueñes, since they did not diagnose the patient's pathology before the second shot of the vaccine was supplied which caused the death of the young woman. <https://healthimpactnews.com/2017/spain-high-court-rules-hpv-vaccine-caused-death-of-young-woman/>

When she got the first shot of the HPV vaccine on July 23, 2012, the woman had a headache and breathing difficulty. Although, she suffered from severe asthmatic exacerbation, she got the second shot on August 23, 2012, and worsened. As a result she suffered severe dyspnea and seizures only 12 hours after receiving the vaccine, and died.

This year India's Ministry of Health and Family Welfare indicated that it was unlikely to include HPV vaccines in the national immunization program.

Last year an empirical study confirmed that the inability to sue vaccine manufacturers in U.S. civil courts since 1986 is associated with a decrease in vaccine safety in FDA-approved vaccines after 1986. Gayle DeLong, Is "Delitigation" Associated with a Change in Product Safety? The Case of Vaccines, Rev. Ind. Org. (June 14, 2017), <https://link.springer.com/article/10.1007/s11151-017-9579-7>.

DeLong found that vaccines licensed after 1986 are associated with approximately 5.2 more reported adverse events per 100,000 vaccine doses than the vaccines that were licensed before the passage of Vaccine Act.

A 2017 investigation by Slate revealed problems with the clinical trials for Gardasil, which was supposed to establish the vaccine's efficacy and safety before it was approved. The article raises questions about why regulators knowingly accepted the company's flawed data. <https://slate.com/health-and-science/2017/12/flaws-in-the-clinical-trials-for-gardasil-made-it-harder-to-properly-assess-safety.html>

"Interviews with five clinical trial study participants and more than

2,300 pages of documents obtained through freedom-of-information requests from hospitals and health authorities suggest inadequacies built into Merck's major clinical tests of Gardasil."

"European health regulators worried about Merck's methods during a review of the company's marketing application for Gardasil 9, the latest version of the vaccine, but have not made their concerns public. In an internal 2014 EMA report about Gardasil 9 obtained through a freedom-of-information request, senior experts called the company's approach "unconventional and suboptimal" and said it left some "uncertainty" about the safety results.

"If I were a research subject, I would feel betrayed," said Trudo Lemmens, a bioethicist and professor of health law and policy at the University of Toronto.

It's worth remembering that former Merck virologists Stephen A. Krahling and Joan A. Wlochowski, filed a lawsuit against Merck in 2010. The scientists alleged that the efficacy tests for the measles, mumps, rubella vaccine (MMR) were faked. They claimed that over the years the effectiveness of the mumps vaccine declined. In 2014 a federal judge rejected Merck's motion to dismiss. The lawsuit is still active with the court ruling class certification is due by 2/15/2019.
<http://ahrp.org/former-merck-scientists-sue-merck-alleging-mmr-vaccine-efficacy-fraud/>

Slate reported when Dr. Rebecca Chandler, at Läkemedelsverket, the Swedish Medical Products Agency began analyzing Merck's safety data for Gardasil 9, three girls vaccinated with Gardasil 9 had been diagnosed with POTS (postural orthostatic tachycardia syndrome), and one with CRPS (Complex regional pain syndrome). There were also several cases of neurological disorders. But none of them had been reported by the company as adverse events.

The suspicion that postural orthostatic tachycardia syndrome is related to the HPV vaccine comes from a 2015 study by Danish researchers who provided some observational evidence about POTS occurrence after HPV vaccines. The authors stated that they "found a close chronologic association to the vaccination. The study found that the average number of days between vaccination and diagnosing POTS was around 11 days.

POTS normally occurs in approximately 1% of adolescents.

The Norwegian press has reported on the case of a 12 years old Norwegian girl, Maria Lysaker Wenersberg, who received the HPV vaccine at school. In April 2015 she was diagnosed with Postural Orthostatic Tachycardia Syndrome which is suspected to be a serious side effect from the vaccine. Most of the time she is now bedridden. Sometimes she faints daily. She has not been able to attend school for the past four and a half years. She has to be pushed in a wheelchair from her bed into the living room.
<http://www.vg.no/nyheter/innenriks/maria-18-har-vaert-alvorlig-syk-i-fem-aar/a/23517356/>

In May 2016, Professor Peter C. Gøtzsche and Cochran Nordic Deputy Director Karsten Juhl Jørgensen, along with others, filed an official complaint about how the European Medicines Agency (EMA) handled the HPV safety issue.

In Australia in 2014 two doctors published in the Journal of Investigative Medicine a case study of a series of teens who had entered premature menopause after vaccination - a phenomenon Dr. Little and Dr. Ward described as ordinarily “so rare as to be also unknown.”

They noted – “Long-term follow-up data after HPV vaccination has not surveyed ovarian function, recorded, measured, or analyzed symptoms or signs of dysfunction. Principles of informed consent, population health, and vaccine confidence require careful, rigorous and independent research to establish ovarian safety following HPV vaccination.”

In a public forum Dr. Little spoke about the poor quality of research being performed on HPV vaccines. She noted a September 2018 article published in Paediatrics which found that women in the USA who received Gardasil were no more likely than those who did not receive Gardasil to have premature ovarian insufficiency meaning that their ovaries were no longer functioning. Little suggest the effect of HPV vaccines on the female ovary needs further study.

The American College of Pediatricians in 2016 released a health warning about the HPV vaccine – “It has recently come to the attention of the College that one of the recommended vaccines could possibly be associated with the very rare but serious condition of premature ovarian failure (POF), also known as premature menopause.”

In January 2016, pathologist Dr. Sin Hang Lee, MD, Director of Milford Medical Laboratory, sent an open letter of complaint to the Director-General of the World Health Organization (WHO), Dr. Margaret Chan, in which he challenged the integrity of the GACVS (Global Advisory Committee on Vaccine Safety) Statement on the Continued Safety of HPV Vaccination.

He wrote: “A series of emails recently uncovered via a Freedom of Information request submitted in New Zealand revealed evidence that Dr. Robert Pless, the chairperson of the Global Advisory Committee on Vaccine Safety (GACVS), Dr. Nabae Koji of the Ministry of Health of Japan, Dr. Melinda Wharton of the CDC, Dr. Helen Petousis-Harris of Auckland University, New Zealand, and others may have been actively involved in a scheme to deliberately mislead the Japanese Expert Inquiry on human papillomavirus (HPV) vaccine safety.”
<https://sanevax.org/wp-content/uploads/2016/01/Allegations-of-Scientific-Misconduct-by-GACVS.pdf>

Dr. Lee found that every one of the 13 Gardasil samples that he examined contained HPV L1 gene DNA fragments. He also found that the HPV DNA fragments were not only bound to Merck’s proprietary aluminum adjuvant but also adopted a non-B conformation, thereby creating a new chemical compound of unknown toxicity.

This non-B conformation, Dr. Lee believes, is responsible for the array of autoimmune illnesses experienced by children and young women following vaccination with Gardasil.

In 2012, he testified at a coroner’s inquest of the death of a New Zealand teenager, 6 months after receiving 3 Gardasil vaccine injections.

During the inquest neuroscientist Professor Christopher Shaw of the University of Columbia in Vancouver told the New Zealand inquest that he was sent the teenager's brain tissue to test. He said there was aluminum in all the samples he tested and there were some abnormalities in the samples. The human papillomavirus (HPV16) was found in her brain, which could have only got there through the vaccine, Prof Shaw said. He said there was a "biological plausibility" that vaccine likely caused her death. He could not say conclusively that was the cause of her death.

Finally, a new study, published in the Journal of Toxicology and Environmental Health, suggests a link between the HPV vaccine and declining fertility. It examined the childbearing capacity of women who received the HPV vaccine – compared to those who didn't, and discovered an alarming correlation. Approximately 60% of women who did not receive the HPV vaccine had been pregnant at least once compared to 35% of women who had had an HPV shot had ever conceived. For married women, 75% who did not receive the shot were found to have conceived, while only 50% who received the vaccine had ever been pregnant.

Considering all this relevant information I would hope that that the Department of Health in all good conscience would not try to force the HPV vaccine on Hawaii's children, when it is known that harm might occur in those more susceptible to injury.

Any decision to vaccinate or not to vaccinate against the sexually transmitted HPV virus is a private medical matter, and definitely not the responsibility of the state.

Jon Woodhouse, M.Ed.





The Senate

STATE CAPITOL
HONOLULU, HAWAII 96813

December 19, 2018

immunization@doh.hawaii.gov

To: Hawaii Department of Health
Hawaii Immunization Program

From: Senator Russell E. Ruderman

Re: Comments on increasing vaccination schedule and reducing opportunities to opt out

These are additional comments from me, not a repeat of my previous comments. After learning that the neighbor island public meetings would lack the decision makers, I write once again with my concerns. Thank you for reading.

You may be surprised to learn that I don't wear a tinfoil hat, or believe the earth is flat. I have a degree in science and view the world scientifically. What you are doing here is not only not 'science,' it is the opposite of true science. Allow me to explain.

A few years ago, against my better judgement, my wife and I got 'flu' shots at the doctor's office. I rarely get them and my wife never had done so. Over the next 2 days, my wife became sick with the first 'flu' of her life! We reported the reaction to our doctor, who did two things:

He pronounced it a coincidence;

He did not record the reaction or report it in any way.

Many others have had similar experiences, so this is not unique or unusual.

Now I ask you as scientists, 'how can you evaluate the rates of adverse reactions if the medical community has a policy of dismissing such, and chooses not to report or track them?' Seriously, how do you justify your conclusions of safety when as a matter of policy the medical community does not track reactions and is discouraged from doing so?

I repeat, this is the opposite of science. Rather it is a coordinated campaign to minimize the awareness of adverse reactions; that is, to hide the truth.

One more personal experience informs my views. I requested a delayed schedule of vaccines for my infant baby in 2016. For the next two weeks, I received at my unlisted home number, a series of over ten phone calls claiming to be from CDC requesting a survey of my opinions on vaccinations. These were live voices, not a robocall. They continued despite my choosing not to return the calls. The tenth such call was at 10:00 PM on a Saturday at my home, calling from a Washington DC number; it would be 4 AM in DC if this is legitimate.

Is this a reasonable thing to expect based on my conversation with my doctor? Or is this an outrageous intrusion into my life, a form of intimidation by our government, and an obscene device by the pharmaceutical industry, in obvious collusion with the CDC.

Did my pediatrician call the CDC to report my 'concerns' because they are compelled to do so? It is a violation of my privacy rights and a red flag for those concerned about vaccines.

By proposing more compulsory vaccines, you are an extension of this outrage. Your obligation is not to this over-reaching industry, it is to the people of Hawaii.

I don't use the word 'outrage' lightly. It is an outrage to me that you propose to compel further injections. Thousands of people feel as I do; most cannot attend your public meetings, or have lost faith that their input matters. If your vaccines are scientifically supported, then educational campaigns and doctors can convince people to take them. We must not lose any more freedoms to this travesty.

Among modern (sometimes called 'industrialized') countries, the U.S. has by far the largest number of 'suggested' vaccines for babies and children. We also have the highest cost of health care among such countries.

Yet, the U.S. is virtually the only such country whose life expectancy is declining, rather than growing.

The U.S. has the worst infant mortality among such countries.

Our health care delivery system has been judged the worst among these countries, while the profits derived from it are the largest.

Can you explain this scientifically? It certainly appears we have something to learn, and that our model, so influenced by large corporations, may be less than scientific after all.

Do the other modern countries use less vaccines because they are less 'scientific?' Or is the multi-billion dollar profit-driven pharmaceutical industry, which is strongest in the U.S., the big difference here?

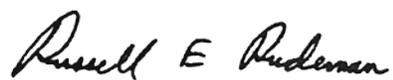
Proposing to increase required vaccines to the highest number in our most-vaccinated nation is irresponsible. I hold you, the decision makers at Department of Health, personally responsible for this outrage. No one is making you do this, yet you proceed in the face of public opposition and lack of safety studies.

Do you have safety studies that analyze the adjuvants as well as the active ingredients? Do you have safety studies that use a true placebo, like in any legitimate scientific study? Do you have studies showing the unprecedented combinations of vaccines, and their adjuvants, are safe in combination and in total?

You do not have any such studies proving the safety of what you propose to compel.

Most medical decisions are, and should be, between a person and his/her medical provider. Yet you propose to interfere with that relationship by compelling more vaccines every year, something virtually no other country does.

The ungodly reach of the pharma industry is using you as a marketing tool. You must find the integrity and strength to oppose this. Forced injections of any kind call to mind the 'experiments' of the Nazi government in the past. No, this is not hyperbole; this is what you are doing to innocent, healthy people. Forced injections that include known toxins, such as the heavy metals in the euphemistically named 'adjuvants' in most vaccines, are even more offensive to those of us who value the American ideal of freedom.



Russell E. Ruderman, Senator
Hawaii State Senate



From: [REDACTED]
To: [REDACTED]
Subject: Immunization
Date: Thursday, December 20, 2018 7:12:32 AM

"When there is risk there must be choice."

Whose facts: vaccines.

We were neither created nor have we evolved to require forced injections for survival. It is a complete human construct for profits and control.

When and if you decide to get a vaccination ask the physician, practitioner, facility owner, vaccine maker or anyone involved to give to you THE unequivocal acceptance of liability for the harm it MAY do to you or your loved one. Additionally, be sure to get your official GUARANTEE of effectiveness.

I assure you that these documents do not and will never exist. While I have empathy for the parents of the child/children who is/are too ill for a vaccination I want to know which of them will assure me or anyone that I/we are not vulnerable to harm from the vaccination serum! There is no such assurance to cause no harm.

Furthermore, if you have such a strong belief in the vaccination then you are protected and in that world of thinking I am the one at risk so why aren't you feeling secure?

Then, humans are born defective and each of us has an (unknown) expiration date. While you may temporarily be saved you can know it is only temporary because infinite is for the gods, legends and hope.

Finally, humans are devolving due to the progressive effects of malnutrition, dehydration and pollution. Survival of the fittest does not mean progressively stronger, just the strongest of the weak. Wake up and see the signs all around you.

John Begg
[REDACTED]

[Sent from Yahoo Mail on Android](#)

From: [REDACTED]
To: [REDACTED]
Subject: Just wanted to ad one more comment
Date: Thursday, December 20, 2018 12:27:53 PM

It also might make sense from a scientific perspective to have a certain percentage of the population (if it is voluntary) that do not receive the mass ordered injections. In this way if an error was made in the vaccine and it caused harmful side effects with long term health, it makes scientific sense to have a percentage of the population that is not at risk of this....so that problems...those who "opted out" could help care for those who were permanently injured by the vaccine.

People do get injured by Vaccines....The documented risks are clearly stated in the insert, the fact that the companies are not liable for damages, and that there is a secret vaccine injury claim court is also very disturbing and concerning.

Finally, even though I personally am not opposed to all Vaccines, I think it is very important to respect other people's beliefs....especially if statistically they tend to be more educated and wealthy. I could understand if the demographics of people opposed to something were a large mass of uneducated people that had been persuaded by some type of fanatical leader ... then I think the experts in power should try to stop them. However, if the people opposed to something are a small minority of concerned citizens, who tend to be highly educated and more financially successful.... it does make basic sense that their point of view should be heard.

That is the case with the anti vaxing debate... my wife has an IQ of over 150 and she is opposed to it.... many other people much smarter than I am who have researched it are opposed to mandatory vaccines as well.

Personally, I am opposed to mandatory vaccines..., unless it is a species wide health emergency, where the entire human race could be at risk....and even then....quarantine areas should be set up for people who choose to "opt out"and all the facts should be clearly presented.

Thank you

David Marshall

[REDACTED] Resident

From: [REDACTED]
To: [REDACTED]
Subject: Oppose mandatory vaccinations
Date: Thursday, December 20, 2018 12:02:10 AM

As a medical provider I am obligated to always look out for the best interests of my patients and I have sworn to do no harm. While medical school stressed the importance of maintaining CDC guidelines I have since come to realize that this may not be the best option for the safety of our children (or our adults). I have seen too many instances of symptoms occurring directly after vaccinations to be able to write them off as all coincidences. Also, simply by comparing the standard patient handouts with the insert of vaccines it is blatantly apparent how sugar-coated the business of vaccines is- and that is exactly what it is... business. While doing my own research as both a doctor and a mother I continue to be amazed not only at the continued increase in the amount of vaccines recommended but also the fact that there is the thought that a company or a practitioner can be objective when there is financial gain involved. While I am not anti-vaccine I am anti-unsafe vaccine practices, of which I feel there are many in this country. I am also very opposed to having people forced to have ANYTHING done to their body without their permission or desire to have it done. When corporations and doctors stand to make large amounts of money off any practice there needs to be far more third party intervention. Furthermore, making vaccines mandatory will simply make many concerned parents find alternatives, such as the number of families that have moved here to escape this same situation in California or those who would feel forced to homeschool their children at the detriment of their professional career. Our medical system continues to have increasing profits while our quality of healthcare continues to decline. This should tell us something. This decision should be between an individual and their physician and both the pros and cons of each vaccination should be discussed as a separate issue, since the risk and benefit ratio is going to be different for each one depending on the person and their particular situation. I have seen parents who chose to vaccinate and regretted it. I have seen parents who chose not to vaccinate and regretted it. There is no right choice but it should be the parent's choice to make- they will always put their child above all else. We should be focusing on things like making sure individuals have adequate vitamin D levels, which have been shown to significantly decrease the risk of contracting viral infections, including the flu. Perhaps if health is truly our goal we should worry less about forced procedures and more about the lack of fresh food in the diets of most children.

I strongly urge you to oppose mandatory vaccinations.

Aloha,

Dr Sarah Strong, ND



Become a fan for recipes and more!

 [Facebook](#)

From: [REDACTED]
To: [REDACTED]
Subject: Public Comment @ Mandatory Vaccinations
Date: Thursday, December 30, 2018 12:46:01 PM

One more point I wanted to add....It would seem wise from a scientific perspective to have a certain percentage of the population (if they volunteered for this)that if a mandatory injection was ordereda certain percentage could "opt out" and not receive the injection In this way if an error was made in the vaccine and it caused harmful side effects and injury (which has happened).. it makes scientific sense to have a percentage of the population that is not at risk of this....so those who "opted out" could help care for those who were permanently injured by the vaccine.

People do get injured by Vaccines....The documented risks are clearly stated in the insert, the fact that the companies are not liable for damages, and that there is a secret vaccine injury claim court is also very disturbing and concerning.

Finally, even though I personally am not opposed to all Vaccines, I think it is very important to respect other peoples beliefs....especially if statistically they tend to be more educated and wealthy. I could understand if the demographics of people opposed to something were a large mass of uneducated people that had been persuaded by some type of fanatical leader ... then I think the experts in power should try to stop them. However, if the people opposed to something are a small minority of concerned citizens, who tend to be highly educated and more financially successful.... it does make basic sense that their point of view should be heard.

That appears to be the case with the anti vaxing debate... my wife has an IQ of over 150 and she is opposed to it.... many other people much smarter than I am who have researched it are opposed to mandatory vaccines as well.

Thank you



Reply Forward

From: [REDACTED]
To: [REDACTED]
Subject: Public email Comment on increasing compulsory vaccine schedule
Date: Thursday, December 20, 2018 11:57:54 AM

I have been a resident of Hawaii for over 20 years and have grown adult and school age children. I am not against the concept of vaccines and have received many myself, but I am against compulsory vaccines and removing religious exemptions. I strongly feel that mandating medical procedures that have documented very serious risks (and also go against people's religious belief system) is a violation of decency, common sense, and the core values that the USA was founded upon.

According to most research, people opposed to mandatory vaccines tend to be more wealthy and highly educated. This is something that should be carefully considered. When people research this issue for themselves they tend to find that the benefits of many vaccines (for non life threatening diseases) do not outweigh the risks. Also, they often learn about the terrible documented corruption that sadly exists in the Pharmaceutical Industry.

Though I do appreciate the good that the pharmaceutical industry does and I usually am very positive about most things and do not like to be overly critical, there are many documented instances of terrible corruption and incompetence in the pharmaceutical and healthcare industries. I urge you to look at all the data. There is a big difference between peer reviewed science and industry funded science and propaganda. Sadly humans are often corrupted by greed and money. The amount of money that is earned through the Vaccine industry alone is estimated at 30 billion per year.

I'm very thankful for our healthcare system and I have many friends who are doctors who are good decent folks. They themselves are victimized by the corruption that has occurred when you have a "for profit" healthcare system. They are truly hoping reforms and more safe guards can be put in place so that the profit motive does not go above caring about people's health.

In many instances the death rate from side effects of the vaccines are greater than the death rate from the disease itself. (research meningitis vaccine) It doesn't make any sense, unless someone is financially benefiting from these vaccines....then it makes sense, but is very much morally wrong and unethical.

I also feel it is important to provide religious exemptions. For some people being injected with anything (especially small amounts of material from aborted fetuses) goes against their core moral religious beliefs. Religious freedom is a cornerstone of our country. Also, sometimes religious beliefs have unintended benefits. In the early 20th century many religious groups were opposed to seeing doctors....and at this time mercury pills were a preferred treatment for many ailments. We now know those religious people were in many instances helping themselves tremendously by not going to doctors and avoiding the terrible effects of injecting mercury.

I hope someone who is making a decision on this issue has taken the time to read this. If you have, thank you. Please consider these arguments and carefully look at other arguments people have made. I know people get very emotional about this subject, for obvious reasons. Being mandated to violate your religious beliefs and put your child at risk of death or serious illness (due to possible documented side effects) in order to attend school is very serious.

Even though we have problems in our healthcare system, Hawaii still has one of the best healthcare services in the country. Lets hope we can keep it this way and make it even better. Lets respect each individuals rights and belief systems. Mandating questionable healthcare practices that have documented serious risksor go against peoples religious beliefs.... is very disrespectful to individuals citizens.... goes against the Hawaiian concept of ALOHA... and has many serious moral and ethical implications...especially when there is a very large profit motive in place.

Wishing you the best,

David Marshall





Renee J
DuFault

Commissioned Corps Award Confirmation

CDR DUFAULT, RENEE J.

With Public Health Service Serial Number: **63672**

has been approved to receive the

The Outstanding Service Medal

In Recognition of: Provide technical assistance & training locally & internationally for containment of infectious disease in hospitals.

For the Period: 12/01 to 12/02

by Surgeon General of the PHS on 05/09/2003

5-16-03
RJS
jsh/usa

Martha J. Boss and Dennis W. Day
URS Corporation, Omaha, Nebraska, USA

This handbook discusses biological risk engineering, an extension of industrial hygiene that involves the assessment, control, and decontamination of indoor biological risks. The book synergizes the knowledge of experts in various fields, from law to toxicology, to provide a compendium of information for applying science to limit biological risk.

Biological Risk Engineering Handbook: Infection Control and Decontamination begins with a microbiological dictionary, using pictures to illustrate the basic morphology and culture appearance of fungi, bacteria, viruses and prions. The text then reviews sampling and laboratory procedures to ensure coordination between sampling teams and their ultimate receiving laboratory. The contributing authors further examine interpretation issues associated with toxicological studies and risk assessment in hopes of providing further impetus for synergistic studies related to risk assessment and management of biohazardous agents. Other topics include ventilation design, infection control, and the use of biocides. The discussion of Legionella control and cooling towers serves as a case study of how design, maintenance, and decontamination should be a seamless process. The contributors also discuss patent utility requirements, insurance processes, laws, and current regulations, including a chapter on Tuberculosis that compares OSHA and CDC guidelines. Finally, security is addressed from the standpoint of both homeland security in the United States and the security of individual laboratories.

From assessment methods to design options, **Biological Risk Engineering Handbook** presents state-of-the-art techniques and practices to measure, control, and contain human exposure to biological contaminants. With the concern of biological risk on the rise and the emerging fear today of biological warfare, this handbook allows you to move into the future armed with the information needed to limit this threat.

*see reverse for other titles of interest
and ordering information*

Catalog no. L1606, November 2002, 624 pp.
ISBN: 1-5667-0606-8, \$149.95 / £105.00



LEWIS PUBLISHERS
A CRC Company

- ◆ Presents bio-risk control measures from the experts actually making these decisions in the field
- ◆ Discusses both the assessment and identification of biological risks and the design and engineering solutions available to remedy these risks
- ◆ Presents monitoring, sampling, and analysis methods and techniques for risk determination
- ◆ Addresses liability issues as well as regulations and industry standards
- ◆ Contains over 200 illustrations to show both laboratory and real-world scenarios, including an 8-page color "pull out" section

*Micro Dictionary, Dennis Day, Martha Boss,
Jerry King, and Melanie Karst*

*Industrial Hygiene Sampling, Dennis Day,
Martha Boss, and Chris Wrenn*

*Biological Sampling and Lab Interpretation,
Vincent Miller and Martha Boss*

*Toxicology, Richard Pleus and
Heriberto Robles*

*Risk Assessment, Harriet Amman,
Vincent Miller and Richard Pleus*

Ventilation System, Martha Boss and Dennis Day
*Maintenance, Martha Boss, Dennis Day, and
Marwan Bader*

*General Infection Control, Renee Dufault,
Martha Boss, and Ed Rau*

*Medical Setting Infection Control, Renee Dufault,
Rita Smith, and Martha Boss*

*Decontamination and Assessment, Brian Wight
and Martha Boss*

*Legionella and Cooling Towers, Martha Boss and
Dennis Day*

Biocides, Martha Boss and Dennis Day

*Laws and Regulations, Jim Hollingshead and
Martha Boss*

Tuberculosis, Martha Boss and Dennis Day

Security, Martha Boss and Dennis Day

Contents

CHAPTER 1	
Micro Dictionary	1
Dennis W. Day, Martha J. Boss, Jerry King, and Melanie Karst	
CHAPTER 2	
Industrial Hygiene Sampling	39
Dennis W. Day, Martha J. Boss, R. Vincent Miller, and Chris Wrenn	
CHAPTER 3	
Biological Sampling and Lab Interpretation	71
R. Vincent Miller and Martha J. Boss	
CHAPTER 4	
Toxicology	97
Richard C. Pleus, Harriet M. Ammann, R. Vincent Miller, and Heriberto Robles	
CHAPTER 5	
Risk Assessment	111
Harriet M. Ammann, R. Vincent Miller, Heriberto Robles, and Richard C. Pleus	
CHAPTER 6	
Ventilation Systems	135
Martha J. Boss and Dennis W. Day	
CHAPTER 7	
Maintenance	157
Martha J. Boss, Dennis W. Day, and Marwan Bader	
CHAPTER 8	
General Infection Control	183
Renee Dufault, Martha J. Boss, and Edward Rau	
CHAPTER 9	
Medical Setting Infection Control	221
Renee Dufault, Rita Smith, and Martha J. Boss	
CHAPTER 10	
Decontamination and Assessment	239
Brian Wight and Martha J. Boss	
CHAPTER 11	
<i>Legionella</i> and Cooling Towers	267
Martha J. Boss and Dennis W. Day	
CHAPTER 12	
Biocides	307
Martha J. Boss and Dennis W. Day	

December 20, 2018

Testimony by Dr. Renee Joy Dufault, Retired Public Health Service Officer, Former FDA Employee (9 years). Currently serve as volunteer Executive Director, Food Ingredient and Health Research Institute, and teach fulltime at Ka'u High School (Special Education)

Qualifications:

Recipient of Surgeon General's Outstanding Service Medal Award in Recognition of Providing Technical Assistance and Training Locally and Internationally for the Containment of Infectious Disease in Hospitals (05/09/2003)

Lead Author of two chapters in highly cited Biological Risk Engineering Handbook: Infection Control and Decontamination – Chapter Titles include "General Infection Control" and "Medical Setting Infection Control."

Served as Environmental Health Officer, Public Health Service, 1993-2008 Last tour of duty U.S. Food and Drug Administration 9 years

Served as Navy Industrial Hygiene Officer 1991-1993, Camp LeJeune Naval Hospital

Served as Medical Laboratory Specialist in the U.S. Army 1976-1980

Thank you for your kind attention as I provide my testimony against most of the proposed changes in the immunization schedule. I've put together this brochure to explain why most of the proposed changes are not needed: Please follow along. First we'll review the statistics and disease facts.

Current Hawai'i County Statistics

Hep B

Hep A

Diphtheria

Measles

Rubella

Pertussis – Mandatory vaccination recommended before children enter pre-school.

Mumps – Mandatory single dose vaccination recommended before children enter pre-school.
(Not part of MMR)

Tetanus

HPV

HPV – This is a sexually transmitted disease. Sexually active children should certainly be offered this vaccine. This should not be a mandatory vaccine, however because its effectiveness in the human population remains unknown. Human papilloma virus cases are not tracked by Hawai'i or the CDC for that matter. There is no way to even measure the HPV vaccine's effectiveness in the U.S. population!

So agencies are recommending a vaccine for which we have no accountability in terms of its effectiveness? Why? How is this logical? This is what we call a **RED FLAG**.

Red Flag

We need to dig deeper. Where is the justification for recommending the HPV vaccine? HPV is only one of several risk factors for cervical cancer. Furthermore, many, many, people with HPV do not develop cancer. In order to understand why we need to pay attention to this red flag we must ask where this nonsensical push to vaccinate is coming from.

Where is this push to vaccinate every child coming from? Private industry (Big Pharma and others) and non-profits that fund the World Health Organization. For example the Gates Foundation is the biggest funder of the World Health Organization through GAVI Alliance (WHO, Voluntary Contributions 2017, https://www.who.int/about/finances-accountability/reports/A71_INF2-en.pdf) The Gates Foundation has collaborated with pharmaceutical companies for many years to push worldwide vaccination. It recently started its own pharmaceutical company. (Forbes, 2018, <https://www.forbes.com/sites/matthewherper/2018/06/07/bill-and-melinda-gates-start-a-nonprofit-biotech-in-boston/#44d498251a45>) Although they are saying that the new company is going to be a non-profit, the partnerships with for profit companies guarantee there will be a profit motive working somewhere. We cannot believe for a minute that there is no profit motive. This is America!! We have a free market economy where profit is more important than even child health.

In addition to opposing the mandatory requirement for the HPV vaccine, I am in opposition to making the following vaccinations mandatory for the reasons specified in the attached brochure: Hep B, Hep A, Diphtheria, Measles, Rubella, Tetanus. Children need to receive vaccinations according to their individual needs when there is a true risk. Hopefully, you can see the real risk of disease is so low for most of these mandated vaccines. I suspect our children have a higher risk of developing diabetes or heart disease from all of the allowable mercury, lead, arsenic and pesticide residues in our food supply. All you have to do is analyze the death statistics in the U.S. to determine where we need to focus our efforts to promote child health. We need to be wary of corporate interests in making public health policies here in Hawai'i.

Having worked at the FDA for nine years of my Public Health Service career, I can tell you the FDA does not have our back when it comes to mitigating the harm to public health that arises from corporate profit interests. I had to retire early and honorably to publish my findings of

mercury in high fructose corn syrup. This finding has been published along with several follow up articles. We now know there is a link between the allowable inorganic mercury in the food supply and several western disease conditions including Type-2 diabetes and autism. (See list of publications at end of testimony).

If you want to improve child health outcomes and reduce the prevalence of diseases impacting the lives of children and their families (autism, ADHD, type-2 diabetes, hypertension, and heart disease), you might want to focus on mandating the placement of warning labels on foods allowed to contain ingredients with detectable and allowable levels of lead, mercury, and arsenic. Warning labels have been associated with lower autism and ADHD prevalence in the United Kingdom. As a teacher, I assure you our classrooms would function better with less child hyperactivity and inattention.

Conclusion

See attached brochure. The only two vaccines currently needed here on Hawai'i Island are pertussis and mumps. These vaccines are justifiable based on the number of cases in the last ten years and the real risk to child health.

Default Publications

See brochure for recent articles. Notable articles and books not listed in the brochure are:

1. Dufault, R. (2017). ***Unsafe At Any Meal: What the FDA Does Not Want You to Know About the Foods You Eat***. Garden City, NY: Square One Publishing
2. Dufault et al. (2012). **A macroepigenetic to identify factors responsible for the autism epidemic in the United States**. *Clinical Epigenetics*, 4:6.
<http://www.biomedcentral.com/content/pdf/1868-7083-4-6.pdf>
3. Dufault et al. (2010, October 29). **The clean label push: what does it all mean?** *Food Manufacturing Journal*. <https://www.foodmanufacturing.com/article/2010/10/clean-label-push-what-does-it-all-mean>
4. Dufault et al. (2009). **Mercury exposure, nutritional deficiencies and metabolic disruptions may affect learning in children**. *Behavioral and Brain Functions*, 5:44.
<http://www.behavioralandbrainfunctions.com/content/5/1/44>
5. Dufault et al. (2009). **Mercury from chlor-alkali plants: measured concentrations in food product sugar**. *Environmental Health*, 8:2. <http://www.ehjournal.net/content/8/1/2>



Commissioned Corps Award Confirmation

CDR DUFAULT, RENEE J.

With Public Health Service Serial Number: **63672**

has been approved to receive the

The Outstanding Service Medal

In Recognition of: Provide technical assistance & training locally & internationally for containment of infectious disease in hospitals.

For the Period: 12/01 to 12/02

by Surgeon General of the PHS on 05/09/2003

5-16-03
PJS
JSP/1128

Martha J. Boss and Dennis W. Day
URS Corporation, Omaha, Nebraska, USA

This handbook discusses biological risk engineering, an extension of industrial hygiene that involves the assessment, control, and decontamination of indoor biological risks. The book synergizes the knowledge of experts in various fields, from law to toxicology, to provide a compendium of information for applying science to limit biological risk.

Biological Risk Engineering Handbook: Infection Control and Decontamination begins with a microbiological dictionary, using pictures to illustrate the basic morphology and culture appearance of fungi, bacteria, viruses and prions. The text then reviews sampling and laboratory procedures to ensure coordination between sampling teams and their ultimate receiving laboratory. The contributing authors further examine interpretation issues associated with toxicological studies and risk assessment in hopes of providing further impetus for synergistic studies related to risk assessment and management of biohazardous agents. Other topics include ventilation design, infection control, and the use of biocides. The discussion of Legionella control and cooling towers serves as a case study of how design, maintenance, and decontamination should be a seamless process. The contributors also discuss patent utility requirements, insurance processes, laws, and current regulations, including a chapter on Tuberculosis that compares OSHA and CDC guidelines. Finally, security is addressed from the standpoint of both homeland security in the United States and the security of individual laboratories.

From assessment methods to design options, **Biological Risk Engineering Handbook** presents state-of-the-art techniques and practices to measure, control, and contain human exposure to biological contaminants. With the concern of biological risk on the rise and the emerging fear today of biological warfare, this handbook allows you to move into the future armed with the information needed to limit this threat.

*see reverse for other titles of interest
and ordering information*

Catalog no. L1606, November 2002, 624 pp.
ISBN: 1-5667-0606-8, \$149.95 / £105.00



LEWIS PUBLISHERS
A CRC Company

- ◆ Presents bio-risk control measures from the experts actually making these decisions in the field
- ◆ Discusses both the assessment and identification of biological risks and the design and engineering solutions available to remedy these risks
- ◆ Presents monitoring, sampling, and analysis methods and techniques for risk determination
- ◆ Addresses liability issues as well as regulations and industry standards
- ◆ Contains over 200 illustrations to show both laboratory and real-world scenarios, including an 8-page color "pull out" section

Micro Dictionary, *Dennis Day, Martha Boss, Jerry King, and Melanie Karst*
Industrial Hygiene Sampling, *Dennis Day, Martha Boss, and Chris Wrenn*
Biological Sampling and Lab Interpretation, *Vincent Miller and Martha Boss*
Toxicology, *Richard Pleus and Heriberto Robles*
Risk Assessment, *Harriet Amman, Vincent Miller and Richard Pleus*
Ventilation System, *Martha Boss and Dennis Day*
Maintenance, *Martha Boss, Dennis Day, and Marwan Bader*
General Infection Control, *Renee Dufault, Martha Boss, and Ed Rau*
Medical Setting Infection Control, *Renee Dufault, Rita Smith, and Martha Boss*
Decontamination and Assessment, *Brian Wight and Martha Boss*
Legionella and Cooling Towers, *Martha Boss and Dennis Day*
Biocides, *Martha Boss and Dennis Day*
Laws and Regulations, *Jim Hollingshead and Martha Boss*
Tuberculosis, *Martha Boss and Dennis Day*
Security, *Martha Boss and Dennis Day*

Contents

CHAPTER 1	
Micro Dictionary	1
Dennis W. Day, Martha J. Boss, Jerry King, and Melanie Karst	
CHAPTER 2	
Industrial Hygiene Sampling	39
Dennis W. Day, Martha J. Boss, R. Vincent Miller, and Chris Wrenn	
CHAPTER 3	
Biological Sampling and Lab Interpretation	71
R. Vincent Miller and Martha J. Boss	
CHAPTER 4	
Toxicology	97
Richard C. Pleus, Harriet M. Ammann, R. Vincent Miller, and Heriberto Robles	
CHAPTER 5	
Risk Assessment	111
Harriet M. Ammann, R. Vincent Miller, Heriberto Robles, and Richard C. Pleus	
CHAPTER 6	
Ventilation Systems	135
Martha J. Boss and Dennis W. Day	
CHAPTER 7	
Maintenance	157
Martha J. Boss, Dennis W. Day, and Marwan Bader	
CHAPTER 8	
General Infection Control	183
Renee Dufault, Martha J. Boss, and Edward Rau	
CHAPTER 9	
Medical Setting Infection Control	221
Renee Dufault, Rita Smith, and Martha J. Boss	
CHAPTER 10	
Decontamination and Assessment	239
Brian Wight and Martha J. Boss	
CHAPTER 11	
<i>Legionella</i> and Cooling Towers	267
Martha J. Boss and Dennis W. Day	
CHAPTER 12	
Biocides	307
Martha J. Boss and Dennis W. Day	

December 20, 2018

Testimony by Dr. Renee Joy Dufault, Retired Public Health Service Officer, Former FDA Employee (9 years). Currently serve as volunteer Executive Director, Food Ingredient and Health Research Institute, and teach fulltime at Ka'u High School (Special Education)

Qualifications:

Recipient of Surgeon General's Outstanding Service Medal Award in Recognition of Providing Technical Assistance and Training Locally and Internationally for the Containment of Infectious Disease in Hospitals (05/09/2003)

Lead Author of two chapters in highly cited Biological Risk Engineering Handbook: Infection Control and Decontamination – Chapter Titles include "General Infection Control" and "Medical Setting Infection Control."

Served as Environmental Health Officer, Public Health Service, 1993-2008 Last tour of duty U.S. Food and Drug Administration 9 years

Served as Navy Industrial Hygiene Officer 1991-1993, Camp LeJeune Naval Hospital

Served as Medical Laboratory Specialist in the U.S. Army 1976-1980

Thank you for your kind attention as I provide my testimony against most of the proposed changes in the immunization schedule. I've put together this brochure to explain why most of the proposed changes are not needed: Please follow along. First we'll review the statistics and disease facts.

Current Hawai'i County Statistics

Hep B

Hep A

Diphtheria

Measles

Rubella

Pertussis – Mandatory vaccination recommended before children enter pre-school.

Mumps – Mandatory single dose vaccination recommended before children enter pre-school.
(Not part of MMR)

Tetanus

HPV

HPV – This is a sexually transmitted disease. Sexually active children should certainly be offered this vaccine. This should not be a mandatory vaccine, however because its effectiveness in the human population remains unknown. Human papilloma virus cases are not tracked by Hawai'i or the CDC for that matter. There is no way to even measure the HPV vaccine's effectiveness in the U.S. population!

So agencies are recommending a vaccine for which we have no accountability in terms of its effectiveness? Why? How is this logical? This is what we call a **RED FLAG**.

Red Flag

We need to dig deeper. Where is the justification for recommending the HPV vaccine? HPV is only one of several risk factors for cervical cancer. Furthermore, many, many, people with HPV do not develop cancer. In order to understand why we need to pay attention to this red flag we must ask where this nonsensical push to vaccinate is coming from.

Where is this push to vaccinate every child coming from? Private industry (Big Pharma and others) and non-profits that fund the World Health Organization. For example the Gates Foundation is the biggest funder of the World Health Organization through GAVI Alliance (WHO, Voluntary Contributions 2017, https://www.who.int/about/finances-accountability/reports/A71_INF2-en.pdf) The Gates Foundation has collaborated with pharmaceutical companies for many years to push worldwide vaccination. It recently started its own pharmaceutical company. (Forbes, 2018, <https://www.forbes.com/sites/matthewherper/2018/06/07/bill-and-melinda-gates-start-a-nonprofit-biotech-in-boston/#44d498251a45>) Although they are saying that the new company is going to be a non-profit, the partnerships with for profit companies guarantee there will be a profit motive working somewhere. We cannot believe for a minute that there is no profit motive. This is America!! We have a free market economy where profit is more important than even child health.

In addition to opposing the mandatory requirement for the HPV vaccine, I am in opposition to making the following vaccinations mandatory for the reasons specified in the attached brochure: Hep B, Hep A, Diphtheria, Measles, Rubella, Tetanus. Children need to receive vaccinations according to their individual needs when there is a true risk. Hopefully, you can see the real risk of disease is so low for most of these mandated vaccines. I suspect our children have a higher risk of developing diabetes or heart disease from all of the allowable mercury, lead, arsenic and pesticide residues in our food supply. All you have to do is analyze the death statistics in the U.S. to determine where we need to focus our efforts to promote child health. We need to be wary of corporate interests in making public health policies here in Hawai'i.

Having worked at the FDA for nine years of my Public Health Service career, I can tell you the FDA does not have our back when it comes to mitigating the harm to public health that arises from corporate profit interests. I had to retire early and honorably to publish my findings of

mercury in high fructose corn syrup. This finding has been published along with several follow up articles. We now know there is a link between the allowable inorganic mercury in the food supply and several western disease conditions including Type-2 diabetes and autism. (See list of publications at end of testimony).

If you want to improve child health outcomes and reduce the prevalence of diseases impacting the lives of children and their families (autism, ADHD, type-2 diabetes, hypertension, and heart disease), you might want to focus on mandating the placement of warning labels on foods allowed to contain ingredients with detectable and allowable levels of lead, mercury, and arsenic. Warning labels have been associated with lower autism and ADHD prevalence in the United Kingdom. As a teacher, I assure you our classrooms would function better with less child hyperactivity and inattention.

Conclusion

See attached brochure. The only two vaccines currently needed here on Hawai'i Island are pertussis and mumps. These vaccines are justifiable based on the number of cases in the last ten years and the real risk to child health.

Default Publications

See brochure for recent articles. Notable articles and books not listed in the brochure are:

1. Dufault, R. (2017). ***Unsafe At Any Meal: What the FDA Does Not Want You to Know About the Foods You Eat.*** Garden City, NY: Square One Publishing
2. Dufault et al. (2012). **A macroepigenetic to identify factors responsible for the autism epidemic in the United States.** *Clinical Epigenetics*, 4:6.
<http://www.biomedcentral.com/content/pdf/1868-7083-4-6.pdf>
3. Dufault et al. (2010, October 29). **The clean label push: what does it all mean?** *Food Manufacturing Journal*. <https://www.foodmanufacturing.com/article/2010/10/clean-label-push-what-does-it-all-mean>
4. Dufault et al. (2009). **Mercury exposure, nutritional deficiencies and metabolic disruptions may affect learning in children.** *Behavioral and Brain Functions*, 5:44.
<http://www.behavioralandbrainfunctions.com/content/5/1/44>
5. Dufault et al. (2009). **Mercury from chlor-alkali plants: measured concentrations in food product sugar.** *Environmental Health*, 8:2. <http://www.ehjournal.net/content/8/1/2>

From:

To:

Date:

[REDACTED]
[REDACTED] HAR 11-157 proposed rules update
Thursday, December 20, 2018 10:51:08 PM

Thank you for this opportunity to provide testimony. As a community member, public health advocate, mother, and licensed psychologist (working at a community health center on the Big Island of Hawaii), I am writing to **strongly oppose the HAR 11-157 proposed rules update.**

The mandate violates a parent's right to informed consent and civil liberties: Where there is a risk of injury or death, no matter how small the perceived risk may be, there *must* be a choice. Vaccines are chemically synthesized biopharmaceuticals with known and documented side effects that include permanent injury and death. And, vaccination is an irreversible medical procedure. To mandate a medical procedure with known risks is medically unethical according to the American Medical Association's code of ethics. It is also inhumane a violation of basic human rights. I implore you to consider these critical reasons to oppose or dismiss HAR-11-157.

Moreover, while we may all be born equal, with equal rights, we are NOT all born the same. Each of us is born with different genes and a unique microbiome influenced by epigenetics that affects how we respond to the environments we live in. We do not all respond the same way to infectious diseases and we do not all respond the same way to pharmaceutical products such as vaccines. Public health laws that fail to respect biodiversity and force everyone to be treated the same are unethical and dangerous.

US ranks last for infant mortality, yet first for immunizations: Compared with other industrialized nations, the US administers the most pediatric vaccinations yet ranks the worst - 34th - for infant mortality rate. Norway, on the other hand, has the lowest mortality rate and yet there are no childhood vaccinations routinely given in the first three months of life. A 2 month old American infant, has typically been vaccinated against at least 4 diseases.

No education options for non-complying families: This bill affects *all* school-aged children registered either in public or private schools, home schools, as well as daycare and preschool facilities. The passing of HAR-11-157 combined with Hawaii's compulsory education laws leave parents with religious beliefs against or conscientious concerns about vaccinations no option other than truancy. Families with truant children will thereby face court-determined penalties such as fines, Child Welfare Services involvement, or even jail time.

Both HIPAA and FERPA laws for medical and educational privacy will become obsolete: The **HIPAA Privacy Rule** establishes national standards to protect individuals' medical records and other personal health information. The Family Educational Rights and Privacy Act of 1974 (**FERPA**) is a federal law that protects the privacy of student education records. The law applies to all schools that receive funds under an applicable program of the U.S. Department of Education. If schools are required to request and send information, including medical exemptions, to the state, either these laws are broken or parents are forced into releasing this information. As I see it, this is no different than the psychological abuse that happens when a person is in a relationship in which s/he has no power or control. Parents will face distress and feelings of helplessness if/when they no longer have the right, or control, to choose when and with whom to share private health or educational information. It will be in the state, and government's hands already. Mental health problems may result.

This is not just about vaccines. Anti-choice medical mandate laws are more than a threat to our current health and freedom. When one agrees to today's mandated vaccine schedule or medical procedure, one is also agreeing to tomorrow's vaccine schedule or medical procedure - in the name of "public health." Yet, there is not good evidence or argument on that end and I would not sign an open-ended, vague, indefinite contract where the other party is unknown and can change at any given time, where I control none of the variables but assume all financial and personal responsibility for all possible results or consequences. Would you?

Pharmaceutical companies have no-liability with vaccine reactions: The National Childhood Vaccine Injury Act of 1986 established the National Vaccine Injury Compensation Program (VICP) as a federal no-fault system to compensate persons (or families of persons) who are injured by childhood vaccines, has paid out over \$2.8 billion to families whose children have died or suffered other adverse reactions. In the past 5 years, an average of \$221,000,000 has been paid out per year, which has nearly doubled from years before. It is worth noting that recipients of compensation are not allowed to speak of their case after its been settled.

Control of our healthcare system seems to be up for grabs. I believe that the choice of if, when and how a child is to be vaccinated needs to remain between a family and their doctor. Who has the right to our lives, our health, our future (or that of your children?). Should we have consumer control of our medical system (with consumer protections) or should policy makers dictate how we care for our and our families health? Should we adhere to an evidence-based, scientific approach to medicine or let profit-motivated pharmaceutical companies, who are free from liability, control our health care options?

Finally, I want to point out that most parents who chose not to vaccinate or not to vaccinate on the government's vaccine

schedule are the very parents who have done their homework. It is the educated, middle and upper class parents who have the time and freedom and will to read, reaseach, and converse about concerning topics affecting their children. It is a media-driven misperception that parents who claim exemptions or don't vaccinate (or don't vaccinate on the CDC schedule) are uneducated or misinformed. It's quite the opposite. However, it is often difficult to speak up. Why?

In the 1970's, Dr. Mendelson warned that medical science has become a "religion" and doctors have turned the act of vaccination into "the new sacrament." In today's world, if one refuses to believe that vaccination is a moral/civic duty and dares to question vaccine safety or advocates for the right to decline one or more government recommended vaccines, s/he is in danger of being branded an anti-science heretic, a traitor, and a threat to public health. S/he will be viewed as a person who deserves to be silenced, humiliated, and punished. Is it any wonder that there are not more who are speaking out? Note that each of us who does, likely does so for 10 more who are too afraid.

In conclusion, this proposed legislation ignores and eliminates the fundamental American value of choice as well as a doctor's ethical obligation to provide their patients informed consent. If we are not free to make informed, voluntary decisions about which pharmaceutical products we are willing to take and which treatment options/medical procedures we want, then we are not free in any sense of the word. If this bill passes it will set a very dangerous precedent and there will be no limit on which individual freedoms the State can remove in the name of the greater good.

For these reasons and many more, I urge you to view this bill as inhumane and medically unethical.

Gina Reyes, Psy.D., LLC
Licensed Psychologist



The contents of this email are for the intended recipient(s). It may contain legally privileged and confidential information that is protected by law. Any unauthorized review, use, disclosure or distribution is prohibited. If you are not the intended recipient, please contact the sender by reply e-mail and destroy all copies of the original message. *E-mail is not a secure, confidential form of communication. Please keep this in mind when deciding whether to send personal information.*

Suicide prevention lifeline: 800-273- 8255

<http://suicidepreventionlifeline.org/>

Crisis Line of Hawaii: 808-832-3100

<http://health.hawaii.gov/amhd/consumer/access/>

From: [REDACTED]
To: [REDACTED]
Subject: Testimony HAR 11-157
Date: Thursday, December 20, 2018 10:10:15 PM

I strongly oppose HAR 11-157.

Mandatory vaccinations are a violation of one of the most important personal freedoms which is control of what we put in our bodies.

While some of the scientific community states an utmost trust in vaccines, my father developed pneumonia, when he was administered vaccines by the army in the 80s and a 2009 Swine Flu vaccine gave a group of NHS(uk) workers narcolepsy, alongside many other documented cases.

I do not believe people should be required to take medications which can and have failed due to neglect and lack of proper testing, which resulted in the ruining and ending of lives.

Sincerely, Noriah Tronier-Langholz.

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: written testimony
Date: Thursday, December 20, 2018 10:50:30 AM
Attachments: [Vaccine Testimony HI.docx](#)

Please find my written testimony attached as well as copied into the email below.
Mahalo!
Catherine Lightfoot Martin

**Testimony RE: Increasing number and type of Mandatory Vaccines for children
Submitted to the Hawaii Department of Health
By Catherine Martin, resident of [REDACTED]
December 20, 2018**

Aloha,

My name is Catherine Lightfoot Martin, I am a Certified Professional Midwife in East Hawaii Island.

I'd like to share a brief history of childhood vaccinations in the US:

1950's-

- 4 vaccines offered to children (diphtheria, tetanus, pertussis & smallpox).
- Children received only 5 shots by age 2 & NEVER more than 1 vaccine at a time.
- US ranked 3rd in Infant Mortality in the world (only 2 countries had Infant mortality rates better than the U.S.)

1970's-

- Increased number of vaccinations to 14 in early childhood
- CDC had to develop a way to address the growing number of adverse affects being reported (the precursor to the Vaccine Adverse Event Reporting System-VAERS)

1980's-

- Combined the Measles, Mumps and Rubella vaccines into 1 injection, called the MMR, children received this Combo shot at 15 months and again at 18 months
- US ranked 17th in Infant Mortality- whoa.

1990's

- Increased number of required vaccinations to 20 injections,
- Added vaccines for Hep B, Herpes and the flu
- Introduction of thimerosal (mercury preservative) in vaccines
- US ranked 23rd in infant mortality- getting much worse

Now-

- Have seen an increase of nearly 414% in # of vaccines being given to our children since the 1950's
- 40 shots are mandated in childhood total
- 7 of those include Combo shots (multiple vaccines in one injection)
- = 54 vaccines total!
- Americans are now required by law to use more vaccines than any other nation in the world.
- US ranked 49th in 2012 in Infant Mortality---- worse than any other developed country!

*Is this really the BEST we can do to **promote and protect the Health of our children?***

The evidence says NO.

In 1975, Japan raised its minimum vaccination age to 2 years old (meaning 0 vaccines to babies until they reach age 2)----after that the infant mortality rate in that country became the best in the world!

In 1995, Japan changed its policy to 6 injections in the 1st year and only 3 more in 2nd year.... Most children in the US today receive 20 vaccine injections in their first 2 years of life (compared to only 9 in Japan)

*Is this really the BEST we can do **to promote and protect the Health of our children?***

The evidence says NO.

More open-minded countries like the Netherlands have studies showing that eliminating childhood infections and episodes of fevers leads to INCREASED numbers of chronic diseases and cancer... that's right, the people who experienced more fevers in childhood have significantly Lower rates of cancer as adults.

*Is increasing the number and types of vaccinations for our children really the BEST we can do to **promote and protect the Health of our children, our future?***

The evidence overwhelming says NO.

Therefore I urge the Hawaii Department of Health:

- Please DO NOT increase the number or types of vaccinations for our Keiki.

And

- Please continue to offer pathways for Informed Refusal of vaccinations for conscientious objectors.

Let's help lead the way, along with other progressive nations of the world, in choosing what

Really IS Best to **promote and protect the Health of our children!**

Here are some Ideas:

- **Promote Breastfeeding-** protective antibodies are passed from mother to child in breastmilk. We must do more to encourage and support our Mothers in breastfeeding their children through age 1 and beyond for optimal Health.
- If you have a baby in the house: require friends and family to wash their hands when they come into your home. This will help Protect children from being exposed to childhood illnesses until their immune system is fully mature and able to handle it.
- Promote optimal Family Leave for working parents- We must do what we can to support Mothers and/or Fathers in staying home with their infants for as long as possible (6 months or longer) in order to protect our infants until their breastfed immune systems are more mature.

If we can do these things, then our babies (an identified at risk population) will be protected so much better than vaccinating the general population in hopes of not exposing the babies... and our children will have stronger immune systems as they grow into adulthood.

As it is now, we are trying to prevent them from getting childhood illnesses that at worst give them fevers and make them miss a couple weeks of school and in exchange we are sacrificing their long-term health and wellness (creating an immune system that is susceptible to auto-immune disorders and cancer.)

I'm not going to ask you to eliminate all vaccination schedules, I understand that may not be feasible in this culture and climate... But what you CAN do, right now, is Please Do NOT make a mandatory requirement for vaccines for our children. The countries who rank best in the world in infant mortality have Recommended vaccine schedules, Not Mandatory vaccine schedules.... Hawaii can join their ranks and lead the US in being the State with the Best in children's health.

Mahalo for your time and consideration!

--



From: [REDACTED]
To: [REDACTED]
Subject: I strongly oppose
Date: Friday, December 21, 2018 2:06:19 PM

We as a family strongly oppose

Re: HAR 11-157,

My name is a Rebecca Hall
I live in [REDACTED]

[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [REDACTED]
Subject: immunization hearing public testimony
Date: Friday, December 21, 2018 11:01:58 AM

An immunized population keeps us all safe, including people who cannot receive vaccines for various health reasons. It's unfortunate that the occasion of updating the immunization requirements to be in line with more current medical recommendations has been taken as an opportunity by people advancing dangerous conspiracy theories to attack the idea of vaccination requirements for public schools. Vaccines are perfectly safe for most people and the presence of medically unjustified unvaccinated students in public schools puts those unvaccinated students at risk as well as those who have legitimate medical reasons for being unvaccinated, those who are too young or too old to be safely vaccinated, and society at large.

The real problem with immunization is that vaccines are available for sale and not provided to everyone who needs them at the point of use for no cost. Whenever prices are involved, some people will go without. It is deeply immoral to provide medicine only to those who can afford to pay, whatever bureaucratic hoops are invented to decide who can "afford" it and who can't.

James Halliday
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Immunization new laws
Date: Friday, December 21, 2018 4:41:55 PM

Aloha

Just letting you know I do not agree with these new laws !!

This is gonna to far to tell us what we have to put in our children bodies!!!

These vaccines have done more damage than good!!!

Stop feeding the pharmsudical company's and selling out the island to make them rich!!!

I am against this law!!!

And am saddened by your sell out by poisoning our kids one way or another!!!

From: [REDACTED]
To: [REDACTED]
Subject: Immunizations
Date: Friday, December 21, 2018 9:03:45 AM

The state of Hawaii should enforce the CDC's recommendation on vaccinations for school age children. If parents opt out of vaccinations their children should not be allowed to attend public school.

The average parent does not have the medical training or knowledge to make an informed decision in this matter, and the internet is not the go-to place for opinions.

Aloha,
Suzy Lauer

From: [REDACTED]
To: [REDACTED]
Subject: In Support of Vaccinations
Date: Friday, December 21, 2018 9:51:42 AM

Hello,

As a mother of a 2 year old and a 4 month old, I support the new immunization requirements. My vulnerable 4-month-old should be exposed to as few diseases as possible, especially if vaccines exist for them. My 2-year-old, as part of a school, has the responsibility of supporting herd immunity.

Best regards,
Crystal Chen
[REDACTED] resident

From: [REDACTED]
To: [REDACTED]
Subject: vaccinations= no
Date: Friday, December 21, 2018 7:16:31 AM

Enough already, I am opposed to more mandated vaccinations.
Please advise,
Mahalo,
Meredith Murphy

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines
Date: Friday, December 21, 2018 9:18:46 AM

To whom it may concern,

I believe vaccines/immunizations should be that of a personal right and a parents choice what goes into their child's body. Adding more vaccines and also making them mandatory, is to me against human rights and putting our loved children at risk for MANY auto immune and other disabilities. Why when a child is trying to develop, would we put foreign substances into their body and introduce a bunch of new things to which are not part of their natural growth? Immunizations have been known to disrupt the brain and it's functioning, as why we are seeing many children with autism and behavioral disorders!! Please I beg of you, help keep our children healthy, help to choose natural remedies that support healthy growth. There ARE other routes to take to increase the care of our loved ones and not put them at risk. There are studies being shown in other countries that homeoprophalaxis works better in communities, than in those that use vaccines. I am grateful for the awareness that is coming out, and I hope it will be curriculum for doctors and pediatricians to know exactly what makes up each vaccine, instead of it being a money gain if they push them.

I am AGAINST mandatory vaccines.

Thank you for your consideration.

From: [REDACTED]
To: [REDACTED]
Subject: "Re: HAR 11-157"
Date: Friday, December 21, 2018 10:55:04 AM

"Re: HAR 11-157, I STRONGLY OPPOSE

I oppose mandating any vaccines (even though I'm generally in favor of vaccines), but on a personal level I strongly oppose mandating the flu shot and the HPV shot.

Teresa Wintersteen (representing myself and my son... currently in 5th grade who has never received a flu shot)

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Opposition to Proposed Increase in Vaccinations
Date: Friday, December 21, 2018 11:10:10 AM

To whom this concern:

I'm writing to express my opposition to the proposed increase in school vaccinations. The proposed list of vaccinations are for non-lethal ailments and pose a harm to many children. I understand that there is scientific evidence to substantiate these vaccines and the evidence is not overwhelming enough to make mandatory vaccinations. This in turn will increase the number of children leaving public schools and increase allergies and autism.

I am a law-abiding, tax paying, voting citizen and respectfully object to the proposed amendments to Title 11, chapter 157.

Sincerely,

Al-Qawi Majidah Lebarre

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Vaccination requirements
Date: Friday, December 21, 2018 11:35:00 AM

Aloha,

I am emailing you to voice my concern of the proposed changes to the requirements of six new vaccines to the list of required vaccinations for school children. In my opinion, no vaccine should be mandated for any child. This should be a decision made by the child's parent. Instead of mandating vaccines, the government should educate parents about the benefits of vaccines, and still allow the parent to make the final decision.

The following vaccines should absolute not be added.

1. HPV vaccine has had several documented adverse effects and so no parent should be mandated to give this (or any) vaccine to their child. HPV is a sexually transmitted infection. This should not be on the list of mandated vaccines.
2. Influenza vaccines are a false sense of security. Influenza vaccine is created from strains from the previous year and there is no proof it will be effective for the current year's flu virus.
3. Rotavirus vaccine is recommended to be started prior to 15 weeks of age and the vaccine series is not recommended to be started after 15 weeks of age. Therefore should not be mandated in school age children vaccinations.

A parent should maintain the right to decide which vaccines he/she wants to give their child and when they want to give them to their child.

The government needs to make safer and more effective vaccines so parents are more willing to have their children vaccinated.

I strongly disagree with mandating any vaccine.

--

In Health,

Gretchen Imdieke, N.D.

[REDACTED]

This message is intended for the sole use of the individual and entity to whom it is addressed, and may contain information that is privileged, confidential and exempt from disclosure under applicable law. If you are not the intended addressee, nor authorized to receive for the intended addressee, you are hereby notified that you may not use, copy, disclose, or distribute to anyone the message or any information contained in the message. If you have received this message in error, please immediately advise the sender by reply email and delete the message. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: vaccine testimony
Date: Friday, December 21, 2018 12:12:28 PM

Aloha,

I am in favor of vaccine requirements and hope that you will pass the proposed amendments.

My name is Amanda Kinsley. I am a resident and home owner in [REDACTED]. I have 2 children, a 4 year old attending Honoka'a elementary preschool and an infant. Both of my children are vaccinated. As a parent I will say, yes at times it can be a little scary taking your child to the doctor and having them get their shots. However, there is no vast conspiracy to cover up the "evils" of vaccines. Rather, there is a great deal of misinformation surrounding vaccines.

I hope that you will vote to pass the proposed amendment based on current science and medicine, rather than on misinformed, emotional based requests of those who are afraid to vaccinate. Vaccines protect us all through 'herd immunity', not just those who are vaccinated. The very young, old, or medically fragile are especially at risk when large groups choose not to vaccinate.

Please vote in favor of science and protecting those who are most vulnerable. Please pass the proposed amendments.

Mahalo and thank you for your time,

Amanda Kinsley

From: [REDACTED]
To: [REDACTED]
Subject: OPPOSITION testimony to mandatory vaccines
Date: Friday, December 21, 2018 2:06:36 PM

Aloha,

As a born and raised [REDACTED] mother, I am completely against mandatory vaccines of any kind. Legally Forced injections of any kind are Completely unethical and take away basic freedom that everyone should have. I am in opposition of any form of mandatory vaccine law or bill to be passed in Hawaii and hope that you take my testimony into consideration. Happy Holidays.

Thank you,
Jenny Hudson

From: [REDACTED]
To: [REDACTED]
Subject: VACCINES
Date: Friday, December 21, 2018 4:33:18 PM

PLEASE BE AWARE !!

<https://www.brighteon.com/5982399562001>

From: [REDACTED]
To: [REDACTED]
Subject: Opposition of HAR-11-157
Date: Friday, December 21, 2018 7:21:43 PM

Aloha,

I would like to express my concern regarding the proposal of HAR 11-157. As Hawaii informed consent states, "Where there is a risk, there must be a choice."

I do not feel it is constitutional to **require** parents to vaccinate their children until further studies have been done on the safety of vaccines. Senate Bill 732 before the 103rd Congress of the United States known as the "Comprehensive Child Health Immunization Act of 1993", made known the fact that there are risks to vaccines.

In addition, there are many concerning ingredients in vaccines, such as carcinogens, neurotoxins, animal blood, allergens, and heavy metals. As a follower of Jesus Christ, and a pro-life supporter the biggest concern of additives in vaccines to our family is aborted fetal tissue.

Consequently, I would like to make it clear that I do **not** support HAR 11-157. I believe in the **freedom of choice** when it comes to our children's healthcare.

Respectfully,

Danielle S. Fields

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Opposed to forced immunizations
Date: Friday, December 21, 2018 7:30:53 PM

Aloha,

Our family is opposed to more mandatory vaccinations for school age childre. The HPV vaccination isn't even safe, my sister got sick from it. A lawmaker in New York recently died after getting the flu shot. The DOH is not a friend of the public by forcing more dangerous vaccines on our kids. This bill will force kids out of public school and into homeschool. Stop violating our right to our bodies.

Sincerely
Danielle Ciccone

[REDACTED]

From: Martina Kalfors
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: Vaccine danger studies added to verbal testimony opppsing HAR 11-157 Martina Kalfors.
Date: Friday, December 21, 2018 7:44:59 PM

Aloha DOH.

After my verbal testimony in [REDACTED]. You stated I could provide more studies. Here you go. Read it all carefully. This will be shared with all legislators to. We the people are NOT ok with this rule change. There was one person in favor of this, she was not a citizen in the U.S. all the other people were affiliated with an organization representing pharmaceutical industry. No individual testimony in favor of HAR-11-157.

But There were over hundred opposing. Why is that? We THE PEOPLE DO NOT WANT THIS. Watch all hearings public on my FB page. Read all the testimonies. Please. Our keiki deserves it.

The added pdf link to the Corvelva study for infrarix hexa contains all contaminates and NO antigens. Came out this week. ALL RISK, NO BENEFIT. This is the trusted science you want us to inject into our keiki. This is absolutely criminal. No question. This should be enough evidence to immediately do a moratorium on vaccines, until all vaccines have been carefully investigated.

Dr. Stephanie Seneff's study pdf. shows traces of Glyphosate in all vaccines. Show us that it is safe to INJECT to our children. Or anyone for that matter.

There are also 60 peer reviewed studies on the danger of hpv vaccine in pdf link.

Thousands of studies on the danger of vaccines on this link. Pick your choice of disease. Many peer reviewed.

<https://medscienceresearch.com/contamination/> <<https://medscienceresearch.com/contamination/>>

<http://www.greenmedinfo.com/blog/200-evidence-based-reasons-not-vaccinate-free-research-pdf-download> <<http://www.greenmedinfo.com/blog/200-evidence-based-reasons-not-vaccinate-free-research-pdf-download>>

New documentary on hpv vaccine danger.

<https://vimeo.com/277078546/7812e25bb1> <<https://vimeo.com/277078546/7812e25bb1>>

<http://vaccinesafetycommission.org/pdfs/Wang%20Yao%202018%20Cytokine%20IL-4%20Hep%20B%20Hippocampus.pdf>
<<http://vaccinesafetycommission.org/pdfs/Wang%20Yao%202018%20Cytokine%20IL-4%20Hep%20B%20Hippocampus.pdf>>

<https://vaccinesafetycommission.org/pdfs/26-2010-Hep-B-Autism.pdf>
<<https://vaccinesafetycommission.org/pdfs/26-2010-Hep-B-Autism.pdf>>

Contaminated vaccines.

<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf> <<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf>>

<https://www.tandfonline.com/doi/abs/10.1080/15287394.2018.1477640?cookieSet=1>
<<https://www.tandfonline.com/doi/abs/10.1080/15287394.2018.1477640?cookieSet=1>>

LIVE VACCINES SHED and spread Infectious Diseases NOT unvaccinated children!

All live virus vaccines contain LIVE viruses. They may be weakened but they can still replicate and infect both the vaccinated, unvaccinated, immunocompromised and "shed" to people around them for weeks after the vaccine is given.

Which vaccines are LIVE?

Chicken Pox- Varivax Section 5.4 (up to 6 weeks):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142812.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142812.pdf>>

MMR- MMRII page 5 (Up to 28 days):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123789.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM123789.pdf>>

Shingles- Zostavax Section 5.2:

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM285015.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM285015.pdf>>

Rotavirus- Rotateq Section 5:5 (Up to 15 days, fecal shedding):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142288.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142288.pdf>>

Small Pox- ACAM2000 Section 5:10 (Only used in the military but highly contagious):

<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142572.pdf>
<<http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142572.pdf>>

But does that REALLY happen? Yes. Yes it can and does as these studies illustrate:

Varicella transfer after vaccine to pregnant mom:

<http://www.ncbi.nlm.nih.gov/pubmed/9255208> <<http://www.ncbi.nlm.nih.gov/pubmed/9255208>>

Pub Med article on Rotavirus shedding:

<http://www.ncbi.nlm.nih.gov/pubmed/18922486> <<http://www.ncbi.nlm.nih.gov/pubmed/18922486>>

Mumps Vaccine sheds:

<http://www.ncbi.nlm.nih.gov/pubmed/24772647> <<http://www.ncbi.nlm.nih.gov/pubmed/24772647>>

Mumps vaccine sheds:

<http://www.ncbi.nlm.nih.gov/pubmed/16266774> <<http://www.ncbi.nlm.nih.gov/pubmed/16266774>>

Measles virus sheds for 1-13 days after vaccination:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC228449/>
<<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC228449/>>

Mumps outbreak in Netherlands linked to those vaccinated twice with MMR:

http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article <http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article>

Measles vaccinated child responsible for outbreak in British Columbia:

<http://www.eurosurveillance.org/images/dynamic/EE/V18N49/art20649.pdf>
<<http://www.eurosurveillance.org/images/dynamic/EE/V18N49/art20649.pdf>>

New York Measles outbreak linked to vaccinated:

<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>
<<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>>

Measles outbreak among the vaccinated:

<http://www.ncbi.nlm.nih.gov/pubmed/8053748> <<http://www.ncbi.nlm.nih.gov/pubmed/8053748>>

We don't know for certain how long shedding occurs because we don't test for it long term or regularly but in rare instances, it has gone on for years:

<http://www.westernmorningnews.co.uk/Vaccinated-man-spread-polio-30-years/story-27693988-detail/story.html> <<http://www.westernmorningnews.co.uk/Vaccinated-man-spread-polio-30-years/story-27693988-detail/story.html>>

Additionally, the Dtap/Tdap and Polio vaccines that are NOT live has been shown to cause the vaccinated to become asymptomatic carriers whenever exposed, thus the vaccinated can be spreading the illness without knowing at any time:

Pertussis carrier:

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376937.htm>
<<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm376937.htm>>

Diphtheria carrier:

<http://www.cdc.gov/diphtheria/clinicians.html> <<http://www.cdc.gov/diphtheria/clinicians.html>>

The polio vaccine “does not stop transmission of the virus.” & “when a person immunized with IPV is infected with wild poliovirus, the virus can still multiply inside the intestines and be shed in the feces, risking continued circulation.”

<http://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/>
<<http://polioeradication.org/polio-today/polio-prevention/the-vaccines/ipv/>>

You can also find that most medical facilities are aware of this. Johns Hopkins and St. Jude hospitals are just a few of many who post precautions for recently vaccinated visitors.

WHY does this matter?

Because society is so deathly afraid of these illnesses that they rush out and load up on vaccines and want to even pass laws forcing others who should never be vaccinated to do the same; but the science shows that it's the vaccinated that are at a higher risk of infections because vaccines heavily suppress the immune system, vaccines are directly linked to spreading illnesses because people are routinely injected with them. Be aware of the infection and carrier risk each vaccine has when making your choice as you will- take cautionary measures being around individuals that are immunocompromised if you have been recently vaccinated or around someone with the illnesses even if you don't show symptoms.

ONE HUNDRED AND FIFTEEN studies on vaccine SHEDDING...

[Www.medscienceresearch.com/shedding/](http://www.medscienceresearch.com/shedding/) <<http://www.medscienceresearch.com/shedding/>>

THE DILEMMA OF VACCINE-INDUCED DISEASE AND UNVACCINATED CHILDREN
VACCINE SHEDDING

It has long been known that vaccines can cause the diseases they were meant to immunise against.

For instance, the live oral polio vaccination can cause polio – a disease named vaccine-associated paralytic polio (VAPP), which is mentioned on the UK dept of health website, immunisation.org.uk
<<http://immunisation.org.uk>>

‘If a baby has had the oral polio vaccine, the live virus can be found in the baby's poop for up to six weeks afterwards.’

It was actually for this reason that the OPV was voted out and injectable polio vaccine re-introduced. The oral vaccine was responsible for the ONLY cases of polio in the developing world. (Committee on Immunization Practices meeting, held 20th June 1996).

According to DRAFT ACIP meeting minutes, February 2001, page 28:

And lastly the myth of herd immunity. A theory that has never been proven to work. Impossible hence booster.

<https://jbhandleyblog.com/home/2018/6/7/herd-immunity-a-dishonest-marketing-gimmick>
<<https://jbhandleyblog.com/home/2018/6/7/herd-immunity-a-dishonest-marketing-gimmick>>

And if you care about the real truth of history. Read Dr. Suzannes book. "Dissolving Illusions".

<https://jbhandleyblog.com/home/2018/5/14/savehumanity>
<<https://jbhandleyblog.com/home/2018/5/14/savehumanity>>

http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR1hPbF_UuhtbtsIMCNp7ukdVWP0bM4Z6eU3XTYriB0-uazolwSXpVd_aQ
<http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR1hPbF_UuhtbtsIMCNp7ukdVWP0bM4Z6eU3XTYriB0-uazolwSXpVd_aQ>

There you go,

Mahalo,
Martina Kalfors.

From: [REDACTED]
To: [REDACTED]
Subject: Request against compulsory vaccinations
Date: Friday, December 21, 2018 8:20:37 PM

Aloha,

We request reconsideration regarding the proposed legislation that would require compulsory vaccinations for all children on the islands.

As parents, we are entrusted with raising our children as best as possible and want to make decisions based on their unique needs.

Being forced to vaccinate on a standard government mandated schedule takes that autonomy away from us and eliminates our ability to work with their pediatrician to give them whatever treatments are best for them as they each grow according to their unique DNA.

Just like Roe vs Wade gave women the liberty to choose how to handle their bodies with regard to pregnancy, having that same choice regarding vaccinations and their timing is the same liberty we hope to maintain as parents while living in America.

Mahalo,

--

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Anti mandatory vaccine statement
Date: Friday, December 21, 2018 9:29:38 AM

Two of my 3 children had severe reactions and disabilities following vaccinations. So I do not want my grand children to get the mandatory injection of massive amounts of aluminum into them. I am a registered nurse and these vaccinations especially the flu have not been properly proven to be safe for the developing brains of children. We need more research from an independent source to prove these are safe and toxin free. - so that an India episode with 450,000 children harmed by inadvertent contamination will not occur here! Then you can make the vaccines mandatory. Melinda Fisher [REDACTED]
Sent from my iPhone

Aloha. My name is Marti Berrett and I am the mother of four children and a resident of [REDACTED]. My first child was born in 1994. Because my husband and I knew nothing about vaccines we decided to postpone vaccinating our first baby. We wanted to do our own research into the possible risks and benefits of vaccines. Since the health risk of vaccination is entirely borne by individuals it is imperative that fully informed consent is observed. Informed consent involves understanding alternatives to suggested treatment, including the option of no treatment, and understanding the risks and benefits of the suggested treatment. Informed consent is central to the practice of medicine and is in direct conflict with anything mandatory.

We quickly discovered that the chicken pox vaccine was going to be added to the CDC's recommended schedule the following year, 1995. This stopped me in my tracks. From my childhood I knew that chicken pox was not a dangerous disease. I thought, "Twenty years from now, young parents might assume chicken pox is a dangerous disease simply because it's on the CDC's schedule." I knew this assumption to be false which spurred me to research other vaccines on the schedule. Following are a few things I have learned.

The National Childhood Vaccine Injury Act of 1986 granted unprecedented, economic immunity to manufacturers for injuries caused by vaccines and eliminated economic incentive for them to make improvements. Congress was aware and concerned by this and, as part of the 1986 Act, charged the Secretary of Health & Human Services (HHS) to submit a biennial report to Congress detailing the improvements in vaccine safety made in the preceding two years. Recently in 2018, HHS shockingly admitted that it never, not even once, submitted a single biennial report to Congress. For the past 32 years HHS and the CDC have touted the safety and efficacy of vaccines without submitting any reports to Congress backing up their claims.

In 1990 the Vaccine Adverse Event Reporting System (VAERS) was established. As a passive reporting system, it relies on individuals to send in reports of their experiences to the CDC. It is estimated that 1 to 10 percent of all vaccine-related health problems are ever reported to VAERS. This means 90% of vaccine injuries go unreported. Total compensation paid over the life of the program is approximately

\$4 billion dollars. US Law regards vaccines as unavoidably unsafe and these payouts are proof of the risks and damages. Keep in mind this payout would be 9 or 10 times higher if 90-100% of vaccine injuries were actually reported.

Since I'm talking money, I would like you to ponder what parents are paid if their child does die from a vaccine versus if a child is injured by a defective car. The National Vaccine Injury Compensation Program will pay parents up to \$250,000 if their child dies from a vaccine. Yes, children and adults have died from vaccines and \$250,000 seems inappropriate and insensitive. Compare that to a family being awarded \$242 million dollars after suing Toyota over a defective front seat. In August 2018 a jury awarded this amount to a family after their two children suffered severe head trauma. \$250,000 for a vaccine induced death versus \$121 million per child from severe car injuries? This is the difference between a manufacturer being protected from liability versus being fully liable for their manufacturing defects. You can bet Toyota is economically incentivized to redesign their seats to avoid further injury. Not so for vaccine manufacturers.

In 2002 the House Government Reform Committee held a hearing on the relationship between childhood vaccinations and autism. Congressman Dan Burton spent time questioning William Egan, the FDA Acting Director. From this hearing I learned that there has only been one test on one ingredient in vaccines, thimerosal. In 1929 Eli Lilly, the manufacturer, tested thimerosal on 27 people that were dying of meningitis. All those people died of meningitis and they concluded there was no correlation between the deaths and the mercury in the vaccines. This is the only human test that has ever been done on thimerosal. Thimerosal is still in vaccines in trace amounts and it is a listed ingredient in the multi-dose flu shot. In fact, other neuro-toxins and hazardous substances in vaccines include: aluminum, formaldehyde, thimerosal, human serum albumin, monkey kidney cells, polysorbate 80, ethanol, and ammonium sulfate just to name a few. High levels of aluminum have been found in the brains of autistic children and people suffering from neurological disorders such as Alzheimer's disease.

In 2012 the House Government Reform Committee held hearings about the autism epidemic. Representative Bill Posey questioned Dr. Colleen Boyle, a Director at the CDC. From this hearing I learned that there has never been a study comparing vaccinated children to unvaccinated children. How can we claim vaccinated children are better off than unvaccinated children if a study does not exist?

In 2014 William Thompson, an expert from the CDC, confessed to having manipulated the data of a key MMR reference study. In 2015 Representative Bill Posey called for Congress to hold a hearing and investigate the CDC's MMR research fraud. No hearing has been called to date.

Today my children are healthy, young adults, and all are vaccine free. I am opposed to the Department of Health adding six new vaccines as a requirement to attend school due to:

1. manufacturer's incurring no liability for vaccine related damages
2. HHS being negligent in their reporting responsibility to Congress, zero reports written in 32 years
3. the risks associated with vaccines including death
4. lack of safety studies conducted on vaccine ingredients, the only one for thimerosal was in 1927
5. no comparative studies on health outcomes of vaccinated versus unvaccinated children
6. the fraud within the CDC as reported by whistleblower William Thompson

Again, vaccines are unavoidably unsafe and must not be mandatory.

Thank you for your time.

Marti Bennett 12/21/18



To Legislators and Administrators Granted Power to Make Decisions Affecting Public Health:

I vehemently OPPOSE HAR 11-157 and any legislation that would prevent me from exercising my human and civil right to freedom of thought, speech, and belief under the Constitution of the United States to make informed voluntary choices regarding my health and the health of those whom God has entrusted into my care.

Nobody should be forced to use pharmaceuticals that carry the risk of harm or failure, especially those made with toxic substances or derived from unethical sources such as aborted human fetuses.

It is religious discrimination to accept exemptions from specific religious organizations and not others. Every individual has the right to exercise their religious beliefs as they so choose. It is my belief that God created our bodies with the power and ability to build and maintain a strong immune system by making healthy choices. Compromising the immune system from birth through the administration of vaccines alters natural immunity for life and is contrary to God's design for the body.

As consumers of anything, we are voting for whatever we put into or on our bodies. Forced vaccinations denies us our "right to vote" against drug and chemical companies, immune from accountability and liability, whose interest is in profit and not our health and well-being.

I strongly encourage you to educate yourself by watching the Youtube video with Del Bigtree called THE IRREFUTABLE ARGUMENT AGAINST VACCINE SAFETY before you attempt to make any more mistakes regarding mandatory vaccinations.

I will pray for each of you to have wisdom to do what is right and for God's mercy when you stand before him accountable for the damage and death that may result from the decisions you make.

Sincerely and respectfully,

Sue Pantano-Saldana

[REDACTED]

[REDACTED]

Miss COHENBERG, NO
639-6437

The Institute of Medicine (IOM) Reports and NVIC Statements

The National Academy of Sciences (NAS) was established in 1863 under President Abraham Lincoln's administration to report on science to policymakers and the public. In 1970 the Institute of Medicine (IOM) of NAS – renamed the Health and Medicine Division in March 2016 - was chartered as the health arm of the NAS to provide evidence to the government and private sector that would assist in informed health decisions.

In the National Childhood Vaccine Injury Act of 1986, and Congress directed DHHS to contract with the Institute of Medicine (IOM), to evaluate and report on adverse effects of federally recommended childhood vaccines. Beginning in 1990, IOM appointed committees of experts to review the evidence in the medical literature and from other sources on the safety of government recommended and mandated childhood vaccines.

NVIC's co-founder and president Barbara Loe Fisher was invited to participate as a consumer representative on an Institute of Medicine Vaccine Safety Forum, which sponsored public vaccine safety workshops and published reports on vaccine adverse detection and response and vaccine safety research, and she was a co-editor of the Forum's 1997 report on Risk Communication and Vaccination. Barbara was also invited to make presentations to IOM expert committees reviewing the evidence for vaccine risks in 2001 and 2012.

IOM Vaccine Safety Reports (1991-2013)

IOM published a series of reports on evidence for adverse effects of vaccines between 1991 and 2013 confirming that:

1. Vaccines can and do carry risks for complications that can be greater for some individuals than others and may lead to chronic brain and immune system damage or death. IOM committees published reports in 1991, 1994a, 1994b, and 2012 and found that the following health problems are causally related to vaccination:
 - o Acute encephalopathy (brain inflammation)
 - o Chronic Nervous System Dysfunction (brain damage)
 - o Anaphylaxis (whole-body allergic reaction)
 - o Febrile Seizures (convulsions with fever)
 - o Guillain-Barre Syndrome (peripheral nerve inflammation)
 - o Brachial Neuritis (arm nerve inflammation)
 - o Deltoid Bursitis (shoulder inflammation)
 - o Acute & Chronic Arthritis (joint inflammation)
 - o Syncope (sudden loss of consciousness/fainting)
 - o Hypotonic/Hyporesponsive Episodes (shock and "unusual shock-like state)
 - o Protracted, Inconsolable Crying and Screaming
 - o Vaccine Strain Infections (smallpox, live polio, measles, varicella zoster vaccines)

- Death (smallpox, live polio, measles vaccines)
2. IOM published a report in 2012 revealing that there were continuing significant gaps in scientific knowledge about the biological mechanisms of vaccine injury and death, a point that was made two decades earlier in 1991 and 1994 IOM reports. Because there are not enough methodologically sound epidemiological and biological mechanism studies evaluating vaccine adverse events, the IOM committee could not come to definitive conclusions about causation for many of the reported vaccine reactions involving chronic brain and immune system dysfunction and death. The Committee also concluded that some individuals are more susceptible to vaccine reactions for genetic, biological, environmental and other reasons that have not been fully identified.
- For eight routinely used vaccines, (MMR, DTaP, hepatitis B, hepatitis A, varicella zoster and meningococcal) there were too few scientifically sound studies published in the medical literature to determine whether more than 100 serious brain and immune system problems are or are not caused by the vaccines, including multiple sclerosis, arthritis, lupus, stroke, SIDS, autism and asthma.
 - Both epidemiologic and biological mechanism research suggest that there are known and unknown biological, genetic and environmental high risk factors, which can increase “individual susceptibility” to vaccine reactions. These predispositions can include genetic variants (in human or microbiome DNA), environmental exposures, behaviors and illness or developmental stage, all of which can interact and, while some of the predispositions may be detectable before vaccination, others are not.
3. IOM published a report in 2013 that revealed the federally recommended birth to six-year old child vaccine schedule had not been fully scientifically evaluated and there was not enough scientific evidence for physician committees to determine if the childhood vaccine schedule *is or is not* associated with the development of the following brain and immune system disorders prevalent among children today:
- Asthma
 - Atopy
 - Allergy
 - Autoimmunity
 - Autism
 - Learning disorders
 - Communication disorders
 - Developmental disorders
 - Intellectual disability
 - Attention deficit disorder
 - Disruptive behavior disorder
 - Tics and Tourette’s syndrome
 - Seizures
 - Febrile seizures

- Epilepsy

Since 1982, NVIC has advocated that well-designed, independent, on-going scientific studies must be conducted to: (1) define the various biological mechanisms involved in vaccine injury and death; (2) identify genetic and other biological high risk factors for suffering chronic brain and immune system dysfunction after vaccination; and (3) evaluate short and long-term health outcomes of individuals, who use many vaccines, and those, who use fewer or no vaccines, to determine the health effects of vaccination on individuals and the public health.

Below are links to selected statements by NVIC to the IOM in the accomplishment of these vaccine safety and research advocacy goals.

- [NVIC's Statement on Childhood Immunization Schedule and Safety: Stakeholder Concerns, Scientific Evidence, and Future Studies. Jan 16, 2013](#)
- [NVIC's Statement on Conducting Research into Health Outcomes of Vaccinated and Unvaccinated Children- 2/9/12](#)
- [NVIC's Statement on the Institute of Medicine Report on Adverse Effects of Vaccines - 8/25/2011](#)
- [IOM Committee on NIP's Procedures & Data Sharing Program - 8/23/04](#)
- [IOM Safety Review Committee: Vaccine Safety Research & Reports - 1/01](#)
- [Institute of Medicine Immunization Safety Committee - 1/11/01](#)
- [IOM Vaccine Safety Forum Workshop on Risk Communication & Vaccination - 5/13/96](#)
- [Statement on Vaccine Safety Research Needs - Perspective From Parents - 4/1/96](#)
- [Vaccine Adverse Event Report Response Methodologies IOM Vaccine Safety Forum - 11/6/95](#)
- [Statement on Vaccine Adverse Event Detection Methodologies - 11/6/95](#)
- [IOM Vaccine Safety Forum Statement: Where we stand? - 11/6/95](#)
- [NVIC Statement Opposing Continued Use of Live Oral Polio Vaccine \(OPV\) - 6/7/95](#)

SimpsonWood Transcript

- June 7-8, 2000 Simpsonwood Retreat Center Norcross, Georgia Dr. Orenstein: My name is Walter Orenstein. I'm Director of the National Immunization Program at CDC and I want to thank all of you for coming here and taking time out of your very busy schedules to spend the next day and a half with us.
- This is how the transcript begins...

SimpsonWood Transcript

- <http://thinktwice.com/simpsonwood.pdf>

Review of the simpsonwood doc

- <https://www.forbes.com/sites/emilywillingham/2014/02/22/is-the-cdc-hiding-data-about-mercury-vaccines-and-autism/#4a24e4341363>
- <https://autismrawdata.net/blog/simpsonwood>

Aloha my name is Abigail schoder.

For many reasons I strongly opposed Har 11-157 specifically in relation to the very serious health and safety risks and conflicts.

This proposal change offers a serious threat of significant increased risk to our Island and society as a whole.

There is more than enough personal claims and documented scientific evidence proving severe detrimental effects from vaccinations. Including but not limited to: the improper proportional dosage to body weight ratio in administering the vaccine, harmful ingredients such as mercury and proven carcinogenic toxic poisons and even contamination. (See 27 page ref. link below)
https://medscienceresearch.com/contamination/?fbclid=IwAR2LczWCTVRnDTeOf9f_GYCuC_dTnD29VR2KJRR28iqtw6hLYn52qZlh9k

Combine this with a "one size fits all" approach to protocol and now a proposal to increase protocol and we have a recipe for disaster and greater injury. The risk is simply too great.

Countless families, communities and school systems are already suffering from the devastating and debilitating negative affects from vaccines. This is reflected with the United States vaccine injury Court paying out over four billion dollars in settlement to date for injuries and even death.

<https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-december-2018.pdf>

The 1986 National Childhood Injury Act law acknowledges that vaccine injuries and deaths are real and that the vaccine injured and their families should be financially supported. For some reason the same law has allowed the vaccine manufacturers to escape liability for these adverse affects and has put the financial burden on the government. Congress created a "vaccine safety task force" to track and take action to reduce these harmful affects and implement measures to improve vaccine safety. The Sec of HHS was mandated to report to senate every two years regarding this. In the past 31 years they have not once reported to the Senate! On top of this **the number of vaccines recommended for our children has significantly increased already (from 24 doses of 7 vaccines by age 18, to 69 doses of 16 vaccines!**

This clearly shows us that our children and citizens are being treated as real live time "guinea pigs" or experiments. This is both unacceptable and downright dangerous. With this as our current situation, why would a proposal such as Har 11-157 even be entertained? Who is this really benefiting?

<https://www.govinfo.gov/content/pkg/USCODE-2016-title42/pdf/USCODE-2016-title42-chap6A-subchapXIX-part2-subpartc-sec300aa-27.pdf>

<http://candecide.org/government/CAN-HHS-Stipulated-Order-July-2018.pdf>

<https://www.nvic.org/cmstemplates/nvic/pdf/downloads/1983-2017-vaccine-schedules.pdf>

Documented scientific evidence and studies show that recently vaccinated individuals shed the virus for weeks and even months to both vaccinated and un-vaccinated people. These recently vaccinated individuals can carry the disease without symptoms and pass it on to others. There are currently no guidelines in place to quarantine recently vaccinated individuals. They are released directly into the public and into our schools while shedding the viruses. Could the vaccinations themselves be increasing the spread of disease? This is a major public health issue and concern. An increase in number of people vaccinated, dosage and frequency could significantly multiply this

problem and harm our society.

<https://www.westonaprice.org/public-health-officials-know-recently-vaccinated-individuals-spread-disease/>

As you know, the Department of Health itself clearly states on their website that no vaccine is 100% effective. We saw proof of this right here on Kauai when mumps vaccinated children and people did indeed contract the mumps during the outbreak last year. The risks are simply and clearly too high and not worth it.

I'm here today to affirm my right, my families rights and any citizens right to have complete sovereignty over our bodies. This is indeed our birth right. I sincerely asked you to truly listen and respond to our concerns as citizens, parents and caregivers. Thank you for your time and consideration.

Additional REFERENCE details:

<https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-december-2018.pdf>

"How many petitions have been awarded compensation? According to the CDC, from 2006 to 2016 over 3.1 billion doses of covered vaccines "were distributed in the U.S. For petitions filed in this time period, 5,576 petitions were adjudicated by the Court, and of those 3,785 were compensated. This means for every 1 million doses of vaccine that were distributed, 1 individual was compensated. Since 1988, over 20,123 petitions have been filed with the VICP. Over that 30-year time period, 17,576 petitions have been adjudicated, with 6,313 of those determined to be compensable, while 11,263 were dismissed. Total compensation paid over the life of the program is approximately \$4.0 billion."

Contamination

Contamination

(<https://medscienceresearch.com/contan>

Recap of the vaccine contaminants below: Mycoplasma, HIV, syphilis, hepatitis B and C, pestiviruses, mouse brain tissue, bacteriophage, reverse transcriptase, SV40 cancer causing virus, porcine circovirus, endotoxins, coliphages, pseudomonas, fungi,

XMRV, foamy viruses of simian origin, nanoparticles with several metals, antifertility drug hCG, Mycobacterium tuberculosis, simian cytomegalovirus

Veterinary vaccines: chicken anaemia virus, egg drop syndrome virus, avian leukosis virus, Torque Teno virus, RD-114 retrovirus, mycoplasma

Absence of antibodies to HTLV-III in health workers after hepatitis B vaccination.

"A proportion of the plasma for the triply inactivated, plasma-derived hepatitis B vaccine produced in the United States is obtained from homosexual men. Because homosexual men are a high-risk group for the acquired immunodeficiency syndrome (AIDS), concern has emerged that the vaccine could harbor the AIDS agent."

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [B #Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/2991619/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/2991619/>)

🔍 **Adventitious agents in viral vaccines: Lessons learned from 4 case studies**

"The four cases are: a) SV40 in polio vaccines; b) bacteriophage in measles and polio vaccines; c) reverse transcriptase in measles and mumps vaccines; and d) porcine circovirus and porcine circovirus DNA sequences in rotavirus vaccines."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

[#Rotavirus \(https://medscienceresearch.com/tag/rotavirus/\)](https://medscienceresearch.com/tag/rotavirus/) [#Measles \(https://medscienceresearch.com/tag/measles/\)](https://medscienceresearch.com/tag/measles/) [#MMR \(https://medscienceresearch.com/tag/mmr/\)](https://medscienceresearch.com/tag/mmr/)
<http://www.sciencedirect.com/science/article/pii/S1045105614000748>
[\(http://www.sciencedirect.com/science/article/pii/S1045105614000748\)](http://www.sciencedirect.com/science/article/pii/S1045105614000748)

🔍 **Adverse effect versus quality control of the Fuenzalida-Palacios antirabies vaccine.**

"We evaluated the components of the Fuenzalida-Palacios antirabies vaccine, which is still used in most developing countries in human immunization for treatment and prophylaxis. This vaccine is prepared from newborn mouse brains at 1% concentration. Even though the vaccine is considered to have a low myelin content, it is not fully free of myelin or of other undesirable components that might trigger adverse effects after vaccination. The most severe effect is a post-vaccination neuroparalytic accident associated with Guillain-Barré syndrome. In the present study we demonstrate how the vaccines produced and distributed by different laboratories show different component patterns with different degrees of impurity and with varying protein concentrations, indicating that production processes can vary from one laboratory to another. These differences, which could be resolved using a better quality control process, may affect and impair immunization, with consequent risks and adverse effects after vaccination. We used crossed immunoelectrophoresis to evaluate and demonstrate the possibility of quality control in vaccine production, reducing the risk factors possibly involved in these immunizing products."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Mouse](https://medscienceresearch.com/tag/mouse/) [#Brain](https://medscienceresearch.com/tag/brain/) [#Guillain \(https://medscienceresearch.com/tag/guillain/\)](https://medscienceresearch.com/tag/guillain/) [#Barre \(https://medscienceresearch.com/tag/barre/\)](https://medscienceresearch.com/tag/barre/) [#Neurological \(https://medscienceresearch.com/tag/neurological/\)](https://medscienceresearch.com/tag/neurological/) [#Rabies \(https://medscienceresearch.com/tag/rabies/\)](https://medscienceresearch.com/tag/rabies/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/) [#Molecular \(https://medscienceresearch.com/tag/molecular/\)](https://medscienceresearch.com/tag/molecular/) [#Mimicry \(https://medscienceresearch.com/tag/mimicry/\)](https://medscienceresearch.com/tag/mimicry/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/10030074> (<https://www.ncbi.nlm.nih.gov/m/pubmed/10030074>)

The African polio vaccine-acquired immune deficiency syndrome connection.

"Seroepidemiological, clinical and molecular findings suggest that the acquired immune deficiency syndrome virus human immunodeficiency virus-1 was introduced into the human species at the time (late 1950s) and in the geographic area (Zaire) in which millions of Africans were vaccinated with attenuated poliomyelitis virus strains that were produced in kidney tissue obtained from monkeys. Since monkeys not only harbor viruses that are remarkably similar to and genetically related to human immunodeficiency virus-1, but also served as tissue donors for the African polio vaccine, it is reasonable to suspect that a then non-detectable monkey virus with human-1-like properties was unknowingly co-cultured with the attenuated poliovirus virus and subsequently

administered to the vaccinees. The possibility of such a polio vaccine-acquired immune deficiency syndrome connection is a reminder of the unpredictable danger of artificially crossing natural species-barriers in biomedical laboratories.”

[#HIV](https://medscienceresearch.com/tag/hiv/) (<https://medscienceresearch.com/tag/hiv/>) [#Polio](https://medscienceresearch.com/tag/polio/) (<https://medscienceresearch.com/tag/polio/>)

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>)

[#AIDS](https://medscienceresearch.com/tag/aids/) (<https://medscienceresearch.com/tag/aids/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>)

[#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)`

<https://www.ncbi.nlm.nih.gov/m/pubmed/9185120/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/9185120/>)

Application of PCR for detection of mycoplasma DNA and pestivirus RNA in human live viral vaccines.

“Although mycoplasma DNA was not detected in any of the vaccines tested, pestivirus RNA was detected in 12 lots (28%).”

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>) [#MMR](https://medscienceresearch.com/tag/mmr/)

(<https://medscienceresearch.com/tag/mmr/>) [#Polio](https://medscienceresearch.com/tag/polio/) (<https://medscienceresearch.com/tag/polio/>) [#Pestivirus](https://medscienceresearch.com/tag/pestivirus/)

(<https://medscienceresearch.com/tag/pestivirus/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>)

[#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)

https://www.ncbi.nlm.nih.gov/m/pubmed/9088554 (https://www.ncbi.nlm.nih.gov/m/pubmed/9088554)

🔍 Association between SV40 and non-Hodgkin's lymphoma.

“Millions of people worldwide were inadvertently exposed to live simian virus 40 (SV40) between 1955 and 1963 through immunization with SV40-contaminated polio vaccines. Although the prevalence of SV40 infections in humans is not known, numerous studies suggest that SV40 is a pathogen resident in the human population today. SV40 is a potent DNA tumor virus that is known to induce primary brain cancers, bone cancers, mesotheliomas, and lymphomas in laboratory animals.”

[#Cancer](https://medscienceresearch.com/tag/cancer/) (<https://medscienceresearch.com/tag/cancer/>) [#Contamination](https://medscienceresearch.com/tag/contamination/)

(<https://medscienceresearch.com/tag/contamination/>) [#Polio](https://medscienceresearch.com/tag/polio/) (<https://medscienceresearch.com/tag/polio/>)

[#Leukemia](https://medscienceresearch.com/tag/leukemia/) (<https://medscienceresearch.com/tag/leukemia/>) [#SV40](https://medscienceresearch.com/tag/sv40/) (<https://medscienceresearch.com/tag/sv40/>)

[#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

(<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/15202523/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/15202523/>)

🔍 Assessment of iatrogenic transmission of HCV in Southern Italy: was the cause the Salk polio vaccination?

“Since the first studies on hepatitis C virus (HCV) prevalence were published, it has been evident that southern

Italy is an area of hyperendemicity. A recent study conducted in southern Italy suggested that the high prevalence of HCV infection might be the result of past iatrogenic transmission. Polio vaccination with the parenteral Salk vaccine between 1956 and 1965 by multiple use of unsafe glass syringes may have been one of the major causes of the spread of HCV infection among southern Italian adults who are now older than 40 years of age. Persons born between the 1940s and early 1960s have a nearly 3-fold increased risk of HCV seropositivity than the younger age group. The findings are consistent with a cohort effect of exposure to the Salk parenteral vaccination."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/12629643> (<https://www.ncbi.nlm.nih.gov/m/pubmed/12629643>)

Bacteriophages and endotoxin in licensed live-virus vaccines

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/805187/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/805187/>)

Bridging the gap: human diploid cell strains and the origin of AIDS.

"Although the theory of a chimpanzee origin of HIV-1 with cross-species transfer to man has now gained popularity, a more likely scenario is that chimps and humans were infected by an HIV-1 precursor virus derived from a contaminated poliovaccine. The reason for the rapidity and ease of cross-species transfer of this precursor virus has not been elucidated. We hypothesize that the poliovaccine was passaged in a human diploid cell strain."

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)
[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/10833351/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/10833351/>)

? Full article here –

<http://www.bmartin.cc/dissent/documents/AIDS/Goldberg.pdf>
<http://www.bmartin.cc/dissent/documents/AIDS/Goldberg.pdf>

Cancer risk associated with simian virus 40 contaminated polio vaccine.

[#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/)
[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Cancer \(https://medscienceresearch.com/tag/cancer/\)](https://medscienceresearch.com/tag/cancer/) [#Simian \(https://medscienceresearch.com/tag/simian/\)](https://medscienceresearch.com/tag/simian/) [#Virus \(https://medscienceresearch.com/tag/virus/\)](https://medscienceresearch.com/tag/virus/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
[https://www.ncbi.nlm.nih.gov/m/pubmed/10472327/ \(https://www.ncbi.nlm.nih.gov/m/pubmed/10472327/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/10472327/)

Clinical implications of endotoxin concentrations in vaccines

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#DTP \(https://medscienceresearch.com/tag/dtp/\)](https://medscienceresearch.com/tag/dtp/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
[https://www.ncbi.nlm.nih.gov/m/pubmed/11978151/ \(https://www.ncbi.nlm.nih.gov/m/pubmed/11978151/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/11978151/)

Clinical Outcomes after Hepatitis C Infection from Contaminated Anti-D Immune Globulin

“Twelve batches, constituting 4062 vials, of contaminated or potentially contaminated anti-D immune globulin were in circulation in 1977 through 1979 (the batches had an expiration date of mid-1979).”

[#Rhogam \(https://medscienceresearch.com/tag/rhogam/\)](https://medscienceresearch.com/tag/rhogam/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/)
[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<http://www.nejm.org/doi/full/10.1056/NEJM199909023411013>
[\(http://www.nejm.org/doi/full/10.1056/NEJM199909023411013\)](http://www.nejm.org/doi/full/10.1056/NEJM199909023411013)

Collective experiences of adventitious viruses of animal-derived raw materials and what can be done about them.

“Contamination of animal-derived raw materials with viruses, mycoplasmas, bacteria and fungi is common. These contaminants can interfere with the diagnosis of viral infection, and vaccines produced using infected cell cultures could lead to seroconversion or disease in the vaccinated animal. The purity, safety and efficacy of viral vaccines requires testing of the ingredients, cell substrates and final product. Methods for detection of viruses, especially bovine viral diarrhea virus, in nutrient serum, cell cultures, seed viruses and viral vaccines, and the frequency of their detection at the Center for Veterinary Biologies are discussed.”

frequency of their detection at the Center for Veterinary Biologics are discussed.

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/19003405/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/19003405/>)

Comparison of methods used for detection of mycoplasma contamination in cell cultures, sera, and live-virus vaccines.

"Contamination by different species of mycoplasma was found in 39% samples tested."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Mycoplasma \(https://medscienceresearch.com/tag/mycoplasma/\)](https://medscienceresearch.com/tag/mycoplasma/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/8206173> (<https://www.ncbi.nlm.nih.gov/m/pubmed/8206173>)

Contaminated vaccine deaths a serious setback for Syria.

(2014)

No abstract available

PMID 25268026

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Death \(https://medscienceresearch.com/tag/death/\)](https://medscienceresearch.com/tag/death/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/25268026/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/25268026/>)

Contamination of Reconstituted Multidose Measles Vaccine Vial and Toxic Shock Syndrome in Tamilnadu

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Death \(https://medscienceresearch.com/tag/death/\)](https://medscienceresearch.com/tag/death/) [#Measles \(https://medscienceresearch.com/tag/measles/\)](https://medscienceresearch.com/tag/measles/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://www.indianpediatrics.net/july2008/606.pdf> (<http://www.indianpediatrics.net/july2008/606.pdf>)



THE COST OF UNSAFE INJECTIONS.

“Unsafe injection practices are associated with substantial morbidity and mortality, particularly from hepatitis B and C and human immunodeficiency virus (HIV) infections.”

“Annually more than 1.3 million deaths and US\$ 535 million are estimated to be due to current unsafe injection practices. With the global increase in the number of injections for vaccination and medical services, safer injecting technologies such as auto-disable syringes must be budgeted for.”

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/)
[#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) B [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) C [#Death \(https://medscienceresearch.com/tag/death/\)](https://medscienceresearch.com/tag/death/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/10593028/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/10593028/>)

Doctors to face disciplinary action over Irish hepatitis C scandal.

“The Irish Medical Council’s fitness to practice committee is to begin a disciplinary examination of the role of several doctors criticised by an official Tribunal of Inquiry into the country’s hepatitis C scandal. More than 1000 mothers were infected through contaminated anti-D immunoglobulin in the mid-1970s.”

[#Rhogam \(https://medscienceresearch.com/tag/rhogam/\)](https://medscienceresearch.com/tag/rhogam/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665410/pdf/9462311.pdf>
[\(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665410/pdf/9462311.pdf\)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2665410/pdf/9462311.pdf)

Don’t ignore the risk of vaccine contamination

“Sir, Your News and Opinion articles about alleged contamination of vaccines should serve as a warning against over-optimism.

These articles highlight the failure to show any evidence for contamination of Wistar Institute polio vaccine stocks by human and simian immunodeficiency viruses (HIV/SIV), and you appeal for a truce. But — although Edward Hooper is quoted as saying that “vaccine samples released did not include any from batches prepared for use in Africa” — lymphocytes have been detected in other polio vaccines. Half of the vervet monkeys in Southern Africa are SIV positive; these animals were used for preparing early polio vaccines.

Considering the many millions of vaccine doses prepared in primary vervet monkey kidney cultures over a 30 year period, it is inconceivable that some SIV did not contaminate many cultures. By the same yardstick, simian

virus 40 (SV40) contaminated millions of doses of poliovirus vaccine until the animals were screened for this tumour virus.

Edward Hooper and others surely do not intend to undermine the polio vaccine efforts. What is needed is a new awareness of the need for caution — remembering the example of BSE — in view of the current impetus towards xenotransplantation and the accompanying danger of contamination. Our aim should be to improve our vaccines, not to undermine public confidence in them.”

[#HIV](https://medscienceresearch.com/tag/hiv/) (<https://medscienceresearch.com/tag/hiv/>) [#Polio](https://medscienceresearch.com/tag/polio/) (<https://medscienceresearch.com/tag/polio/>)
[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>)
[#AIDS](https://medscienceresearch.com/tag/aids/) (<https://medscienceresearch.com/tag/aids/>) [#SV40](https://medscienceresearch.com/tag/sv40/) (<https://medscienceresearch.com/tag/sv40/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)
(<https://medscienceresearch.com/tag/vaccine/>) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)
(<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.nature.com/nature/journal/v408/n6808/full/408018b0.html>
(<https://www.nature.com/nature/journal/v408/n6808/full/408018b0.html>)

Endogenous retroviruses as potential hazards for vaccines.

“Retroviruses are classified as exogenous or endogenous according to their mode of transmission. Generally, endogenous retroviruses (ERVs) are not pathogenic in their original hosts; however, some ERVs induce diseases. In humans, a novel gammaretrovirus was discovered in patients with prostate cancer or chronic fatigue syndrome. This virus was closely related to xenotropic murine leukemia virus (X-MLV) and designated as xenotropic murine leukemia virus-related virus (XMRV). The origin and transmission route of XMRV are still unknown at present; however, XMRV may be derived from ERVs of rodents because X-MLVs are ERVs of inbred and wild mice. Many live attenuated vaccines for animals are manufactured by using cell lines from animals, which are known to produce infectious ERVs; however, the risks of infection by ERVs from xenospecies through vaccination have been ignored. This brief review gives an overview of ERVs in cats, the potential risks of ERV infection by vaccination, the biological characteristics of RD-114 virus (a feline ERV), which possibly contaminates vaccines for companion animals, and the methods for detection of infectious RD-114 virus.

2010 The International Association for Biologicals. Published by Elsevier Ltd. All rights reserved.”

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)
(<https://medscienceresearch.com/tag/vaccine/>) [#XMRV](https://medscienceresearch.com/tag/xmr/) (<https://medscienceresearch.com/tag/xmr/>)
[#Cancer](https://medscienceresearch.com/tag/cancer/) (<https://medscienceresearch.com/tag/cancer/>) [#Chronic](https://medscienceresearch.com/tag/chronic/) (<https://medscienceresearch.com/tag/chronic/>)
[#Fatigue](https://medscienceresearch.com/tag/fatigue/) (<https://medscienceresearch.com/tag/fatigue/>) [#Syndrome](https://medscienceresearch.com/tag/syndrome/)
(<https://medscienceresearch.com/tag/syndrome/>) [#Veterinary](https://medscienceresearch.com/tag/veterinary/) (<https://medscienceresearch.com/tag/veterinary/>)
[#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)

<http://www.sciencedirect.com/science/article/pii/S1045105610000801?via%3Dihub>
(<http://www.sciencedirect.com/science/article/pii/S1045105610000801?via%3Dihub>)



Evidence of pestivirus RNA in human virus vaccines.

"We examined live virus vaccines against measles, mumps, and rubella for the presence of pestivirus RNA or of pestiviruses by reverse transcription PCR. Pestivirus RNA was detected in two measles-mumps-rubella combined vaccines and in two monovalent vaccines against mumps and rubella."

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>) [#MMR](https://medscienceresearch.com/tag/mmr/) (<https://medscienceresearch.com/tag/mmr/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>) [#Pestivirus](https://medscienceresearch.com/tag/pestivirus/) (<https://medscienceresearch.com/tag/pestivirus/>) [#Mumps](https://medscienceresearch.com/tag/mumps/) (<https://medscienceresearch.com/tag/mumps/>) [#Rubella](https://medscienceresearch.com/tag/rubella/) (<https://medscienceresearch.com/tag/rubella/>) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/8077414> (<https://www.ncbi.nlm.nih.gov/m/pubmed/8077414>)

Experience with preparation an laboratory control of oral poliomyelitis vaccine in Czechoslovakia.

"Among the many problems connected with the preparation and laboratory control of oral poliomyelitis vaccines, one of the most vexed is that of the presence of undesirable, extraneous viruses of simian origin, particularly the foamy viruses. In Czechoslovakia, as elsewhere, these have been encountered in the production of live poliomyelitis vaccine from Sabin strains. Of 596 single lots of primary monkey kidney cell cultures intended for use in vaccine, only 143 lots successfully passed laboratory control tests, mainly because foamy viruses were found. Comparison tests showed that monkey and rabbit kidney cells were equally sensitive for the detection of foamy viruses but that dog kidney cells were less so and, in addition, in 8% of cases contained endogenous cytopathogenic virus agents. The presence of vacuolating agent was not tested for in the control tests discussed in this paper. All vaccine lots which passed control tests and were administered to children in the course of mass vaccination campaigns in Czechoslovakia in 1960 and 1961 proved safe and effective."

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>) [#Polio](https://medscienceresearch.com/tag/polio/) (<https://medscienceresearch.com/tag/polio/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/13913913/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/13913913/>)

🔍 Experimental oral polio vaccines and acquired immune deficiency syndrome.

The simian immunodeficiency virus (SIV) of the common chimpanzee is widely acknowledged as the direct ancestor of HIV-1. There is increasing historical evidence that during the late 1950s, kidneys were routinely excised from central African chimpanzees by scientists who were collaborating with the polio vaccine research of Dr Hilary Koprowski, and sent – inter alia – to vaccine-making laboratories in the USA and Africa, and to unspecified destinations in Belgium. While there is no direct evidence that cells from these kidneys were used as a substrate for growing Dr Koprowski's oral polio vaccines, there is a startling coincidence between places in

Africa where his CHAT vaccine was fed, and the first appearances in the world of HIV-1 group M and group-M-related AIDS. Because of the enormous implications of the hypothesis that AIDS may be an unintended iatrogenic (physician-caused) disease, it is almost inevitable that this theory will engender heated opposition from many of those in the scientific establishment, and those with vested interests.

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/)

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/11405924/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/11405924/>)

🔍 Hepatitis B Vaccines—to Switch or Not to Switch

“Shortly after the licensure of Heptavax-B in 1981 and its general availability in July 1982, the discovery of the acquired immunodeficiency syndrome (AIDS) among male homosexuals threatened the success of this product, since some of the hepatitis B surface antigen (HBsAg)-positive plasma donors were members of this high-risk group. Intensive epidemiologic, virological, and serological evaluations were launched, which eventually found no evidence for the transmission of AIDS to recipients of the plasma-derived HBsAg vaccine.”

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) B [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)

[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://jamanetwork.com/journals/jama/article-abstract/366144> (<http://jamanetwork.com/journals/jama/article-abstract/366144>)

Hepatitis vaccine pluses outweigh threat of AIDS.

Fraser B. Dent Stud. 1983.

No abstract available

PMID 6583121

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) B [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)

[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/6583121/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/6583121/>)



The injection century: massive unsterile injections and the emergence of human pathogens.

"Unsterile medical injections are common in the less-developed world, where most visits to a doctor result in the (generally unnecessary) administration of intramuscular, or subcutaneous drugs. WHO estimates¹ that every year unsafe injections result in 80 000–160 000 new HIV-1 infections, 8·16 million hepatitis B infections, and 2·3–4·7 million hepatitis C infections worldwide (this figure does not include transfusions). Together, these illnesses account for 1·3 million deaths and 23 million years of lost life."

#HIV (<https://medscienceresearch.com/tag/hiv/>) #Hepatitis (<https://medscienceresearch.com/tag/hepatitis/>) B
 #Contamination (<https://medscienceresearch.com/tag/contamination/>) #Error
 (<https://medscienceresearch.com/tag/error/>) #Death (<https://medscienceresearch.com/tag/death/>) #Vaccine
 (<https://medscienceresearch.com/tag/vaccine/>) #MedScienceResearch
 (<https://medscienceresearch.com/tag/medscienceresearch/>)

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(01\)06967-7/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(01)06967-7/abstract)

([http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(01\)06967-7/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(01)06967-7/abstract))

● Injection Safety Practice among Health Workers in Static Immunisation Centres in an Urban Community of Nigeria.

"However, reports have it that about one-third of immunisation injections are unsafe in many countries of the world including Africa."

"The common infections associated with unsafe injection listed by the subjects were abscess, HIV and Hepatitis in that order of frequency."

"Re-use of syringe for vaccine withdrawal and re-capping of used needles before discard were common practices observed while accidental needle stick injury was reported by about half (49%) of the subjects."

#HIV (<https://medscienceresearch.com/tag/hiv/>) #Hepatitis (<https://medscienceresearch.com/tag/hepatitis/>)
 #Contamination (<https://medscienceresearch.com/tag/contamination/>) #Error
 (<https://medscienceresearch.com/tag/error/>) #Vaccine (<https://medscienceresearch.com/tag/vaccine/>)
 #MedScienceResearch (<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/16160716/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/16160716/>)

ncbi.nlm.nih.gov Share

to be safer than therapeutic injections.
 However, reports have it that about one-third of immunisation injections are

unsafe in many countries of the world including Africa!

Investigation of a regulatory agency enquiry into potential porcine circovirus type 1 contamination of the human rotavirus vaccine, Rotarix: approach and outcome.

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)

[\(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/24056737/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/24056737/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/24056737/)

Veterinary

Isolation and characterization of an adventitious avian leukosis virus isolated from commercial Marek's disease vaccines.

"The data indicate that commercial MD vaccines produced by two manufacturers were contaminated with endogenous subgroup E and an exogenous subgroup A.ALV."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Animal](https://medscienceresearch.com/tag/animal/)

[\(https://medscienceresearch.com/tag/animal/\)](https://medscienceresearch.com/tag/animal/) [#Veterinary \(https://medscienceresearch.com/tag/veterinary/\)](https://medscienceresearch.com/tag/veterinary/)

[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

https://www.ncbi.nlm.nih.gov/m/pubmed/17039837 [\(https://www.ncbi.nlm.nih.gov/m/pubmed/17039837\)](https://www.ncbi.nlm.nih.gov/m/pubmed/17039837/)

Jonathan Hutchinson on Vaccination Syphilis

"A century ago, even as today, the opponents of compulsory vaccination for smallpox argued that the complications of the procedure might be worse than the disease. One of the most resolute advocates of compulsory vaccination at the time was Jonathan Hutchinson, then a newly elected honorary member of the New York Dermatological society. Hutchinson made no secret of his contempt for the misguided zealots who supported the antivaccination movement. One may well imagine, therefore, how painful it must have been for him to report in detail his findings on the transmission of syphilis by arm-to-arm vaccination. Hutchinson met the problem with characteristic courage. How he did so is summarized in this article."

[#Syphilis \(https://medscienceresearch.com/tag/syphilis/\)](https://medscienceresearch.com/tag/syphilis/) [#Contamination](https://medscienceresearch.com/tag/contamination/)

[\(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Smallpox \(https://medscienceresearch.com/tag/smallpox/\)](https://medscienceresearch.com/tag/smallpox/)
[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)
[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://jamanetwork.com/journals/jamadermatology/article-abstract/530942>
[\(http://jamanetwork.com/journals/jamadermatology/article-abstract/530942\)](http://jamanetwork.com/journals/jamadermatology/article-abstract/530942)

Live oral poliovirus vaccines and simian cytomegalovirus.

“Live oral poliovirus vaccines (OPV) are often produced in primary Cercopithecus monkey kidney (CMK) cells. The kidneys of these monkeys are often latently infected with simian cytomegalovirus (SCMV), and CMK cultures are frequently contaminated with SCMV. We tested human, monkey and rabbit tissue culture systems, and found that MRC-5 cells are most sensitive for detection of SCMV. To address the question of whether OPV could be contaminated with infectious SCMV, we inoculated MRC-5 cells with neutralized OPV manufactured in the United States between 1972 and 1998. Infectious SCMV was not found in any of the vaccine lots tested. We also used the polymerase chain reaction (PCR) to search for SCMV DNA in live oral poliovirus vaccines; SCMV DNA sequences were found in several of the vaccine lots manufactured prior to 1992.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio](https://medscienceresearch.com/tag/polio/)
[\(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Simian \(https://medscienceresearch.com/tag/simian/\)](https://medscienceresearch.com/tag/simian/)
[#Cytomegalovirus \(https://medscienceresearch.com/tag/cytomegalovirus/\)](https://medscienceresearch.com/tag/cytomegalovirus/) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)
[\(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/12217341/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/12217341/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/12217341/)

Mortality and morbidity among military personnel and civilians during the 1930s and World War II from transmission of hepatitis during yellow fever vaccination: systematic review.

“During World War II, nearly all US and Allied troops received yellow fever vaccine. Until May 1942, it was both grown and suspended in human serum. In April 1942, major epidemics of hepatitis occurred in US and Allied troops who had received yellow fever vaccine. A rapid and thorough investigation by the US surgeon general followed, and a directive was issued discontinuing the use of human serum in vaccine production. The large number of cases of hepatitis caused by the administration of this vaccine could have been avoided. Had authorities undertaken a thorough review of the literature, they would have discovered published reports, as early as 1885, of postvaccination epidemics of hepatitis in both men and horses. It would take 4 additional decades of experiments and epidemiological research before viruses of hepatitis A, B, C, D, and E were identified, their modes of transmission understood, and their genomes sequenced.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Hepatitis](https://medscienceresearch.com/tag/hepatitis/)
[\(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [#Yellow \(https://medscienceresearch.com/tag/yellow/\)](https://medscienceresearch.com/tag/yellow/) [#Fever](https://medscienceresearch.com/tag/fever/)

(<https://medscienceresearch.com/tag/tever/>) #Veterinary_(<https://medscienceresearch.com/tag/veterinary/>)
 #Military_(<https://medscienceresearch.com/tag/military/>) #Vaccine_(<https://medscienceresearch.com/tag/vaccine/>)
 #MedScienceResearch_(<https://medscienceresearch.com/tag/medscienceresearch/>)`
<https://www.ncbi.nlm.nih.gov/m/pubmed/23327242/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/23327242/>)

Multiple sclerosis and hepatitis B vaccination: could minute contamination of the vaccine by partial hepatitis B virus polymerase play a role through molecular mimicry?

“Reports of multiple sclerosis developing after hepatitis B vaccination have led to the concern that this vaccine might be a cause of multiple sclerosis in previously healthy subjects. Some articles evidenced that minor Hepatitis B virus (HBV) polymerase proteins could be produced by alternative transcriptional or translational strategies. Their detection is very difficult because they are in minute concentration and probably enzymatically inactive, however, it was shown that they could be exposed on the outside of the virus particles and also be immunogenic. In addition, HBV polymerase shares significant amino acid similarities with the human myelin basic protein. We hypothesise that some of the apparent adverse reactions to the vaccine could be due to a process called of molecular mimicry, the HBV polymerase, which could be a contaminant in the recombinant or plasma-derived vaccines, could act as autoantigens and induce autoimmune demyelinating diseases such as multiple sclerosis.”

#Multiple_(<https://medscienceresearch.com/tag/multiple/>) #Sclerosis_(<https://medscienceresearch.com/tag/sclerosis/>) #Hepatitis_(<https://medscienceresearch.com/tag/hepatitis/>) B
 #Autoimmunity_(<https://medscienceresearch.com/tag/autoimmunity/>) #Molecular_(<https://medscienceresearch.com/tag/molecular/>) #Mimicry_(<https://medscienceresearch.com/tag/mimicry/>)
 #Contamination_(<https://medscienceresearch.com/tag/contamination/>) #MedScienceResearch_(<https://medscienceresearch.com/tag/medscienceresearch/>)
<https://www.ncbi.nlm.nih.gov/m/pubmed/15908138/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/15908138/>)

Need for new technologies for detection of adventitious agents in vaccines and other biological products.

“From an industrial perspective, the conventional in vitro and in vivo assays used for detection of viral contaminants have shown their limitations, as illustrated by the unfortunate detection of porcine circovirus contamination in a licensed rotavirus vaccine.”

#Contamination_(<https://medscienceresearch.com/tag/contamination/>) #Rotavirus_(<https://medscienceresearch.com/tag/rotavirus/>) #Vaccine_(<https://medscienceresearch.com/tag/vaccine/>)
 #MedScienceResearch_(<https://medscienceresearch.com/tag/medscienceresearch/>)
<https://www.ncbi.nlm.nih.gov/m/pubmed/25475629/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/25475629/>)

New Quality-Control Investigations on Vaccines: Micro- and Nanocontamination

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccines](https://medscienceresearch.com/tag/vaccines/)

[\(https://medscienceresearch.com/tag/vaccines/\)](https://medscienceresearch.com/tag/vaccines/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf> (<http://medcraveonline.com/IJVV/IJVV-04-00072.pdf>)

Of Mice and Men: On the Origin of XMRV.

“The novel human retrovirus xenotropic murine leukemia virus-related virus (XMRV) is arguably the most controversial virus of this moment. After its original discovery in prostate cancer tissue from North American patients, it was subsequently detected in individuals with chronic fatigue syndrome from the same continent. However, most other research groups, mainly from Europe, reported negative results. The positive results could possibly be attributed to contamination with mouse products in a number of cases, as XMRV is nearly identical in nucleotide sequence to endogenous retroviruses in the mouse genome. But the detection of integrated XMRV proviruses in prostate cancer tissue proves it to be a genuine virus that replicates in human cells, leaving the question: how did XMRV enter the human population? We will discuss two possible routes: either via direct virus transmission from mouse to human, as repeatedly seen for, e.g., Hantaviruses, or via the use of mouse-related products by humans, including vaccines. We hypothesize that mouse cells or human cell lines used for vaccine production could have been contaminated with a replicating variant of the XMRV precursors encoded by the mouse genome.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#XMRV](https://medscienceresearch.com/tag/xmr/)

[\(https://medscienceresearch.com/tag/xmr/\)](https://medscienceresearch.com/tag/xmr/) [#Cancer \(https://medscienceresearch.com/tag/cancer/\)](https://medscienceresearch.com/tag/cancer/) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)

[\(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/21687768/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/21687768/>)

Oral polio vaccine and human cancer: a reassessment of SV40 as a contaminant based upon legal documents.

“The confirmation of the removal by one drug manufacturer, Lederle, has been made public at an international symposium in January 1997, where its representatives stated that all of Lederle’s seeds had been tested and screened to assure that it was free from SV40 virus. However, in litigation involving the Lederle oral polio vaccine, the manufacturer’s internal documents failed to reveal such removal in all of the seeds. The absence of confirmatory testing of the seeds, as well as testimony of a Lederle manager, indicate that this claim of removal of SV40 and the testing for SV40 in all the seeds cannot be fully substantiated. These legal documents and testimony indicate that the scientific community should not be content with prior assumptions that SV40 could not have been in the oral polio vaccine.”

have been in the oral polio vaccine.

[#Cancer \(https://medscienceresearch.com/tag/cancer/\)](https://medscienceresearch.com/tag/cancer/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Corruption \(https://medscienceresearch.com/tag/corruption/\)](https://medscienceresearch.com/tag/corruption/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/11205211> (<https://www.ncbi.nlm.nih.gov/m/pubmed/11205211>)

🔍 **The origin of acquired immune deficiency syndrome: Can science afford to ignore it?**

“Scientific discussion of the polio vaccine hypothesis for the origin of acquired immune deficiency syndrome (AIDS) has been systematically suppressed for more than 12 years. The author calls for an international multidisciplinary inquiry into the origin of AIDS, arguing it is essential to human health, prevention of new pandemics, and to protect the integrity of science in the eyes of the public.”

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

Full article here:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1088489/pdf/TB010935.pdf>
(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1088489/pdf/TB010935.pdf>)

🔍 **Polio, hepatitis B and AIDS: an integrative theory on a possible vaccine induced pandemic.**

“The hypothesis that simian virus 40 (SV40) infected polio vaccines may be linked to the evolution of acquired immunodeficiency disorder (AIDS), and certain cancers, has been advanced. Most recently, investigators discussed the likelihood of gene-reshuffling following SV40 infection as a precursor to acquired immune dysfunction. Findings of recent SV40 infections in four children born after 1982 suggest infections were transmitted vertically along gene lines. Earlier observations proved activation of a retrovirus gene by a hepatitis B virus (HBV) protein. This paper proposes a new integrative theory on the origin of AIDS. It advances the possibility of genetic recombinations with oncogene activation by HBV involving simian viruses that likely infected polio vaccinated blood donors to the initial hepatitis B (HB) vaccine trials conducted on gay men in New York City and Ugandan Blacks in the early to mid-1970s. The socio-economic and even military ramifications associated with this politically challenging thesis are discussed.”

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)

[\(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#Cancer \(https://medscienceresearch.com/tag/cancer/\)](https://medscienceresearch.com/tag/cancer/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)
[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/11388787/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/11388787/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/11388787/)

Full article here-

<http://www.originofaids.com/articles/polio.htm> [\(http://www.originofaids.com/articles/polio.htm\)](http://www.originofaids.com/articles/polio.htm)

Polio vaccines and the origin of AIDS.

"In particular, it is now known that the early polio vaccines were contaminated with at least one monkey virus, SV40. The transfer of monkey viruses to man via contaminated vaccines is particularly relevant to the acquired immunodeficiency syndrome (AIDS), since the causative agent of AIDS, human immunodeficiency virus (HIV), is thought to be derived from a simian precursor virus. Furthermore, human infection with this virus appears to be a relatively recent event. We hypothesize that the AIDS pandemic may have originated with a contaminated polio vaccine that was administered to inhabitants of Equatorial Africa from 1957 to 1959. The mechanism of evolution of HIV from this vaccine remains to be determined."

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#SV40](https://medscienceresearch.com/tag/sv40/)
[\(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Contamination](https://medscienceresearch.com/tag/contamination/)
[\(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/)

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/7935079/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/7935079/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/7935079/)

Porcine circovirus (PCV) removal by Q sepharose fast flow chromatography.

"The recently discovered contamination of oral rotavirus vaccines led to exposure of millions of infants to porcine circovirus (PCV). PCV was not detected by conventional virus screening tests. Regulatory agencies expect exclusion of adventitious viruses from biological products. Therefore, methods for inactivation/removal of viruses have to be implemented as an additional safety barrier whenever feasible. However, inactivation or removal of PCV is difficult. PCV is highly resistant to widely used physicochemical inactivation procedures. Circoviruses such as PCV are the smallest viruses known and are not expected to be effectively removed by currently-used virus filters due to the small size of the circovirus particles. Anion exchange chromatography such as Q Sepharose®) Fast Flow (QSFF) has been shown to effectively remove a range of viruses including parvoviruses. In this study, we investigated PCV1 removal by virus filtration and by QSFF chromatography. As expected, PCV1 could not be effectively removed by virus filtration. However, PCV1 could be effectively removed by QSFF as used during the purification of monoclonal antibodies (mAbs) and a log₁₀ reduction value (LRV) of 4.12 was obtained.

© 2013 American Institute of Chemical Engineers.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Rotavirus \(https://medscienceresearch.com/tag/rotavirus/\)](https://medscienceresearch.com/tag/rotavirus/)

[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/24039195/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/24039195/>)

Possible origins of AIDS.

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/)
[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/)
[#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://science.sciencemag.org/content/256/5061/1260.1.long>
<http://science.sciencemag.org/content/256/5061/1260.1.long>

Richard Pearson Strong and the iatrogenic plague disaster in Bilibid Prison, Manila, 1906.

“In November 1906, Richard Pearson Strong, then head of the Philippine Biological Laboratory, inoculated 24 men–inmates of Manila’s Bilibid Prison–with a cholera vaccine that somehow had been contaminated with plague organisms; 13 men died.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Death \(https://medscienceresearch.com/tag/death/\)](https://medscienceresearch.com/tag/death/)
[#Cholera \(https://medscienceresearch.com/tag/cholera/\)](https://medscienceresearch.com/tag/cholera/)
[#Corruption \(https://medscienceresearch.com/tag/corruption/\)](https://medscienceresearch.com/tag/corruption/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)
[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/2690293> (<https://www.ncbi.nlm.nih.gov/m/pubmed/2690293>)

The Risk of AIDS After Hepatitis Vaccination

“In the recent decision analysis article by Sacks et al¹ in the Dec 28, 1984, issue of The Journal, the authors claim to have calculated the maximum rate of hepatitis B vaccine-induced acquired immunodeficiency syndrome (AIDS) to be eight per 100,000 with 95% confidence. This calculation is based on a study of 40,000 persons who had been vaccinated prior to mid-1982. I do not believe that an extrapolation from this population can be expected to hold true for a vaccine manufactured from today’s pool of donors.”

[#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/)

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [B #Statistics \(https://medscienceresearch.com/tag/statistics/\)](https://medscienceresearch.com/tag/statistics/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<http://jamanetwork.com/journals/jama/article-abstract/398638> (<http://jamanetwork.com/journals/jama/article-abstract/398638>)

Should the risk of acquired immunodeficiency syndrome deter hepatitis B vaccination? A decision analysis.

"The current epidemic of acquired immunodeficiency syndrome (AIDS) and fear that its causative agent contaminates the currently available hepatitis B vaccine may have deterred vaccine use. We formulated a decision-analytic model that compares the risk of death from hepatitis B and AIDS in those vaccinated with the risk of death from hepatitis B alone in those who wait two years for a synthetic vaccine. For individuals with 5% annual risk of hepatitis B, the best current estimate is that vaccination now would save 25 lives per 100,000. The best current estimate of the rate of vaccine-induced AIDS is zero, and one can be 95% confident that the rate is less than eight per 100,000. The rate would have to be considerably higher before postponement of vaccination would be rational for those for whom vaccination has been recommended."

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [B #Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Statistics \(https://medscienceresearch.com/tag/statistics/\)](https://medscienceresearch.com/tag/statistics/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/6239044/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/6239044/>)

Simian cytomegalovirus and contamination of oral poliovirus vaccines.

"In the 1950s the use of primary rhesus macaque kidney cultures to propagate poliovirus for vaccine production led to the contamination of vaccines with simian virus 40 (SV40). African green monkey kidney (AGMK) cultures free of SV40 were used as an alternative cell substrate for vaccine manufacture. In this study we evaluate oral poliovirus seeds, vaccine bulks and vaccines themselves for the presence of a common contaminant of AGMK cultures, simian cytomegalovirus (SCMV). Using sensitive polymerase chain reaction (PCR) techniques, nearly half of the samples analysed were found to be contaminated with SCMV sequences. However, vaccine bulks, positive by PCR for SCMV failed to show any evidence of infectious virus in these studies. One poliovirus vaccine and one seed, propagated on rhesus macaque kidney cultures were found to be positive for the rhesus monkey CMV by PCR."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Simian \(https://medscienceresearch.com/tag/simian/\)](https://medscienceresearch.com/tag/simian/)

<https://medscienceresearch.com/tag/polio/> <https://medscienceresearch.com/tag/sv40/>

[#Cytomegalovirus \(https://medscienceresearch.com/tag/cytomegalovirus/\)](https://medscienceresearch.com/tag/cytomegalovirus/) [#SV40](https://medscienceresearch.com/tag/sv40/)

[\(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/12623061/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/12623061/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/12623061/)

Simian cytomegalovirus-related stealth virus isolated from the cerebrospinal fluid of a patient with bipolar psychosis and acute encephalopathy.

“A cytopathic ‘stealth’ virus was cultured from the cerebrospinal fluid of a patient with a bipolar psychotic disorder who developed a severe encephalopathy leading to a vegetative state. DNA sequencing of a polymerase chain reaction-amplified product from infected cultures has identified the virus as an African green monkey simian cytomegalovirus (SCMV)-related stealth virus. The virus is similar to the SCMV-related stealth virus isolated from a patient with chronic fatigue syndrome. The findings support the concepts that stealth viruses can account for a spectrum of dysfunctional brain diseases and that some of these viruses may have arisen from live polio viral vaccines.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio](https://medscienceresearch.com/tag/polio/)

[\(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Cytomegalovirus](https://medscienceresearch.com/tag/cytomegalovirus/)

[\(https://medscienceresearch.com/tag/cytomegalovirus/\)](https://medscienceresearch.com/tag/cytomegalovirus/) [#Psychiatric](https://medscienceresearch.com/tag/psychiatric/)

[\(https://medscienceresearch.com/tag/psychiatric/\)](https://medscienceresearch.com/tag/psychiatric/) [#Encephalopathy](https://medscienceresearch.com/tag/encephalopathy/)

[\(https://medscienceresearch.com/tag/encephalopathy/\)](https://medscienceresearch.com/tag/encephalopathy/)

[#Chronic \(https://medscienceresearch.com/tag/chronic/\)](https://medscienceresearch.com/tag/chronic/) [#Fatigue \(https://medscienceresearch.com/tag/fatigue/\)](https://medscienceresearch.com/tag/fatigue/)

[#Syndrome \(https://medscienceresearch.com/tag/syndrome/\)](https://medscienceresearch.com/tag/syndrome/) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)

[\(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

[\(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/8888270/> [\(https://www.ncbi.nlm.nih.gov/m/pubmed/8888270/\)](https://www.ncbi.nlm.nih.gov/m/pubmed/8888270/)

Some oral poliovirus vaccines were contaminated with infectious SV40 after 1961.

“Some polio vaccines prepared from 1954 to 1961 were contaminated with infectious SV40. It has been assumed that all polio vaccines were SV40 free in the United States after 1961 and in other countries after 1962. Following a WHO requirement that was prompted by the detection of SV40 in some human tumors, we conducted a multilaboratory study to test for SV40 polio vaccines prepared after 1961. Vaccine samples from 13 countries and the WHO seed were initially tested by PCR. The possible presence of intact and/or infectious SV40 DNA in PCR-positive samples was tested by transfection and infection of permissive CV-1 cells. All results were verified by immunohistochemistry, cloning, and sequencing. All the vaccines were SV40 free, except for vaccines from a major eastern European manufacturer that contained infectious SV40. We determined that the procedure used by this manufacturer to inactivate SV40 in oral poliovirus vaccine seed stocks based on heat

inactivation in the presence of MgCl₂ did not completely inactivate SV40. These SV40-contaminated vaccines were produced from early 1960s to about 1978 and were used throughout the world. Our findings underscore the potential risks of using primary monkey cells for preparing poliovirus vaccines, because of the possible contamination with SV40 or other monkey viruses, and emphasize the importance of using well-characterized cell substrates that are free from adventitious agents. Moreover, our results indicate possible geographic differences in SV40 exposure and offer a possible explanation for the different percentage of SV40-positive tumors detected in some laboratories.”

[#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/16288015/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/16288015/>)

Suffolk County to conduct test of special safety syringes.

“The syringes will be used in administering vaccines and performing routine medical health procedures in the public health department and jail. The study was prompted by several cases in which health-care workers accidentally or carelessly exposed patients to HIV and other blood-borne diseases through the reuse of syringes labeled for one-time use.”

[#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/11366592/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/11366592/>)

A survey of mycoplasma detection in veterinary vaccines.

“Nine live virus veterinary vaccines from six sources were found to be contaminated with mycoplasma. The vaccines were for use in canine, feline and avian species, and 53 batches of the products were at fault. The isolates were identified as *Mycoplasma hominis*, *M. arginini*, *M. orale*, *M. hyorhinis* and *M. gallinarum*.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Veterinary \(https://medscienceresearch.com/tag/veterinary/\)](https://medscienceresearch.com/tag/veterinary/) [#Error \(https://medscienceresearch.com/tag/error/\)](https://medscienceresearch.com/tag/error/) [#Animal \(https://medscienceresearch.com/tag/animal/\)](https://medscienceresearch.com/tag/animal/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#Mycoplasma \(https://medscienceresearch.com/tag/mycoplasma/\)](https://medscienceresearch.com/tag/mycoplasma/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)
<https://www.ncbi.nlm.nih.gov/m/pubmed/3799018> (<https://www.ncbi.nlm.nih.gov/m/pubmed/3799018>)

[SV40 as a possible cofactor in the etiopathogenesis of mesothelioma and other human tumors].

"Simian virus 40 (SV40) has been introduced into the human population with contaminated polio vaccines between 1955 and 1963. Previous research conducted by southern blot hybridization and recent analysis by PCR have shown the presence of SV40 sequences in human brain tumors, mesotheliomas and osteosarcomas as well as in normal tissues such as blood and sperm fluids. SV40 RNA and T antigen were detected in the same tissues. All the samples were coinfecting by BK Virus (BKV), suggesting that BKV may have a helper function for SV40 replication in human cells. The presence of SV40 in human tumors suggests that the virus may be a cofactor in the etiopathogenesis of human neoplasia. In addition, blood and semen may represent the vectors for transmission of SV40 by horizontal infection in the human population."

[#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/9987613/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/9987613/>)

Veterinary

Testing for viral contaminants of veterinary vaccines in Hungary.

"The safety of veterinary vaccines is of paramount importance and it is significantly jeopardised by extraneous agents such as bacteria, mycoplasma, Chlamydia and viruses. Several critical steps of vaccine manufacture involve a potential risk of viral contamination. Viruses, as extraneous, agents can be divided into two main groups. Group 1 agents, such as Pestivirus, chicken anaemia virus (CAV), and egg drop syndrome virus (EDSV) are well-known to manufacturers and authorities. Compendial detection methods, clear guidelines and legislation have been established to minimise the risk of contamination with these agents. Contrary to group 1, group 2 agents like Torque Teno virus (TTV) or RD114, a replication-competent feline gamma-retrovirus, have only recently been recognised and their role as contaminants needs further investigation. Randomly selected veterinary vaccines used between 1992 and 2009 were tested by nucleic acid amplification for CAV, EDSV, and TTV. Pestivirus contamination was examined in 33 vaccines used between 1996 and 2006 and a further 27 vaccines used between 2007 and 2009 based on random selection of these vaccines. In addition to random tests done on vaccines used from 2007 on, 12 batches of live Aujeszky's disease vaccines submitted to our laboratory for Official Control Authority Batch Release (OCABR) were also tested for Pestivirus."

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Veterinary \(https://medscienceresearch.com/tag/veterinary/\)](https://medscienceresearch.com/tag/veterinary/) [#Animals \(https://medscienceresearch.com/tag/animals/\)](https://medscienceresearch.com/tag/animals/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)



<https://www.ncbi.nlm.nih.gov/m/pubmed/20338783> (<https://www.ncbi.nlm.nih.gov/m/pubmed/20338783>)

🌐 **Tetanus vaccine may be laced with anti-fertility drug. International / developing countries.**

“A priest, president of Human Life International (HLI) based in Maryland, has asked Congress to investigate reports of women in some developing countries unknowingly receiving a tetanus vaccine laced with the anti-fertility drug human chorionic gonadotropin (hCG). If it is true, he wants Congress to publicly condemn the mass vaccinations and to cut off funding to UN agencies and other involved organizations. The natural hormone hCG is needed to maintain pregnancy. The hormone would produce antibodies against hCG to prevent pregnancy. In the fall of 1994, the Pro Life Committee of Mexico was suspicious of the protocols for the tetanus toxoid campaign because they excluded all males and children and called for multiple injections of the vaccine in only women of reproductive age. Yet, one injection provides protection for at least 10 years. The Committee had vials of the tetanus vaccine analyzed for hCG. It informed HLI about the tetanus toxoid vaccine. HLI then told its World Council members and HLI affiliates in more than 60 countries. Similar tetanus vaccines laced with hCG have been uncovered in the Philippines and in Nicaragua. In addition to the World Health Organization (WHO), other organizations involved in the development of an anti-fertility vaccine using hCG include the UN Population Fund, the UN Development Programme, the World Bank, the Population Council, the Rockefeller Foundation, the US National Institute of Child Health and Human Development, the All India Institute of Medical Sciences, and Uppsala, Helsinki, and Ohio State universities. The priest objects that, if indeed the purpose of the mass vaccinations is to prevent pregnancies, women are uninformed, unsuspecting, and unconsenting victims.”

[#Corruption \(https://medscienceresearch.com/tag/corruption/\)](https://medscienceresearch.com/tag/corruption/) [#Contamination](https://medscienceresearch.com/tag/contamination/)

[\(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Tetanus \(https://medscienceresearch.com/tag/tetanus/\)](https://medscienceresearch.com/tag/tetanus/)

[#hCG \(https://medscienceresearch.com/tag/hcg/\)](https://medscienceresearch.com/tag/hcg/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/12346214/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/12346214/>)

Transmissible spongiform encephalopathies: vaccine issues.

“The recent emergence of bovine spongiform encephalopathy (BSE) and variant Creutzfeldt-Jakob Disease (vCJD) suggests that transmissible spongiform encephalopathies (TSEs) pose an ongoing threat to human and animal health. To avoid iatrogenic transmission of TSEs in vaccines, strategies must be developed to obviate TSE agent infectivity in cellular substrates, cell culture media components and enzymes, and excipients, and to validate the safety of these components and field vaccines efficiently.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine](https://medscienceresearch.com/tag/vaccine/)

[\(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/)

[#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/11761262/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/11761262/>)

Tuberculosis in Newborns: The Lessons of the “Lübeck Disaster” (1929-1933).

Fox GJ, et al. PLoS Pathog. 2016.

“In an accident later known as the Lübeck disaster, 251 neonates were orally given three doses of the new Bacille Calmette-Guérin (BCG) antituberculosis (TB) vaccine contaminated with Mycobacterium tuberculosis. A total of 173 infants developed clinical or radiological signs of TB but survived the infection, while 72 died from TB.”

[#Death](https://medscienceresearch.com/tag/death/) (<https://medscienceresearch.com/tag/death/>) [#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>)

[#Failure](https://medscienceresearch.com/tag/failure/) (<https://medscienceresearch.com/tag/failure/>) [#BCG](https://medscienceresearch.com/tag/bcg/) (<https://medscienceresearch.com/tag/bcg/>)

[#Tuberculosis](https://medscienceresearch.com/tag/tuberculosis/) (<https://medscienceresearch.com/tag/tuberculosis/>) [#Contamination](https://medscienceresearch.com/tag/contamination/)

(<https://medscienceresearch.com/tag/contamination/>)

[#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/) (<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/26794678> (<https://www.ncbi.nlm.nih.gov/m/pubmed/26794678>)

Vaccination-induced syphilis and the Hübner malpractice litigation.

“Dr. Georg Hübner, the defendant, was accused of having initiated a small epidemic of syphilis by using the lymph of a syphilitic infant to vaccinate 13 infants.”

[#Syphilis](https://medscienceresearch.com/tag/syphilis/) (<https://medscienceresearch.com/tag/syphilis/>) [#Contamination](https://medscienceresearch.com/tag/contamination/)

(<https://medscienceresearch.com/tag/contamination/>) [#Smallpox](https://medscienceresearch.com/tag/smallpox/) (<https://medscienceresearch.com/tag/smallpox/>)

[#Vaccine](https://medscienceresearch.com/tag/vaccine/) (<https://medscienceresearch.com/tag/vaccine/>) [#MedScienceResearch](https://medscienceresearch.com/tag/medscienceresearch/)

(<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/22643719/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/22643719/>)

The XIX century smallpox prevention in Naples and the risk of transmission of human blood-related pathogens.

“Although Galbiati established the retro-vaccination (1803) and developed the “calf” lymph vaccine, recognized and implemented since 1864 as the optimal smallpox vaccine in the following hundred years, Naples general population was mainly vaccinated with “human” lymph from abandoned children until 1893. Mini-epidemics of syphilis and serum hepatitis were periodically reported as results of arm-to-arm procedure. The risk of transmission of blood-related pathogens was higher in Naples where >80% of abandoned children, used as repository of cowpox virus, were dying in their first year of life.”

[#Contamination](https://medscienceresearch.com/tag/contamination/) (<https://medscienceresearch.com/tag/contamination/>) [#Syphilis](https://medscienceresearch.com/tag/syphilis/)

(<https://medscienceresearch.com/tag/syphilis/>) [#Hepatitis](https://medscienceresearch.com/tag/hepatitis/) (<https://medscienceresearch.com/tag/hepatitis/>) [^](#)

[#Smallpox](https://medscienceresearch.com/tag/smallpox/) (<https://medscienceresearch.com/tag/smallpox/>) [#Death](https://medscienceresearch.com/tag/death/) (<https://medscienceresearch.com/tag/death/>)

#Liver (<https://medscienceresearch.com/tag/liver/>) #Vaccine (<https://medscienceresearch.com/tag/vaccine/>)

#MedScienceResearch (<https://medscienceresearch.com/tag/medscienceresearch/>)

<https://www.ncbi.nlm.nih.gov/m/pubmed/25622683/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/25622683/>)

< ncbi.nlm.nih.gov Share

smallpox vaccine in the following
 hundred years, Naples general
 population was mainly vaccinated with
 "human" lymph from abandoned
 children until 1893. Mini-epidemics of
 syphilis and serum hepatitis were
 periodically reported as results of arm-
 to-arm procedure. The risk of
 transmission of blood-related pathogens
 was higher in Naples where >80% of
 abandoned children, used as repository
 of cowpox virus, were dying in their first
 year of life. Recent vaccinology

Tweet

G+

Search

DATABASE

A B C D E F G H I J K L M N O P R S T U
 (https://www.ncbi.nlm.nih.gov/m/pubmed/25622683/)
 A) B) C) D) E) F) G) H) I) J) K) L) M) N) O) P) R) S) T) U)

(<https://www.medscienceresearch.com/contamination/#letter->

V) W) Y)

ABOUT US

Med Science Research brings you evidence-based information, straight science, and data from medical journals.

Med Science Research is not designed to review studies, but instead to highlight and categorize them in an organized fashion for the user to review.

A special thank you is in order to our Scientific Advisory Board for all of their assistance.

Call to action: "Those who have the privilege to know have the duty to act."

Please share this website with the world!

Note: It is not uncommon for authors of studies to place an obligatory mention of vaccine safety in order to have their research accepted for publication in pharmaceutical funded journals.

This website is not designed to give medical advice.

MedScienceResearch@gmail.com (<mailto:MedScienceResearch@gmail.com>)

RECENT POSTS

[Acute Flaccid Paralysis \(https://medscienceresearch.com/acute-flaccid-paralysis/\)](https://medscienceresearch.com/acute-flaccid-paralysis/)

[Kawasaki \(https://medscienceresearch.com/kawasaki/\)](https://medscienceresearch.com/kawasaki/)

[HIV \(https://medscienceresearch.com/hiv/\)](https://medscienceresearch.com/hiv/)

 (<https://www.facebook.com/MedScienceResearch/>)

IF YOU WOULD LIKE TO SUPPORT OUR MISSION, PLEASE CONSIDER DONATING TO OUR CAUSE SO THAT WE CAN CONTINUE TO BRING YOU THE VERY BEST INFORMATION POSSIBLE. ANY AMOUNT HELPS.

[Make A Donation \(https://www.paypal.com/cgi-bin/webscr?cmd=donations&business=MedScienceResearch@gmail.com&item_name=Support+MedScienceResearch.com\)](https://www.paypal.com/cgi-bin/webscr?cmd=donations&business=MedScienceResearch@gmail.com&item_name=Support+MedScienceResearch.com)

© 2017 Med Science Research. All Rights Reserved. Crafted By: [32 Bit Solutions \(http://32BitSolutions.com\)](http://32BitSolutions.com)



The Weston A. Price Foundation

Public Health Officials Know: Recently Vaccinated Individuals Spread Disease

MARCH 3, 2015 BY LESLIE MANOOKIAN

([HTTPS://WWW.WESTONAPRICE.ORG/AUTHOR/LMANOOKIAN/](https://www.westonaprice.org/author/lmanookian/))

WASHINGTON, D.C. –March 3, 2015– [[GlobeNewsWire \(http://globeonewswire.com/news-release/2015/03/03/712042/10123084/en/Public-Health-Officials-Know-Recently-Vaccinated-Individuals-Spread-Disease.html\)](http://globeonewswire.com/news-release/2015/03/03/712042/10123084/en/Public-Health-Officials-Know-Recently-Vaccinated-Individuals-Spread-Disease.html)] — Physicians and public health officials know that recently vaccinated individuals can spread disease and that contact with the immunocompromised can be especially dangerous. For example, the Johns Hopkins Patient Guide warns the immunocompromised to “Avoid contact with children who are recently vaccinated,” and to “Tell friends and family who are sick, or have recently had a live vaccine (such as chicken pox, measles, rubella, intranasal influenza, polio or smallpox) not to visit.”¹

A statement on the website of St. Jude’s Hospital warns parents not to allow people to visit children undergoing cancer treatment if they have received oral polio or smallpox vaccines within four weeks, have received the nasal flu vaccine within one week, or have rashes after receiving the chickenpox vaccine or MMR (measles, mumps, rubella) vaccine.²

“The public health community is blaming unvaccinated children for the outbreak of measles at Disneyland, but the illnesses could just as easily have occurred due to contact with a recently vaccinated individual,” says Sally Fallon Morell, president of the Weston A. Price Foundation. The Foundation promotes a healthy diet, non-toxic lifestyle and freedom of medical choice for parents and their children. “Evidence indicates that recently vaccinated individuals should be quarantined in order to protect the public.”

Scientific evidence demonstrates that individuals vaccinated with live virus vaccines such as MMR (measles, mumps and rubella), rotavirus, chicken pox, shingles and influenza can shed the virus for many weeks or months afterwards and infect the vaccinated and unvaccinated alike. ^{3,4,5,6,7,8,9,10,11,12}

Furthermore, vaccine recipients can carry diseases in the back of their throat and infect others while displaying no symptoms of a disease.^{13,14,15}

Both unvaccinated and vaccinated individuals are at risk from exposure to those recently vaccinated. Vaccine failure is widespread; vaccine-induced immunity is not permanent and recent outbreaks of diseases such as whooping cough, mumps and measles have occurred in fully vaccinated populations.^{16,17} Flu vaccine recipients become more susceptible to future infection after repeated vaccination.^{18,19}

Adults have contracted polio from recently vaccinated infants. A father from Staten Island ended up in a wheel chair after contracting polio while changing his daughter's diaper. He received a 22.5 million dollar award in 2009. ^{20,21}

"Vaccine failure and failure to acknowledge that live virus vaccines can spread disease have resulted in an increase in outbreaks of infectious disease in both vaccinated and unvaccinated individuals," says Leslie Manookian, producer of The Greater Good. "CDC should instruct physicians who administer vaccinations to inform their patients about the risks posed to others by those who've been recently vaccinated."

According to the Weston A. Price Foundation, the best protection against infectious disease is a healthy immune system, supported by adequate vitamin A and vitamin C. Well-nourished children easily recover from infectious disease and rarely suffer complications.

The number of measles deaths declined from 7575 in 1920 (10,000 per year in many years in the 1910s) to an average of 432 each year from 1958-1962.²² The vaccine was introduced in 1963. Between 2005 and 2014, there have been no deaths from measles in the U.S. and 108 deaths reported after the MMR vaccine.²³

The Weston A. Price Foundation is a 501(c)(3) nutrition education foundation with the mission of disseminating accurate, science-based information on diet and health. Named after nutrition pioneer Weston A. Price, DDS, author of Nutrition and Physical Degeneration, the Washington, DC-based Foundation publishes a quarterly journal for its 15,000 members,

supports 600 local chapters worldwide and hosts a yearly international conference. The Foundation phone number is (202) 363-4394, www.westonaprice.org, info@westonaprice.org.

MEDIA CONTACTS:

Kim Hartke, 703-860-2711, press@westonaprice.org

Leslie Manookian, 208-721-2135, leslie@greatergoodmovie.org

(<http://www.westonaprice.org/wp-content/uploads/Johns-Hopkins-Patient-Guide-p-113.jpg>)

Hospital Warning about Potential Vaccine Shedding

REFERENCES:

1. Since this press release was issued the hospital has revised this Patient Guide. These are screen shots of the original, see first two images above. The third image is the redacted

(<http://www.westonaprice.org/wp-content/uploads/Package-Insert.png>)

Close Up of Warning about Vaccines Potential to Transmit Disease

version.

2. <http://www.stjude.org/stjude/v/index.jsp?>

[vgnextoid=20206f9523e70110VgnVCM1000001e0215acRCRD](http://www.stjude.org/stjude/v/index.jsp?vgnextoid=20206f9523e70110VgnVCM1000001e0215acRCRD)

(<http://www.stjude.org/stjude/v/index.jsp?>

(<http://www.westonaprice.org/wp-content/uploads/Patient-Guide-After-WAPF-press-release.jpg>)

Redacted version of patient guide was put online after this WAPF press release

[vgnextoid=20206f9523e70110VgnVCM1000001e0215acRCRD](#) (This document was taken down since this press release was issued, see image four, above)

3. Outbreak of Measles Among Persons With Prior Evidence of Immunity, New York City, 2011

<http://www.westonaprice.org/wp-content/uploads/St-Jude-Patient-Guide-LG.jpg>

St. Jude Patient Guide Informs Parents about Live Virus Vaccine Risk for Immune Compromised Children

<http://cid.oxfordjournals.org/content/ear> Since this press release was issued the hospital has revised this page.
<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>

<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>

4. Detection of Measles Virus RNA in Urine Specimens from Vaccine Recipients

<http://www.ncbi.nlm.nih.gov/pubmed/7494055>

<http://www.ncbi.nlm.nih.gov/pubmed/7494055>

5. Comparison of the Safety, Vaccine Virus Shedding and Immunogenicity of Influenza Virus Vaccine, Trivalent, Types A and B, Live Cold-Adapted, Administered to Human

Immunodeficiency Virus (HIV)-Infected and Non-HIV Infected Adults

<http://jid.oxfordjournals.org/content/181/2/725.full>

(<http://jid.oxfordjournals.org/content/181/2/725.full>)

6. Sibling Transmission of Vaccine-Derived Rotavirus (RotaTeq) Associated with Rotavirus

Gastroenteritis <http://pediatrics.aappublications.org/content/125/2/e438>

(<http://pediatrics.aappublications.org/content/125/2/e438>)

7. Polio vaccination may continue after wild virus fades <http://www.cidrap.umn.edu/news-perspective/2008/10/polio-vaccination-may-continue-after-wild-virus-fades>

(<http://www.cidrap.umn.edu/news-perspective/2008/10/polio-vaccination-may-continue-after-wild-virus-fades>)

8. Engineering attenuated virus vaccines by controlling replication fidelity

<http://www.nature.com/nm/journal/v14/n2/abs/nm1726.html>

(<http://www.nature.com/nm/journal/v14/n2/abs/nm1726.html>)

9. CASE OF VACCINE-ASSOCIATED MEASLES FIVE WEEKS POST-IMMUNISATION, BRITISH COLUMBIA, CANADA, OCTOBER 2013 <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20649>

(<http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20649>)

10. The Safety Profile of Varicella Vaccine: A 10-Year Review

http://jid.oxfordjournals.org/content/197/Supplement_2/S165.full

(http://jid.oxfordjournals.org/content/197/Supplement_2/S165.full)

11. Comparison of Shedding Characteristics of Seasonal Influenza Virus (Sub)Types and Influenza A(H1N1)pdm09; Germany, 2007–2011 <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0051653>

(<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0051653>)

[id=10.1371/journal.pone.0051653](http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0051653))

12. Epigenetics of Host–Pathogen Interactions: The Road Ahead and the Road Behind

<http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1003007>

(<http://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1003007>)

13. Animal Models for Influenza Virus Pathogenesis and Transmission

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063653/>

(<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063653/>)

14. Acellular pertussis vaccines protect against disease but fail to prevent infection and

transmission in a nonhuman primate model

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063653/>

(<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3063653/>)

15. Study Finds Parents Can Pass Whooping Cough to Babies

http://www.nytimes.com/2007/04/03/health/03coug.html?_r=0

(http://www.nytimes.com/2007/04/03/health/03coug.html?_r=0)

16. Immunized People Getting Whooping Cough

<http://www.kpbs.org/news/2014/jun/12/immunized-people-getting-whooping-cough/>

(<http://www.kpbs.org/news/2014/jun/12/immunized-people-getting-whooping-cough/>)

17. Vaccine Failure — Over 1000 Got Mumps in NY in Last Six Months

<http://articles.mercola.com/sites/articles/archive/2010/03/06/vaccine-failure-over-1000-get-mumps-in-ny-in-last-six-months.aspx>

18. Impact of Repeated Vaccination on Vaccine Effectiveness Against Influenza A(H3N2) and B During 8 Seasons <http://cid.oxfordjournals.org/content/early/2014/09/29/cid.ciu680.full>

(<http://cid.oxfordjournals.org/content/early/2014/09/29/cid.ciu680.full>)

19. [http://articles.mercola.com/sites/articles/archive/2012/09/18/flu-shot-increases-flu-](http://articles.mercola.com/sites/articles/archive/2012/09/18/flu-shot-increases-flu-illness.aspx)

[illness.aspx](http://articles.mercola.com/sites/articles/archive/2012/09/18/flu-shot-increases-flu-illness.aspx) (<http://articles.mercola.com/sites/articles/archive/2012/09/18/flu-shot-increases-flu-illness.aspx>)

20. [http://www.nydailynews.com/new-york/staten-island-dad-22-5m-polio-case-lederle-](http://www.nydailynews.com/new-york/staten-island-dad-22-5m-polio-case-lederle-laboratories-article-1.369105)

[laboratories-article-1.369105](http://www.nydailynews.com/new-york/staten-island-dad-22-5m-polio-case-lederle-laboratories-article-1.369105) (<http://www.nydailynews.com/new-york/staten-island-dad-22-5m-polio-case-lederle-laboratories-article-1.369105>)

21. <http://naturalsociety.com/woman-contracts-polio-virus-vaccinated-infant/>

(<http://naturalsociety.com/woman-contracts-polio-virus-vaccinated-infant/>)

22. <http://www.cdc.gov/mmwr/preview/mmwrhtml/00056803.htm>

(<http://www.cdc.gov/mmwr/preview/mmwrhtml/00056803.htm>)

23. [http://vaccineimpact.com/2015/zero-u-s-measles-deaths-in-10-years-but-over-100-](http://vaccineimpact.com/2015/zero-u-s-measles-deaths-in-10-years-but-over-100-measles-vaccine-deaths-reported/)

[measles-vaccine-deaths-reported/](http://vaccineimpact.com/2015/zero-u-s-measles-deaths-in-10-years-but-over-100-measles-vaccine-deaths-reported/) (<http://vaccineimpact.com/2015/zero-u-s-measles-deaths-in-10-years-but-over-100-measles-vaccine-deaths-reported/>)

About Leslie Manookian

This site uses Akismet to reduce spam. [Learn how your comment data is processed \(https://akismet.com/privacy/\)](https://akismet.com/privacy/).

Copyright © 2018 Weston A. Price · Site by [Site a la Carte \(http://sitealacarte.com\)](http://sitealacarte.com)

To whom it may concern,

December 21, 2018

On behalf of the Kauai Community College Nursing program we are here in support of the new Hawai'i school mandated HPV and Hep A vaccine initiative. The Human papillomavirus causes various genital cancers including cervical cancer. In a study done by Tom et al., in 2016, it was found that the HPV vaccine has been available to the Hawai'i pediatric population; however, since 2013 vaccine use has been suboptimal with only 38% of females and 31% of males ages 13-17, completing all three doses of the vaccine. This new school mandate will increase the completion rates of the three step vaccination series among the adolescent population thus preventing cancer. It is important that parents are informed about this vaccine's ability to prevent cancer in their children as well as protecting themselves. The Center for Disease Control recently expanded their recommendation for HPV vaccinations to men and women between the ages of 27-45 because of its effectiveness. However, the recommendation is that children be vaccinated between 9 and 11 years old. The reason for the early vaccination is prevention of HPV BEFORE being exposed. In 2018, Robert et al., studied school located vaccination policies, currently only two states, Virginia and Rhode Island, and Washington D.C., have school mandated HPV vaccination requirements. In their study, all three have high uptake and completion rates of the HPV vaccination series. With the new vaccine requirements in Hawaii, we should expect similar improvements in vaccine completion rates and hopefully a reduction in cancer.

Ask yourselves, if you could get an injection that would prevent cancer, would you?

Roberts, M. C., Murphy, T., Moss, J. L., Wheldon, C. W., & Psek, W. (2018). A qualitative comparative analysis of combined state health policies related to human papillomavirus vaccine uptake in the United States. *American Journal of Public Health*,

108(4), 493–499. Retrieved from

<https://kauaproxy.lib.hawaii.edu:2291/10.2105/AJPH.2017.304263>

Dirty Vaccines: New Study Reveals Prevalence of Contaminants

Celeste McGovern

Every Human Vaccine Tested Was Contaminated by Unsafe Levels of Metals and Debris Linked to Cancer and Autoimmune Disease, New Study Reports

Researchers examining 44 samples of 30 different vaccines found dangerous contaminants, including red blood cells in one vaccine and metal toxicants in every single sample tested – except in one animal vaccine.

Using extremely sensitive new technologies not used in vaccine manufacturing, Italian scientists reported they were “baffled” by their discoveries which included single particles and aggregates of organic debris including red cells of human or possibly animal origin and metals including lead, tungsten, gold, and chromium, that have been linked to autoimmune disease and leukemia.

In the [study](#), published this week in the *International Journal of Vaccines and Vaccination*, the researchers led by [Antonietta Gatti](#), of the National Council of Research of Italy and the Scientific Director of [Nanodiagnostics](#), say their results “show the presence of micro- and nano-sized particulate matter composed of inorganic elements in vaccine samples” not declared in the products’ ingredients lists.

Lead particles were found in the cervical cancer vaccines, Gardasil and Cervarix, for example, and in the seasonal flu vaccine Aggripal manufactured by Novartis as well as in the Meningetec vaccine meant to protect against meningitis C.

Samples of an infant vaccine called Infarix Hexa (against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and haemophilus influenzae type B) manufactured by GlaxoSmithKline was found to contain stainless steel, tungsten and a gold-zinc aggregate.

Other metal contaminants included platinum, silver, bismuth, iron, and chromium. Chromium (alone or in alloy with iron and nickel) was identified in 25 of the human vaccines from Italy and France that were tested.

GSK’s Fluarix vaccine for children three years and older contained 11 metals and aggregates of metals. Similar aggregates to those identified in the vaccines have been shown to be prevalent in cases of [leukemia](#), the researchers noted.

Many of the vaccines contained iron and iron alloys which, according to the researchers, “can [corrode](#) and the [corrosion products](#) exert a toxicity affecting the tissues”.

CMSRI_Corrosive Debris Meme_v1.pngThe researchers supply an image of an

area in a drop of Sanofi Pasteur MSD's Repevax (diphtheria, pertussis, tetanus, polio) vaccine "where the morphology of red cells - we cannot tell whether they are human or animal- is clearly visible" along with the presence of "debris" composed of aluminum, bromine, silicon, potassium and titanium.

Feligen, the only veterinary vaccine tested in the 44 total vaccines sampled, proved to be the only sample free from inorganic contamination.

The investigation revealed aluminum and sodium chloride, the usual component of saline, as was expected, because they are named ingredients of most vaccines. Using a Field Emission Gun Environmental Electron Scanning Microscope, the researchers produced photos of this aluminum salt which formed white crystalline branches similar to frost on a windowpane on the top of the droplets of vaccine liquid. A German-made vaccine against allergies produced a layer of inorganic salts so thick that the researchers could not penetrate the drop to detect other particulate contaminants.

Aluminum has a documented neurotoxicity all by itself. The French veterinary vaccines exclude it for this reason. The human ones don't. The researchers express concern about synergy of multiple toxins added to this known neurotoxin. "It is a well-known fact in toxicology that contaminants exert a mutual, synergic effect, and as the number of contaminants increases, the effects grow less and less predictable. The more so when some substances are unknown."

"The quantity of foreign bodies detected and, in some cases, their unusual chemical compositions baffled us," the researchers note. "In most circumstances, the combinations detected are very odd as they have no technical use, cannot be found in any material handbook and look like the result of the random formation occurring, for example, when waste is burnt. In any case, whatever their origin, they should not be present in any injectable medicament, let alone in vaccines, more in particular those meant for infants."

Donate to support independent research:

**Drug companies shouldn't do it, but they do.
Government agencies should do it, but they don't.
Unbiased, independent medical research - it's up to us.
Please Help.
Donate Today**

Undesirable impact

The study explains that these foreign injected impurities may explain a vast array of apparently unrelated adverse events associated with vaccination from headaches and seizures to fatigue, muscle pain, paralysis and sudden infant death syndrome. More likely than not, they speculate, vaccine contaminants will "have a more serious impact on very small organisms like those of children."

Once inside a body, foreign material in a vaccine shot, whether it is meant to be there as in the case of an aluminum, or not, in the case of contaminants, launches the formidable immune system into action.

As with anything small and foreign, its reaction to vaccine ingredients is potent, poorly understood, unpredictable, and as the Italian researchers say, may be “undesirable.” The immune system may dispatch an army of large white blood cells called macrophages to engulf the foreign bodies and contain them in swellings and granulomas at the injection site. But if the contaminants are swept away in the blood’s circulation to any distant site or organ including the microbiota, which regulate numerous functions including the immune system, their effect could be felt long after they covertly entered the body.

In some cases, the immune system may initiate an inflammatory assault against what it perceives as invader. This may include the launch of a host of players called cytokines. Some of these chemical messengers like interleukin-6 are incriminated in autism.

Because these contaminants may persist in the body and stimulate the immune system, they may induce chronic inflammation and can manifest as autoimmune diseases when the immune system turns on its host's own cells as in multiple sclerosis or type 1 diabetes.

It’s also been shown that the contaminants found in the vaccines can enter cell nuclei and interact with DNA, the researchers note. No one knows what that can do.

Vaccine DangersDark history

Vaccines have a long and sordid history of contamination. In 1955 batches of polio vaccine containing live polio virus infected and paralysed hundreds of children. The tragedy became known as the Cutter Incident for the laboratory where the vaccines had passed safety tests with flying colors.

But there are dozens of other “incidents” which would better be called acts of criminal negligence, including:

- The polio vaccine doled out between 1955 and 1963 was contaminated with simian virus 40 (SV40) from monkey kidney cells used to produce the vaccine. It’s been linked to the growing epidemic of cancer.
- In 2007, Merck & Company, Inc. recalled 1.2 million doses of Hib vaccines due to contamination with bacteria called *cereus*, a potentially lethal food-poisoning bug.
- In 2009, more than 40,000 doses of a meningitis C vaccine for babies were withdrawn from the British market when they were found to be contaminated with blood-poisoning bacteria, *S aureus*.
- In 2010, deep sequence analysis of eight different live attenuated virus vaccines revealed unexpected viral sequences in three of them: retrovirus avian leukosis was found in a measles vaccine, a virus similar to simian retrovirus was identified in Rotateq anti-diarrhea vaccine developed by CDC consultant Paul Offit, and the entire genome sequence of porcine cirovirus1 was found in Rotarix leading the FDA to suspend the rotavirus vaccine.
- In 2014, The US Food and Drug Administration ordered GlaxoSmithKline to

review the manufacturing operation of its flu vaccine when it found microbiological contamination of products purporting to be sterile.

- In 2013, Merck & Company, Inc. recalled one batch of Gardasil when glass particles were discovered in several phials.
- Recently it was reported that Sanofi Pasteur refused to recall its ActHIB vaccine for babies, even though it knew it was contaminated with glass shards. The FDA didn't object.

There are dozens of these cases, and even if vaccine manufacturers are issued multiple "warnings" action is rarely ever taken to clean the vaccine manufacture process. Since pharmaceutical companies have blanket indemnity from lawsuits for faulty vaccines, there is no incentive for them to clean up their act.

Clear and present danger

The study investigators conclude that the vaccine contamination they found is likely accidental. "Our hypothesis is that this contamination is unintentional, since it is probably due to polluted components or procedures of industrial processes (e.g. filtrations) used to produce vaccines, not investigated and not detected by the Producers".

Discussion about why pharmaceutical companies don't produce clean vaccines is one thing. But the reality of vaccines as they are now is another. It doesn't change what is being injected into millions of people today. Dangerous unintended toxins are in every one of the vaccines tested in this investigation, except one for cats.

This research doesn't just show that vaccines are full of crud that top scientists can't even define. It makes a mockery of health oversight agencies like the FDA and CDC and their lies that vaccines undergo adequate safety checks and risk assessment.

It doesn't merely reveal that the long-term consequences of vaccinating cannot even be assessed. If anti-cancer vaccines like Gardasil and Cervarix contain cancer-causing aggregates of toxic metals, their use as a weapon against a cancer a girl has zero chance of getting before age 21 is not just useless. It is egregious abuse.

Now, every vaccine's claims to saving lives must be weighed against its risks of causing cancer, neurodevelopmental disease, autoimmune disease and every other immune-mediated "mystery" disorder now epidemic and soaring.

The results of these investigations not only negate every assertion that vaccines are "safe and effective", but they confirm that they are actually a clear and present danger.

Topics: [vaccine safety studies](#), [vaccines and autoimmunity](#)

Contamination

© 2017 Med Science Research. All Rights Reserved. Crafted By: [32 Bit Solutions \(http://32BitSolutions.com\)](http://32BitSolutions.com)



Contamination

(<https://medscienceresearch.com>

/contamination/)

Recap of the vaccine contaminants below: Mycoplasma, HIV, syphilis, hepatitis B and C, pestivirus: mouse brain tissue, bacteriophage, reverse transcriptase, SV40 cancer causing virus, porcine circovirus, endotoxins, coliphages, pseudomonas, fungi, XMRV, foamy viruses of simian origin, nanoparticles with several metals, antifertility drug hCG, Mycobacterium tuberculosis, simian cytomegalovirus

Veterinary vaccines: chicken anaemia virus, egg drop syndrome virus, avian leukosis virus, Torque Teno virus, RD-114 retrovirus, mycoplasma

—
Absence of antibodies to HTLV-III in health workers after hepatitis B vaccination.

“A proportion of the plasma for the triply inactivated, plasma-derived hepatitis B vaccine produced in the United States is obtained from homosexual men. Because homosexual men are a high-risk group for the acquired immunodeficiency syndrome (AIDS), concern has emerged that the vaccine could harbor the AIDS agent.”

[#AIDS \(https://medscienceresearch.com/tag/aids/\)](https://medscienceresearch.com/tag/aids/) [#HIV \(https://medscienceresearch.com/tag/hiv/\)](https://medscienceresearch.com/tag/hiv/) [#Hepatitis B \(https://medscienceresearch.com/tag/hepatitis/\)](https://medscienceresearch.com/tag/hepatitis/) [#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

<https://www.ncbi.nlm.nih.gov/m/pubmed/2991619/> (<https://www.ncbi.nlm.nih.gov/m/pubmed/2991619/>)

—
● **Adventitious agents in viral vaccines: Lessons learned from 4 case studies**

“The four cases are: a) SV40 in polio vaccines; b) bacteriophage in measles and polio vaccines; c) reverse transcriptase in measles and mumps vaccines; and d) porcine circovirus and porcine circovirus DNA sequences in rotavirus vaccines.”

[#Contamination \(https://medscienceresearch.com/tag/contamination/\)](https://medscienceresearch.com/tag/contamination/) [#SV40 \(https://medscienceresearch.com/tag/sv40/\)](https://medscienceresearch.com/tag/sv40/) [#Polio \(https://medscienceresearch.com/tag/polio/\)](https://medscienceresearch.com/tag/polio/) [#Vaccine \(https://medscienceresearch.com/tag/vaccine/\)](https://medscienceresearch.com/tag/vaccine/) [#MedScienceResearch \(https://medscienceresearch.com/tag/medscienceresearch/\)](https://medscienceresearch.com/tag/medscienceresearch/)

Search

DATABASE

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	R	S	T	U	
(http://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...)																				
#letter-																				
(http://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...)																				
A)	B)	C)	D)	E)	F)	G)	H)	I)	J)	K)	L)	M)	N)	O)	P)	R)	S)	T)	U)	
#letter-	#letter-																			
V)	W)	Y)																		

ABOUT US

Med Science Research brings you evidence-based information, straight science, and data from medical journals.

Med Science Research is not designed to review studies, but instead to highlight and categorize them in an organized fashion for the user to review.

A special thank you is in order to our Scientific Advisory Board for all of their assistance.

Call to action: "Those who have the privilege to know have the duty to act."

Please share this website with the world!

Note: It is not uncommon for authors of studies to place an obligatory mention of vaccine safety in order to have their research accepted for publication in pharmaceutical funded journals.

This website is not designed to give medical advice.

[MedScienceResearch@gmail.com \(mailto:MedScienceResearch@gmail.com\)](mailto:MedScienceResearch@gmail.com)

RECENT POSTS

[Acute Flaccid Paralysis \(https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...\)](https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...)

[Kawasaki \(https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...\)](https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...)

[HIV \(https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...\)](https://medscienceresearch.com/contamination/?fbclid=IwAR1Qizvs...)



<https://www.MedScienceResearch.com>

**IF YOU WOULD LIKE TO !
OUR MISSION, PLEASE C
DONATING TO OUR CAU
WE CAN CONTINUE TO E
THE VERY BEST INFORM
POSSIBLE. ANY AMOUN**

Make A Donation

https://www.paypal.com/cgi-bin/webscr?cmd=_donations&business=MedScienceResearch@gmail.com&item_name=Support+MedScienceResearch.com&%2e00¤cy_code=USD



From: [REDACTED]
To: [REDACTED]
Subject: STOP this maiming & killing of our children
Date: Friday, December 21, 2018 4:30:12 PM

There is so much imperial, science-base evidence as to the extreme damage, including incapacitating perfectly healthy children and adults - also including death, that it is extremely hard to believe that anyone in their right mind would even consider forcing vaccinations upon all the people.

In all fairness, "all sides" of this proposition should very carefully be investigated and considered.

I know that all of us - each and every one - are super busy these days - - especially at this holiday time - when it was decided to have so-called public discussion on this matter.

I include links that are clear and concise - thus will take up little of your time to check out.

I implore you to "do due diligence" before proceeding in this matter, and unbiasedly be aware of all the ramifications of this proposal.

There are thousands of cases of human lives being destroyed by vaccines and it is proved many times over that the vaccinated children/ people expose others to the very "illness" the vaccines are propertied to protect against.

<https://www.youtube.com/watch?v=ZDg7CUh53ys>

Please check out at least a few of these 335 Abstracts regarding vaccines - PLEASE BE INFORMED !!

.....

100s Reject Vaccine - timesofindia.indiatimes.com

MEERUT: Hundreds of madrassas across western Uttar Pradesh have refused permission to health officials to administer measles-rubella vaccines to students, putting lakhs of children at risk. In Meerut alone, at least 70 of the 272 seminaries have refused entry to health officials. According to these messages, the vaccine can make a child impotent.". R eports from across the country of children falling sick after vaccination have added to the fear. According to a government report, over 49,000 children were killed in 2015 due to it.

From: [REDACTED]
To: [REDACTED]
Subject: Support HAR 11-157
Date: Friday, December 21, 2018 10:31:34 PM

To whom it may concern,

I am a Nurse Practitioner and a mother, writing to express my concern for the opposition toward this bill. Following the CDC schedule of vaccines is well-studied and established, and it makes sense. Disease burden and associated financial and emotional costs are slashed by preventing disease.

People who are fortunate enough to be able to afford medical care perceive the risk of foregoing vaccination as minimal, but this is short-sighted. Transmitting disease to those who cannot afford proper medical care can be devastating. Children have the right to go to school and be protected, not exposed to potentially life threatening or altering disease.

As a society, we must do better, we have a duty to protect our own youth, as well as those in our community who cannot stand up for themselves. It is unacceptable to have abundant knowledge and access to science and to blatantly disregard it because we "feel" differently. This has nothing to do with feelings, and everything to do with knowledge.

Please, I urge you to help protect our future generations and support HAR 11-157.

Kindly,

Jennifer Nill, DNP, FNP-BC

Sent from mobile device.

From: [REDACTED]
To: [REDACTED]
Subject: Supporting The Updated Immunization Guidelines
Date: Friday, December 21, 2018 10:31:43 AM

I am writing to strongly support the updated immunization guidelines. The proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The science beyond vaccine safety is not questionable, and I am dismayed by the efforts of the anti-vaccination proponents to make their opposition appear anything other than isolated misguided voices fueled by unfortunate misconceptions and fears.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Alex Khomenko
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: I OPPOSE HAR 11-157
Date: Saturday, December 22, 2018 6:29:58 AM

I OPPOSE HAR 11-157.

I am a 29 year resident of the State of Hawaii, a husband, a father, and a citizen of the United States of America. Compulsory and/or mandatory vaccinations are a misuse of the of the power of the state, which is the use of aggressive force.

It is an aggressive act to compel what decisions are made concerning my body and the body and the bodies of my family. It is a violation of and an assault on the body. The state has no right to do that, because I am a flesh and blood human being.

The subject of vaccines is highly debated and controversial. I am basing my opposition on many things but a few are most concerning. There has not been enough time to truly know if the long term effects are safe enough so that the benefits outweigh the risks. There is evidence that the ingredients used as preservatives in vaccines are dangerous and toxic. I have met and experienced many parents whom report injuries inflicted upon the children after receiving vaccinations. The anecdotal evidence is overwhelming when one searches on the internet for reports of vaccine injuries.

A separate argument could be made about the effectiveness of vaccinations. It seems that many who receive vaccinations end up getting infected and sick from what they were trying to prevent, seasonal flu shots are one example. Why must they be compulsory if those who voluntarily get vaccinations are supposed to be protected from those who do not. My opting out is not a violation of someone's inalienable rights. To cite ideas about herd health are invalid arguments. They only prove that vaccinations are less effective than advertised.

There may be some merit to vaccine theory but as of its current application it is an assault on the sovereignty of the body of the individual.

I oppose injecting heavy metals and chemical preservatives into my body or the bodies of my family.

This legislation might not work to increasing the number of people taking vaccines. It will increase the number of parents who opt out of the DOE school system. If this legislation, passes my family will be obligated to homeschool. This is an attack on equality. My child will not have the equal right to public education because the state has taken away the rights of the parent to choose whether or not to vaccinate. It should be unlawful to use tax payer funds for public education and then make it impossible for parents to enjoy their right to public education.

From: [REDACTED]
To: [REDACTED]
Subject: OPPOSE HAR 11-157
Date: Saturday, December 22, 2018 9:40:14 AM

I strongly oppose HAR 11-157. My children have been vaccinated according to the schedule set out by our doctor up until this point but under no circumstances will I allow them to have the HPV vaccine. A vaccine that prevents STD's is a private decision between parents, children and their doctor. The flu vaccine should also be decided upon privately. Vaccines in general should not be required in order to go to school. What goes into my child's body should not be decided by the government.

Sincerely,
Michelle Scotti

--
[REDACTED]
Ph: [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Oppose Mandatory Vaccinations
Date: Saturday, December 22, 2018 7:26:31 AM

I highly oppose mandatory vaccinations.

They are not safe for our children.

I pay lots of taxes and my children have a right to attend public school.

We have a right to choose whether to vaccinate or not.

It is against my religion.

This is America, where we are supposed to have these simple freedoms to live a life of liberty and the pursuit of health and happiness.

No one has a right to force the poisoning of children.

[REDACTED]

Joyce Kehoe Smith

From: [REDACTED]
To: [REDACTED]
Subject: Vaccinations
Date: Saturday, December 22, 2018 6:58:54 AM

As a mother and health care professional, the state of Hawaii has a duty to ensure the health and well-being of its people. One way to fulfill that duty is through stricter vaccination rules. This is the best way to protect the community.

As a therapist, I have seen how the elderly suffer because of the flu. There is a huge cost upon everyone when the flu hits. A vaccine can help protect the vulnerable and should become a priority.

Alternative health and a distrust in science and evidence-based medicine is very popular but dangerous. This is what's driving the need to reestablish stricter guidelines to keep our community healthy. Fake medicine claims to help people but when someone gets a preventable disease, real medicine is what will alleviate suffering and help one recover.

Joni Kamiya
Mother, Occupational Therapist

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: Re: HPV paper
Date: Saturday, December 22, 2018 9:03:13 AM

[REDACTED]

Irene thank you for being active. I know, I'm pissed too, that we have to fight as the Gov tries to piece by piece take our freedoms. I can't sit quietly as I see this happen. I don't want my children to not have choice and the right to make informed decisions about their health and what is put into their bodies.

Sent from my iPhone

> On Dec 22, 2018, at 8:44 AM, Irene Kelly [REDACTED] wrote:
>
> <khvi-11-10-1066948.pdf>

From: [REDACTED]
To: [REDACTED]
Subject: OPPOSE HAR 11-157
Date: Saturday, December 22, 2018 9:40:14 AM

I strongly oppose HAR 11-157. My children have been vaccinated according to the schedule set out by our doctor up until this point but under no circumstances will I allow them to have the HPV vaccine. A vaccine that prevents STD's is a private decision between parents, children and their doctor. The flu vaccine should also be decided upon privately. Vaccines in general should not be required in order to go to school. What goes into my child's body should not be decided by the government.

Sincerely,
Michelle Scotti

--
[REDACTED]
Ph: [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: testimony on proposed rules title 11
Date: Saturday, December 22, 2018 1:35:40 PM

I am a retired family physician. In my 35 year career with Kaiser Permanente, I was also a professor of family medicine and had teaching appointments at three Southern California Medical Schools. I approved of thousands of childhood immunizations.

I favor some immunizations and acknowledge their effectiveness.

I am opposed to adding more immunizations to the Hawaii childhood regulations.

The child's new immune system is overwhelmed by all these foreign body injections.

In my view, most of the present immunizations are either not very effective or not even necessary. The new ones are even worse. Often times, their side effects are worse than the possibility of acquiring the targeted the disease.

In all cases, the parents should be able to opt out.

Gordon LaBedz, MD

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Strongly OPPOSE rule change of HAR 11-157
Date: Saturday, December 22, 2018 9:02:22 PM
Attachments: [khvi-11-10-1066948.pdf](#)
[khvi-11-10-1066948.pdf](#)

My name is Irene Kelly. I am a tax paying resident of Hawaii residing at:
[REDACTED]

I am writing to DOH in STRONG OPPOSITION of HAR 11-157. I would like to submit the following published paper in testimony to support that the HPV vaccine is highly flawed. I am also strongly against the government and the pharmaceutical industry using our children as experimental pawns so that legislators and the pharmaceutical industry can profit.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4635939/>

Further I am strongly against mandatory medical procedures and firmly believe that if there is a risk there must be a choice. The Vigibase database of the World Health Organization has compiled more than 86,000 serious advert reactions to the HPV vaccine, with over \$5 million paid to families injured by HPV vaccine.

Will the state of Hawaii, DOH and DOE be responsible and liable for injuries caused by this mandate? Injuries that include: nervous system and autoimmune disorders, respiratory disorders, vascular disorders, reproductive system disorders, cardiac disorders, blood and lymphatic system disorders, seizures, paralysis, blindness, pancreatitis, and death!!

HPV is not a communicable disease. Children cannot pass HPV like a cold in school. Plus HPV can take years (10-30 years) to result in cancer which is plenty of time for screening, treatment and prevention. There is nothing wrong with annual pelvic exams. We should be teaching children about reproductive health in school, the value of annual exams and safe sex. Further, my own pediatrician believes this vaccine to be deeply flawed and does not recommend it!! MY DOCTOR!! This important decision should be left to doctors and families.

Again, I and my family strongly oppose the HPV vaccine and refuse to allow my tax dollars to be used to support such an unethical and deeply flawed vaccine and mandatory program in Hawaii.

Regards,
Irene Kelly
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Immunization
Date: Sunday, December 23, 2018 12:14:30 PM

To Whom it may concern,
Mandatory vaccination has no place in America. Taking away our rights as to how we protect our children is a clear violation of our rights. You simply can not make something mandatory that has clear evidence to show the potential for very dangerous side effects. I will pull my very healthy child from school before I would expose him to the ridiculous vaccination schedule the pharmaceutical company's have decided upon. I do not think it would be in the best interest of Hawaii's precious Keiki to make vaccination mandatory.
Mahalo for your consideration,
Amy Arnett-Smith

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Immunization Requirements
Date: Sunday, December 23, 2018 3:45:13 PM

To Whom It May Concern,

I am emailing to support the immunization requirements being proposed as administrative law. Participation in the immunization process should be required for all students. Those applying for exemption should need to demonstrate that they meet the exemption requirements with substantial evidence. It is imperative that we all participate in the program to prevent the spread of deadly diseases.

Respectfully,
Erin Petrosian

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: immunization rights
Date: Sunday, December 23, 2018 6:10:39 PM

HAR 11-157

It should be our right as parents to choose what we think is right for the health of our children!

Many will have to choose between their rights and their job

HB 1722

SB 2316

SB 2393

SB 2394

HB 1945

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: OPPOSING CH 11-157
Date: Sunday, December 23, 2018 9:15:01 AM

Aloha,

I strongly oppose CH11-157.

First of all, when there is a risk there must be a choice!! There has been numerous vaccine related injuries and even deaths that occurred specifically from the HPV vaccine that you are planning on mandating all 7th graders with this bill. HPV is a SEXUALLY TRANSMITTED DISEASE!!! To require all 7th graders to be vaccinated against HPV is wrong especially given that the nature of this disease is an STD. This is a decision that must and should be made by the parents! Why would a parent want to vaccinate their child if their child is not sexually active especially given the numerous reports of its vaccine injuries from this particular vaccine.

In addition, all vaccines should be a decision made by the parents including flu vaccines and should not be required for preschoolers. Vaccine injuries are a real issue for some parents. Mandating vaccines when there are clear evidence of possible vaccine injuries. Would parents be permitted to sue the state if a vaccine injury occurs and the state policies and regulations force parents to vaccinate? These vaccine injuries vary in severity but can cause permanent health issues, complications for life and even death in severe cases.

Thank you!

<https://www.ncbi.nlm.nih.gov/m/pubmed/20869467/>

<https://www.nvic.org/NVIC-Vaccine-News/July-2012/merck-lawsuit-reignites-vaccine-safety-concerns.aspx>

<https://healthwyze.org/reports/208-the-lead-vaccine-developer-comes-clean-so-she-can-sleep-at-nightq-gardasil-and-cervarix-dont-work-are-dangerous-and-werent-tested>

<http://www.herbs-info.com/blog/lead-developer-of-hpv-vaccines-comes-clean-warns-parents-and-young-girls/>

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Opposing Proposed Changes to HAR 11-157
Date: Sunday, December 23, 2018 1:17:56 PM

To whom it may concern at the DOH,

I am writing to express my heartfelt opposition to the proposed rule changes to HAR 11-157. As a father and concerned citizen I am also alarmed and disturbed by the general shifting trends in the DOH's approach to vaccination issues which these proposed changes seem to reflect. They strike me as both un-democratic and un-Hawaiian.

I and my family are NOT "anti-vaccination." I and my wife have received immunizations and at this time plan to have our children receive certain shots as well, as and when appropriate. I do not question the fundamental medical science of artificial immunization, nor its ability to spare countless people from life-threatening or truly life-altering diseases such as Smallpox, Polio, and Ebola.

However, we ARE alarmed by the trend toward more and more vaccines being given to younger and younger children for less and less serious diseases, as well as the increasing pressure from pharmaceutical companies to gradually erode patients' fundamental human right to choose and/or refuse medical treatment (ie vaccines), under the guise of "protecting public health" or "promoting the common good"—while the successful efforts by vaccine manufacturers to lobby for the passage of legislation to exempt themselves for liability from injuries caused by their products is particularly disturbing, immoral, and unprecedented (not to mention seemingly hypocritical on some level). Such trends serve only to polarize the debate and side-line legitimate, evidence-based discussion and independent study around vaccinations, while further alienating much of the public and eroding trust in our government entities.

Skepticism and even outright concern regarding the aggressive scheduling, sheer overwhelming quantity, and specific timing of shots currently recommended by the CDC is not in any way a fringe idea. The widespread conflict of interest in the sprawling body of vaccine research is also of concern--again, this is not a "conspiracy theory," but well documented. Some of the recommendations are apparently not even evidence-based--such as administering Hep B starting at birth to ALL babies, despite the fact that Hep B is NOT a childhood illness and is not (according to the CDC themselves) spread by casual contact. Many pro-vaccination doctors have spoken out about their concerns with the CDC recommendations, such as Dr Robert Sears, MD, FAAP, and Dr. Paul Thomas, MD, who have both written whole books that mention these issues, in an attempt to provide parents with the information to make more informed decisions. In his popular book The Vaccine Book, Dr Sears writes that he is pro-vaccine, but also that his is pro-informed consent, and that while he believes most vaccines are indeed safe for most children, there is also an inherent risk with any vaccine (some more than others), and that any doctor who tells you otherwise is lying. Both these doctors have created their own "alternative schedules"--as have countless others--in an attempt to best serve and protect their patients. Such modifications as avoiding giving multiple live vaccines at one time, avoiding giving more than one shot containing aluminum at one time, and delaying certain less critical and/or more problematic shots till a child is older (with a more developed immune system) are common themes. None of these concerns is addressed by the CDC recommendations (in fact, they violate all three of these evidence-based

cautionary principles).

The CDC's blanket, statistically-modeled schedule also makes no allowance for circumstances that greatly affect disease risk (both the individual's risk of contraction, severity of illness, and risk of complications, as well as risk of transmission to others), such as whether a child is breastfed and for how long, whether he/she will be in daycare from infancy or kept at home until school age, family diet and lifestyle habits, and so much more--all of which can have HUGE impacts. Vaccinations are really only a tiny piece of the puzzle when it comes to raising healthy children.

Ultimately, our children are not statistics. Each case is different, and every parent wants the best for their child, and every doctor the best for their patients. And for the reasons mentioned above and others, the science is absolutely not "settled." Nor are all vaccines equally vital to public health or equally safe for the recipients. Therefore medical decisions regarding if, when, and how to administer immunizations should be left to patients (or their parents) in cooperation with their doctor. For the State to use coercion (no matter how well-intentioned), either directly or indirectly, to infringe upon an individual's right to choose or refuse care, is nothing less than a violation of human rights.

Thank you for your serious consideration of these concerns, and your work on our behalf. I wish you and yours health and happiness for the holidays and the new year!

Mahalo nui loa,

Sky Roversi-Deal

From: [REDACTED]
To: [REDACTED]
Subject: Testimony
Date: Sunday, December 23, 2018 7:47:21 PM

I would like to share my testimony in support of vaccinations and maintaining mandatory immunizations as a doctor and parent of a nine-month old.

Vaccinations have been proven to be safe through multiple scientific studies over the past few decades. They protect us from preventable diseases that can kill or seriously impair our children. Antivaccine rhetoric is becoming concerning in Hawaii, and is putting our Hawaii keiki at risk of multiple preventable diseases. Anti-vaccine advocates use inaccurate information and pseudoscience to scare parents who get nervous about the vaccination process. In order for our children to be safe from these diseases, I strongly recommend we adhere to the CDC guidelines for mandatory vaccinations. We have seat belt laws for the same reasons; it benefits our collective health and safety when we all abide by those safety laws and rules. In the case of vaccinations, these laws not only promote our own safety, but also the safety of people around us.

I attended the public hearing in Kailua Kona at the West Hawaii Civic Center on December 20th, 2018. Many of the speakers expressed misinformed views against vaccinations. I was shocked at how many speakers clearly had a financial conflict of interest in testifying against mandatory vaccinations. This presents a clear conflict of interest in their testimony.

For example, one speaker began by promoting her own book. She brought it with her and held it up to promote it to the people in the room or anyone watching the video recording. She subsequently brought up many disproven claims, such as the link between autism and thimerosal, which has shown to be false in multiple studies conducted since 1999.

Another speaker used this platform to promote a group that he leads. He acknowledged that this group is something that he modeled off of Tony Robbins, the self help writer and entertainer with no medical or scientific background. This speaker was moved by Robbins' sentiment that germ theory is not accurate, and that diseases actually come from within. He apparently claims that you can fight disease by changing your mindset. These speakers, and others like them, stand to benefit from the dissemination of inaccurate or false information to promote their own self-interest, and instill unfounded fear in vaccinations and their benefits.

Additionally, there was a doctor that claimed to be putting herself at risk by speaking against mandatory vaccinations. She practices in an area on Hawaii Island which has a growing population of non-vaccinators. Most doctors in the area understand the risk that not vaccinating poses to the greater community, and will not accept nonvaccinators into their practice. The nonvaccinators in this area of Hawaii find themselves in need of a doctor that will see their children despite not having the mandatory vaccinations. Often, these

patients tend to be from more affluent socio-economic backgrounds, and will pay a lot of money to see someone who identifies with their views. Therefore, a doctor willing to accept and promote an anti-vaccine viewpoint would see a direct financial benefit from more patients joining their practice. Again, this demonstrates a clear conflict of interest and goes against all advice of the major medical associations, like the American Association of Pediatrics.

I was unable to stay for all of the speakers at this public hearing and provide my direct testimony. However, I could see that many of these speakers had much to gain from their testimony in supporting their anti-vaccine views. There is great harm that can be done to our community by spreading inaccurate information for personal or other financial gain. This is extremely dangerous to our safety and most of all, our keiki. These conflicts of interest could mean the difference of life or death for some children when it comes to vaccinations.

I would like to acknowledge that I personally have no financial incentives or conflicts of interest in the vaccine argument. I am an optometrist, and I do not administer vaccines. I am solely concerned about the safety of my own child and the children in my community. I strongly believe that the State of Hawaii Department of Health needs to conduct educational sessions to counter the misinformation that is being disseminated by anti-vaccine groups. There have been more and more outbreaks in the State of Hawaii, and we need to prevent outbreaks like the one that occurred in Disneyland in 2014 with measles. Let's not wait until there are preventable deaths that have occurred to take action. I strongly support mandatory vaccinations and immunizations.

Thank you for your time.
Dr. Janet Mitchell, O.D.

From: [REDACTED]
To: [REDACTED]
Subject: Opposition of HAR-11-157
Date: Sunday, December 23, 2018 8:05:03 PM

Aloha,

I would like to express my concern regarding the proposal of HAR 11-157. As Hawaii informed consent states, "Where there is a risk, there must be a choice."

I do not feel it is constitutional to **require** parents to vaccinate their children until further studies have been done on the safety of vaccines. Senate Bill 732 before the 103rd Congress of the United States known as the "Comprehensive Child Health Immunization Act of 1993", made known the fact that there are risks to vaccines.

In addition, there are many concerning ingredients in vaccines, such as carcinogens, neurotoxins, animal blood, allergens, and heavy metals. As a follower of Jesus Christ, and a pro-life supporter the biggest concern of additives in vaccines to our family is aborted fetal tissue.

Consequently, I would like to make it clear that I do **not** support HAR 11-157. I believe in the **freedom of choice** when it comes to our children's healthcare.

Respectfully,

Robert R. Fields
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Re: Supporting The Updated Immunization Guidelines
Date: Sunday, December 23, 2018 11:35:18 PM

In addition to my previous message of support, I hope that the DoH can take a cue from a state like California and recommend removal of personal and religious belief exemptions. The public health interest should prevail.

On Fri, Dec 21, 2018 at 10:31 AM Alex Khomenko [REDACTED] wrote:

I am writing to strongly support the updated immunization guidelines. The proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The science beyond vaccine safety is not questionable, and I am dismayed by the efforts of the anti-vaccination proponents to make their opposition appear anything other than isolated misguided voices fueled by unfortunate misconceptions and fears.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Alex Khomenko
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Feedback on HAR 11-157 proposed rule change hearing process
Date: Sunday, December 23, 2018 1:41:41 PM

Dear folks at the DOH,

I attended the hearing for Kaua'i County on Friday 12/21 for testimony regarding the proposed changes to HAR 11-157. I hoped to help bring some serious concerns regarding the hearing and how it was conducted to your attention.

The room in which the hear was held could only hold 40 people at one time, which was vastly inadequate for the number of people attending (mostly to voice opposition to the rule change, I noticed), as was the time allotted (2 hours), which meant only a fraction of the people who came from all over the island to give spoken testimony were able to do so, while some were never able to enter the building at all. (Nor was there anyone present from the DOH in person listening to testimony that I could see--aside from the facilitator). I would like to give the organizers the benefit of the doubt and assume they were simply caught unprepared for the volume of attendees and/or were limited by scheduling constraints and budget concerns. Because otherwise, unfortunately, one would be more likely to view the entire hearing as a sham and a mockery of the democratic process, as well as an insult to the dozens of people who took time out of their lives on a busy, pre-holiday week to attend and give heartfelt testimony--which I sincerely have to hope was not the intent. However, I noted that many people attending DID quickly make such assumptions, creating a generally tense mood at the hearing of frustration, anger, and cynicism.

Thank you for your time and consideration of this matter, and a very happy holidays.

Sincerely,
Sky Roversi-Deal

From: [REDACTED]
To: [REDACTED]
Subject: FW: Message submission from DOCD Contact Form
Date: Monday, December 24, 2018 8:38:13 AM

Please see below. Not sure if a response is needed.

From: DOH webmaster
Sent: Monday, December 24, 2018 8:28 AM
To: Yoshiura, Corliss [REDACTED] Ungos-Markham, Jocelyn [REDACTED]
[REDACTED]
Subject: FW: Message submission from DOCD Contact Form

Forwarding an inquiry below.

Thank you,
DOH Web Mail (vc)

NOTICE: Individuals should always review or confer with their supervisors about the request and composed responses to ensure it conforms with current DOH position on various policy areas. If a question and or response is current on potential "hot topic" or a "controversial" issue review and approval from the appropriate deputy may be required.

From: [REDACTED]
Sent: Sunday, December 23, 2018 6:30 AM
To: DOH webmaster [REDACTED]
Subject: Message submission from DOCD Contact Form

Please select a category:
Other Department of Health inquiries
Name
Michele Sorensen
Email
[REDACTED]
Your Message
I OPPOSE HAR 11-157

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Sunday, December 23, 2018 9:38:07 PM

I am writing in request to oppose
HAR 11-157.

Parents should always have a choice on the health care of their children, especially when there are risks associated with the treatments being mandated.

I have a friend whose daughter now suffers from frequent seizures after a bad reaction to vaccines.

Some people argue that their kids will be at risk if not everyone is vaccinated. If vaccines are effective, there should be no risk of exposure for the children whose parents have decided to vaccinate.

Thank you for keeping our rights safe as parents. No matter what one believes is best on the vaccine issue, it should always be the parents right to decide what's safest for their children.

Thank you for your time and attention to these matters.

Sincerely,
Emily Gambino

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: testimony Clare Loprinzi
Date: Sunday, December 23, 2018 9:15:59 PM
Attachments: [Aloha DOH clare testimony written.docx](#)

Aloha Kakou

I am hoping you read this testimony, it would have been more respectful for DOH to attend the hearings, make sure all could come that worked, the deciding board come to the hearing and show aloha. This is a violation of human rights. ethical rights and sovereign rights. This is cultural insensitive for many reasons including violating protocols that should be adhered to in the time of Lonoikamakahiki. These are war crimes and we love our keiki.

here is my testimony although I testified in person too.
lonoikamakahiki, Clare

clare loprinzi traditional midwife

[REDACTED]
birth sovereignty advisor

Birth Sovereignty supports basic public health measures and projects that create sovereignty in birth choices, health care access and environmental health as a vital component of broader cultural, social, economic and environmental sovereignty and justice issues.

From: [REDACTED]
To: [REDACTED]
Subject: Testimony HAR:11-157
Date: Sunday, December 23, 2018 4:52:32 PM

Aloha!

As a mom and resident of Hawaii I would like to express my concerns towards proposed rule changes to include new VACCINE REQUIREMENTS for Hawaii children .

I have come to find that freedom is often an illusion awarded to those who do as they are told. When it comes to vaccines it's exactly what happened.

We trusted governments and doctors and our children started to become more and more sick with autoimmune diseases neurological disorders and started dying.

This isn't about whether or not you are for or against vaccines, this is about having the power to choose.

Here are my reasons why I don't agree with the proposed rule HAR 11-157, why I decided not to continue in vaccination of my son and why I don't consider vaccines as "safe and effective"

1. Vaccines Have Never Been Confirmed To Increase Immunity or Resistance To Disease
<http://www.whale.to/vaccines/antibody.html>

2. Vaccine Manufacturers Refuse To Conduct Any Research To Prove Vaccines Increase Resistance to Disease or Immunity and The Government OKs This Entire Process – so after we learned that vaccines were never proven to make a person more immune to disease in the real world (*because vaccine research only tests antibody response, which doesn't relate to increased immunity*), we asked why this research isn't being done. At that point we discovered that the government themselves along with both science and medicine all block this research from being done because they deem such research unethical.

3. Babies Don't Have Fully Developed Immune Systems Until 1-4 Years After Birth – infants do not have fully developed (*or even close to developed*) immune systems until [between 1-4 years of age](#). ([Baby's Immune System](#))

Baby's Immune System

As with all other organs and systems in the body, a newborn is not born with a fully developed immune system at birth. Rather, their immunity – a protective function consisting of cells, proteins, and

depending on what research is being reviewed. Regardless, all research is firm that no fully active immune system is available inside an infant less than 1 year of age. When we asked our doctor why vaccines were required for newborns, our doctor responded that vaccines were used to increase function of the immune system to help with greater disease resistance. I asked, “*how can a vaccine stimulate an infant’s immune system when no immune system is fully present to stimulate?*”

4. We Actually Read A Vaccine Insert – under the international medical law of informed consent, each patient exposed to a procedure that could kill or permanently injure them, must be given the related documents legally warning of that risk. We weren’t even aware at the time that each vaccine insert legally declares that each and every vaccine can either kill our child (*directly or indirectly*) or that our new born son could be crippled for life from the vaccine, which has never been proven to increase immunity in the real world. We also must remember that government, medicine and science block the research that would clarify if vaccinated people are actually more immune to disease compared to non vaccinated people. So no research exists to prove if the vaccine will increase immunity or resistance to disease in my son plus the vaccine is legally documented to have the potential to kill or permanently injure my daughter. This decision was becoming clear for my husband and I, as we were both more than a little shocked at what we were discovering. In the end we had to ask for the vaccine insert and that request was delayed as much as possible. When we received a vaccine insert it was more than obvious why the international medical law of informed consent was being broken in regards to providing one. If all parents were forced to read one of these inserts, very few would move ahead with vaccination of themselves or their children. Basically, we were now stepping out of discovering that vaccination was unscientific, immoral and unethical but we were also stepping into an area where not forwarding the vaccine insert was in contravention of a well documented international medical law. [Click here to read the vaccine inserts \(FDA Product Approval: View All](#)

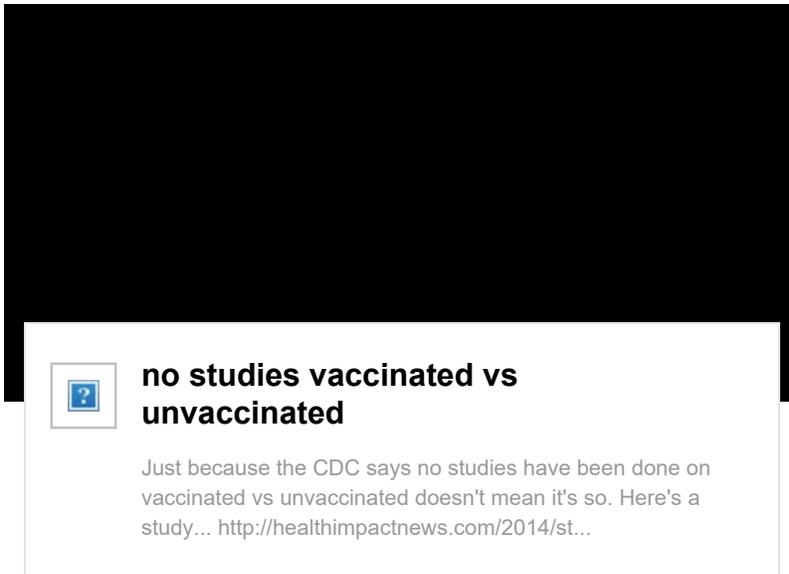


FDA Product Approval: View All

of the vaccines you may be considering.

5. A Blatant Disregard for the Most Basic of Scientific Protocol – it was beyond obvious that pro vaccine science was flying in the face of the most basic and most accepted conventional scientific protocols. For example, in high school we all learned the scientific

method. The scientific method revolves around forming a hypothesis and then testing that hypothesis. Pro vaccine science proposes the hypothesis that vaccinating increases someone's immunity and resistance to disease compared to doing nothing. (*not taking the vaccine*) There's only problem though. As stated earlier, [that research has never been done.](#) ([no studies vaccinated vs unvaccinated](#))



 **no studies vaccinated vs unvaccinated**

Just because the CDC says no studies have been done on vaccinated vs unvaccinated doesn't mean it's so. Here's a study... <http://healthimpactnews.com/2014/st...>

How does this pass as science where I'm supposed to inject my child with an untested vaccine that comes with the side effects death and/or permanent injury? I guess it can pass as science when you don't question your role as patient and your commands from the top of the government or science pyramid but where I'm originally from, that sort of behavior gets you into a whole wack of trouble. As a kid from a rough neighborhood, where the people in power were caught regularly abusing children, I got used to questioning things... especially when government and authority were involved. Science is also supposed to be an unbiased quest for truth but all the negative data on vaccines is being ignored by everyone selling or pushing the vaccines and the appropriate research that should have been done decades ago, is being blocked for reasons that sound official but make little sense. Would it be so hard to study the vaccinated vs the unvaccinated for disease incidence, when people walk in sick every day to hospitals around the world? If someone has the flu at a hospital, how hard would it be to ask, "Did you get the flu shot this year?" Are we really to believe that this sort of research can't be done? I know nurses and they have told me that when there's a flu outbreak declared at the hospital it's well known that every single person in that hospital who has the flu, has taken their flu shot in that current year. Also regarding pro vaccine research, which takes longer to read over in its entirety, the companies conducting the research always were vaccine makers and the government never questioned or reviewed their findings. Claims of research involving "unvaccinated control groups" often documented that the unvaccinated groups were also injected with highly toxic material. It's not scientific on any grounds to allow parties with a vested interest in the research outcomes to conduct the research and of course injecting people with known poisons and calling them the "unvaccinated control group" isn't scientific either. It's corruption. There were red flags all over the place and when it comes to the health of a child, it was starting to become clear that the public were not being told anywhere near the truth regarding vaccination.

6. **Vaccines and Autism** – like everything else along the way, the research showed the

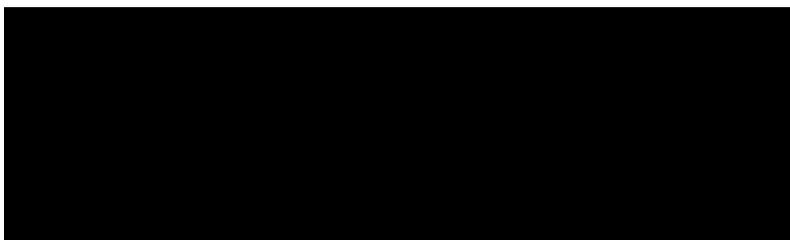
opposite of what we were being told was true. The amount of evidence that vaccines do cause Autism is massive and [I documented most everything I found \(Is There Any Evidence That Vaccines Cause Autism?\)](#)

Is There Any Evidence That Vaccines Cause Autism?

1. Some vaccine inserts have listed Autism and death (SIDS) as occurring to children receiving the vaccination, after the vaccine was approved for use by the public. A vaccine insert is where the truth of the vaccine must be listed legally, in case a

to show my wife and then moved it into papers that I could share with other parents. [Click here to see the evidence I compiled](#) (same link as above) regarding vaccinations having a direct link to Autism. What was also odd is that when I talked to doctors about the vaccine and Autism link, they told me it was unproven. I then asked them if Autism was a form of brain damage and they agreed it was. Then I showed them the vaccine insert I carried with me regarding the side effects of the very common MMR vaccine and I circled every side effect that I believed could cause brain damage. I asked the doctor if the side effects I circled could cause brain damage in a vaccinated child, as a direct side effect of vaccination and they admitted yes it could. If a vaccine can cause brain damage and Autism is brain damage, how can vaccines be proven not to cause Autism just because a doctor calls the damage a different name? After very little research it became obvious that no one selling, producing or administering the vaccines wanted anything to do with our logical questions and wanted to hurry us out of the doctor's office and hurry in the next parent, who would take the vaccinations without question or resistance. The non questioning patient who did exactly as they were told was always welcome. We were not.

7. Medical Doctors and PhD Scientists That Warn About The Dangers of Vaccination – I came across a [long list of medical doctors and PhD scientists \(Medical Doctors and PhD Scientists Speak Out Against Vaccinations\)](#)



Medical Doctors and PhD Scientists Speak Out Against Vaccinations

Below is a list of videos (and some articles) where medical doctors and PhD scientists come forward to discuss the unhealthy effects of vaccines. Each professional presents documented research, facts and statistics to prove, when taken in its' total

who openly try to warn the public about the dangers of vaccination regarding the same exact points I reviewed above plus much more. What is also odd is that no doctor I ran into, who was in favor of vaccination, could do anything but verbally declare that vaccines were safe and effective, that vaccines prevent disease, that vaccines were the greatest invention in the history of health care and that vaccines don't cause Autism. Behind the advertised slogans and catch phrases of conventional vaccine mythology there was no real science to back these claims. So we have people who just utter these magic pro vaccine phrases without scientific validation and then we have this very long list of [medical doctors and scientists](#) who take their time to explain exactly how vaccination isn't safe or effective. So there was the bullying and pressure packed approach of the system that manufacturers, sells and administers the vaccines compared to medical doctors (*with nothing to gain and everything to lose*) taking their time to explain clearly that the public is being lied to about vaccination, on all levels. I may not know everything about vaccination but I know enough to tell the difference between a self serving bully and someone who truly cares about children. That I know for sure.

8. The Place Where They Give The Most Vaccines To Infants Has The Greatest Rate of Infant Deaths In The World – the United States has the most numerous vaccine schedule before the age of 1 in the world, suggesting 26 separate vaccinations. The US has one of the [highest infant mortality](http://healthimpactnews.com/2011/studies-show-that-the-countries-with-the-most-vaccines-have-the-worst-infant-death-rate/) (<http://healthimpactnews.com/2011/studies-show-that-the-countries-with-the-most-vaccines-have-the-worst-infant-death-rate/>)

rates out of all developed nations....DESPITE the highest health budget expenditure on the planet. Inside the US is the state of Mississippi, where vaccines are mandatory save very few exemptions, [Mississippi has the highest infant mortality rates inside the US](http://healthimpactnews.com/2014/mississippi-first-in-infant-vaccination-rates-last-in-infant-mortalities/). (<http://healthimpactnews.com/2014/mississippi-first-in-infant-vaccination-rates-last-in-infant-mortalities/>)

I took statistics in University and although this isn't conclusive regarding the conclusion that it's only the vaccines that are killing infants, it definitely means there's a significant correlation. Taken by itself, these statistics raise a massive red flag. Combine these statistics with everything else I discovered and the big picture comes into focus.

9. MORE THAN HALF A MILLION REPORTED VACCINE INJURIES IS CONSIDERED "RARE?!?!?"

I KNEW that "government" and media were lying to us about the safety of vaccines, but I had no idea just how bad it really is until I decided to do a little investigating.

I went to VAERS: [Search VAERS Database](#)

Search VAERS Database

I located the download links for the "government" data bases of vaccine injuries:

<https://vaers.hhs.gov/data/data>

I clicked on and downloaded the data reports for ALL 25 years listed since VAERS started keeping records. I wrote down all the figures and then totalled them up. MORE THAN 531,000 cases have been reported ... JUST in the U.S.!!!

How many cases are missed (or OVERLOOKED) because the "science professionals," doctors and/or coroners refuse to admit damages caused by vaccines?

HOW CAN OVER HALF A MILLION INJURIES EVER BE CONSIDERED "RARE?"

DO YOUR RESEARCH BEFORE VACCINATING!

Secret Government Database of Vaccine-Damaged Children

Federal Admission of Vaccine Risks:

In 1986, Congress officially acknowledged the reality of vaccine-caused injuries and death by creating and passing The National Childhood Vaccine Injury Act (Public Law 99-660). The safety reform portion of this law requires doctors to provide parents with information about the benefits and risks of childhood vaccines prior to vaccination, and to report vaccine reactions to federal health officials. Doctors are required by law to report suspected cases of vaccine damage. To simplify and centralize this legal requisite, federal health officials established the Vaccine Adverse Event Reporting System (VAERS) -- operated by the Centers for Disease Control and Prevention (CDC), and the Food and Drug Administration (FDA).

[ThinkTwice Global Vaccine Institute: Secret Vaccine Database](#)

ThinkTwice Global Vaccine Institute:

Secret Vaccine Database

THINKTWICE! Vaccine reactions can be avoided. The U.S. government keeps a secret database of several thousand children recently injured or killed by immunizations. Thinktwice!

BREAKING NEWS FROM ITALY:

NO ANTIGENS found in the Infanrix Hexa vaccine, only chemicals.

"With the onset of government vaccine mandates, which suddenly required Italian children to be injected with 11 vaccines to attend school, the Italians are fighting back. First, they voted out the government that pushed for the mandates calling their movement #GovernmentofChange. Then on December 4, the new Italian health minister kicked out all 30 members of the health policy advisory board.

On December 13, Corvelva, a scientific research group, announced it had received €10,000 (US\$11,350) from the Italian National Order of Biologists with plans to use the money to test the contents of every vaccine currently on the market. The result of their first test was released on December 16, and the report is a doozie.

You certainly won't hear this in the MSM.

The first vaccine they thoroughly tested was Infanrix Hexa – a six-in-one vaccine manufactured by GlaxoSmithKline (GSK) that is *supposed* to contain the following antigens: tetanus, diphtheria and pertussis toxoids; inactivated poliomyelitis viral strains 1-2-3; and hepatitis B surface antigen. Shockingly, Corvelva found NONE of these antigens in the vaccine, meaning, that NO antibodies to the intended antigens will be created.

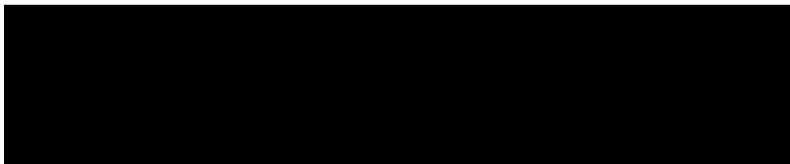
And it gets worse. In addition to no vaccine antigens, they found the following:

traces of 65 chemical cross-contaminants from other manufacturing lines;
chemical toxins;
unrecognizable macromolecules;
various free bacterial peptides that are potential allergens and are capable of inducing autoimmune reactions.

These findings could bring justice to parents who lost their children in 2009 when 36 children died and more than 1,700 were injured in a "clinical trial" – the nice name for human experimentation.

I suspect that as they continue to test each of the vaccines in the childhood schedule, they will find metallic compounds, nanotechnology and a long list of chemical contaminants."

[Vaccinegate: Initial results on Infanrix Hexa chemical composition](#)



Vaccinegate: Initial results on Infanrix Hexa chemical composition

By Staff Corvelva

When we started these analysis, from the metagenomics to the chemical ones, we had a lot of questions and we were only looking for answers... After...

-Dr. Sherri Tenpenny

Hawai'i please don't become the place with the most vaccinated children in US.
Hawai'i please leave parents the right to choose what's the best for their children because everyone is different!

Hawai'i please don't become a Big Pharma poppet.

WHERE THERE IS A RISK THERE HAVE TO BE A CHOICE!!!!

Jaroslava Sibilja



[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11=157 Vaccinations
Date: Sunday, December 23, 2018 1:44:29 PM

Aloha,

In Hawai'i we are blessed with abundant Sunshine. In Hawai'i we are blessed with abundant pure water. In Hawai'i we are blessed with some of the freshest air on the planet. We are blessed with pleasant weather unmatched the world over. We have a warm fresh Ocean to play in, to enjoy, like Hawaiians of Old. We have so much Fresh healthy food, we are blessed to have the fresh healthy food. We have more and more Organic Farmers, working with Nature, balancing the environment in the soil to bring us food full f Nutrients WITHOUT Toxins. We have an active outdoor life for anyone who chooses to enjoy that. I see all ages enjoying it daily in my time here. There is a trail up from Sunset Beach elementary school, a trail that in some places is VERY Steep, Very Challenging, to the extent that ropes are provided in many places so assist one if needed to prevent falls or slipping in the sometimes muddy conditions. I hike this trail regularly when I am spending time at Sunset Beach. I see children, at time barely past the toddler stage, climbing this trail with wonder coming from their voices and eyes. Excitement, Glee, all the things we want to see in our Keiki. It brings such a smile to my face and heart. All the things I describe here are the makings of Health. They are the makings of Strong Natural Immunity.

Given what I have described above, Why in God's name, Why in the Name of all the God's of old Hawai'i, would we now propose rules forcing deadly Toxins into our most valued Treasure, Our Very Future, Our Keiki?

Health, REAL Health, does NOT come from a Needle. Health, REAL Health, does NOT come from a Pill. It comes from what I described in my first paragraph.

You know, if the History I have read of Hawai'i is accurate, Moneyed Interests Stole this beautiful land from the Hawaiians of Old. Will you let this happen a second time? This time stealing a more valuable treasure than the land, our Keiki

Vaccine Injuries are REAL. Vaccine DEATHS are REAL. The FACT is, since it was created in the Reagan Era, in the 80's I believe, the Vaccine injury Compensation Program has paid out over 4 BILLION Dollars, \$4,000,000,000, in claims for Vaccine Injury and Death. I have heard it said that this is a Fraction of what would have been paid out if all the Vaccine Injuries and Deaths had been taken into account. Let that sink it. I mean really, take a moment and let that sin in...

I will share one Real Life Tragedy, of the thousands that are out there. It is with the HPV

Vaccine given to a young boy. This young boy is now Dead. He was an athlete, an outdoorsman, a bright promising young man with good parents. He is now dead, from a Vaccine given to prevent a cancer that is SO RARE, and So Preventable by what I said in my first paragraph above, that I would classify his death as a Homicide. Why do I say this? Because some of the people who push these vaccines KNOW the problems with Vaccines, and they push them for WHAT?

PROFIT, GREED, SELFISH EGO... Very similar reasons this Beautiful land was stolen from the Old Hawaiians.

Here is the young man's story.

<https://healthimpactnews.com/2018/utah-teen-dies-from-gardasil-vaccine-injuries/>



Utah Teen Dies from Gardasil Vaccine Injuries - Health Impact News

In 2016 we published the story of Colton Berrett, who received the Gardasil HPV vaccine at the age of 13 and became paralyzed from the neck down. We published

healthimpactnews.com

These people who push these Vaccine think they know what is right for everyone. They tell you the Science is IN. You know who's science is in? Their Science. NOT ALL THE SCIENCE. This past fall, an event was organized called "One Conversation". This event was organized so that folks who have serious concerns about vaccines, could get together with folks who favor and push vaccines could sit down and discuss the issue openly and honestly. So ALL the Science could be discussed. NOT just the Science that say Vaccines are Great and Necessary. So there were to be six folks who had concerns and six folks who favored vaccines. It was all set to happen. Well, guess what happened? At the last moment, the folks, Doctors and Researchers who favored vaccines, BACKED OUT? Why? I think it was because they knew they would have to face Facts, Science, that showed the REAL DANGERS of Vaccines. Here is the link to this event, that went on with six empty chairs...

https://oneconversationatatime.com/participants?fbclid=IwAR1M8qSfkPLU_gAw_JKoJzwCu2R0pD7gaoIVzN8reNM1_DcQF_rSqVSuvjM

Here is a video of the event...

<https://www.facebook.com/HighWireTalk/videos/492160047964629/?t=1704>

I am a 69 years old man, who has not taken an over the counter or prescription Drug, for over 47 years. I have not been to a doctor for ANY sickness for over 47 years. I had full medical insurance coverage on my railroad job for 33 years. I never used that insurance ONCE, NOT EVER, for any sickness. I have had Medicare since 2002, when a work injury ended my railroad career. I have NEVER used that Medicare for ANY Sickness EVER, since 2002. You see as a young man, I took my own advice described in my first paragraph above, and made Food, Nutritious Organic Food, and Lifestyle my medicine. I am no Rocket Scientist. I am a regular guy who became a Scientist of Healthy living. If I can do this. I did do this, if taught, others can do this. Think about the BILLIONS Hawaii and the Nation could save on Healthcare if Folks did what I did. It CAN be done. I did it. Why not create a system based on HEALTH, Balance with the Aina, Not toxic Vaccines? Why NOT? We could do this. We could create an economy Based on Health, NOT Toxic Vaccines and Pills. I am willing to share my story, my life with anyone who wants to know more.

Please, PLEASE at least delay this new proposal on Vaccines for our Keiki. There is no rush. There is NO emergency. Their IS a big lack of the WHOLE Story. Take the time to find the WHOLE Story on Vaccines. You ALL Owe this to our Keiki.

With all due respect,

Thomas MILCAREK

Spending time at [REDACTED]
[REDACTED]
[REDACTED]

P.S. Pardon any errors in my letter here. You see I was severely vaccine Injured in 2002, when I had the aforementioned work injury. I was taken to the hospital and in a dazed state I was given the Tdap vaccine, without my permission by the way, and was left very brain damaged for many years. I was and still am blinded in my right eye by this Vaccine. This happens from Ischemic Stroke. I was suicidal for many years due to this Vaccine. I know first hand the dangers of Vaccines and only recovered because I practiced what I described in this e-mail...

P.S.S. I will leave you with one more link.

https://duckduckgo.com/?q=Dr.+Andrew+mouldenon+Vaccines&atb=v111-5_y&ia=web

P.S.S.S. I will leave you with stories of 50 Honest Knowledgeable Doctors on Vaccines.

<https://www.youtube.com/watch?v=5yNcaLjb45k>



VaxXed Stories: The ER Doctor in Seattle

An ER doctor and his wife speak frankly about the dangerous and inefficacies of vaccines with the VaxXed team in Seattle. Camera and editing by Joshua Coleman.

www.youtube.com

Sent from [Outlook](#)

From: [REDACTED]
To: [REDACTED]
Subject: Immunization Hawaii
Date: Monday, December 24, 2018 3:28:51 PM

To whom it may concern,

I am a long time 30 year resident of Hawaii, and raised family here without vaccines and without any adverse effects. I oppose this new recommendation HAR 11-157 becoming law. There is no proof that it has any benefit to anyone, especially young children. You must act responsibly and do not impose this dangerous ruling. There are countless cases of people young and old having severe if not disabling effects from the additives used in making the immunization products. **Let it always be the choice of informed adults and parents to decide what is best for them!**

Sincerely, Steven Line. ([REDACTED] resident, tax payer, and business owner)

From: [REDACTED]
To: [REDACTED]
Subject: immunization plan
Date: Monday, December 24, 2018 2:48:04 PM

Dear DOH:

Please do not be swayed by the testimony of those conspiracy theorists who have shown up at public meetings to demand the cessation of common sense public health measures that protect all of us.

Please adhere to the recommendations and findings of credible institutions such as CDC, NIH, and WHO. Those zealots that would have you halt immunizations of students based on paranoid claims backed by fully discredited “research” are putting the health of all of us at risk. For most citizens, childhood immunizations are a no-brainer, so we have no motivation to show up and mouth off at a public meeting. I’m appalled that so many are getting their misinformation from alternative “news” sources that they can show up en masse at a hearing that most of us didn’t even know was happening and appear to constitute some short of majority of opinion. As public health officials it is your duty to follow the facts and serve the public good regardless of how many nut cases come out of the woodwork to voice their adherence to the nonsense-de-jour.

Thank you.

Doug Perrine

[REDACTED]

please do not send any attachments larger than 1MB without advance permission

if your e-mail doesn't go through, try my travel account:

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: immunization
Date: Monday, December 24, 2018 8:05:03 AM

Hawaii State Department of Health
1250 Punchbowl St.
Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Joe Roth

From: [REDACTED]
To: [REDACTED]
Subject: Immunizations update
Date: Monday, December 24, 2018 8:59:31 AM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Dr. Lois Gregg

Family Physician, 22 years in [REDACTED]

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: Vaccinations
Date: Monday, December 24, 2018 7:13:34 AM

December 23, 2018

Hawaii State Department of Health

1250 Punchbowl St.

Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Henry J. Roth, Ph. D.



From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157, I OPPOSE
Date: Monday, December 24, 2018 2:28:16 PM

To whom it may concern,

As a mother of an unvaccinated toddler I strongly oppose passing a law that makes vaccines mandatory. It is a violation of people's personal and religious beliefs and we live in a country that has separation of church and state.

Here is some of the personal research I have done:

[Vaccines:](#)

<https://www.cdc.gov/nceh/drywall/docs/whatyoushouldknowaboutformaldehyde.pdf>

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf>

22 contain formaldehyde

<https://www.westonaprice.org/studies-show-that-vaccinated-individuals-spread-disease/>

<http://www.tandfonline.com/doi/figure/10.1080/15287394.2011.573736?scroll=top&needAccess=true>

Sincerely,
Jessica Qsar
--
Jessica Qsar

From: [REDACTED]
To: [REDACTED]
Subject: Please NO
Date: Monday, December 24, 2018 3:33:54 PM

Re: HAR 11-157, I STRONGLY OPPOSE this bill. Please do not make vaccines mandatory EVER. Big Pharma does not own our lives and our health. Vaccines have not been proven safe and studies for them are funded by the corporations that make them.

My name is Bentley Kalaway. I represent myself.
Thank you

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: opposition to HAR 11-157
Date: Monday, December 24, 2018 4:36:17 PM

To whom it may concern,

I am writing on behalf of myself, Crystal Dudoit, and my spouse, Frederick Huihui, to oppose HAR 11-157. We are the parents of two healthy, unvaccinated boys. I myself have only had a couple vaccines that my mother thought that I needed for school. She didn't know there was a "religious exemption" or she would have gone that route. I developed asthma after a tetanus shot I received when I was 12, and I'm not the only one who's reported that. But beyond the reported side effects and the lack of scientific research on these effects, I'd like to bring it back to basic human rights.

As parents our job is to keep our children safe. We take our knowledge and beliefs and make the best decisions that we can for our children. There are many beliefs about what safety and health mean. We can't force people to eat fruits and vegetables, even though its good for them. We can't force people to stop drinking and smoking even though it will inevitably lead to a serious illness. We can't force a person who is dying from cancer to do chemotherapy, or any type of therapy. So tell me why we would want to force healthy kids to take a controversial drug, that may or may not have negative side effects, that their parents may or may not approve of?

I respect other parents decisions and I hope that others will respect ours. After all if they immunize their children, then theoretically their children should be "protected" right?

We are free to choose our religion. We are free to choose our own political beliefs. We are free to do with our bodies as we wish. Why should our choice for immunizations for ourselves and our children be any different?

Mahalo

Crystal Dudoit and Frederick Huihui

Sent from [Mail](#) for Windows 10

From: [REDACTED]
To: [REDACTED]
Subject: Written Testimony Opposing HAR 11-157
Date: Monday, December 24, 2018 5:59:21 PM

Alicia 'Ilikea Kam
Written Testimony Opposing HAR 11-157
12.24.2018

To the Hawai'i Department of Health,

*Mai ka la hiki a ka la kau
Mai ka ho'oku'i a ka halawai
Mai ka hina kua
Mai ka hina alo
Mai ka 'akau o ka lani*

Aloha mai kakou, my name is Alicia 'Ilikea Kam. I am a parent and an educator as well as a cultural practitioner. I work for the Department of Education and I am deeply concerned about the effects of the DOH making a blanket inclusion of additional vaccinations in the State of Hawai'i education entrance policies.

My first concern is for the health and well-being of my children. There is enough research about the risk of vaccinations yet the majority of our health industry ignores that research for the better good of their businesses such as that of the infamous pharmaceutical companies for example who use non FDA approved equipment, practices and drugs without proper research then issue costly recalls due to malpractice suits and patient deaths. According to HRS 671-3 (1), parents should be given informed consent. Never have I been given proper informed consent as described by law. I have not been provided all of the risks involved in such treatment (vaccinations). I have not been provided with alternatives to such treatment including the benefits of alternative treatments. What I have been given is a piece of paper that I need to read and sign stating that I decline vaccinations which is then kept on file in the doctor's office.

We do not even know what ingredients are used in the vaccinations today. I doubt that the nurses who administer them even know themselves. When

I told a nurse once that I wanted her to check the ingredients for Thimerosal or any related ingredients, she looked at me puzzled because all she had in her hand was a vaccination-filled needle. She did not know what was used as the preservative of the vaccination. She could not tell me what the ingredients were. Don't even get me started on the unstoppable agony and pain a baby experiences when getting a vaccination shot. What about the red solid raised bump around the injection area? Isn't that an allergic reaction to the shot followed by fever and sickness?

My second concern is that as parents and Hawaiians, we are being culturally denied! Less than 20 years ago here in Hawai'i a cultural right of Hawaiian people was vastly denied. All around our state women who gave birth in a hospital were forced to "incinerate" the placentas of their newborns. Whether or not the 'iewe, or placenta really were incinerated is unknown. What is known is that at the time the medical world was denying us a cultural birth right that the most respected elders of our mo'oku'auhau were treated as "medical waste." How dare you call my 'iewe, produced by my own body, which brought forth life, light out of darkness as described in the oldest chant of our people (the Kumulipo)(2). How dare you call my 'iewe containing my DNA and the DNA of my ancestors medical waste! It took many testimonies, oppositions and protests to overturn this policy within our state. It is now allowable to take home your newborn's placenta instead of volunteer it to the hospital. How long will it take until we can parent our keiki the way we feel is fit? How long will it take before the state of Hawai'i allows us to parent by making our own informed medical decisions? How long until this cultural practice is no longer denied to us?

My last concern is the effect this will have on schools. State law and board policy 4140 requires all children age 5 and older to attend public or private schools (there are exceptions for home schooling although all home schooled children are in fact enrolled at public schools under 4140). I will not give my children an additional amount of vaccinations (up to 75 perhaps) to comply to this law and attend school unknowing the result on my child. I know a number of parents who feel the same way. How will the schools react when hundreds of children per school are not attending school? Schools will lose federal funding by count day. School administrators will be cornered into taking parents to court for compulsory

education non compliance. How will the courts react? If I stay home with my children because they are not allowed at school, not only do I suffer financially but so does my family and the school I work at! Have all of these facets even been considered??? This last concern alone can be explored further with many more scenarios that could only result in disaster!

Please consider these points when making a decision.

na‘u me ka mahalo ha‘aha‘a,

Alicia M. ‘Ilikea Kam



(1) Hawaii Revised Statutes 671-3, Informed Consent Law. Retrieved From https://www.capitol.hawaii.gov/hrscurrent/Vol13_Ch0601-0676/HRS0671/HRS_0671-0003.htm

(2) The Kumulipo chant
<http://www.kauainenehcp.com/uploads/8/1/8/0/81802884/kumulipo-text.pdf>

(3) State of Hawaii and board policy 4140 Hawai‘i Compulsory Education
https://www.capitol.hawaii.gov/hrscurrent/Vol05_Ch0261-0319/HRS0302A/HRS_0302A-1132.HTM

From: [REDACTED]
To: [REDACTED]
Subject: Opposition to HAR 11-157
Date: Monday, December 24, 2018 9:55:25 PM

Thank you for this opportunity to provide testimony. As a parent and community member I STRONGLY OPPOSE HAR-11-157.

I believe the requirements to mandate the HPV vaccine for 7th graders and the Flu vaccine for all children attending school violates a parent's freedom of choice for healthcare for their children. These two vaccine in particular are controversial. The HPV vaccine protects against a sexual transmitted disease and has nothing to do with school. Children do not have sex in school! In addition, the long term research about this vaccine is conflicting and some of the potential side effects are very serious. It is each family's right to choose to risk those side effects or not. Especially since this is a sexually transmitted disease and can otherwise be prevented.

The same is true for the flu vaccine. This is a controversial vaccine that has been proven to work in 60% of case at best and only 10% at worst. No vaccine is without risk and it should be the family's choice to accept the possible side effects or risk catching the disease, especially with a flawed vaccine such as this one.

I do want to note that our family is not generally against vaccines. All 3 of our children are vaccinated and us parents also receive necessary vaccines. We do strongly believe that it is our choice for our family which vaccines to get when. HAR 11-157 will take that choice away. This is why I strongly OPPOSE.

Thank you for your time,

Katja Bajema

May you have a wonderful day.
Aloha, Katja

From: [REDACTED]
To: [REDACTED]
Subject: Vaccinations
Date: Monday, December 24, 2018 7:11:14 AM

December 23, 2018

Hawaii State Department of Health

1250 Punchbowl St.

Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis**(whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since**

1955. In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Lorraine Roth, M. D.



From: [REDACTED]
To: [REDACTED]
Subject: comments on immunization schedule update
Date: Monday, December 24, 2018 3:12:47 PM

Hello,

As much as I understand your desire to update immunization protocols, there are a couple of issues that warrant your consideration in my opinion:

(1) From my perspective the immunization system is not broken, and even if there are now new vaccines recommended, more restrictions on parental choice are not necessary, .

(2) freedom of choice: medical choices are an individual human right not to be dictated by the government. People should always have the ability to opt out, as long as they are aware of the consequences to themselves and others of doing so.

(3) the lack of good research is a real issue: I've read the studies that illustrate that correlation is not causation when it comes to the onset of adverse childhood reactions to vaccines, but in science the precautionary principle should apply. Some people think this means that we should all weigh the risk of getting a serious, even life-threatening illness against the risk of long-term health concerns that arise as a result of vaccinations - and opt for vaccination. But what isn't clear is that there is proof that vaccines are actually safe. Much research has been published showing that they don't appear to directly cause certain diseases or conditions, but as we know, research can only isolate a few variables, and the human body is incredibly complex, so it doesn't seem that any of the research has actually proven that vaccines don't cause harm just because groups of people with and without vaccines appear to have the same prevalence of diseases in the short-term. This is of no comfort to people who not only experience acute adverse reactions or watch their children doing so, but it ignores the potential for negative health affects that might come to be in the long-term. Such a longitudinal analysis is nearly impossible to conduct accurately given how many variations there are among human beings over time, but there are so many relatively new conditions and diseases that we currently don't understand or know how to cure, and as such we have no idea what may be causing them. Because we cannot prove with certainty that vaccinations are not contributing causes to such conditions and diseases, doesn't the precautionary principle apply?

Most people will continue to vaccinate because they are willing to take the risk of adverse immunization effects compared with the impacts of the diseases, and this is fine. And I understand that public health agencies must take a firm stance on this issue in an effort to keep these diseases in check, if not eradicate them. But there is in fact collateral damage, which the federal government knows given the existence of the VAERS system and the millions of dollars in payments made to families to address neurological and other permanent conditions without parents needing to "prove" causation. This may seem to be a small price for society to pay for low disease rates, but that's only easy to say when it's not you or your child. As such, parents deserve the right to decide for themselves what risks they are willing to take. Yes, non-vaccinators do benefit from the safety of herd mentality, which only exists because so many have vaccinated, but choosing to vaccinate is a choice just as choosing to opt out is, and people deserve the right to decide for themselves.

Thank you for accepting public comment on this issue.

Michael Kramer

From: [REDACTED]
To: [REDACTED]
Subject: STRONGLY OPPOSE HAR 11-157
Date: Monday, December 24, 2018 2:44:16 PM

I, George Walter Chyz, STRONGLY OPPOSE HAR 11-157.

Individuals have a constitutional right to bodily autonomy that must be respected. By requiring children to take a vaccine in order to attend compulsory schooling violates their right to bodily autonomy.

Informed consent upholds people's rights while offering a service.

Vaccines have risks and WHEN THERE IS RISK THERE MUST BE A CHOICE!

Stop HAR 11-157

Thank you,

George Walter Chyz

From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose HAR 11-157
Date: Monday, December 24, 2018 4:19:38 PM

HAR 11-157, I, Michelle lejeune, **STRONGLY OPPOSE** mandatory vaccines because it causes autism and other autoimmune disorders to our children. Shame on you for trying to propose this law.

From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose HAR 11-157 proposed new rules.
Date: Monday, December 24, 2018 8:15:37 PM

Aloha,

I am grateful for this opportunity to provide testimony. As a community member and concerned parent, I am writing to strongly oppose the HAR 11-157 proposed rules update.

I write this on Christmas Eve, as it is that important to me and many people I know.

I oppose HAR 11-157 because medical health and freedom is of utmost importance to me. There have been no long term double blind safety studies done on this cocktail of vaccines given to our children. I believe they are more harmful than the diseases they aim to give immunity to. Did you know that the aluminum adjuvant in many vaccines crosses the blood brain barrier and can create heavy metal-induced diseases such as Alzheimer's? I have studied the effects of vaccines for years and am appalled at the lack of awareness and social irresponsibility with which they are associated.

I oppose including early-child-hood centers into this rule, is not acceptable without consent of the early-child-hood centers themselves and parents, to my knowledge none have been informed or been invited into the process of this proposal. It creates extra expenses, training and equipment and enrollment for new children.

I request the attorney of the DOH to legally check if this reporting system in conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g and making schools involuntary break the law by following your current rule.

I oppose HAR 11-157 for being incomplete proposal and by not offering the draft of the standard medical and religious exemption forms. I not accept that DOH decides without public input on their final form and should have been a part of this proposal. They can make needed medical exemptions unnecessary more complicated or easy. We simply don't know, because they are missing.

The HPV that would be compulsory for all 7th graders is especially dangerous and there have been many side effects and deaths associated with it.

I respectfully request that the proposed changes to HAR 11-157 be opposed and request that for further changes on immunization a communication link will be established between the DOH & DOE to inform all schools, teachers, parents and who else will be affected by the change, by informing us about the intentions including a summary of the full implication of the rule change.

Please consider the long term safety and health of our innocent school children.
Vaccines do not give long term immunity, but they do reduce overall health and burden the immune system.

Mahalo,
Maluhia Abhayada

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Subject: HAR 11-157, I OPPOSE
Date: Monday, December 24, 2018 2:11:02 PM

Aloha Hawaii Department of Health,

I STRONGLY OPPOSE THE HAR 11-157 PROPOSED RULES UPDATE.
I OPPOSE INCREASING VACCINE REQUIREMENTS.

Vaccinations are a medical procedure which carries risk of serious health consequences including autism, autoimmune disease, seizures, paralysis, and death. GreenMedInfo.com has compiled a document containing over 300 pages of abstracts from peer reviewed journals demonstrating that vaccines are neither as safe nor as effective as their proponents claim. These abstracts cover every vaccine currently mandated by Hawaii law and all of the proposed additional vaccines. Here is a link to the document. gmipub_58635_anti-therapeutic_action_vaccination_all-3.pdf

To bring a human component to this discussion, I offer this video testimony from Brenda and David McDowell, whose three healthy, normally developing 9 month old triplets each became severely autistic within hours of receiving a single dose of pneumococcal vaccine. While correlation does not prove causation, the circumstantial evidence in favor of the vaccine causing this severe decline is enormous and geneticists have told the family it is statistically impossible for this have been caused by genetics alone. Note that the parents received no compensation because they were told they could not sue anyone because they had signed for the shots. By the time the parents learned about the vaccine reporting system, it was past the deadline for reporting an adverse effect. <https://www.naturalnews.com/2018-12-23-triplets-all-become-autistic-within-hours-of-vaccination-see-shocking-video.html>

The proposed rules update would substantially increase the number of vaccinations required in Hawaii, however, there has never been a study done to test the efficacy or safety of the combined vaccines already mandated, let alone a study that includes the additional proposed vaccines.

I OPPOSE INCREASING REQUIREMENTS FOR MEDICAL AND RELIGIOUS EXEMPTION.

'The US Supreme Court has ruled that vaccines are "unavoidably unsafe". Vaccine manufacturers are exempt from liability in the event of adverse reaction to their products. Meanwhile the Vaccine Injury court has paid out over \$3 billion in damages.

The Universal Declaration on Bioethics and Human Rights, adopted by UNESCO October 19, 2005 states:

'Any preventative, diagnostic and therapeutic medical intervention is only to be carried out with the prior, free and informed consent of the person concerned, based on adequate information.'

It is essential that individuals and parents retain the right of refusal for any medical procedure that may damage their or their child's health. Parents and individuals must also have the right to refuse procedures that violate their religious beliefs or conscience.

While this proposed bill seeks to further restrict those rights, the federal HHS has recently established the Conscience and Religious Freedom Division to protect those rights. I would like to see the Hawaii DHS move in the direction of greater protection of individual rights, adding a philosophical exemption to the current medical and religious exemptions.

Thank you,

Shosannah Chantara



From: [REDACTED]
To: [REDACTED]
Subject: Support for Immunization
Date: Monday, December 24, 2018 10:50:05 AM

December 24, 2018

Hawaii State Department of Health

1250 Punchbowl St.

Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article "Economic Evaluation of the Routine Childhood Immunization Program in the United States" published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of

vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Jack Mitchell

Sent from my iPad

From: [REDACTED]
To: [REDACTED]
Subject: Support Immunizations
Date: Monday, December 24, 2018 1:22:22 PM

December 23, 2018

Hawaii State Department of Health
1250 Punchbowl St.
Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis**(whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000

deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Mary Sanchez

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: TESTIMONY HR 11-157
Date: Monday, December 24, 2018 3:03:30 PM

ALOHA

Thank you for reading my testimony.

I am strongly opposed to the proposed rule changes to HR 11-157.

As a religious leader in this community I have witnessed adverse effects following the immunization of some children here. There are many studies out now questioning the safety as well as the efficacy of these immunizations, as well as whether they are causing negative side-effects.

Please do not force families to be required to have their children immunized. If there's even a question about these immunizations being unsafe and possibly causing harm, then parents must have the choice to immunize or not.

I speak for the community and my grandchildren here on Maui.

Thank you,
Reverend Bodhi Be

Showing Up For Death Nourishing Life

Reverend Bodhi Be, Executive Director

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157
Date: Monday, December 24, 2018 12:29:23 PM

To the Disease Outbreak Control Division,
To the Department of Health,
To the Humans working for the public's well-being,

I strongly oppose HAR 11-157.

I also orally testified at the Kaua'i public hearing on Dec. 21, 2018 strongly opposing HAR 11-157.

I strongly oppose any proposal of rules taking away the right to autonomy.

This is a violation of human rights and constitutional rights.

How do you continue to bulldoze over known and said violations?

The public hearings are for YOU to hear what the public opinions are to help YOU gather what the public needs are.

It is very clear that the public says NO to HAR 11-157 throughout the entire Hawaiian islands. It is NOT OK to continue to ignore DEATHS and BAD OUTCOMES from vaccines received in human bodies.

We are not experiments, samples nor robots to test how vaccines are effective or not.

One death is enough to acknowledge vaccines are not safe.

One bad outcome is enough to acknowledge vaccines are not safe.

It is not about scientific proof, the deaths has occurred, the bad outcomes have occurred.

Very clear.

The many bad outcomes the families have had to deal with, it is their experience that matters and speaks the loudest and most clearly that deaths and bad outcomes have occurred and that they have chosen after the bad outcome in one or more of their children that they have decided not to vaccinate the others, showing the grand difference in a healthy NORMAL child versus a dead child/mentally disabled child.

You cannot take away choice.

It is the parent's choice through thorough informed consent that they choose to vaccinate or not, their children who THEY care for for 24/7.

The government shall not mandate vaccines into any human being, ever.

Please educate yourself and others with some of the resources provided here for you.

1. The literature demonstrates clearly negative impacts of aluminum on the nervous system across the age span:

[Immunol Res](#). 2013 Jul;56(2-3):304-16. doi: 10.1007/s12026-013-8403-1.

Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine adjuvants, and autoimmunity.

[Shaw CA](#)¹, [Tomljenovic L](#).

2. Science: Increase in cancer cases as a consequence of eliminating febrile infectious

diseases:

https://www.wanttoknow.info/health/cancer_link_vaccination_fever_research.pdf

3. Vaccines manufactured in human fetal cell lines contain unacceptably high levels of fetal DNA fragment contaminants. The human genome naturally contains regions that are susceptible to double strand break formation and DNA insertional mutagenesis. The "Wakefield Scare" created a natural experiment that may demonstrate a causal relationship between fetal cell-line manufactured vaccines and ASD prevalence:

[Issues Law Med](#). 2015 Spring;30(1):47-70.

Epidemiologic and Molecular Relationship Between Vaccine Manufacture and Autism Spectrum Disorder (ASD) Prevalence.

[Deisher TA](#), [Doan NV](#), [Koyama K](#), [Bwabye S](#).

And we/you very much know that the vaccinated people are the carriers of the specific viruses they have been vaccinated for since the “immune system has created antibodies against that virus to circulate in that body” they can tolerate being carriers of the virus.

*The solution is for the government to apply support/fund/access to build healthier soils, eat fresh garden vegetables, have clean water, exercise, educate how to prepare home remedies to keep the immune system healthy and strong, to stay home if the child is sick, to stay home if a parent is sick, to offer genuine help to families who are sick, to cover healthcare costs.

A healthy happy community will build everlasting support to the government that helps out the people who make up the community!

Kapa'a, Kaua'i
Home Birth Midwife
Mieko Aoki, CPM



From: [REDACTED]
To: [DOH.Immunization](#)
Cc: [REDACTED]
Subject: HAR 11-157
Date: Tuesday, December 25, 2018 7:33:40 PM

My name is Valerie Nelson. I am a resident of [REDACTED] and I was born here. I am strongly opposed to HAR 11-157. It should be a right as an American and as a parent to choose whether or not to inject substances into my body or my child's body. Thank you.

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HAR 11-157
Date: Tuesday, December 25, 2018 4:50:57 PM

Thank you for this opportunity to provide testimony.
As a former school teacher for children with severe disabilities, mom and community member,
I OPPOSE THE PROPOSED RULE CHANGES HAR 11-157.

I am opposed to mandatory vaccines and over regulation for school children. I have met many children whose condition was caused or made worse by vaccinations. I believe that it is a parent's right to choose whether or not they want their children to be vaccinated.

I am also concerned that the requirements to report on children who aren't vaccinated does not comply with privacy laws (The Family Educational Rights and Privacy Act (FERPA), *20 U.S.C. § 1232g, requires written parental consent before personally identifiable information from your child's education records is disclosed to the health department.* & HIPPA) in our schools and I miss the draft for new standardized medical & religious exemption forms are not part of this proposal, even so they very important part of the process and need to be discussed with professionals and public.

At this point, there is not enough evidence to prove that vaccines are safe for all children and especially for this population demographic. There is no one fits all solution. Informed consent, medical freedom are very important for this country and its people.

There is a huge list of potential side effects that may come from vaccinations. In fact, there is even a special court known as vaccine court created to handle issues with side effects and damages to children.

Toxic ingredients are allowed to be added to vaccinations without any responsibility on the part of the vaccine companies. The rules for safety in vaccines are almost non-existent.

For these reasons and many more, I strongly oppose bill 11-157 requiring mandatory vaccinations for school children. Parents need choices on what's best for their kids!

Sincerely,
Kamala Knudsen, Kauai

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HAR 11-157
Date: Tuesday, December 25, 2018 8:46:51 PM

I strongly oppose any and all mandatory immunization programs. We have a human right to our own health decisions and those for our children.

Oppose HAR 11-157

Thank you

Marilyn Powers

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HAR 11-157
Date: Tuesday, December 25, 2018 7:48:09 PM

I am writing to oppose HAR 11-157 for reasons these additional changes impose our community more mandately immunization and takes away our choice to not to immunize our children. I have worked with children with autism in public school system for over 10 years and I have been exposed to testimony from parents of autistic children stating strong link of immunization and autism. This experience led me to deeper research of immunization and autism link and have learned that certain heavy metals such as Mercury are used in vaccine as ingredients. There are more harmful toxic ingredients in vaccines that I do not choose to put in my child body. Immunization should remain to be personal choice and I strongly oppose HAR 11-157.

Chie Takahashi

[REDACTED]

From: Dr Valerie Simonsen
To: [REDACTED]
Subject: I Oppose
Date: Tuesday, December 25, 2018 7:49:13 AM

Aloha...

I strongly Oppose HAR 11-157.

As a physician specializing in integrative medicine I have had the great fortune to serve young people for decades that have had been adversely affected by vaccines.

In 2007 I had 2 high school girls neurologically impaired within 24 hours of receiving the HPV vaccine.

I can tell more stories... hundreds.... but I will save you the agony of sifting through the details. Please reconsider these new standards.

Thank you as you have my support to oppose the HAR 11-157.

mahalo Dr Valerie Simonsen ND

[REDACTED]

Return.... Restore..... Renaissance!

YOU KNOW MORE!

Dr Valerie

Dr. Valerie Lane Simonsen, ND

Global Naturopathic Physician (License [REDACTED])

hOMe to: you kNOW more

USA phone: [REDACTED]

Welcome to your online pharmacy at your fingertips!

Products delivered to your door!

Enhancing & simplifying your life!

Get a 10% discount today!

Free Standard shipping (3-6 business days) is available on all orders of \$49 or more.

Just go to the link below & set up an account today!

[REDACTED]

Skype: [REDACTED]

Email: [REDACTED]

Facebook: Valerie Simonsen

[REDACTED]

Websites:

[REDACTED] (re-creating now)

[REDACTED] (under construction)

Blog:

[REDACTED]

2 options of HONOR FEES: \$\$\$

You can send a check to:

Valerie Lane Simonsen, ND

[REDACTED]

[REDACTED]

~ or ~

Pay Pal account:

[REDACTED]

use my email address to send money:

[REDACTED]

USE FRIENDS & FAMILY OPTION please.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: I oppose strongly HAR 11-157
Date: Tuesday, December 25, 2018 4:10:26 PM

Thank you for this opportunity to provide testimony. As a community member of the island of [REDACTED], and human rights advocate, graphic designer, doula, founder of a former pre school coop and a mom.

I spend my last holiday month informing people about this rule change and explaining its implications in balanced view as possible. I talked to moms, dads, nurses, midwives, child care center directors, school principals and nurses people of this and other islands that vaccinate, selectively vaccinate, not vaccinate at all and experienced vaccine injuries.

I speaking for myself and also will reflect my over all impressions from discussing this rule change. I am not a anti-vaxxer, I am pro choice, for informed consent and balanced communication. I come from a family of nurses and medical professionals and able to read scientific studies and papers in certain areas that i was taught on and taught myself, nerveless I am not calling myself a medical professional, and inviting balanced talk from all sides with open hearts and ears.

I am writing to **strongly oppose the HAR 11-157 proposed rules update.**

I oppose HAR 11-157

1. for being a incomplete proposal, by not offering the draft of the standard medical and religious exemption forms. I not accept that DOH assumes power to decide without public input on their final form and the drafts should have been a part of this proposal. Medical exemptions can be made unnecessary more complicated or beneficial. We the public simply don't know, because they are missing.

I oppose HAR 11-157-2 definitions:

1. extending the rules to child hood center, to any early child hood center I spoke, was not aware of this at all. Who got even informed on this? , especially for smaller businesses this will change alot, incl the enrollment procedure and the reporting security, training and equipment needed. Some where worried it will alter the amount of kids that will enroll in future and open gates to more unprofessional child care solutions.
2. Blanket adopting the "ACIP's - General best practice guidelines for immunization" and its further amendments as as part to our rule and let go of the freedom and independence as a State of Hawaii to compile our own Guidelines.

I oppose HAR 11-157-6.4 Reporting

1. I request the general attorney of the DOH to legally check if this already done reporting system in conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g and making schools involuntary break the law by following your current rule and either pause the reporting with names and change to pure statistics or and offer options for parents a. to be informed and b to opt out or in.
2. No parent that filed for medical or religious exemption with a child in the DOE schools to my knowledge can recall to sign or had any option to agree or disagree with the consent that the school will be reporting their children's names, The Family Educational Rights and Privacy Act (FERPA), 20 U.S.C. § 1232g, requires written parental consent before personally identifiable information from your child's education records is disclosed to the health department. In fact most thought that was a new addition to the rule, because they did not know that their schools already doing this including me.
3. Informed Choice is already mandated by the State of Hawaii and is failing to be abided by many healthcare practitioners. Healthcare Practitioners must give an informed choice, that includes speaking about the alternatives to the procedure that they are using. Vaccines need to by law show both sides.

I oppose HAR 11-157 Exhibit A,

1. The added six vaccines (baby-college) are NOT tested with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 vaccines to 9 vaccines (k-12) and as one example adds HPV as a requirement, making us one of the most regulated states in all USA. Safety & Risk assessment needs to be done first. For example, HPV been taken out of Japans requirements for 5 years due to many adverse reactions. <https://www.hpv-yakugai.net/2018/06/29/5years-english/>
2. The time frame was to short for me to look deeper from both sides into the other six vaccines or current regulated once that may need a update.
3. The proposed rules update is especially disturbing for students first entering 7th grade or higher to receive the HPV. This is especially true for the HPV vaccine which may prevents HPV-related cancers and spread not in school, with that is not a school measure and should stat a choice for parents and thier teenager to make.

I oppose HAR 11-157 Exhibit B

- Please keep in mind we do have many ethnics reside on these islands, and safety studies, to my knowledge and research ACIP guidelines where never designed or tested for this unique demographic. There is no one fits all solution.
- I oppose to Exhibit B, blanket adopting the “best practice guidelines for Immunization”

We all must revisit the safety, health benefit and risk balance here

No vaccine is 100% effective for everyone and not everyone can handle the same amount of vaccination. Additional vaccination needs to stay a choice a parent, guided with respect by their Pediatrician/MD/ND/RN....

The medical community is urged to offer informed consent. Parents & Patient should

be given opportunity to ask questions and clarify all doubts. There must not be any kind of coercion. Consent must be voluntary, and patient should have the freedom to revoke the consent. Consent given under fear of injury/intimidation, misconception or misrepresentation of facts can be held invalid.

The process of the public hearing and your efforts of informing the people of Hawaii been unacceptable. Initially DOH Hawaii planed only one public hearing, with outside pressure you extended the meeting to the outer islands. The timings often excluded teacher, educators, small business child care center to attend, beside it was already heart for parents in one for many very special holiday times. On top of that no key decision maker was present, you ignored the petition delivered to you before the Maui hearing, a request from the public and we were told that you will review the hours of testimony using the transcript. Please explain this process.

I missed the effort to inform the public and any PR to this issue from your side was not explaining all the implication and selling it as a harmless little update to what? Most states do not have 9 vaccines as requirement, especially not HPV (only 3 do as of November 2018) California as comparison has only 5 vaccines required. Their problem is the difficult medical exemption and loss of religious exemption. I urge you to study what that meant for California. For me this is a wolf in a sheepskin, a Trojan. Also I request to consider all testimonies as valid even so they thought its about mandatory vaccination which equals taken the exemption away, because you did not inform the public in detail. Also many know, and so I had to learn in the last month, that the DOH tried to take it away in the past via legislation and also its clear that you would prefer it, after reviewing the interviews of Dr.Park and HIC intentions.

I request to invite open communication and informed consent with the next approach, and invite Parents, Schools and any one affected with an letter about your approach.

Please check if you received my first testimonial (nov 26), i never revived a confirmation. This is my follow up to my oral testimony on Kaua'i that I could hardly finish within 2 min.

I hope you open up a opportunity offering a open heart to the people of Hawaii that experienced vaccine injuries, and how the process was is for them, and for to how many did had to go through a hell for not being accepted as a vaccine injury and had to report to VEARS themselves, even so their once healthy child has now a diagnose for autism spectrum or other diagnoses of chronic illnesses and autoimmune disorders and the timing of the change is very clearly documented, with this behavior of the medical community is breaking their own oath, to nor harm the people. which seems to be a result of not being educated on this issue but being educated rather how to deal with vaccine denier, in a way to keep them out. Senator Russell Ruderman explained the process well in his testimony, its not uncommon. I know one thing as a mom and assisting moms with their birth and children, they do know their babies and they need to be listened to and not ignored or talked down. If you want truth about this, create a better reporting system and demand your

professionals to use VEARS and a local system and ability to recognize adverse events to see what really is going on. Hawaii is not the mainland. I have upmost respect for the medical community over all, and I hope in future we can foster a balanced communication and strife away to create a black and white situation.. all or nothing. The truth for me is in the middle, and all sides need to open up and have a discussion on it. We are the best vaccinated state as HIC sais. So why we need to force down a huge update. We all will be watching all the rule changes and legislation form this time on closely.

I respectfully request that the proposed changes to HAR 11-157 be opposed and request that for further changes on immunization a communication link will be established between the DOH & DOE to inform all schools, teachers, parents and who else will be affected by the change, by informing us about the intentions including a summary of the full implication of the rule change. Also to create a essay to any rule change to explain the details for the public to translate the intentions, implications and changes.

Merry Christmas to you all

Astrid Drolson, [REDACTED] Dec 26 2018

From: [REDACTED]
To: [REDACTED]
Subject: I STRONGLY OPPOSE HAR 11-157
Date: Tuesday, December 25, 2018 8:11:33 AM

Aloha,

I represent myself, Neal Chantara, a father of 3, now adult, very healthy children, all unvaccinated.

I choose not to receive flu shots nor any other such things.

My wife and I extensively researched the pros and cons of vaccinating 30 years ago and made the decision not to vaccinate for very good reasons.

From what I have loosely followed over the years, vaccinations seem to only be getting worse. We now know there is mercury in many of them and the vaccination to autism connection is statistically significant.

If the vaccinations really work, why are those vaccinated afraid of others not receiving the vaccine?

Regardless, I strongly believe we have the freedom and God given right to choose for ourselves and our young children.

Many thanks,
Neal Chantara

[REDACTED]

--

Neal Chantara [REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Immunizations
Date: Tuesday, December 25, 2018 6:12:23 AM

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis**(whooping cough) were reported to the

Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Sent from Joanne Zeidman

From: [REDACTED]
To: [REDACTED]
Subject: Letter for Support of Immunizations for Hawaii
Date: Tuesday, December 25, 2018 6:10:54 AM

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article “Economic Evaluation of the Routine Childhood Immunization Program in the United States” published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family

education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Joanne Zeidman

From: [REDACTED]
To: [REDACTED]
Subject: Oppose Mandatory Vaccinations Until There is Mandatory Disclosure
Date: Tuesday, December 25, 2018 3:18:36 PM

TWIMC:

Oppose mandatory vaccinations until there is authentic mandatory disclosure.
I am a board certified internist licensed to practice medicine in Hawaii.

In these current shameful times of rampant corruption in business, government, health care, science, media, education, and law enforcement I am unable to support new mandates for vaccination until there is proven reliable science to support such mandates. Also necessary would be public accountability and support for the consequences, intended and unintended, of such mandates. When honesty, accountability, transparency, life, people, and the planet finally become more important than money, then maybe we will be able to make informed decisions based on truth and not based on biased toxic profiteering.

Stop poisoning my patients from the toxic air, water, food, clothing, shelter, communication (5G), and health practices that currently dominate our American deathstyle. Human experimentation without consent are War Crimes. Everyone involved in promotion, implementation, and profiteering from this toxic deathstyle will be held personally and financially responsible for all harms inflicted.

Thank you for your very kind attention.

Joseph Kohn MD

[REDACTED]

From:
To:
Subject:
Date:

██████████
██████████; ██████████; ██████████; ██████████
HAR-11-157

Tuesday, December 25, 2018 8:33:56 PM

My name is Jessica Penner and I strongly oppose HAR-11-157.

I was born and raised on ██████████, and I am a mother of 3. I am here to advocate for the health of our children. This includes limiting their exposure to *any* toxic chemicals including the ones present in vaccines.

This rule doubles the number of vaccines required for our children to enter school.

Growing up on Kauai in the 80's and 90's, I can recall less than a handful of peers that had any type of serious or chronic issue.

Fast forward to today and I could stand here and testify all day long about all the people I know and their very real and debilitating health issues.

Is this all in my head? Or are we really sicker than ever?

Let's look at the facts.

We in the US spend over 10k per person per year on healthcare. This is twice as much all other developed nations.

<https://www.healthsystemtracker.org/chart-collection/health-spending-u-s-compare-countries/#item-start>

Despite this fact: According to the CDC and AAP:

60% of all US adults have one chronic health condition and 40% have two or more.

<https://www.cdc.gov/chronicdisease/pdf/nccdphp-overview-508.pdf>

As of 2011: 54% of all children in the US have a chronic health condition such as Asthma, Eczema, Hay Fever, Life threatening food allergy, celiac disease, obesity, diabetes, autism, ADHD, learning disability, or severe mental health issues.

<https://www.academicpedsjnl.net/article/S1876-2859%2810%2900250-0/abstract>

1 in 6 children has a developmental disability, and 13% of our children now require special education.

<https://nces.ed.gov/fastfacts/display.asp?id=64>

The CDC will tell you that they don't know what is driving these chronic conditions, but that they are sure it's NOT VACCINES.

Can we trust them though?

Members of the CDC and ACIP (the people who decide which vaccines become mandated) can and do individually own or share ownership in over 50 vaccine patents.

Here is what ACIP member at the time Dr. Paul Offit had to say when asked about his potential conflict of interest in 1999:

"I am a co-holder of a patent for a (rotavirus) vaccine. If this vaccine were to become a routinely recommended, I would make money off of that," Offit said. "When I review safety data, am I biased? That answer is really easy: absolutely not."

Well, rights to Dr. Offit's Rotavirus vaccine were sold in 2009 for 182 million dollars. Estimates of the money he received for this sale are between 29 and 42 MILLION dollars.

Rotavirus IS ONE OF THE NEW VACCINES REQUIRED FOR OUR KIDS DUE TO THIS RULE CHANGE. (show Exhibit A)

<https://www.ageofautism.com/2009/02/voting-himself-rich-cdc-vaccine-adviser-made-29-million-or-more-after-using-role-to-create-market.html>

But that's not even the worst information I'm presenting today.

The national childhood vaccine injury act of 1986 removed all liability from vaccine manufacturers and tasked Health and Human Services with the sole responsibility of ensuring vaccine safety. This law also stipulated that HHS file reports every two years documenting their efforts on vaccine safety and reducing adverse events.

Did you know that HHS was recently sued for access to these reports and lost? They conceded **that they have NEVER, NOT ONCE IN 31 YEARS** done a safety study OR reported to the Senate on their efforts regarding vaccine safety. **The are in direct violation of the law.**

This fact alone is enough to invalidate their demand on us to vaccinate.

<https://www.upi.com/UPI-Investigates-The-vaccine-conflict/44221058841736/#ixzz5aG0jNgwt>

<http://www.lawfirms.com/resources/environment/environment-health/cdc-members-own-more-50-patents-connected-vaccinations>

Global vaccine revenues have gone from hundreds of millions in the 80's to over 32.2 Billion in 2014. And expected to almost double to nearly 60 billion dollars by 2020.

<https://www.statista.com/statistics/265102/revenues-in-the-global-vaccine-market/>

Pharmaceutical companies are the most powerful lobbying group in the united states and have spent over 4 Billion dollars persuading our politicians to enact favorable legislation. They spend 50% more money than the next most powerful lobbying group - the insurance industry.

And they outspend oil and gas 2 to 1.

<https://www.opensecrets.org/lobby/top.php?indexType=i>

Our government has a history of failing to protect us from high profit industry. Big Lead, Big Oil, Big Ag, Big Tobacco, Big Pharma... this situation is unfortunately just another chapter of the same old story.

We as parents are the last line of our children's defense. Do not make us choose between more vaccines or the free education granted to us by the United States constitution.

To force this on us or take away our rights as citizens is coercion, harassment, and persecution. It is just plain wrong.

December 25th 2018

Christmas Day eve

Testimony in regards to *HAR 11-157 Immunization and Examination*

There is no human right more fundamental than the freedom to think rationally and follow our conscience when making a decision whether to risk our life or the lives of our children for any reason.

The Bill of Rights in the US constitution makes it clear that the respect for the natural rights of individuals limits the power of the state. As Thomas Jefferson put it “minorities possess their equal rights which equal laws must protect and to violate would be oppression”.

Unequal vaccine risk is a burden on vulnerable children in the name of public health.

There are only two laws that ask American citizens to risk their lives.

- 1) Federal law - the military draft. Requires all healthy adult males to risk their lives in a war declared by the government to protect National security. Adults objected to a war for religious beliefs or conscience can obtain a conscientious objection exemption without being punished.
- 2) State law- Requires all healthy children to risk their lives in a war doctors declared on microbes more than two centuries ago. But unlike adults who are not punished for following their conscience in refusing to fight in a war to protect national security. Parents can be punished for following their conscience and refusing to risk their children’s lives in a war to theoretically protect public health.

State Sanctions include- Segregation, loss of the unvaccinated child right to public school, permitting pediatricians to deny medical care to children who have not received one or more vaccines.

These two different laws require healthy US citizens to risk injury or death.

One conscripting adults in what governments clearly defines as an emergency military action, the other conscripting children in the mandatory vaccine program that is not defined as an emergency military action but is treated like one.

No two children are alike I am sure we agree. Vaccine risks are not shared equally by all. Some children are more at risk than others. Either biologically, genetically or environmentally at risk to be killed or damaged by vaccines. Please do not sweep this inconvenient truth under the rug. In 1987- congress gave doctors the broad liability shield (similar to the one congress gave Vaccine Manufactures in 1986), to protect them from a broad range (most) of vaccine injury lawsuits. Doctors don’t have to worry about getting sued for being militant enforcers of vaccines.

There should be limits placed on the authority that public health officials and their physician’s colleges exercise in a constitutional democracy. They should not be given unchecked power to

order parents to play vaccine roulette with their child's lives and punish them for refusing to obey that order.

Laws that fail to respect biodiversity and force parents to risk their children's lives in a war that they cannot refuse to fight without being punished are not American in nature.

Science that cannot be ignored:

1) Sun Yat-sen University's (In the top 10 universities in China) Dr. Zhibin Yao American-educated (University of Pittsburgh) and the author of 33 peer-reviewed studies, but he's also the lead author of the three most important biological studies ever done analyzing how, exactly, the Hepatitis B vaccine can cause autism. In 2015, Dr. Yao was the lead author of "[Neonatal vaccination with bacillus Calmette-Guérin and hepatitis B vaccines modulates hippocampal synaptic plasticity in rats](#)," the first study that ever looked at the impact ANY vaccine might have on the brains of rats.

Dr. Zhibin's did 3 studies with the Hep B vaccine.

2015- This is the first study to test the effects of immune activation by vaccination on brain development. All other studies of immune activation have used essentially pathological conditions that mimic infection and induce a strong fever. A criticism I have heard often from vaccine advocates is that the immune activation experiments are not relevant to vaccines because vaccines cause a milder immune activation than injections of poly-IC or lipopolysaccharide (two types of immune system activators). This new study demonstrates that vaccines can affect brain development via immune activation. Hence, the immune activation experiments are relevant to vaccines...The hep B vaccine increased IL-6 in the hippocampus (the only brain region analyzed for cytokines).

2016 - "This work reveals for the first time that early HBV vaccination induces impairments in behavior and hippocampal neurogenesis. This work provides innovative data supporting the long suspected potential association of HBV with certain neuropsychiatric disorders such as autism and multiple sclerosis."

2018- "These findings suggest that clinical events involving neonatal IL-4 over-exposure, including neonatal hepatitis B vaccination and asthma in human infants, may have adverse effects on neurobehavioral development."

Above can be referenced to: <https://jbhandleyblog.com/home/hepatitsb2018>

Please see Exhibit 1

I say to myself "this is just one vaccine being researched, there are so many more" but "no other research about them is yet available like this one". I would say that would leave me skeptical about its true safety.

Definition of safety from the Merriam Webster's dictionary- the condition of being safe from undergoing or causing hurt, injury, or loss.

The insert in every vaccine administered contradicts the above definition of safety.

You CANNOT say vaccines are SAFE!

Please also see

Exhibit 2 Vaccine Safety

Exhibit 3 Peer Review

- 2) STAFFORDSHIRE, England—In early December 2017, [Dr. Chris Exley of Keele University](#) in England and his colleagues published a paper that for the first time looked at the brain tissue of subjects with autism to determine the level of aluminum (note: they spell “aluminum” as “aluminium” in the United Kingdom) found within their brain tissue. For anyone trying to convince the world that “the science is settled and vaccines don’t cause autism,” the study’s findings are deeply contradictory to that statement. In a [blog post](#) written by Professor Exley on the day his study was published, he explained the groundbreaking results:

“...while the aluminium content of each of the 5 brains [of people with autism] was shockingly high it was the location of the aluminium in the brain tissue which served as the standout observation...The new evidence strongly suggests that aluminium is entering the brain in ASD [autism spectrum disorders] via pro-inflammatory cells which have become loaded up with aluminium in the blood and/or lymph, much as has been [demonstrated](#) for monocytes at injection sites for vaccines including aluminium adjuvants.”

Dr. Exley’s study — [“Aluminium in brain tissue and autism”](#) — is the final piece of a puzzle that first started to come together in 2004, and picked up steam since 2010, that has dramatically furthered the scientific understanding of exactly how a vaccine can trigger autism. This timeline is critical to recognize, because the Vaccine Court in the United States dismissed the vaccine-autism hypothesis in 2009, long before most of what I’m about to explain even existed. Science is a continuum, an emergence of truth through many different studies that often have to be pieced together before the picture becomes clear. And, scientific progress can sometimes move slowly until that moment when an emerging truth presents itself in such a way that it can no longer be denied.

Mystifyingly, aluminum has never experienced biological testing to consider its safety for being injected into babies, having been “grandfathered” into our modern safety standards. Canadian scientists Dr. Chris Shaw and Dr. Lucija Tomljenovic addressed this omission in a critical study they published in 2011 in *Current Medicinal Chemistry* titled, “Aluminum Vaccine Adjuvants: Are they Safe?” They wrote:

*“Aluminum is an experimentally demonstrated neurotoxin and the most commonly used vaccine adjuvant. Despite almost 90 years of widespread use of aluminum adjuvants, medical science’s understanding about their mechanisms of action is still remarkably poor. There is also a concerning scarcity of data on toxicology and pharmacokinetics of these compounds. **In spite of this, the notion that aluminum in vaccines is safe appears to be widely accepted.** Experimental research, however, clearly shows that aluminum adjuvants have a potential to induce serious immunological disorders in humans. In particular, aluminum in adjuvant form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences.”*

Above reference at: <https://jbhandleyblog.com/home/2018/4/1/international2018>

Please see Exhibit 4 Exley

Please see Exhibit 5 Mitkus

Science is NEVER closed!!

Science is forever on going and those of us who doubt and question are the very reason why science gets better!

The US vaccinates the most out of the top developed countries in the world- Yet we have the highest rate of SIDS, Autism, maternal death and we have a seriously sick young population. Something is wrong!

It is your duty to review this science!!

Prove to Kauai that you are really questioning these injections and how they are affecting our Children's bodies!

Regarding the actual public hearing on 12/21/2018. The time, date, and capacity of the room brings suspicion that this mandate is being passed through without true openness and notification to the public. There was NOT enough seating, nor a TV supplied so those of us waiting outside. There were just as many people outside as there were inside and we could NOT be part of the "Public hearing". We had to wait in the blazing hot sun for over 90 min with no idea of what was being discussed inside. The one government official that did attend the hearing gave ample notice to the DOH that there was going to be a large turnout of people. The room provided could hold max 40 people! There was no shown effort to make accommodations available, it actually looked like it was purposeful... This did not go unnoticed but those who attended nor by those not able to make the hearing due to the heat of the holidays, also noted.

The DOH has not conducted/provided safety reports about vaccines to congress for over 30 years, why would we trust your mandates? Either they have been lazy or are hiding information from the public.

There is no liability by the vaccine manufacturers who create these products or liability for doctors administering them. If my child or myself is injured or killed by a vaccine no one is held liable for its damage. Why would I trust an entity with no incentive to provide a safe product??

There is ample hard science that PROVES that vaccines are causing BRAIN DAMAGE and are causing autism and an assortment of other ailments. This science is growing and will be most available in countries other than the US (which is gaged by big pharma).

All around us there are more and children who become autistic, sick or have chronic immune system problems... interestingly enough after they received a round of vaccines.

We are noticing, we are concerned and these "mandates" are only making us more enraged about what we are seeing.

You are being held accountable, you need to listen to your public!

Mahalo,

Kelly Morgan

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157
Date: Tuesday, December 25, 2018 8:01:35 AM

Hanna Blumenfeld
[REDACTED]

Re: HAR 11-157, I Strongly Oppose.

For many reasons this is dangerous, we as a community should not be forced to inject our growing children with substances that could harm them. All vaccines have side effects stated in there packaging if there is a risk we should have a choice. By taking away our children's opportunity to go to school with requiring parents to play roulette with there health, you are limiting our freedom. Not to mention other economic and sociological aspects that will change. Please keep our freedoms.

Much Appreciated

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Opposing mandatory vaccinations
Date: Tuesday, December 25, 2018 8:49:11 AM
Attachments: [Hawaii Revised Statutes 671 informed choice .docx](#)

To whom it may concern,
My name is misha kassel, I'm a board certified emergency Medicine physician here on Oahu. I'm not opposed to vaccines if they are a choose made a by a patient or parent after receiving risks and benefits. Having a right to informed consent is critical as a patient and also as part of the physician patient relationship. Mandatory vaccinations take out this critical component of physician patient relationship and patients rights. There are risks with vaccinations and risks without and that decision should be left to parents and patients after reviewing those. Please do the reasonable and decent thing and not remove that. If you have further questions or would like to talk with me further, please contact me. Sincerely with aloha,
Misha kassel md

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]; [REDACTED]
Subject: TESTIMONY RE-HAR11-157
Date: Tuesday, December 25, 2018 12:15:30 PM

Martha Stephens
[REDACTED]

December 25, 2019

Dear Governor Ing, Dr. Pressler and all Hawaii DOH and DOH Partners,

Hawaii RE-HAR11-157 is an unethical and blatant criminal overreach of the Hawaii DOH under Corporate Federal Government of the United States and would strip Hawaii people of their basic human rights of informed consent about their personal health and the health of their children. I strongly oppose RE-HAR-157.

The Geneva Conventions specifically protect Informed Consent – the right to say “NO!” to any medical intervention, including vaccination, without penalty, pressure or punishment.

“Very few, if any, prospective vaccine recipients, or their natural guardians, know vaccine ingredient/content facts or are given valid factual information about a vaccine, especially the toxic ingredients, contraindications and adverse reactions for each vaccine as listed on its package insert, so as to make an intelligent informed consent before the injection of toxic chemicals, viruses, metals, foreign DNA, excipients, cell fragments, drugs, adjuvants, bacteria, fungi and nano-particles contained in vaccines, into one’s body or one’s children’s bodies.

Since vaccinations are both medical procedures [breaking the skin or otherwise inserting a foreign solution] and pharmaceutical drugs, there is “double-indemnity” of sorts involved, which healthcare consumers are not educated about and to which they are subjugated, unknowingly. Since vaccinations are both medical procedures [breaking the skin or otherwise inserting a foreign solution] and pharmaceutical drugs, there is “double-indemnity” of sorts involved, which healthcare consumers are not educated about and to which they are subjugated, unknowingly.

The Centers for Disease Control, under the aegis of the Food and Drug Administration, have failed the Public Trust and have lost public confidence. The agency, like so many other Federal agencies, is viewed by the public as serving the interest of politically connected “crony” corporations, but not the safety interests of the public. Under such circumstance, the urgency of the redress for which this Petition is submitted should be compelling. The Public will not trust the Federal Public Health Authorities without a clear Regulation faithfully implementing Informed Consent as the sine qua non [essential element or condition] of Public Health interventions. The Public Interest can only be met by imposing on the regulated drug companies the obligation to include in their Package Inserts strong acknowledgment of the Right to Informed Consent.

Counsel Fucetola asserted, “The Constitution for the United States of America requires the President, and all Executive Agencies, such as the FDA, to see to it that the laws be ‘faithfully executed...’ (Article II, Section 2). This means that requirements of law, such as Informed Consent, are a proper subject for reasonably implementing regulations. We are asking FDA to implement Informed Consent to the fullest extent required by law. There are regulations and statutes covering the situation where there is a formal experiment with an Independent Review Board protecting Informed Consent, but no implementing regulations where there is no IRB. This includes all drugs and vaccines after they have been approved and released to the public.”

Something the CDC/FDA, medical profession and Big Pharma seem to ignore is that the United States is bound to observe the Nuremberg Code by virtue of the US having promulgated the Code in the first place! Furthermore, the Geneva Conventions, which form the core of international humanitarian law, are also binding upon the USA. Both bind the USA by treaty to implement fully Informed Consent, which does not happen regarding vaccinations in the USA!

The Petition states that

A key element in the international protections secured by the Allied Victory [of which the USA was a party] and subsequent codification of health-related international law was recognition that no person could be forced to accept any medical intervention that was contrary to conscience and that all medical interventions were to be carried out only with fully informed [and therefore meaningfully willing] consent.

To which I would like to interject that, however, preceded Big Pharma's strong arm (sic) "consensus science" and marketing strategies which, essentially, have been the vaccine industry's "claim to fame."

According to Counsel Fucetola, while Humanitarian Law was given great impetus by the horrors of World War II, these basic ideas have also been distorted to further an internationalist depopulation program, called Agenda 21, including the Global Health Security Initiative (GHSI) that perverts the meaning of fundamental human rights to further justify tyrannical globalist control. We need a clear regulation for Informed Consent to prevent "deemed" or "assumed" consent from being used to justify mass, involuntary vaccination or other "treatment" programs through aerial spraying, vaccine-bearing GMO vectors and other methodologies that do not include direct injection by needle.

The Petition to the FDA alleges an emergency situation, invoking provisions of the Administrative Procedures Act that lets FDA act expeditiously without first providing many months of fact-finding and public comment. This is to prevent delays in implementing the Informed Consent Regulation. Under emergency circumstances (such as the current clear and present threat to Informed Consent represented by various State enactments revoking religious and philosophical conscientious objections to vaccination) the public hearings can happen after the initial emergency regulation.

Interestingly, I found the Petition states that "The United States Government has no legitimate interest in promoting FDA-approved vaccination mandates in violation of Informed Consent."

Counsel Fucetola explained this assertion is based on several Supreme Court cases cited in the Petition. The Court has held that the U.S. government has no "interest" in preventing the public from making what it considers bad decisions with truthful information. *Thompson vs Western States*, 2002.

The intent of the Petition is to clarify that Federal Law, which must implement the Right of Informed Consent, supersedes state-law restrictions on freedom of choice in vaccination. Even if state laws mandating vaccines are adopted, individuals retain their fundamental human rights which supersede state restrictions on conscientious objection.

Here's another question that both the Petition and I ask, "How is one to effectively assert the Right to Informed Consent, enshrined in International Humanitarian Law, for oneself and those over whom one has guardianship?"

Dr. Rima reminds us that Advanced Care Directives and similar documents should always reference Informed Consent and can include statements such as "I do not give informed consent to any vaccinations."

Counsel Fucetola explained, "Without clear regulations protecting Informed Consent, people will have to litigate, on a case-by-case basis, how the right is to be enforced, greatly burdening the exercise of that right. Since the law is settled, that the Right to Informed Consent is a fundamental human right, it is a waste of judicial resources to have to litigate case after case to vindicate the right. This is what we expect the regulation we've requested will prevent. The FDA simply has to require that all drug (including vaccine) 'package inserts' clearly explain the Right to Informed Consent."

I'd like to end this interview with reminding readers of the Hippocratic Oath most physicians take where in part they say, "Nor shall any man's entreaty prevail upon me to administer poison to anyone." I guess either the medical professions disregard and don't read vaccine package inserts, or somehow they've convince themselves that injecting poisons into infants and children is permissible. Is it possible that it's because it is so profitable? " By Catherine J. Frompovich

The Geneva Conventions specifically protect Informed Consent – the right to say "NO!" to any medical intervention, including vaccination, without penalty, pressure or punishment.

Governor Ing, Dr. Pressler and decision makers of Hawaii DOH the underlying agenda of the United Nations, United States Corporation of DC/Federal Government and its donors shame on you for now by passing legislation. This is not about health but Corporate interests in profit and depopulation.

All the data is available and you have now seen it. There is more research and statistics done by the public than any other entity involved. I wonder why?

Regardless of your belief in vaccines, All our rights are taken allowing a for profit Corporation backed by unknown entities to inject ANY and ALL citizens with unknown substances. This is the end game of this nefarious world agenda in the day and age of nano particulate technology and bio warfare. Vaccines are ineffective and uncontrollable.

Do the right thing and end this war on the Hawaiian peoples rights.

"When people vaccinate their children, they're not doing it because of the documented research. They're doing it because they're afraid not to, because the entire system is designed to punish people who don't comply. Vaccination is about compliance and given vaccines are proven to cripple and kill children, without an increase in immunity or

resistance to disease, people are literally being bullied to inject poison into their own children. The need to "belong" is strong within the human animal and this is the only thing moving a parent to vaccinate. It certainly isn't the documented research that's getting a parent to inject their children with poison. That we know for sure."

--Jason Christoff

<https://www.nvic.org/informed-consent.aspx>

Thank you for your time. I implore of you to kill RE-HAR11-157 now.

Sincerely,

Martha Stephens

From: [REDACTED]
To: [REDACTED]
Subject: Oppose Mandatory Vaccinations Until There is Mandatory Disclosure
Date: Tuesday, December 25, 2018 3:18:36 PM

TWIMC:

Oppose mandatory vaccinations until there is authentic mandatory disclosure.
I am a board certified internist licensed to practice medicine in Hawaii.

In these current shameful times of rampant corruption in business, government, health care, science, media, education, and law enforcement I am unable to support new mandates for vaccination until there is proven reliable science to support such mandates. Also necessary would be public accountability and support for the consequences, intended and unintended, of such mandates. When honesty, accountability, transparency, life, people, and the planet finally become more important than money, then maybe we will be able to make informed decisions based on truth and not based on biased toxic profiteering.

Stop poisoning my patients from the toxic air, water, food, clothing, shelter, communication (5G), and health practices that currently dominate our American deathstyle. Human experimentation without consent are War Crimes. Everyone involved in promotion, implementation, and profiteering from this toxic deathstyle will be held personally and financially responsible for all harms inflicted.

Thank you for your very kind attention.

Joseph Kohn MD

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: WE STRONGLY OPPOSE MANDATORY VACCINATIONS
Date: Tuesday, December 25, 2018 3:34:15 PM

Re: HAR 11-157,

I am shocked that such a proposal would even be put forward.

I have been tracking the vaccination issue since my first child was born 42 years old. There is clearly more risk of danger to the body by having immunizations. Personally, I educated myself with the reasons to choose not to vaccinate and choose not to have any of our 3 children vaccinated. All the grown children have been healthy their whole lives. I have close friends who did immunize with vaccine and it went bad for their children. One became paraplegic and the other diagnosed with Asperger's Autism. He is not able to function in a normal capacity and needs supervision.

I strongly believe that it is MORE DETRIMENTAL TO THE HEALTH OF A CHILD TO BE VACCINATED. I strongly believe that the parents of the child needs to right to opt out of vaccines. There are just too many court cases and documented stories of children being healthy and normal and then had a great degenerative decline shortly after receiving them.. I do not believe it is constitutional to force vaccines on anyone. WE INSIST ON OUR RIGHT TO INFORMED CONSENT !
thank you, Laura Binstock, on behalf of our Ohana of 7 adults

From: [REDACTED]
To: [REDACTED]
Subject: Right to choose
Date: Tuesday, December 25, 2018 4:04:20 PM

To whom it may concern,

I am a parent who believes in having a choice in what vaccinations are giving to my children and when. I ask that you please consider that mandatory vaccines could be detrimental to our child and their futures. We should have a right to decide what goes in our children's body. I appreciate your time and hope that we continue to follow our countries guidelines of freedom to choose.

Mahalo, Carrie Larita

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]
Subject: Re: HAR 11-157, I OPPOSE" or "STRONGLY OPPOSE" against vaccination and immunization
Date: Tuesday, December 25, 2018 4:34:54 PM

I strongly oppose the proposal to require vaccinations and immunizations for children. I represent my self .

please file and record my plea to vote against mandatory vaccinations and immunizations for children.

there is massive research pointing against the benefit to children to be forced to do this. this should b e a choice of parents. injecting children with disease is an ancient arcaic practice.

please vote against.

I am a naturopathic practitioner, acupncturist and nutritionist and KNOW how bad this is.

thanks you....grace purusha [REDACTED] [REDACTED]

--

Grace Purusha

[REDACTED]
[REDACTED]

From:
To:
Subject:
Date:

██████████
Testimony to Oppose HAR 11-157
Tuesday, December 25, 2018 5:53:53 PM

Dear Department of Health,

Aloha and a warm Happy Holidays to you all. I am writing to strongly oppose HAR 11-157. I am informing the Hawaii Department of Health that according to the CDC's website, there are "limitations in our knowledge of the risks associated with vaccines" and vaccinations have the following problems:

1. Limited understanding of biological processes that underlie adverse events
2. Incomplete and inconsistent information from individual reports
3. Poorly constructed research studies (not enough people enrolled for the period of time)
4. Inadequate systems to track vaccine side effects
5. Few experimental studies were published in the medical literature. (1)

The above very revealing admissions from the US Centers for Disease Control (CDC) completely undercut the overconfidence exhibited by the Hawaii Department of Health which is pushing for more mandatory vaccinations with HAR 11-157. Similarly, the Vaccine Injury Compensation Program compensation numbers are, not only not reassuring, but, frankly astonishing, and should give not just all parents, but all people in general (including the DOH), serious pause. If vaccines are "safe and effective" as our medical practitioners and politicians constantly tell us via mainstream media outlets, then why is there a running payout total from 1988 up to now of over \$4 billion, according to the US Health Resources and Services Administration. This is the elephant in the room, and the DOH is either unaware, looking the other way or blindly following orders from the CDC and ACIP. Whichever the case, all are unacceptable, because children are being harmed every day and the DOH is allowing it to happen and about to worsen the situation with the HAR 11-157 changes. If I can find Adverse Event information on the CDC and VAERS websites in a 30 second Google search, so can you. It's your duty.

When there is risk there must be a choice. The risks are real and proven. I will leave you with some shocking information for the public record: In the manufacturer insert label for Gardasil-9 (made by Merck) it states the following on page 7, Section 6.1:

"Serious Adverse Events in Clinical Studies: Serious adverse events were collected throughout the entire study period (range one month to 48 months post-last dose) for the seven clinical studies for GARDASIL 9. Out of the 15,705 individuals who were administered GARDASIL 9 and had safety follow-up, 354 reported a serious adverse event; representing 2.3% of the population." (2)

Let me make this crystal clear - 1 out of 50 children will suffer a serious adverse event after taking Gardasil-9. That's 2% of our children. How can the DOH mandate a vaccine that has this high a number of guaranteed adverse events? In post-market safety surveillance here's what Merck found, adverse events that include:

“Blood and lymphatic system disorders: Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, lymphadenopathy.

Respiratory, thoracic and mediastinal disorders: Pulmonary embolus.

Gastrointestinal disorders: Nausea, pancreatitis, vomiting.

General disorders and administration site conditions: Asthenia, chills, death, fatigue, malaise.

Immune system disorders: Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

Musculoskeletal and connective tissue disorders: Arthralgia, myalgia.

Nervous system disorders: Acute disseminated encephalomyelitis, dizziness, Guillain-Barré syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonic-clonic movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis.

Infections and infestations: Cellulitis.

Vascular disorders: Deep venous thrombosis.” (3)

The DOH must put HAR 11-157 on the shelf and not sign it in to law. The HPV Vaccine is NOT SAFE. There may be promise for future versions of vaccines for this cancer, but Merck's current Gardasil-9 is not the one, it is a total failure. Mark my words, Gardasil-9 will become the next Vioxx. Merck is in court right now for fraudulent premarket trials. I've seen the data, they will be found guilty. If the Hawaii DOH, who swears to protect and improve the health and environment for all people in Hawai'i, pushes HAR 11-157 through, the DOH will be implicit with Merck's poorly and fraudulently studied product. Why take this chance? Why risk our children's lives?

Need I remind you - the Hawaii DOH philosophy states the following, “Health, that optimal state of physical, mental, social and environmental well-being, is a right and responsibility of all of Hawaii's people.” Well, I am Hawaii's people, and I am saying that we have a right to philosophically say no to Gardasil-9, a harmful

medical product that has 500mcg of AAHS (aluminum adjuvant) in it. 500mcg of a known neurotoxin! (4). Informed consent must be allowed, there must be a choice that the parent can make without the need for a Religious or Medical Exemption.

Please, Department of Health, I respectfully ask that you do thorough research on Gardasil-9 and it's severe and numerous risks before mandating it for all of Hawaii's children. Consult the VAERS data and read the entire manufacturers insert label. Read the plethora of studies on aluminum and it's toxicity in humans. It will show you that the benefits do not outweigh the risks of adverse events in this case. The science is there, the numbers are there, all you have to do is look. The people of Hawaii are depending on you to do what's right. It's your kuleana. Don't forget that the CDC and ACIP only make recommendations, not laws. The DOH doesn't have to mandate what they recommend. Many states and countries are doing the research and not implementing ACIP or CDC guidelines. Many states and countries are well aware of the extreme conflicts of interest with ACIP members being patent holders for the very vaccines they recommend. I urge you to heed all of this and make Hawaii a shining example of optimal health and limited severe adverse reactions to vaccines like Gardasil-9 by not signing HAR 11-157. This bill puts us all at risk. What's at stake is literally the future of the human race. Please, I beg you, do not knowingly harm our children with this bill.

References submitted for the public record:

1. http://www.cdc.gov/vaccinesafety/Vaccine_Monitoring/history.html
2. https://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf (page 7, Section 6.1)
3. https://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf (page 9-10, Section 6.2)
4. <https://aacijournal.biomedcentral.com/track/pdf/10.1186/s13223-018-0305-2>

Thank You,

Eric Day

Citizen of Hawaii



From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157
Date: Tuesday, December 25, 2018 5:55:15 PM

Shannah Fagundes, representing myself and my children. Re: HAR 11-157, I STRONGLY OPPOSE. This really resonates with me. My kids are homeschooled. My son expressed interest in trying out public school. I have to decide if it's really worth it to expose him to the dangers of vaccines, when we already have a child who reacted negatively to a vaccine. He should be able to attend, regardless of his vaccination status. It isn't fair to him to be excluded. He's a healthy child, rarely ever getting sick. He deserves to be in public school with his peers.

Thank you,
Shannah Fagundes

From:
To:
Subject:
Date:

[REDACTED]
Re: HAR 11-157
Tuesday, December 25, 2018 6:30:56 PM

I strongly oppose the above proposed rule because I question the safety of many vaccines and the number of vaccines proposed especially for infants and toddlers.. Many people have negative reactions to certain ingredients in vaccines which should be studied further. There must be a choice for any vaccine. Mandatory vaccination should not be allowe

https://academic.oup.com/cid/article/33/Supplement_4/S319/302320

Susan C. Friar

From: [REDACTED]
To: [REDACTED]
Subject: Vaccines testimony
Date: Tuesday, December 25, 2018 6:55:21 PM

My child was perfectly healthy until she received her vaccines. Shortly after, she developed over 15 allergies. I will never give her another vaccine. Forcing kids to be vaccinated is an over reach of power and should be punishable by jail. You have no right to bully or force parents to vaccinate their child. Any public official that forces unsafe drugs from criminal pharmaceutical companies should be jailed. The pharmaceutical companies and DOH should be held liable for any damages. Not allowing a child to get an education based on not polluting their bodies is criminal! YOU Should ALL BE JAILED FOR NEGLIGENCE!!! One day you will answer to YHVH, the creator and the injury or death of innocent kids will be on your hands!!!! STOP PROMOTING CRIMINAL DRUGS!!! Just remember when someone's kid dies or is permanently injured from the HPV vaccines it's your fault! You sided with pharmaceutical companies and lobbyists vs the safety and personal choice of the people!

<http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/>

Tracy Adams

From: [REDACTED]
To: [REDACTED]
Subject: "Re: HAR 11-157, I OPPOSE" "STRONGLY OPPOSE" even the thought that this personal matter of choice is anyone elses business.
Date: Tuesday, December 25, 2018 7:54:15 PM

My name is Aerie Waters. My address is [REDACTED]
I strongly oppose Har11-157.
It is not someone else's right to make this personal choice for me, or anyone else.
This is unconstitutional. My health care is my liberty.
With Aloha, Aerie Waters

From: [REDACTED]
To: [REDACTED]
Subject: Testimony on increasing vaccination schedule and reducing opportunities to opt out.
Date: Tuesday, December 25, 2018 9:08:15 PM

To Hawaii Department of Health
Comments on increasing vaccination schedule and reducing opportunities to opt out.

I represent myself and my family, and I STRONGLY OPPOSE!!!!!!

The number of vaccines increases every year, and along with them the number of injuries, and even worse, deaths. Such risk should NOT be mandatory, no matter how big or small. No matter what side of the argument we stand on. NO MATTER WHAT!! Don't take away our right to choose.

Taking away the choice for a parent to decide what is injected into our babies, when we feel there is the possibility of dangerous injury or death as a result, goes against everything this country stands for. It's taking away our American rights, and even the idea shocks me, but so did Donald Trump running for president, and that became a reality. I feel so strongly about this that I am taking time away from my family to testify to you, on Christmas Day, and plead with you- Please don't **INFRINGE** on my **RIGHT TO INFORMED CONSENT**.
IT IS UN- AMERICAN!

Sincerely,

Katherine E. Roberts

[REDACTED]
[REDACTED]
[REDACTED]



Virus-free. www.avast.com

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157, STRONGLY OPPOSE
Date: Tuesday, December 25, 2018 11:49:18 PM

Please give these decisions a little more time. The latest microbiology studies are showing a huge pending breakthrough and medical knowledge relating to the symbiotic relationships between human cells bacteria and even virus. Horizontal gene transfer is a topic in biology that is on the minds of every researcher, and Physicians who are keeping up. Even though now there seems to be nothing but positive affects from almost every vaccine, the negative effects may prove to be a lot more subtle. The healthy human biome contains many thousands of species, horizontal gene transfer now a fact between these microbes and the human cells, may very well play a part in how combating one potential threat may decrease the resistance to a subtle multitude of threats by changing the biome.

I want my Granddaughters health to be optimized to protect them from the revenges of noncommunicable diseases, especially cancers, not influenza vaccines which do not even have effectiveness above 70%.

<https://www.nature.com/articles/srep26934>

https://www.amazon.com/Human-Superorganism-Microbiome-Revolutionizing-Pursuit/dp/1101983906/ref=sr_1_1?ie=UTF8&qid=1545817250&sr=8-1&keywords=the+human+superorganism

https://www.amazon.com/Tangled-Tree-Radical-History-Life-ebook/dp/B075RX2QY4/ref=sr_1_1?ie=UTF8&qid=1545817300&sr=8-1&keywords=the+tangled+tree+a+radical+new+history+of+life

Steven Slater
[REDACTED]

December 25, 2018

Aloha DOH,

This is the second testimony of Clare Loprinzi, an Indigenous Practitioner in Hawaii in opposition to HAR 11-157. This law is culturally offensive and insensitive to many peoples in Hawaii, and to the Indigenous Practitioners who hold traditions of healing much safer and more effective than the mandatory vaccines. We have generations of proof and we are strong.

The indigenous rights belong to those who, being indigenous peoples, are defined by being the original people of a land that has been conquered and colonized by outsiders. The issue of indigenous rights is also associated with other levels of human struggle. Mandatory Vaccines is now a human struggle for their children. Indigenous communities, peoples, and nations are those that, having a historical continuity with pre-invasion and pre-colonial societies that developed on their territories, consider themselves distinct from other sectors of the societies now prevailing in those territories, or parts of them. Indigenous Practitioners continue to use the ancestral wisdom that preserves food, land and cultural sovereignty including relevant diverse healthcare options throughout life. Vaccines contain DNA from aborted fetuses and other toxic components which change DNA. To create a mandatory law that would force children to get vaccines in order to be educated not only violates the DOH Human Right of the child to obtain education in schools but violates cultural rights to keep our DNA to be passed down to future generations as documented in the Kumulipo. (1)(4)(5)(6)(8) The taking of stem cells from the 'iewe (placenta), the cord blood, and the foreskin is a human right and something that the child was given to keep them healthy. As stated by Hawaiian Cultural Practitioner and DOE kumu, Ilikea Kam, "Less than 20 years ago here in Hawai'i a cultural right of Hawaiian people was vastly denied. All around our state women who gave birth in a hospital were forced to "incinerate" the placentas of their newborns. Whether or not the 'iewe, or placenta really were incinerated is unknown. What is known is that at the time the medical world was denying us a cultural birth right that the most respected elders of our mo'okū'auhau were treated as "medical waste." Indigenous Practitioners know that the taking of stem cells from the baby's cordblood or foreskin, using aborted stem cells, or the illegal taking of the first stem cells that produced what they wanted from Henrietta Lacks in unethical and violation of human rights of the child, indigenous rights and not mentioned in an "informed choice for vaccines."

The mandatory vaccination contains other DNA, adjuvants, aluminum and other toxicities that Indigenous rights object to as they already their natural medicines that protect human health.(1) Imposing mandatory vaccination schedules originating from the Federal agency of the occupying power, the CDC, this is in fact a War Crime, since no such vaccination schedule exists for the occupied Hawaiian Kingdom. (2)(5)(9)In fact Medical Doctors, under Hawaii Revised Statutes 671-3, requires a thorough informed consent for vaccinations since they are a treatment or procedure, that also includes recognized alternative treatments or procedures. (3) This is not for the most part being done, instead bullying parents and paying Pediatricians a big bonus if 90 % of their patients (babies and children) are vaccinated and forcing programs to endorse vaccinations or funding will be cut is happening .

Lastly in my added testimony in opposition to oppose HAR 11-157, is to address the topic of the inclusion of Naturopathic Physicians as providers capable of assessing Medical exemptions, while imposing stringent adherence to an alien allopathic Medical paradigm for making such assessments is a hollow and patronizing inclusion. This is not only rude but again illegal since they are recognized Physicians in the State of Hawaii. It is time that the DOH collaborates instead of confrontation with all branches of healthcare.

I demand that the DOH listen to the people, it has been overwhelming opposition at each hearing. The time is now for a diverse committee of representations of healthcare practitioners, community members, Native Hawaiians, Legislatures (all who must not have an invested interest in the billion dollar business of vaccines) and parents to come together and talk. I suggest that Lt. Governor Dr. Josh Green is a good person to moderate this discussion. If not we all know if approved, this law will be in the courts and the people will be there. We can not allow this to happen because so many children and young adults will be effected. This is our kuleana.

Me ka haahaa o Lonoikamakahiki,

Clare Loprinzi, Indigenous Practitioner, Traditional Midwife, MCH (Maternal/Child Healthcare) Degree

1. https://www.google.com/search?client=safari&channel=mac_bm&source=hp&ei=WtMhXIaxG7ywOPEPn9adiAY&q=indigenous+rights+movement&oq=indigenous+ri&gs
2. <https://hawaiiankingdom.org/blog/united-states-falsely-reports-to-united-nations-hawaiiis-status/>
3. Hawaii Revised Statutes 671-3 – Informed consent Current as of: 2016 | Check for updates | Other versions https://www.capitol.hawaii.gov/hrscurrent/Vol13_Ch0601-0676/HRS0671/HRS_0671-0003.htm
4. <https://hawaiiankingdom.org/blog/united-states-falsely-reports-to-united-nations-hawaiiis-status/>
5. <http://www.kauainehcp.com/uploads/8/1/8/0/81802884/kumulipo-text.pdf>
6. MCH 789 Case Stud/Research/MCH Program 2008 Clare Loprinzi Portfolio MCH 789 Case Stud/Research/MCH Program 2008 Clare Loprinzi Portfolio Dr. Horowitz , Professon Lorreta Fuddy Statistics , Birth Studies MCH JABSON Degree 2008 Clare Loprinzi Violation of Hawaii Revised Statutes 671-3 – Informed consent
7. Blood Money The taking of STEM Cells AIMS Journal Vol. 16, NO 4 2005 pg 6,7 AIM Journal Vol. 17 p 25, 26
8. The Worldwide Traditional Midwifery/Indigenous Practitioner Council, 2018 statement
9. The Immortal Life of Henrietta Lacks, Rebecca Skloot, “ Broadway Books Ney York”, 2010

From: [REDACTED]
To: [REDACTED]
Subject: Freedom to choose
Date: Tuesday, December 25, 2018 7:50:48 AM

To Whom It May Concern,

I understand that your job is to protect the population of our precious state, but not at the cost of a parent's right to choose.

The vaccines have been proven dangerous, of late, and I do not want this issue to be legislated to force these chemicals into our children's bodies.

We shall find the pono way to protect all of us!

Do not bow to the pharmaceutical industry and accept money from them !

We have had enough, dealing with Monsanto and Roundup ruining Paradise.

We are watching you, and trust you to protect our rights!

Merry Christmas, blessed ones.

Thank You Very Much,
Reverend Roma Carlisle

From: [REDACTED]
To: [REDACTED]
Subject: STRONGLY OPPOSE MANDATORY Vaccines!
Date: Tuesday, December 25, 2018 4:05:50 PM

To Whom it may concern,

I am a healthcare practitioner living on the island of [REDACTED]. In no way does it make sense to take away a right to choose which vaccines are appropriate from the parents! This is no one else choice! I am shocked that this is even being considered. This is insanity!

Thank you,

Myrica Morningstar

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: STRONGLY OPPOSE VACCINATION BILL
Date: Tuesday, December 25, 2018 9:01:37 AM

This is UNCONSTITUTIONAL!!!
Make more accessible but allow CHOICE! BAD BILL!!!!

Sincerely,
Anne Trygstad

[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Input on HAR 11-157
Date: Tuesday, December 25, 2018 8:11:22 AM

I am writing to share my thoughts on the importance of keeping immunization rates high in the state of Hawai'i.

I am the parent of a nearly six year old child who will be attending Haiku Elementary, starting in January, who just finished three and a half years of chemotherapy for acute leukemia. My child is the reason people who care about others vaccinate- even though they themselves may be healthy/lucky enough, if exposed to a life threatening illness, to fight it off with minimal effect and no long term damage, my child has an immune system that may take years to recover after being suppressed with chemo for so long. There are much greater odds than normal, for my child, that an illness as simple as chicken pox could go systemic, attacking his organs, including his brain. We are simply hoping the humans around us are vaccinated, because with his damaged immune system, even once he gets all his vaccines again after having his immunity wiped out by treatment, they will likely not be as effective in protecting him as they would be a normal, healthy child. He will always be more at risk, and dependent on those around him to form a wall of protection around him with their immunity.

I get that there are risks to vaccinating. They are frightening for a parent who thinks reading google sites filled with pseudoscience and conspiracy theories qualifies as research, who only hears the worst stories of vaccine reactions and never knows how many devastating epidemics vaccines have saved us all from, and how much disease-related death there was only 100 years ago. It is easy to assume our greatest threat comes from the pharmaceutical industry when the success of modern medicine has removed other threats so effectively. Please consider our family and so many others like us, and work on our behalf to pass laws protecting us.

Thank you.

Bobby, Susan, Daniel, and Alexander Koehn

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157 OPPOSE
Date: Wednesday, December 26, 2018 10:48:45 PM

To whom it may concern:

The vaccine behemoth was a 1 billion dollar industry when I was a student 30 years ago. Presently this industry stands at 61 billion. We'd be fools to disregard that this industry has a financial incentive. Especially since the USA vaccinates more per capita by far than any other developed country and yet we are still very sick with escalating morbidity and diminishing life expectancies. Is this liability from vaccines? Well we don't know because there are no long term studies!

Our Hawaii State constitution states in the Bill of Rights:

1. All political power of this State is inherent in the people; and the responsibility for the exercise thereof rests with the people. All government is founded on this authority.
2. All persons are free by nature and are equal in their inherent and inalienable rights. Among these rights are the enjoyment of life, liberty and the pursuit of happiness, and the acquiring and possessing property. These rights cannot endure unless the people recognize their corresponding obligations and responsibilities.

You, our government officials are bound by oath to fulfill these obligations to the People. I personally cannot pursue happiness if I or my children must sacrifice themselves for the greater good by disregarding **informed consent**. It is my right to refuse any other kind of treatment if it is not agreeable to my best determinations. Why should vaccines be any different? ESPECIALLY when vaccine manufacturers are indemnified against any liability and vaccine compensation requirements have been amended many times that legitimate claims must wait for unreasonable periods to be considered. Still many claims are disregarded and compensation is nil for deaths or serious AE's from vaccines. Hawaii wants to take on more liability?

Currently there is no methodology to *screen* patients for vaccines that might possibly maim or exterminate the recipient. Where else in medicine does this same dynamic stand? If a physician advises surgery or toxic chemotherapy shouldn't I have a choice?

The Institute of Medicine (IOM) now known as the National Academy of Medicine is the premier overseer of US policy on healthcare. In the 1991 they published a paper reviewing vaccine research and concluded that this research was 'woefully inadequate'. Subsequent papers seem to exonerate this proclamation without due diligence by the IOM. However, they had published a nearly 900 page document outlining vaccine adverse events.

Adverse Events of Vaccines: Evidence and Causality
released Aug 25, 2011

Furthermore, the Association of American Physicians and Surgeons, a conservative group of MD/DO physicians numbering more than 40,000 members have placed a moratorium on mandatory vaccines. This policy stands today since there are no long term studies, most short term studies are on monovalent vaccines not polyvalent vaccines and there is no screening methodology.

Additionally, the New Zealand medical Journal published an important paper on 5/24/96 that former N I H researcher J. Barthelow Classen, M.D. concluded that there was a whopping 60% increase in juvenile diabetes from Hep B vaccine. He advocated waiting at least until the infants were 2 years old to reduce the risk.

Regarding HPV vaccine: the vaccine adverse event reporting system (VAERS) received 58,000 adverse event reports. HPV as you may know accounts for 3% of all cancers. To date HPV has caused 14 deaths and 376 serious injuries. Less than a third of all claims received have not been compensated. Under reporting all vaccine injuries is common place.

Please reconsider this mandate and let the People determine their fate not misled bureaucrats endeavoring to do the right thing.

Thank you for your consideration. OPPOSE HAR 11-157

Miles Greenberg

██████████

██████████

██████████

██████████████████

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: Har 11-157
Date: Wednesday, December 26, 2018 12:01:51 AM

I am a father and community leader. I strongly appose har 11-157 because it takes away our free will as individuals, hinders opportunity for our children and supports a corrupt corporate owned medical system.

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: Har 11-157
Date: Wednesday, December 26, 2018 1:54:00 PM

Aloha,

I strongly oppose 11-157 for many reasons. We need to have medical freedom. Vaccine manufacturers have no one holding them accountable.

Thank you,

Kendra Schneider

Sent from my iPhone

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157, I oppose
Date: Wednesday, December 26, 2018 4:02:50 PM

To whom this concerns:

I am writing to oppose HAR 11–157.

The trend toward more and more vaccines being given to younger and younger children for less and less serious diseases is alarming and needs to be abruptly stopped until science proves beyond a shadow of a doubt that this trend is actually benefiting the children's and communities health now and into the future.

The CDC recommendations are apparently not even evidence-based--such as administering Hep B starting at birth to ALL babies, despite the fact that Hep B is NOT a childhood illness and is not (according to the CDC themselves) spread by casual contact. Many pro-vaccination doctors have spoken out about their concerns with the CDC recommendations,

Many pediatricians have employed more sane strategies for vaccinating their patients. Avoiding giving multiple live vaccines at one time, avoiding giving more than one shot containing aluminum at one time, and delaying certain less critical and/or more problematic shots till a child is older (with a more developed immune system) are common themes. None of these concerns is addressed by the CDC recommendations (in fact, they violate all three of these evidence-based cautionary principles).

The HPV vaccine has been found to have huge negative consequences for young girls and should not be given to anyone until it is studied with the gold standard double blind real placebo studies.

The successful efforts by vaccine manufacturers to lobby for the passage of legislation to exempt themselves for liability from injuries caused by their products is particularly disturbing, immoral, and unprecedented.

Thank you for your time, Maria Maitino

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157 Testimony
Date: Wednesday, December 26, 2018 3:41:09 PM

Aloha again,

I am writing to oppose HAR 11-157 but also to add/ask:

1. Why were no deciding members of the DOH at outer island meetings? It makes the community feel unheard.
2. Can you please add more outer island hearings so that everyone has a chance to be heard? Maui's meeting was too short for everyone in attendance.
3. What proof can you provide those who testify that our opinions, research, questions, etc. are being considered?
4. What kinds of gatherings are happening in schools that Hawaii's children need supposed "protection" from HPV, a sexually transmitted disease?

I do not believe the suggested changes listed in HAR 11-157 are necessary or best for Hawaii's keiki. I am also left feeling unheard as a citizen of Hawaii. What does the DOH plan to do about this? I would appreciate a response other than "we received your email."

Mahalo,
Lori Auldridge, M.A., M.F.A.

From: [REDACTED]
To: [REDACTED]
Subject: HAR11-157...vaccination proposal
Date: Wednesday, December 26, 2018 12:46:00 PM

Aloha,

My name is Lisa Kerman and I've been a resident of [REDACTED] for the past 8 years. I am writing today in strong opposition to the proposed HAR11-157. I am actually appalled that the state is looking at mandating these vaccines. I strongly disagree that the state take it in their hands to determine how we're going to raise our children and to what degree we're willing to poison them in order to enroll them in the public & private school system.

It is not okay by me that we're looking at the possibility of mandating vaccines. It's not okay by me that it could become mandatory for human beings to be injected with foreign matter such as mercury, aluminum, animal & human cells, cells from abortive fetal tissue, formaldehyde, bacterial, viruses (some of which are known carcinogens that are known to cause breast cancer), antibiotics, to name a few. And, it's not okay by me that big business could make a financial killing on the many people that these vaccines may kill or at least compromise over time.

The U.S. supreme court has ruled that vaccinations are unavoidably unsafe...yes, unavoidably unsafe. The many side effects from the proposed vaccines include asthma, allergies, eczema, ADD, ADHD, ear infections, insulin dependent diabetes, autoimmune diseases (autoimmune diseases are increasing at an alarming rate), just to name a few. This sounds like a human experiment to me, and a very lethal one at that.

The CDC is reputed to be an independent government agency making vaccine recommendations to the public. They are the agency charged with vaccine safety oversight, and yet the CDC owns patents on at least 56 different vaccines. They purchase and sell 4.1 billion dollars in vaccines annually including vaccines for Flu, Rotavirus, Hepatitis A, HIV, Anthrax, Rabies, Dengue Fever, West Nile Virus, Group A Strip, Pneumococcal Disease, Meningococcal Disease, RSV, Gastroenteritis, Japanese Encephalitis, SARS, Rift Valley Fever, Chlamydomphila Pneumoniae, among various other patents. There clearly appears to be a huge conflict of interest here. The CDC...Center for Disease Control that is supposedly and independent government agency...is actually a subsidiary of Big Pharma.

The vaccine industry is a 54 billion dollar industry and the side effects elicited from these vaccines also make up a huge business for the pharmaceutical industry. The first drugs make you sick, then there's more drugs prescribed to try to clear up the problems that the first drugs created. Sounds like great job security to me. The vaccine injury compensation program that went into effect in 1986 has paid out 3.2 billion dollars in vaccine injury claims through a government program, which is actually estimated to be only 10% of the total vaccine injured population. So no, it's definitely not okay by me that we douse our children with up to 69 doses of recommended childhood vaccines. Enough already!

If vaccines become mandatory for children entering school here in Hawaii, we will be the highest vaccinated state in the nation. Out of all the dozens of people that testified in Kauai on December 21st, there were only three people in favor of implementing mandatory vaccinations in the state of Hawaii.. It's pretty obvious that the majority of people in our state are opposed to HAR11-157. If this proposal passes, I know a number of parents who will be withdrawing their children from public school and will be opting to home school them instead.

One last thing. I attended the hearing at the health department in Lihue, on December 21st...4 days before Christmas when people are either off island for the holidays or else they're busy with loved ones on island (many of us felt that this was intentional as to keep the hearing " short & sweet" and unattended). I arrived just a little before 2:00 when the meeting was due to begin. The room held 40 people, but when I arrived...the room was at full capacity. Another several dozen people were lined up at the door to get in. I stood outside for the first hour of the hearing and as one person left the room, another one from the line was allowed in. They didn't have it broadcasted outside so that we could at least hear what was being said. I did find out that Dr. Jannet Berreman, the Director of the Department of Health was in attendance which I was appreciative of. So, I am requesting that 1) when an issue of such grand importance arises, please supply a room that will hold all the attendees, 2) I would really appreciate it if hearings around issues of great importance, (as this one obviously is) would be held at times other than busy holidays and 3) that the deciding politicians actually listen to the transcripts from the statewide hearings.

From the attendance that took place at the various hearings around the state, it's obvious that the majority of Hawaii residents...are passionate about keeping mandatory vaccinations out of the equation.

Thank you for your time, happy holidays and please, don't be convinced by the profiting CDC & Big Pharma that vaccinating is the necessary action to take here,

Lisa Kerman



From: [REDACTED]
To: [REDACTED]
Subject: Hawaii Mandatory Vaccine
Date: Wednesday, December 26, 2018 3:23:44 PM

Dear Dept. of Health,

I am outraged and alarmed to learn that you are considering injecting students with the highly questionable and controversial vaccine. I consider such action to be a violation of the Helsinki Protocol which requires informed consent before such experiments.

I agree with Sen. Ruderman's comments that "Proposing to increase required vaccines to the highest number in our most-vaccinated nation is irresponsible."

I oppose mandatory medical procedures of any kind. Forced injections of any kind call to mind the notorious Tuskegee experiments.

Experiment on innocent, healthy people is a crime. There is ample evidence of the harmful side effects of these injections. That's why the pharmaceutical industry pressured congress to pass a law making it nearly impossible to sue Merck and their ilk.

This proposal seems a violation of the your department stands for.

Please do not experiment on our children.

Thank you
Anita Hallard

From:

To:

Subject:

Date:

[REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Hawaii Vaccination Regulations & Laws

Wednesday, December 26, 2018 3:25:03 PM

With regards to the proposed changes to Hawaii vaccination regulations and laws, I'm writing to oppose ALL mandatory vaccinations. This means I oppose all additions to the current schedule of vaccinations that are required for attendance at public educational institutions. This also means I oppose any reduction of exemptions, such as exemptions for medical, religious, philosophical, or personal reasons.

To take away a parent's right to make an informed medical decision for their child is unconstitutional.

Sincerely
L. Bowlin

From: [REDACTED]
To: [REDACTED]
Subject: HPV Vaccination Program
Date: Wednesday, December 26, 2018 10:10:37 AM

Dear Dept. of Health,

I am outraged and alarmed to learn that you are considering injecting students with the highly questionable and controversial vaccine. I consider such action to be a violation of the Helsinki Protocol which requires informed consent before such experiments.

I agree with Sen. Ruderman's comments that "Proposing to increase required vaccines to the highest number in our most-vaccinated nation is irresponsible."

I oppose mandatory medical procedures of any kind. Forced injections of any kind call to mind the notorious Tuskegee experiments.

Experiment on innocent, healthy people is a crime. There is ample evidence of the harmful side effects of these injections. That's why the pharmaceutical industry pressured congress to pass a law making it nearly impossible to sue Merck and their ilk.

This proposal seems a violation of the your department stands for.

Do not experiment on our children.

Mark Sheehan, Ph.D.

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: I am in opposition of HAR 11-157 proposal rules
Date: Wednesday, December 26, 2018 2:59:23 PM

To Whom it may concern ,I'm writing to state that I strongly oppose changes to the proposal rules.Everyone has the right to decline for themselves or for their children vaccines ,for medical and religious values. Thanks for protecting our civil rights by making it mandatory for the children to participate in schools we pay for with our taxes.And please have a real conversation and allow each island adequate time and space for testimonials,and public comments regarding the proposal. Sayuri Handa and Govinda Rubin
Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HAR-11-157 mandatory vaccines.
Date: Wednesday, December 26, 2018 10:57:11 AM

I , Amy Cutler, oppose HAR-11-157 mandatory vaccines.

I am citing Hawaii Revised Statues 671-3, informed consent as my reason for opposition.

I want freedom of choice when it comes to what happened to my body and the bodies of my children. Also, all of the children of hawaii and their parents.

Thank you for your consideration in this matter. Do what's right and oppose HAR-11-157!!

Amy Cutler

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Subject: I OPPOSE HAR 11-157
Date: Wednesday, December 26, 2018 3:26:09 PM

Aloha Hawaii Department of Health,

Thank you for this opportunity to provide testimony.

I STRONGLY OPPOSE THE HAR 11-157 PROPOSED RULES UPDATE!

I OPPOSE INCREASING VACCINE REQUIREMENTS. The risks of adverse reactions include death, seizures, paralysis, infertility, autoimmune disorders, seizures, developmental disorders, allergies, and more. Over 500,000 adverse effects to vaccines have been reported to VAERS. Over 59,000 adverse effects from the HPV vaccine have been reported to VAERS, including 425 deaths.

**THERE IS NO DENYING THAT VACCINES CAN CAUSE ADVERSE REACTIONS!
\$4 BILLION HAS BEEN GIVEN BY THE NATIONAL VACCINE INJURY COMPENSATION PROGRAM FOR INJURIES AND DEATHS CAUSED BY VACCINES.**

The most compensated vaccine injuries are for the Influenza vaccine. Please read the data available at the website:

<https://www.hrsa.gov/vaccine-compensation/data/index.html>

Please read this study by the National Center for Biotechnology Information that concludes:

"NATIONS THAT REQUIRE MORE VACCINE DOSES TEND TO HAVE HIGHER INFANT MORTALITY RATES."

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3170075/>

I OPPOSE INCREASING VACCINE REQUIREMENTS BECAUSE IT WILL INCREASE ADVERSE REACTIONS AND DEATHS!

I OPPOSE INCREASING REQUIREMENTS FOR MEDICAL AND RELIGIOUS EXEMPTION. Complicating the exemption process would contribute to more allergic reactions and adverse reactions for susceptible genetic types. We must be allowed to refuse the injections of toxic metals, harmful chemicals, allergens, and xenobiological agents such as animal and fetal derived DNA.

I OPPOSE ADOPTING THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP) RECOMENDATIONS. These recommendations have not been proven safe and pose risks of severe adverse reactions.

HEALTH FREEDOM AND INFORMED CONSENT ARE BASIC HUMAN RIGHTS! Everybody must be allowed the right to chose or refuse what it put into the body. Vaccination is a medical intervention that carries a risk of injury or death. The right to informed consent to any medical intervention that can kill or injure you or your child is a human right.

Please consider the health concerns of everyone susceptible to adverse reactions to immunizations.

Thank you again for the opportunity to provide testimony opposing the HAR 11-157 proposed rules update and the adverse consequences it would cause.

Mahalo,
Michael Donaldson
Hawaii resident and father of 3 children

[REDACTED]

"When we feel love and kindness toward others, it not only makes others feel loved and cared for, but it helps us also to develop inner happiness and peace." The 14th Dalai Lama (1935)

From: [REDACTED]
To: [REDACTED]
Subject: I OPPOSE HAR 11-157 proposed rules
Date: Wednesday, December 26, 2018 2:31:12 PM

Aloha & thank you for this opportunity to provide testimony. As a community member and mother I am writing to **strongly oppose the HAR 11-157 proposed rules update.**

I oppose HAR 11-157 Exhibit A, are NOT made with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 to 9 (k-12) and adds HPV as a requirement, making us one of the most regulated states in all USA. Safety & Risk assessment needs to be done first. For example, HPV been taken out of Japans requirements for 5 years due to many adverse reactions. <https://www.hpv-yakugai.net/2018/06/29/5years-english/>

Please keep in mind we do have many ethnics reside on these islands, and safety studies, nor ACIP guidelines where never designed or tested for this unique demographic. There is no one fits all solution.

I oppose to Exhibit B, blanket adopting the “best practice guidelines for Immunization” as part to our rule and let go of the freedom and independence as a State of Hawaii to compile our own Guidelines.

I oppose including early-child-hood centers into this rule, is not acceptable without consent of the early-child-hood centers themselves and parents, to my knowledge none have been informed or been invited into the process of this proposal. It creates extra expenses, training and equipment and enrollment for new children.

I request the attorney of the DOH to legally check if this reporting system in conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g and making schools involuntary break the law by following your current rule.

I oppose HAR 11-157 for being incomplete proposal and by not offering the draft of the standard medical and religious exemption forms. I not accept that DOH decides without public input on their final form and should have been a part of this proposal. They can make needed medical exemptions unnecessary

more complicated or easy. We simply don't know, because they are missing.

Thank you,

Meredith Cross

From: [REDACTED]
To: [REDACTED]
Subject: I OPPOSE HAR 11-157 proposed rules
Date: Wednesday, December 26, 2018 12:44:36 PM

Aloha & thank you for this opportunity to provide testimony. As a community member, sister, auntie, and member of [REDACTED]

I am writing to **strongly oppose the HAR 11-157 proposed rules update.**

I oppose HAR 11-157 Exhibit A, are NOT made with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 to 9 (k-12) and adds HPV as a requirement, making us one of the most regulated states in all USA. Safety & Risk assessment needs to be done first. For example, HPV been taken out of Japans requirements for 5 years due to many adverse reactions. <https://www.hpv-yakugai.net/2018/06/29/5years-english/>

Please keep in mind we do have many ethnics reside on these islands, and safety studies, nor ACIP guidelines where never designed or tested for this unique demographic. There is no one fits all solution.

I oppose to Exhibit B, blanket adopting the “best practice guidelines for Immunization” as part to our rule and let go of the freedom and independence as a State of Hawaii to compile our own Guidelines.

I oppose including early-child-hood centers into this rule, is not acceptable without consent of the early-child-hood centers themselves and parents, to my knowledge none have been informed or been invited into the process of this proposal. It creates extra expenses, training and equipment and enrollment for new children.

I request the attorney of the DOH to legally check if this reporting system in conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g and making schools involuntary break the law by following your current rule.

I oppose HAR 11-157 for being incomplete proposal and by not offering the draft of the standard medical and religious exemption forms. I not accept that DOH decides without public input on their final form and should have been a part of this proposal. They can make needed medical exemptions unnecessary more complicated or easy. We simply don't know, because they are missing.

Mahalo,

Amanda Kilroy

[REDACTED] HI

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: I OPPOSE HAR 11-157 proposed rules
Date: Wednesday, December 26, 2018 11:49:50 AM

Aloha & thank you for this opportunity to provide testimony.

As a community member and mother, I am writing to strongly oppose the HAR 11-157 proposed rules update.

I oppose HAR 11-157 Exhibit A, are NOT made with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 to 9 (k-12) and add HPV as a requirement, making us one of the most regulated states in the entire USA. Safety & Risk assessments need to be conducted first. For example, HPV has been removed from Japan's requirements for the past 5 years due to many adverse reactions. <https://www.hpv-yakugai.net/2018/06/29/5years-english/>

Please keep in mind we do have people of many ethnicities residing on these islands, and neither safety studies nor ACIP guidelines where ever designed or tested for this unique demographic. There is no one-size-fits-all solution.

I oppose Exhibit B, blanket adopting the "best practice guidelines for Immunization" as part of our rule and it would require relinquishing of the freedom and independence of the State of Hawaii to compile our own Guidelines.

I oppose including early-childhood centers into this rule. This is unacceptable given the lack of consent on the part of the early-childhood centers themselves as well as of parents or legal guardians. To my knowledge none have been informed or been invited into the process of this proposal. It would add extra expenses, and the need for training and equipment in the enrollment for new children.

I request the attorney of the DOH to legally check if this reporting system in conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g and making schools involuntary break the law by following your current rule.

I oppose HAR 11-157 for being an incomplete proposal and for not offering the draft of the standard medical and religious exemption forms. I do not accept, that DOH is making decisions without public input on their final form which should have been a part of this proposal. They can make required medical exemptions unnecessary, more complicated or easy. We simply don't know, because they are missing.

No parent who filed for medical or religious exemption with a child in the DOE schools can to my knowledge recall to sign or had any option to agree or disagree with the proposal, that the school will be reporting their children's names. The Family Educational Rights and Privacy Act (FERPA), 20 U.S.C. § 1232g, requires written parental consent before personally identifiable information from one's child's education records is disclosed to the health department. In fact, most thought, that was a new addition to the rule, because they did not know that their schools are already doing, this including myself.

Informed Choice is already mandated by the State of Hawaii and is failing to be abided by many healthcare practitioners. Healthcare Practitioners must, by law, give an informed choice, which includes speaking about the alternatives to the procedures and vaccines that they are using, and provide options to patients.

We all know that the State of Hawaii is unique, we need to do our best to preserve as much independence as possible till all the question of whose land this is are answered. And anyone looking into history and the process can answer the question, even if we are avoiding it.

The proposed rule update is especially disturbing for students first entering 7th grade or higher

who may receive the HPV vaccine. This is especially true for the HPV vaccine which claims to prevent HPV-related cancers which cannot be spread in school, thereby rendering it a measure that is not applicable to schools.

We all must revisit the safety, health benefit and risk balance here

No vaccine is 100% effective for everyone and not everyone can handle the same amount of vaccination. Additional vaccination needs to stay a choice for parents and legal guardians, guided with respect by their predication/MD/ND. The medical community is urged to offer informed consent. Parents & Patient should be given an opportunity to ask questions and have all their doubts clarified. There must not be any kind of coercion. Consent must be voluntary, and patients should have the freedom to revoke their consent. Consent given under fear of injury/intimidation, misconception or misrepresentation of facts can be held invalid. The process of the public hearing and your efforts of informing the people of Hawaii have been unacceptable. Initially, you planed only one public hearing, with pressure you extended the meeting to the outer islands. The timing often excluded teachers, educators, small business and childcare center owners to attend, beside which, it was already difficult for parents with the nearing holidays and school pick-up times coinciding with meeting start times. On top of that, no key decision maker was present at any meeting. You ignored the petition delivered to you before the Maui hearing, a request from the public, and we were told that you will review the hours of testimony using the transcript. Please explain this process. Also, I missed the effort to inform the public and read with disgust, labeling up front anyone who will oppose the proposed rules, with a name and category.

This issue affects especially people who vaccinate, and if they oppose any part, they are labeled by your public relations staff which creates assumptions about those going to speak up. I request to invite open communication and informed consent with the next approach, and stay away from labeling the opposition as one group, negating their diversely.

I respectfully request that the proposed changes to HAR 11-157 be opposed and request, that with further changes on immunization, a communication link be established between the DOH & DOE to inform all schools, teachers, parents and all others who would be affected by the change, by informing us about the intentions. including a summary of the full implication of the rule change.

Respectfully,

December 26, 2018 Lucia Kocak, [REDACTED]

PS. Despite lack of official independent research to back the current vaccine schedule as noted by the recent lawsuit led and won by Mr. Robert F Kennedy against the HHS for the lack of vaccine safety testing and effectiveness over the past 30 plus years (<https://healthimpactnews.com/2018/hhs-sued-for-not-upholding-vaccine-safety-testing-mandated-by-law/>), research HAS been done by independent doctors and researcher since vaccines were first introduced, proving their harmful ingredients and negative effects on the human gut biome, which is responsible for our health, thereby rendering most harmful to the human body. Herd immunity has also been proven an unsound myth. The authors of these types of rule changes ought to do their due diligence and first conduct their own thorough research on vaccine safety and effectiveness, and not simply rely on the proven-to-be inaccurate and in some cases non-existent or falsified tests offered by the billion-dollar industry selling them. It behoves anyone willing to take on the responsibility for the health and well-being of other people's children by injecting them with foreign substances without their parents consent, to know the facts and the full implications of such an action as they will then be fully liable for any damage done to the children.

Sent from [Outlook](#)

From:
To:
Subject:
Date:

[REDACTED]
I oppose HAR 11-157
Wednesday, December 26, 2018 12:12:05 PM

You

Aloha my name is Abigail schoder.

For many reasons I strongly opposed Har 11-157 specifically in relation to the very serious health and safety risks and conflicts.

This proposal change offers a serious threat of significant increased risk to our Island and society as a whole. I am writing today to affirm my right, my families rights and any citizens right to have COMPLETE sovereignty over our bodies.

There is more than enough personal claims and documented scientific evidence proving severe detrimental effects from vaccinations. Including but not limited to: the improper proportional dosage to body weight ratio in administrating the vaccine, harmful ingredients such as mercury and proven carcinogenic toxic poisons and even contamination. (See 27 page ref. link below)
https://medscienceresearch.com/contamination/?fbclid=IwAR2LczWCTVRnDTeOf9f_GYCuC_dTnD29VR2KJRR28iqtw6hLYn52qZlh9k

Combine this with a "one size fits all" approach to protocol and now a proposal to increase protocol and we have a recipe for disaster and greater injury. The risk is simply too great.

Countless families, communities and school systems are already suffering from the devastating and debilitating negative affects from vaccines. This is reflected with the United States vaccine injury Court paying out over four billion dollars in settlement to date for injuries and even death.

<https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-december-2018.pdf>

The 1986 National Childhood Injury Act law acknowledges that vaccine injuries and deaths are real and that the vaccine injured and their families should be financially supported. For some reason the same law has allowed the vaccine manufacturers to escape liability for these adverse affects and has put the financial burden on the government. Congress created a "vaccine safety task force" to track and take action to reduce these harmful affects and implement measures to improve vaccine safety. The Sec of HHS was mandated to report to senate every two years regarding this. In the past 31 years they have not once reported to the Senate! On top of this **the number of vaccines recommended for our children has significantly increased already (from 24 doses of 7 vaccines by age 18, to 69 doses of 16 vaccines!**

This clearly shows us that our children and citizens are being treated as real live time "guinea pigs" or experiments. This is both unacceptable and downright dangerous. With this as our current situation, why would a proposal such as Har 11-157 even be entertained? Who is this really benefiting?

<https://www.govinfo.gov/content/pkg/USCODE-2016-title42/pdf/USCODE-2016-title42-chap6A-subchapXIX-part2-subpartc-sec300aa-27.pdf>

<http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

<https://www.nvic.org/cmstemplates/nvic/pdf/downloads/1983-2017-vaccine-schedules.pdf>

Documented scientific evidence and studies show that recently vaccinated individuals shed the virus for weeks and even months to both vaccinated and unvaccinated people. These recently vaccinated individuals can carry the disease without symptoms and pass it on to others. There are currently no guidelines in place to quarantine recently vaccinated individuals. They are released directly into the public and into our schools while shedding the viruses. Could the vaccinations themselves be increasing the spread of disease? This is a major public health issue and concern. An increase in number of people vaccinated, dosage and frequency could significantly multiply this problem and harm our society.

<https://www.westonaprice.org/public-health-officials-know-recently-vaccinated-individuals-spread-disease/>

As you know, the Department of Health itself clearly states on their website that no vaccine is 100% effective. We saw proof of this right here on Kauai when mumps vaccinated children and people did indeed contract the mumps during the outbreak last year. The risks are simply and clearly too high and not worth it.

Again, I'm writing today to affirm my right, my families rights and any citizens right to have COMPLETE sovereignty over our bodies. This is indeed our birth right. I sincerely asked you to truly listen and respond to our concerns as citizens, parents and caregivers. Thank you for your time and consideration.

Abigail Schoder

Additional REFERENCE details:

<https://www.hrsa.gov/sites/default/files/hrsa/vaccine-compensation/data/monthly-stats-december-2018.pdf>

"How many petitions have been awarded compensation? According to the CDC, from 2006 to 2016 over 3.1 billion doses of covered vaccines "were distributed in the U.S. For petitions filed in this time period, 5,576 petitions were adjudicated by the Court, and of those 3,785 were compensated. This means for every 1 million doses of vaccine that were distributed, 1 individual was compensated. Since 1988, over 20,123 petitions have been filed with the VICP. Over that 30-year time period, 17,576 petitions have been adjudicated, with 6,313 of those determined to be compensable, while 11,263 were dismissed. Total compensation paid over the life of the program is approximately \$4.0 billion."

..

From: [REDACTED]
To: [REDACTED]
Subject: I oppose HR 11-157
Date: Wednesday, December 26, 2018 3:02:56 PM

Aloha DOH,

Mahalo for the opportunity to submit testimony.

This is Yana. I spoke a couple times so you guys should know who I am. Sorry if I got a little serious during my testimony. I'm not suing anyone anytime soon :).

However I will keep researching this topic and continue to try and find new and innovative SCIENTIFIC information on this topic for you all to consider in your decision making process.

You all have an amazing and unique opportunity to stand for TRUTH AND JUSTICE right now. We all truly want health and happiness for ourselves and our babies.

Lets try and have a mature, healthy happy conversation about this and have a civil question and answer discussion panel as many that have given testimony request.

I very much so, hope that the DOE and everyone making decisions is yearning for truth and information as much as I am and that you find it within yourselves, for the sake of our children to come to the table and have a good discussion with the community about this topic.

A panel where not only do you hear testimony, but also answer our questions and demonstrate that you fully acknowledge and answer our concerns into the matter of mandatory vaccinations.

Just for fun, here is one more study I'd like for you to consider:

Dec 22, 2018 by Richard Harris

Research published in a major medical journal concludes that a parachute is no more effective than an empty backpack at protecting you from harm if you have to jump from an aircraft.

But before you leap to any rash conclusions, you had better hear the whole story.

The gold standard for medical research is a study that randomly assigns volunteers to try an intervention or to go without one and be part of a control group.

For some reason, nobody has ever done a randomized controlled trial of parachutes. In fact, medical researchers [often use the parachute example](#) when they argue they don't need to do a study because they're so sure they already know something works.

[Cardiologist Robert Yeh](#), an associate professor at Harvard Medical School and attending physician at Beth Israel Deaconess Medical Center, got a wicked idea one day. He and his colleagues would actually attempt the parachute study to make a few choice points about the potential pitfalls of research shortcuts.

They started by talking to their seatmates on airliners.

"We'd strike up a conversation and say, 'Would you be willing to be randomized in a study where you had a 50 percent chance of jumping out of this airplane with — versus without — a parachute?' " Yeh says.

Only a few people said yes to this outrageous invitation, and they were excluded for reasons of questionable mental health.

The scientists had much better success asking members of their own research teams from Harvard, University of California, Los Angeles (Where Yeh's brother is a surgery professor), and University of Michigan (where a buddy works) about volunteering to participate in the experiment on other aircraft.

In all, 23 people agreed to be randomly given either a backpack or a parachute and then to jump from a biplane on Martha's Vineyard in Massachusetts or from a helicopter in Michigan.

Relying on two locations and only two kinds of aircraft gave the researchers quite a skewed sample. But this sort of problem crops up frequently in studies, which was part of the point Yeh and his team were trying to make.

Still, photos taken during the experiment show the volunteers were only too happy to take part. "I think people are laughing all of the way to the ground," Yeh says.

Oh, there's one important detail here. The drop in the study was about 2 feet total, because the biplane and helicopter were parked.

Nobody suffered any injuries. Surprise, surprise. So it's technically true that parachutes offered no better protection for these jumpers than the backpacks.

"But, of course, that is a ludicrous result," Yeh says. "The real answer is that that trial did not show a benefit because of the types of patients who were enrolled."

If they had enrolled people at high risk for injury, that is people in *flying* aircraft, the results would have been quite different (not to mention unethical).

But something like this happens in everyday medical research. It's far too easy for scientists who have already anticipated the outcome of their research to cherry-pick patients and circumstances to achieve the results they expect to see. This research paper carried that idea to the ridiculous extreme.

The [study's findings](#) were published in the traditionally lighthearted Christmas issue of the medical journal, *BMJ*.

"It's a little bit of a parable, to say we have to look at the fine print, we have to understand the context in which research is designed and conducted to really properly interpret the

results," Yeh says. Scientists often read just the conclusion of a study and then draw their own conclusions that are far more sweeping than are justified by the actual findings.

This is a real problem in science.

"I know that people often don't look detailed enough into what is being investigated to know how to interpret the results of a trial," says [Cecile Janssens](#), an epidemiology professor at Emory University.

Janssens was delighted to come across the paper on Twitter. She says like a lot of research, its results are accurate as far as they go, but "the results can only be generalized to situations where people jump out of an aircraft within a few feet above the ground."

She plans to give this paper to her students with a straight face and see how long it takes for them to get the deeper points about scientific methodology buried in this absurd experiment.

"It will be unforgettable," she says — far better than assigning a straight-ahead scientific study.

Yeh is pleased to see that the fun he had with his colleagues is turning into a teaching tool. He also savors some of the more subtle lessons buried in the paper.

For example, the scientists attempted to submit it to a government registry of research studies, which is required for many studies involving human subjects. They chose one in Sri Lanka to reduce the risk that it would be discovered in advance, spoiling the joke. It was rejected.

"They thought that a trial conducted in this manner could not lead to scientifically valid evidence," he said.

"They're right!" he adds with a laugh.

In fact, the paper acknowledges that the research team members cracked themselves up so much that "all authors suffered substantial abdominal discomfort from laughter."

"Our greatest accomplishment from all of this was we felt very good that we were able to cite Sir Isaac Newton in the paper," he says. They referred to Newton's classic 1687 paper establishing the law of gravity.

Yes, gravity is a law. Mess with it at your own risk.

You can reach NPR science correspondent Richard Harris by email: rharris@npr.org.

Copyright 2018 NPR. To see more, visit <https://www.npr.org>.

Thank you again for this opportunity to testify and I look forward to hearing good news about your organizations.

Mahalo,
Yana

From: [REDACTED]
To: [REDACTED]
Subject: I oppose RE 11-157
Date: Wednesday, December 26, 2018 1:58:51 PM

Dear Sirs:

I am writing to oppose RE 11-157

This is not about the dangers of vaccination and the amount of children that have been damaged by them. This is about our choice as parents to make an informed decision and for our right to choose what is best for our children.

The medical industry is as corrupt as it gets as we can see when look at the amount of people that are addicted to opioids that were launched although the pharmaceuticals behind them knew they were addictive.

Someone is pushing for extra vaccines, doctors are getting paid in the form of Bonuses for pushing vaccines and other medications without researching the background of their patients. Please ,help children to have a chance and protect them from the greed in the medical industry.

Some articles

<https://foreverconscious.com/former-pharmaceutical-executive-speaks-out-about-the-corrupt-industry>

<https://www.marketwatch.com/story/purdue-pharma-execs-knew-about-opioid-addiction-risks-long-before-publicly-admitting-them-court-papers-claim-2018-10-24>

Sincerely,

--
Joanna Wheeler
Registered voter [REDACTED]

--
[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: I strongly oppose 11-157 proposed rules
Date: Wednesday, December 26, 2018 4:00:15 PM

Aloha,

I strongly oppose 11-157 proposed rules.

I am a licensed Naturopathic Doctor as well as a mother and grandmother. In my family practice as a primary care doctor in Vermont and Hawaii for 24 years, I have had many vaccine injured babies, children, and adults come to me for treatment.

There are many reasons that I oppose the 11-157 proposed rules. I will mention a few of the important reasons due to time.

It is unlawful to require more vaccinations, especially for a child to be able to enter schools and preschools.

Unfortunately, vaccines are not safe and many children and adults have been injured and often debilitated. Reported vaccine injuries can be seen on the VAERS database.

There have never been proper scientific, double- blind studies done to determine the safety and efficacy of individual vaccines, and no studies have been conducted to evaluate the safety of combining multiple vaccinations in one shot or in one office visit , or the cumulative affects of 48 vaccinations starting from birth through early childhood on the current recommended vaccine schedule (before the added proposed vaccines)!

It is absolutely unlawful to require medical interventions that have a history of causing harm and death, and that have not been studied adequately individually , combined, or cumulative over time.

The vaccines are manufactured with many chemicals and adjuvants that are neurotoxic and toxic to living beings in general like aluminum, mercury compounds, formaldehyde, phenol, polysorbate 80, to name a few. Some contain material from aborted human fetuses, dog kidneys, genetically modified insects and viruses. How do these interact with a baby or adult's DNA? Do you know? No studies have been done. Animal and aborted human cells can easily be contaminated by other unknown viruses, which may lead to the recipient developing cancer , autoimmune and other conditions. Has this been studied? No.

Gardasil, an hpv vaccine, that is being proposed for requirement, has been shown to have many terrible side effects and reactions, yet hpv is a very slow growing cancer that is easily treated and screamed for.

Due to time I must end here,

Mahalo,

Dr. Donna Caplan, ND
[REDACTED]

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: I support HAR 11-157
Date: Wednesday, December 26, 2018 12:49:43 PM

I support HAR 11-157.
Dr Lester Harunaga

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Immunization
Date: Wednesday, December 26, 2018 1:32:16 PM

December 26, 2018

Hawaii State Department of Health
1250 Punchbowl St.
Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article "Economic Evaluation of the Routine Childhood Immunization Program in the United States" published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,
Ally Brown

From: [REDACTED]
To: [REDACTED]
Subject: Immunization policy
Date: Wednesday, December 26, 2018 3:21:52 PM

I'm writing in my testimony against the immunization mandate. I don't believe in creating mandates that exclude people who do or don't decide to vaccinate their children. I believe vaccinations have done great harm to many children all across the world. I don't think there has been enough testing to prove these vaccines are harmless. I would not feed my kids something I believe bad for them, let alone knowingly inject something into my precious child that I believe harmful. I'm asking you to prove to me these products your pushing on us are safe and do more good than harm. If mandates expand and normal things like joining public schools and sports and what not are decided upon by your vaccine status, many people will pull away from that society and create their own where they feel safe and free. We all want to live our lives the best we can and I'm asking to be able to live mine with freedom of choice and freedom to decide what is best for my children. As I am sure you want that choice for yourself and yours.

~ A very concerned citizen Samantha Calderon

From: [REDACTED]
To: [REDACTED]
Subject: Immunizations
Date: Wednesday, December 26, 2018 3:43:48 PM

Aloha to whom it may concern,

Please do not insist on immunization it is all poison. All humans should have the right to choose. Do not take our freedom away.

Deb

From: [REDACTED]
To: [REDACTED]
Subject: Immunizations
Date: Wednesday, December 26, 2018 1:32:52 PM
Attachments: [image001.png](#)

December 26, 2018

Hawaii State Department of Health
1250 Punchbowl St.
Honolulu, HI 96813

Dear Dr. Bruce Anderson and Hawaii State Department of Health Staff:

I am writing on behalf of myself, my family, and my community to express unequivocal support for vaccines. I want to strongly support the Hawaii State Department of Health in affirming the importance of mandatory vaccinations, for the following reasons:

- 1. Vaccines protect the health of children and adults and save lives.**
- 2. Vaccines prevent life-threatening diseases, including forms of cancer.**
- 3. Vaccines have been part of the fabric of our society for decades and are one of the most significant medical innovations of the modern era.**

The impact from vaccines improving the health of the planet and our local communities is indisputable. Here are few facts from this incredible and important history of vaccines:

- As a result of the introduction of mass vaccinations, smallpox was declared eradicated from the world in 1977.
- Polio, a disease that routinely afflicted 13,000 to 20,000 Americans every year in the United States before the availability of the vaccine, was officially eliminated from the Western Hemisphere in 1991.

As has been extensively documented and studied by the United Nations and UNICEF, globally, vaccines prevent the deaths of roughly 2.5 million children per year. According to the article "Economic Evaluation of the Routine Childhood Immunization Program in the United States" published in the journal *Pediatrics* in 2009, data shows that just for children born in the United States in 2009, routine childhood immunizations will prevent approximately 42,000 early deaths and 20 million cases of disease with savings of more than \$82 billion in societal costs.

Although vaccines are the safest and most cost-effective way of preventing disease, disability and death, the United States has witnessed outbreaks of vaccine-preventable diseases, as highlighted by the measles outbreak at Disneyland in 2014. We should do everything we can in Hawaii to prevent these vaccine-preventable outbreaks from occurring here

In another example in 2012, **48,277 cases of pertussis** (whooping cough) were reported to the Centers for Disease Control and Prevention (CDC), including 20 pertussis-related deaths, as reported and documented by the CDC. **This was the most reported cases of pertussis since 1955.** In addition, each year, more than 200,000 individuals are hospitalized and 3,000-49,000 deaths occur from influenza-related complications, which could be greatly reduced with increased vaccinations.

Claims that vaccines are unsafe when administered according to expert recommendations have been disproven by a robust and thoroughly researched body of medical literature, including an exhaustive review by the National Academy of Medicine. Delaying or not requiring vaccines only leaves our State and our communities at risk of disease, particularly children. Hawaii State Department of Health should redouble efforts to make needed investments in patient and family education about the importance of vaccines in order to increase the rate of vaccination among all populations.

In conclusion, the Hawaii State Department of Health should vigorously promote and defend the importance of vaccines. The Hawaii State Department of Health should share this message, loudly and clearly:

Vaccines are safe. Vaccines are effective. Vaccines save lives.

Our communities across the state of Hawaii need accurate and detailed information regarding the robust, extensive scientific evidence supporting vaccine safety and effectiveness. Please continue to require and promote vaccinations to keep our beautiful State of Hawaii healthy and safe!

Sincerely,

Best Regards,
Tim Brown



Sue Brown Realty & Associates



direct |



fax |



From:

To:

Subject:

Date:

Informed Consent / NO Mandated Vaccines

Wednesday, December 26, 2018 12:12:01 PM

Aloha ~

Ask the teachers about the increase of ADHD/ autism and learning/ health issues! (especially in SPED) I taught here for 35 years and believe me ~ the children are in DANGER!

https://www.naturalnews.com/052265_vaccine_experiments_Bill_Gates_India.html

<http://mauiindependent.org/hawaii-dept-of-health-tries-to-force-hazardous-ineffective-hpv-vaccine-on-all-public-school-children/?fbclid=IwAR1dvnQrBqhKaBTuNbGZ7DK98mFI03fwMSjrF5Bx45ZHYlrZgDPulAcDyyo>

“ALL the Vaccines Are Contaminated - Every Last One of Them

"The chief, if not the sole, cause of the monstrous increase in cancer has been vaccination" - Dr. Robert Robert Bell, CM, MSc, MD, FACS, FRCSC Cancer Clinical Research Unit (CCRU), once Vice President International Society for Cancer Research at the Princess Margaret Cancer Centre

(WASHINGTON, D.C.) - Have you been rushing out to get a yearly flu vaccine or diligently taking your children for the 40 or so mandated childhood vaccines?

That's really a shame because you have unwittingly been trading a run-of-the-mill flu or just the measles, for loading up your or your children's bodies with cancer and other deadly viruses, a destructive bacteria, a chemical selected to damage fertility, and with synthetic DNA that threatens to damage your own DNA - the biologic code for your existence.

Who is saying the vaccines are contaminated?

None other than the (now deceased) head of vaccines at Merck, Dr. Maurice Hillerman, who on camera admitted that Merck's Hepatitis B vaccines, contaminated with a virus, caused the AIDS epidemic in the US. He went on to say that all of Merck's vaccines are contaminated with cancer and other viruses. (The US government has conceded the HEB B vaccine causes Lupus. That vaccine is mandated for every infant in the US on the day of birth, and is associated with MS as well.)

<http://www.salem-news.com/articles/november292011/vaccines-contaminated-se.php>

Or they might recognize that so is Dr. Larry Palevsky, a board certified NY pediatrician, who for ten years routinely gave vaccines to his patients until he noticed them losing eye contact and then began looking into the vaccines he had blindly trusted. He found that they are ALL contaminated with viruses that are so small they can never be removed. He no longer gives any vaccines. He now treats his young patients for autism and other neurologic injuries from vaccines.

Donald W. Scott, the editor of The Journal of Degenerative Diseases and the co-founder of the Common Cause Medical Research Foundation, links vaccines to AIDS (as did Hillerman) and

to US bio-weapons research, and says they are contaminated with mycoplasma, a primitive bacteria that takes apart cell walls.

Perhaps the highest scientific authority saying vaccines are contaminated is Garth Nicolson. He is a cell biologist and editor of the Journal of Clinical and Experimental Metastasis, and the Journal of Cellular Biochemistry. He is one of the most cited scientists in the world, having published over 600 medical and scientific peer-reviewed papers, edited over 14 books, and served on the editorial boards of 28 medical and scientific journals. He is not just saying that vaccines are contaminated with mycoplasma but is warning the US that they are. Nicolson goes further and says that we are all being damaged by them and contracting chronic degenerative diseases that.

That damage translates into lifelong patients (and thus life-long profit) for the pharmaceutical industry making the vaccines and he says doesn't appear to be accidental.

According To CIA Statistics: As Shots Increase, U.S. Lifespan Is DECREASING

All the vaccines mandated to children and many other vaccines as well, including the seasonal flu vaccines being mandated to health care workers, are contaminated with polysorbate 80, the central ingredient in a pharmaceutical industry patent to damage fertility. The pharmaceutical industry has a long history of seeking a vaccine that would covertly sterilize whole populations. So, in addition to being contaminated with cancer and other viruses, and with the bacteria mycoplasma, vaccines are intentionally "contaminated" with a chemical as well, which is, given the patent, a "patently" sought-after sterilizing agent.

Beyond containing polysorbate 80 and cancer and other viruses, and likely mycoplasma, the Gardasil vaccines are contaminated in an additional way. It and all the new vaccines are contaminated with genetically engineered DNA. It can contaminate people's DNA, just as genetically engineered crops can contaminate normal crops. Gardasil itself is contaminated with a man-made version of the HPV DNA, the very virus it was supposed to protect against, which now it threatens not only altering kids' healthy DNA with synthetic DNA (!) but with a diseased version.

The California law even approves in advance, ALL yet-to-be made (and completely untested) vaccines for sexually transmitted diseases, though of the two current Merck vaccines they are pushing on children, one Merck vaccine caused AIDS and causes Lupus and the other Merck vaccine is contaminated in multiple ways and proving highly lethal. Children will be the ones to decide whether to take the vaccines, and they will make that decision after being forced to see videos of people dying terrible deaths from cancer. Not only would the vaccine be given without parental consent, but parents are denied knowledge that the vaccine is going to be given or that it was given. If the child has a seizure or dies afterward, parents may not see their own children's medical records.

This is what is left of the "informed consent" meant to provide human rights to protect the world from pharmaceutical industry abuses against mankind.

After World War II, it was Merck which received the flight capital of the pharmaceutical industry indicted for crimes against humanity, human enslavement and mass murder.

In the case of children, rather than their facing childhood diseases of insignificant threat, they

are, by legal mandate, being bombarded repeatedly throughout their childhood with viruses that cause diseases (including cancer), a cell-destroying bacteria, a threat to the very integrity of their DNA, and a chemical specifically chosen to impair fertility. And laws are being written to add to the already long list of vaccines they must take, including two mandated Merck vaccines. One is an old Merck vaccine that caused AIDS and is causing Lupus. The other is a Merck vaccine claiming to prevent cervical cancer though girls have little chance of contracting it in the first place (and boys, none!) and it can easily be detected by pap smear and treated successfully and there is NO evidence the vaccine prevents it. Meanwhile, it is killing children.

--S. Edmonson for Salem-News.com

<http://www.salem-news.com/articles/november292011/vaccines-contaminated-se.php>”

From: [REDACTED]
To: [REDACTED]
Subject: OPPOSE HAR-A57
Date: Wednesday, December 26, 2018 2:34:00 PM

To the DOH Hawaii,

My name is Ione Chittenden and I OPOPOSE HAR 11-157! As the mother of an autistic child, I saw what vaccines did to my child and I don't want the same to happen to other families. I've been called crazy for believing that vaccines harmed my child but unless you've seen it happen to your own, many won't believe it. She is our only child and she was very much wanted. We tried for many years to have a child and finally had her with the help of in vitro fertilization. We adored her every sound & movement. Then she had the MMR shot and everything changed. We saw the changes that the MMR vaccine did to her. But we didn't make the connection to the vaccines until we took her back for more shots. That is when the more severe symptoms of autism appeared. She stopped talking and behaviorally, she was out of control! We needed speech therapy, occupational therapy and consulted with specialists, non of which was covered by our health insurance so we had to pay out of pocket! We tried to get DDD services for our child but was denied for 7 years!!!!!! In 2015, things got so bad! Our child was destroying our house, her school cut her school hours down to only 2 a day and we could not find help!!! I finally contacted Senator Rudderman's office for help and his office helped to get us on the waiver program.

You, the DOH, want to force vaccines, but then hold back services to the families of the children who get hurt by the vaccines. I know of other families that had a hard time getting DDD services as well. If this bill passes, I fear that many more families will go through the same hardship that we went through when we were looking for help! We've exhausted all of our retirement by paying out of pocket for therapies that weren't covered under our medical. Now we are left worrying what will happen to our child after we die.

I believe that passing this bill is fueled by the greed of the pharmaceutical companies. Please do not pass this bill. More children will be hurt, more families will have their hopes and dreams destroyed and their lives turned upside down. In closing, I would like for you to please look at your DOH mission statement and goals. Passing this bill goes against what your mission statement stands for!

MISSION STATEMENT

The mission of the Department of Health is to protect and improve the health and environment for all people in Hawai'i .

Philosophy

Health, that optimal state of physical, mental, social and environmental well-being, is a right and responsibility of all of Hawaii's people.

Goals

- Promote health and well-being
- Prevent disease and injury
- Promote healthy lifestyles and workplaces
- Promote the strength and integrity of families and communities

To prevent pollution and promote and preserve a clean, healthy and natural environment

- Promote resource conservation (recycling)
- Protect and enhance air and water quality

To assure basic physical and mental health care (the five A's)

- Affordable
- Appropriate
- Assured quality
- Available
- Accessible

Guiding Principles

- Ensure that core public health functions – assessment, policy, and assurance – are implemented or maintained.
- Ensure that federal mandates, including court-ordered settlements are satisfied.
- Ensure that resources are directed at those problems that pose the greatest risk to the public's health and the environment.
- Ensure that appropriate and cost-effective resources are dispersed geographically and satisfy principles 1 to 3.
- Ensure that the health department is the service provider of last resort for uninsurable populations and where there is no other satisfactory alternative.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Oppose increased mandatory vaccinations
Date: Wednesday, December 26, 2018 3:44:21 PM

To the Immunization Branch
Hawaii State Department of Health

The very topic of mandatory vaccinations is abhorrent to many people. It reeks of authoritarianism, communism and nazism - virtually every negative "ism" is evoked when the term "mandatory vaccinations" is heard. It assumes that the individual's right to privacy and freedom of choice is non-existent. It strikes at the heart of what it means to be an American living in a Constitutional republic.

Not only Americans are horrified at the thought - in the words Dr. Hiroko Mori, former head of the infectious disease section at the former Institute of Public Health, Japan: "The right to choose should be recognized as a fundamental human right."

<https://www.japantimes.co.jp/life/2014/10/04/lifestyle/vaccination-choice-two-unknowns/>

'Mandatory vaccinations' implies not only that the individual has no such rights, but that they are incapable of deciding, based on the facts, what is best for their own health and the health of their children.

Therein lies the rub - in today's information age, in a climate of medicine for profit, where pharmaceutical corporations wield their billions of dollars like weapons of war and saturate the airwaves with direct-to-consumer advertising, (U.S. being only one of two countries in the world to allow this), and pay their lobbyists to write the legislation that protects them from vaccine liability, in this climate it is exceedingly difficult to find any facts on the topic of vaccines efficacy and safety.

Let's go back in time and look at the early polio vaccines. The original Salk vaccine made of inactivated viruses was replaced by the Sabin oral polio vaccine of three vaccine strain polioviruses cultured from primary cell monkey kidneys. One of the monkeys carried a virus known to cause cancer tumors - SV40. In spite of this fact, public health officials recommended that all children receive this oral polio vaccine. Between 1954 and 1961 over 100 million children and adults received this vaccine. Doctors assumed that the cancer causing virus was removed from the vaccine, however it was discovered that up until 1978 it was still present in the vaccine. (Cutrone r, Lednicky J, Dunn G et al. [Some Oral Poliovirus Vaccines Were Contaminated with Infectious SV40 after 1961](#). *Cancer Res* 2005; 65: 10273-10279.)

Of course, the fact that half of all people today will have some kind of cancer must simply be a coincidence...right? "Correlation is not causation" is the mantra we hear so often from those scientists dependent on corporate dollars.

Speaking of which, let's look at the vaccine studies done by scientists funded by the protected class of vaccine manufacturing pharmaceutical corporations, which the CDC relies on. Can we be assured that they present all the pertinent data, free of bias? Hardly.

In the opinion of the Chief Editor of the world's most prestigious medical journal, The Lancet:

“The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness.” - “Offline: What is medicine's 5 sigma?” Richard Horton, editor The Lancet www.thelancet.com vol385 April 11, 2015.

But that's not all. Listen to what the editor at the New England Medical Journal has to say: Marcia Angell: “it is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor of *The New England Journal of Medicine*”

So, Hawaii Department of Health now asks us to follow the recommendations made by the CDC for these ‘mandatory vaccinations’. Vaccinations are violent, invasive procedures that may result in death, paralysis or permanent disability. And we are asked to do so, because the CDC says it is a good thing.

Let's watch a video as the CDC's "Advisory Committee on Immunization Practices" decides whether to approve the new Hep B vaccine: <https://thevaccinereaction.org/2018/09/acip-voting-on-a-new-vaccine/>

"Is there any comment on using this vaccine at the same time as other adjuvanted vaccines? *We have no data to make a recommendation one way or the other.* So just to sort of put this in context of other vaccines, while pre-clinical studies were not done using this vaccine simultaneously, our general approach to immunizations is that they can be given at the same time in different limbs.

Are multiple adjuvanted vaccines used in Europe or other markets?

Not to my knowledge. Okay, I think unless there's any further discussion we will take a vote on this recommendation. *So... the voting is completed and it is unanimous to support this recommendation to approve the hepatitis B vaccine.*”

In other words, this committee has decided to approve a vaccine known to cause myocardial infarctions and see what happens to the millions of guinea pig people who will unwittingly be testing it.

Is the entire CDC corrupted beyond all repair by pharmaceutical money? Thanks to the efforts of independent journalists we can look at former CDC Director Thomas Frieden for a glimmer of just how bad it could be. Not simply that he was arrested for sexual abuse, but the possible billions in scandals. <https://www.coreysdigs.com/cdc/cdc-thomas-frieden-billions-in-potential-scandals/>

There are too many reasons to list here as to why I oppose mandatory vaccinations. Suffice it to say that not only should the CDC recommendations not be implemented, but the philosophical exemption should be reinstated.

Sincerely,

Vicki Vierra



From:

To:

Subject:

Date:

[REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
OPPOSE MANDATORY VACCINATION

Wednesday, December 26, 2018 5:13:31 PM

My name Debra Parzych and I STRONGLY oppose mandatory vaccination! There is a huge list of dangers associated with vaccines and when there are dangers present there MUST be a choice!!

Debra Parzych

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Opposition Testimony to HAR 11-157
Date: Wednesday, December 26, 2018 10:11:05 AM

Dear Sir or Madam,

Please oppose HAR11-157 mandating the extremely unsafe HPV vaccine and terribly inefficient Flu shot for children to attend public school.

I urge you to listen to the countless stories of harm these shots have caused.

I urge you to please understand we are not a "1 size fits all" population- especially when it comes to our health!

I was in the military for 4 years and subjected to over 40 doses of vaccines.

Within a few months I was experiencing hair loss, and psoriasis. I was only 23 yrs old! Years later with genetic testing I found out that I have a genetic mutation called MTHFR, which in short means my body is unable to properly detox like normal. This means any toxins I'm exposed to stay within me leading to autoimmune diseases without me making effort to detox with supplements and interventions.

I have kids. My 9yr old daughter was fully vaccinated according to schedule and she has had problems with anxiety, sensory disorder (extremely sensitive to noises and lights and crowded places), she also suffered from damage to her development in executive processes due to her inability to detox from the toxic ingredients in the vaccines.

HPV vaccine is dangerous and does not prevent cancer. Young children are not at risk and this should just be optional for sexually active teens and adults.

The flu shot does not prevent anyone from contracting the influenza virus- it simply reduces your symptoms, therefore you may have the virus, and still attend school and spread the virus infecting others because you aren't displaying symptoms! This is not acceptable. My son had the flu this year and we kept him home, we let him rest and gave him extra vitamin C, elderberry Syrup, probiotics, and kept him hydrated, he was better in 3 days.

I do not fear disease simply because someone is selling a vaccine for it.

You shouldn't either. Please take time, & due diligence to understand how these vaccines are made, how they supposedly work, what the true risks are, and why they only give a "1 size fits all dose"... why so many parents are afraid of being forced to inject toxic substances into their children.

HPV vaccine has been pulled from schedule in many countries due to safety concerns and flu vaccine has the most reported vaccine for injury . These vaccines are not going to contribute to better health but may actually cause more health issues than the could hypothetically prevent.

Thank you for your time and consideration.

Please be pono.

Respectfully,
Jessica Oliveira

[REDACTED]

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Cc: [REDACTED]
Subject: TESTIMONY OPPOSING Ch 11-157
Date: Wednesday, December 26, 2018 7:54:58 AM

RE: Testimony STRONGLY OPPOSING the Hawaii DOH's proposed amendments to HAR Ch. 11-157, Examination and Immunization

The Department of Health held several public hearings across the islands, on Honolulu, Maui/Molokai (video conference), Lanai, Kauai, Hilo, and Kona as per the public schedule posted on their website.[\[1\]](#)

Although oral testimony was provided in front of a DOH hearings officer, Steven Jacobsen and Unknown, both publicly stated at every meeting that they had not read or was not familiar with the proposed language and that they were not there to make any decisions.

None of the decision makers were present at any of the hearings, only DOH staffers. The only senior DOH staff seen a couple of hearings was Ron Balajadia of the Immunization Branch, under Dr. Sarah Park, State Epidemiologist.

The DOH recorded over 12 hours of oral testimony from the public on the proposed amendments and requested written testimony. An overwhelming majority of testifiers described personal stories of vaccine injuries, facts and evidence of vaccine injuries and dangers. Only a handful of practitioners testified in support.

The Hearings Officers stated that the DOH would review the audio and written testimonies and would make a decision. Neither Hearings Officer could provide any time frame. When pressed for the names of the decision makers, the Hearings Officers could not provide any names for the record.

This lack of transparency in the administrative process demonstrated that the DOH, specifically the Disease Outbreak Control Division, Immunization Branch under Dr. Sarah Park cannot be allowed to amend, repeal or adopt any administrative rules without additional oversight.

Ch. 11-157 amendments proposes to adopt ACIP guidelines while also mandating several additional vaccines at various school levels, with the additional authority to adopt future amendments as they occur. However, important decisions related to our children cannot be left to individuals who make decisions but are not responsible for the health consequences that may occur from these mandates.

Under the National Childhood Vaccine Injury Act of 1986, specifically 42 USC 300aa-27, the Department of Health and Human Services (DHHS) is required "to improve the safety profile of childhood vaccines, which includes licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on

vaccines, in order to reduce the risks of adverse reactions to vaccines.” These are the same childhood vaccines recommended by the CDC on behalf of the federal government.

However, a recent FOIA request showed that DHHS admitted that it has never conducted any studies or research demonstrating the safety of childhood vaccines recommended by the federal government as required by 42 USC 300aa-27.[2] The federal government was unable to show and continues to be unable to show that childhood vaccines are any safer than they were when they were first introduced onto the market, in some instances, many decades ago.

As the Hawaii DOH attempts to mandate these very same vaccines recommended by the ACIP, a federal advisory committee to the CDC, which falls under DHHS, the issues remain the same. If DHHS has not conducted any studies in the last 30 years on the safety of vaccines, then the ACIP, which has never conducted any clinical studies itself, by default, cannot also claim that its recommendations regarding the CDC recommended childhood vaccines are safe related to adverse reactions.

ACIP guidelines and its vaccine recommendations should not be mandated by the DOH in the proposed Ch. 11-157. These recommendations are intended to only be recommendations where parents and doctors discuss the risks and benefits of vaccines before making an informed decision. To mandate vaccines without evidence of safety is unconscionable and irresponsible by the Hawaii Department of Health, the Director of Health, the State Epidemiologist, the Governor and the State of Hawaii and any other individual involved in making this monumental decision.

Please find included, a link to 50 studies questioning the safety of vaccines published since 2010[3] which I am submitting as evidence for DOH review to OPPOSE Ch. 11-157.

Thank you,

Teresa Chao, RPh, MBA, MJ

[1] <https://health.hawaii.gov/opppd/files/2018/11/11-157-Public-Hearing-Additional-dates.pdf>

[2] <http://www.icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

[3] <http://vaccinesafetycommission.org/pdfs/50-Studies.pdf>

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: TESTIMONY OPPOSING CH 11-157
Date: Wednesday, December 26, 2018 3:26:04 PM

TESTIMONY STRONGLY OPPOSING DOH Ch. 11-157 for the following reasons:

The DOH submitted an application to the Small Business Regulatory Review Board (SBRRB) entitled, "Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board" received on June 27, 2017.

At the Maui public hearing held on December 14, 2018, the DOH hearings officer, Steve Jacobson stated that the public could submit questions via email so that the DOH would have the opportunity to address public concerns. Therefore, I am requesting the DOH Immunization Branch and the DOH Disease Outbreak Control Division to provide a written response to the following questions related to the above Impact statement and DOH responses. The questions are as follows:

1. Through a request to the SBRRB, records showed that the SBRRB received the DOH's Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board on June 27, 2017. In addition the DOH also submitted at that time, two documents, and a version of HAR Chapter 11-157, dated May 26, 2017 and a copy of the ACIP guidance.

On July 19, 2017, the SBRRB voted to send the proposed rules dated May 26, 2017 to a public hearing. However, the version of Chapter 11-157 dated May 26, 2017 is **DIFFERENT** from the version that is currently posted on the DOH website which is dated September 5, 2018. The September 5, 2018 version was also the version that was debated on at the public hearing on Oahu on November 1, 2018 and will be the same version for the remaining hearings on the outer islands.

There are substantive differences in these versions of Ch. 11-157 relating to the tuberculin testing and the process to move these proposed rules to public hearing should have been readdressed but was not.

QUESTION: Was the DOH legally or ethically required to submit an up-dated Ch. 11-157, at minimum to the SBRRB and when did the DOH disclose this change of information to the SBRRB?

2. Page 2, question 1, basically asks how small businesses may be adversely affected by the proposed rules. The DOH responded "The health care providers should not be adversely affected by the proposed rules. Child care centers, compulsory schools and post-secondary should not be affected by the proposed rules."

QUESTION: What documents, notes, or additional information did the DOH use to support their assertion that these providers "should not be adversely affected?"

QUESTION: What additional written information, testimonies or summaries of information were submitted by health care providers, child care centers, compulsory schools and post-secondary providers that support the DOH's claim that these providers "should not be adversely affected?"

3. Page 2, question 2, asks for dollar amounts of increased direct costs in fees, fines, and indirect costs including reporting, recordkeeping, equipment construction, labor, professional services, revenue

loss, or other costs associated with compliance.

The DOH response was "Increased indirect costs associated with enhance screening and recordkeeping may be incurred by some schools and post-secondary schools. The Department does not anticipate any increased costs associated with compliance to health care providers." However, no dollar amounts were provided as required.

QUESTION: The DOH admitted that "some schools and post-secondary schools" may incur increased costs. What are these estimated dollar amounts?

QUESTION: What information did the DOH use to assert that health care providers are not anticipated to incur any increased costs?"

4. Page 2, question 3, asks for the probable monetary costs and benefits to the agency or other agencies directly affected.

QUESTION: The DOH stated that it estimates that the additional requirements necessary for implementation have been determined to be \$60,000 for the 1st year and \$5,000 for additional years. Where is the cost analysis showing how the DOH arrived at both of these figures and what is the plan the DOH intends to implement to achieve these goals?

QUESTION: Since the Department of Education is another agency that will be affected by the additional recordkeeping and monitoring as described in the proposed rules, what information did the DOH use to determine the probable monetary costs for the Department of Education to implement these additional requirements?

5. Page 3, question 4, asks for the methods the DOH considered or used to reduce the impact on small business. The DOH's response was that "the training provided would assist the providers and affected organizations to understand the changes to the requirements so that they would be able to screen records appropriately."

QUESTION: When small businesses are required to provide the man-power to implement the recommendations proposed by Ch. 11-157, exactly what are the expected duties necessary to properly screen the documents and what are the estimated costs in man-power and supplies needed to satisfy this requirement?

6. On page 3, question 7, the question asks how the DOH involved small business in the development of the proposed rules.

DOH's response was that "the 'School and Immunization Requirements Working Group' was made up of representatives from private compulsory and post-secondary institutions, the American Academy of Pediatrics, Hawaii Chapter, the Hawaii Association of Independent Schools, and Kaiser Permanente, Department of Education, the Department of Human Services, and Tuberculosis Control, Public Health Nursing, Disease Investigation, and Immunization Branches of the Department of Health."

However, there are NO small businesses or individuals represented in this working group. Therefore, it is questionable as to whether any small businesses were involved in the development of the proposed Ch.11-157 rules.

QUESTION: If there were small businesses or individuals in the 'School and Immunization Requirements Working Group,' please identify them by name or by name of business.

7. On Page 3, question 7a, asks if there were any **recommendations** made by small businesses and whether the recommendations were incorporated in the proposed rule. If yes, explain, if no, why not.

Instead of answering "yes" or "no" to this question, the DOH stated that the 'School and Immunization Requirements Working Group' member organizations emphasized the need for delayed effective date to allow training materials and training to take place of the rules' effective date.

QUESTION: Why did the DOH fail to directly answer this question? Is it because they did not appear to have solicited any responses from small businesses such as daycare business owners, individual providers or the like in their working group?

The exclusion of small businesses from the working group implies that small businesses such as daycare centers and individual providers did not provide any recommendations and thus their input were not incorporated into the proposed rule.

Further, the DOH's solution of providing training and training materials was created by LARGE businesses which included Kaiser Permanente, the HAIS for private schools, and post-secondary institutions which include community colleges and universities.

This omission of small businesses from the working group should invalidate this entire application and the DOH should be required to properly solicit input from small businesses such as daycare centers, other child-care facilities, and individual small business owners before the proposed amendment is allowed to move forward.

1. On page 3, question 8, asks whether "the proposed rules include provisions that are more stringent than those mandated by a comparable or related federal, state, or county standards, with an explanation of the reason for imposing the more stringent standard."

The DOH's response states that "the proposed school examination and immunization regulations are consistent with the United States Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP) recommendations and are comparable to and in some instances less stringent than other states' school and post-secondary school immunization and examination requirements. The proposed rules are not more stringent than any comparable or related federal, state or county standards."

The DOH's statement is false. There are three problems with the DOH response:

- A. The DOH states that "their school examination and immunization regulations are consistent with the ACIP recommendations." However, the issue is that the DOH appears to be misrepresenting ACIP guidelines as federal, state, and county standards when they are not. ACIP guidelines are only recommendations issued by a federal advisory committee. They are not mandates or laws from the federal or state governments.
- B. The DOH claims that the ACIP recommendations are comparable to and in some instances less

stringent than other state immunization requirements. However, some states have philosophical exemptions but Hawaii does not. Also, ACIP guidelines support very specific recommendations for medical exemptions which would make Hawaii's medical exemptions more strict compared to other states. Hawaii's religious exemption is also more strict in that the document must be certified and the "person's religious beliefs must prohibit the practice of immunization" compared to other states with looser requirements.

In states that only have medical restrictions such as Mississippi,[\[1\]](#) only 9 vaccinations (DTap, IPV, Hepatitis B, MMR, Varicella)[\[2\]](#) are required for school entry from K to 12th grade and only Tdap is required for 7th grade for a total of 17 injections. West Virginia[\[3\]](#) only requires 9 vaccinations (DTap, IPV, MMR, Varicella, Hepatitis B) [\[4\]](#) for school entry from K to 12th grade for a total of 14 injections. California's K-12 children require 9 vaccinations (DTap, IPV or OPV, Hepatitis B, MMR and Varicella)[\[5\]](#) for a total of 16 injections.[\[6\]](#) The Hepatitis A, HPV, and meningococcal vaccines are not required compared to the DOH's proposed rules which would require these vaccinations.

Further, only 2 states require HPV. Virginia[\[7\]](#) requires HPV for 6th graders, however, the parent or guardian, at the parent or guardian's sole discretion, may elect for the child to not receive the HPV vaccine, unlike DOH's proposed rules which would mandate HPV for all 7th graders. Rhode Island allows a simple religious exemption form[\[8\]](#) which does not require the "certification of a person's religious beliefs prohibit[ing] the practice of immunization" as per DOH's current rules.

The current Hawaii immunization requirements for K-12 are 9 vaccinations (DTP, IPV or OPB, MMR, Hepatitis B and Varicella)[\[9\]](#) for a total of 16 to 17 injections (depending on timing) which is currently similar to other states. However, with DOH's the proposed rules, children from K-12, would also be required to receive an additional 3 vaccinations, including Hepatitis A, HPV, and MCV as 6 injections for a total of 23 to 24 injections for K-12. For post-secondary students the number of vaccines could increase by 5 vaccinations or as 8 injections or more but the number of doses may vary since number of doses are not specifically outlined in the DOH's proposed rules. *(The number of vaccinations were based on my interpretation of DOH's proposed rules. Many doses are open to interpretation since the rules do not stipulate the number of doses, address timing of doses that overlap into other grades, and need for extra doses due to timing or age, and the need for additional series of vaccines for older adults attending post-secondary schools.)*

Thus, the DOH's Ch. 11-157 appears to be **MORE** stringent rather than less stringent than any comparable or related federal, state or county standards. These findings contradict the DOH's written statement of being "not more stringent" than any comparable or related federal, state or county standards.

- A. Most states comply with the Federal Educational Rights to Privacy Act (FERPA) in their state laws and rules which require written parental consent before releasing any educational records, including vaccinations records and exemptions, except for limited emergency situations. Hawaii's Department of Education, HAR Ch. 8-34[\[10\]](#) protects these educational records, and does not authorize the DOE to release educational records to the DOH. Yet, both the current[\[11\]](#) and proposed DOH rules[\[12\]](#) require DOE schools to automatically release educational records on a regular basis from the schools to the DOH thus violating FERPA. The DOH does not have the authority to force schools to violate federal FERPA law.

Since the Hawaii Department of Education receives millions of dollars in federal funding from the US Department of Education and from the Office of Special Education Programs, known violations of FERPA could result in the withholding of these federal funds.

1. In a follow-up to page 3, question 8, if the DOH has misrepresented their response where their proposed rules are actually MORE stringent rather than “not more stringent” than any comparable or related federal, state or county standards, as they have claimed, then this “Pre-Public Hearing Small Business Impact Statement” should again be deemed invalid.

Because if the answer is supposed to be “yes” to question 8 where these rules are more stringent, then the DOH would be required to provide information comparing the costs and benefits of the proposed rules to the costs and benefits of the comparable federal, state or county laws which would require responses to the additional 5 items below requiring a more in depth analysis of the following:

- the public purposes of the proposed rule,
- the text of the related federal, state, or county law, including information about the purposes and applicability of the law,
- a comparison between the proposed rule and the related federal, state, or county law, including a comparison of their purposes, application, and administration,
- a comparison of the monetary costs and benefits of the proposed rule with the costs and benefits of imposing or deferring to the related, federal, state or county law, as well as a description of the manner in which any additional fees from the proposed rules will be used and,
- a comparison of the adverse effects on small business imposed by the proposed rule with the adverse effects of the related federal, state or county law.

QUESTION: Will the DOH conduct a cost analysis presenting the costs and benefits of the proposed rules to the costs and benefits of the comparable federal, state or county law, which includes the above 5 items.

QUESTION: If the DOH will not conduct a cost analysis, can the DOH definitively demonstrate that the DOH’s proposed rules are “not more stringent than any comparable or related federal, state or county standards?”

In conclusion, the DOH’s “Pre-Public Hearing Small Business Impact Statement to the Small Business Regulatory Review Board” dated June 27, 2017 has many questionable items and the public deserves answers before Ch11-157 hearings are adopted including the following:

1. **The differences in the Ch. 11-157 versions submitted to the SBRRB which was voted on in July 19, 2017 and moved to public hearing.**
2. The vague and non-committal responses provided by the DOH when dollar amounts were specifically asked for.
3. The absence of a daycare provider, or child care center representative, or individual small business representatives on the School Examination and Immunization Requirements Working Group and the inappropriate DOH response provided when recommendations from these small businesses were required.

4. The DOH's claim that their proposed rules are not more stringent than any comparable or related federal, state or county standards when there is evidence to the contrary.
5. The need for a cost analysis if the DOH's their proposed rules are indeed MORE stringent than any comparable or related federal, state or county standards.

The issues raised related the impact of the DOH's Chapter 11-157 proposed rules on small businesses must be more thoroughly evaluated and reviewed before any further consideration can be given to move these changes forward through the SBRRB process. Please provide a written response for public review.

Mahalo,

Teresa Chao, RPh, MBA, MJ



Testimony as a member of Hawaii for Informed Consent

[1] http://www.msdh.state.ms.us/msdhsite/_static/resources/2029.pdf

[2] Indicates each antigen, i.e. MMR is 3 antigens, measles, mumps and rubella

[3] <https://dhhr.wv.gov/oeps/immunization/requirements/Documents/8-31-17%20%20NewSchoolEnterers.pdf>

[4] Indicates each antigen, i.e. MMR is 3 antigens, measles, mumps and rubella

[5] Indicates each antigen, i.e. MMR is 3 antigens, measles, mumps and rubella

[6] <https://www.shotsforschool.org/k-12/>

[7] <http://www.vdh.virginia.gov/immunization/requirements/>

[8]

<http://www.health.ri.gov/forms/exemption/ReligiousImmunizationExemptionCertificateForSchools.pdf>

[9] Indicates each antigen, i.e. MMR is 3 antigens, measles, mumps and rubella

[10] <http://boe.hawaii.gov/policies/AdminRules/Pages/AdminRule34.aspx>

[11] <http://health.hawaii.gov/docd/files/2013/07/11-157.pdf>

[12] <https://health.hawaii.gov/opppd/files/2018/09/HAR-11-157-Ramseyer-9.6.18.pdf>

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157, I OPPOSE
Date: Wednesday, December 26, 2018 8:12:43 AM

To Whom It May Concern:

My name is Alison Miller, I am a [REDACTED] resident of over 15 years and a parent and I strongly oppose bill Har 11-157. There is enough research and information circling the medical communities that raises strong health concern as to the safety of vaccinations, the effectiveness of them or adverse reactions caused by them. I have peers in the medical community and have researched and viewed documentaries that demonstrate the ingredients in vaccinations can potentially be damaging and create harm while questionably.

Health News articles report, vaccines Are 'Unavoidably Unsafe'. Both the U.S. Congress and the Supreme Court have concluded that government licensed vaccines are "unavoidably unsafe,"² and this is what precipitated the decision to grant drug companies immunity against vaccine injuries and deaths. See more documentation.

<https://www.nvic.org/NVIC-Vaccine-News/June-2016/defending-religious-exemption-to-vaccination.aspx>

Thank you for your opposition to this bill.

Sincerely,

Alison Miller

From: [REDACTED]
To: [REDACTED]
Subject: Protest Mandatory Immunization
Date: Wednesday, December 26, 2018 8:23:16 AM

We have a right to choose what we inject into our bloodstream.

“Imagine if you will a country where 1% control almost all the wealth and power (big pharma). And the other 99% are so brainwashed they fight vigorously to keep it that way.”

First, our entire mainstream food, supplement and drug supply has become so corrupted, companies we've trusted for decades are committing heinous crimes in the name of profit. Just today, Johnson and Johnson is charged because a three year old was hospitalized due to metal in her intestines from her vitamin gummy bears! This same company also admitted to using asbestos in their baby powders. These companies that rule the market place our ruining lives for the sake of profit.

Daily I read articles on vaccine injury. A new father hospitalized for the flu vaccine with extreme nerve damage, he can not move or open his eyes. He's blinded. Lou Ferigno—aka the Hulk—hospitalized after the pneumonia vaccine. Very sick but recovering. Deaths from the HPV vaccine are climbing now that this is mainstream. And countless other mothers and fathers who claim their once bright lively toddler suddenly turned to stone, days or within weeks of the MMR vaccine. Injuries from DTAP range as the highest—none of this is reported in mainstream news because big pharma controls the media. They also control the government. There are two pharmaceutical lobbyists per one senator in the US government today! Think about that. That means their ears are filled with lies and their pocket books are being filled with money to campaign to make every American take their drugs! They want us sick and dependent for our entire lives.

Now the science behind vaccines might make good sense, but it is the adjuvants and metals they add to preserve [the vaccines](#) that are monumentally damaging to your health. Would you in good conscience inject your children (or yourself) with the following lethal ingredients?

--Mercury -- most toxic substance/metal known to man, they claim to have removed it, however, it continues to show up in the flu vaccine, and others. It's a powerful immunosuppressant amongst myriad other things. When you hear from the vaccine safety promoters that new studies have shown that ethylmercury (in thimerosal) disappears from the blood within several days. Actually, the mercury

leaves the plasma and enters the brain, where it is de-ethylated and remains for a lifetime, wreaking havoc on the brain.

--Aluminum—first added in 1926, another known neurotoxin—DNA damage, cell damage, binds to ATP and affects energy production in all cells. It's linked to dementia, autism, Parkinsons—1 in eight seniors have dementia now (hello flu shot), in less than a decade, it'll be one in four. What's the common thread here?

--Formaldehyde—used to embalm dead bodies. Need we say more? You want that in your kids?

--Peanut oil – why was there a plague of children suddenly with peanut allergies. No one could explain. Well, it was used in vaccines as a preservative for a time. Hmm.

--MSG—a known neurotoxin! You won't eat it, but you'd inject it?

--Also DNA residues, gelatin, antibiotics—like we need more of those!

--And not listed on official ingredient lists are bacterial and viral contaminants, which can include their particulate, fragmented matter.

This is frightening! Connect the dots! They are not saving lives.

In 1983, before the autism epidemic began, children received 10 vaccinations before attending school and the autism incidence was 1 in 10,000. Today, they receive 24+ vaccines before they turn 1, and 36+ by the time they start school and the autism rate is now 1 in 150 births! Do the math!

There are over one million children with autism and the numbers continue to grow. This is a medial disaster of monumental proportions. The link to the vaccine program is scientifically and logically compelling but these same medical elitists refuse to listen. Like smoking and lung cancer, we have enough proof today to call a halt to the present excessive vaccine program and ban any level of mercury in vaccines.

Vaccines are tested for a brief period if at all!!! Three weeks. They have never tested what repeated vaccinations and the current volume/quantity of vaccinations do to animals/humans. We are guinea pigs for big pharma's bottomline—making them BILLIONS of dollars. The vaccine schedule for an infant born in America, before the age of one, is the equivalent of giving an adult one shot a day. Our bodies are so polluted from these toxic injections.

Independent third party studies are vilified and struck from record, almost none are accepted into medical literature. That's what billions of dollars will do.

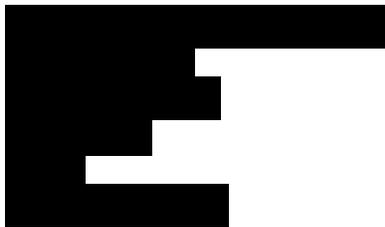
Lastly -- CHINA -- The Chinese are now the largest vaccine manufacturers in the world, with over 400 biopharmaceutical companies making vaccines and poor quality drugs for the world. The FDA admits that it inspects only 1.8 percent of the 714 drug firms in China and that, according to a GAO study, FDA inspections may be done 13 years apart (In the US it's spaced 2 years apart).

--More frightening is that the inspectors must depend on Chinese translators and US companies who purchase [the vaccines](#) must have a Chinese communist official serve as its legal representative. One CEO was quoted as saying "every piece of information you get (from the Chinese) is suspect."

--With thousands of people dying and getting sick, not only in China, but in hundreds of nations receiving China's tainted pharmaceutical products, future vaccines are an even greater danger.

No thank you. Count my children out of this twisted program that claims to protect our health while destroying bodies and minds. But hey, it does make the 'elite few' billions of dollars!

Jack Ringler



From: [REDACTED]
To: [REDACTED]
Subject: testimony regarding mandatory immunizations HR 11-157
Date: Wednesday, December 26, 2018 8:54:29 AM

I am writing in opposition for mandatory immunizations. This is unconstitutional! There is absolutely no evidence that immunizations are safe, and to force our children to be immunized is a communist act! Our country is based on freedom! Freedom to choose what is right for our own bodies and minds. There are far to many complications with immunizations to force them on our human race.

My grandmother was opposed to vaccinations, because my uncle was affected by them. She educated our family about the threat of complications from immunizations my cousin was not vaccinated. My cousin was valedictorian of her class with a full scholarship to Berkley! She has never been affected by her lack of immunization. My son was vaccinated as a child, and he was clearly affected by the immunizations that he received. As he has grown I have not given him any more vaccinations because it is DANGEROUS!

There is no proof that having a child vaccinated will protect them! There is considerable information that vaccinations are dangerous, please educate yourselves on this matter, before you choose to put our children at risk!

We have the right to informed consent, we have the right to freedom of of religion, and should be able to opt out if we choose to do so!

Sincerely,
Marisa provost

From:

To:

Cc:

Subject:

Date:

RE: HAR 11-157

Wednesday, December 26, 2018 8:59:13 AM

Aloha Bruce,

Thank you for the returned call...

Here are my concerns – first and foremost the right to choose the best healthcare regime for ourselves.

The practice of one size fits all vaccines/immunizations clearly is not working. By making this a requirement to attend school, we are limiting our kid's future.

The choice between risks of becoming vaccine injured or not going to school, is not fair!

Vaccines need better outcomes for all, before being required.

The U.S. Supreme Court ruled vaccines are “unavoidably unsafe” and the U.S. government has paid out approximately \$3.9 billion for vaccine injury claims..

Thank you for your consideration, Luan Vick

From: [REDACTED]
To: [REDACTED]
Subject: : I OPPOSE HAR 11-157 proposed rules
Date: Wednesday, December 26, 2018 10:35:05 AM

Aloha & thank you for this opportunity to provide testimony. As a community member and mother of 3,

I oppose HAR 11-157 Exhibit A

It is made without taking the diverse demographic in Hawaii in mind and will over regulate our school requirements from 5 to 9 (k-12). Further, it adds HPV as a requirement, making us one of the most regulated states in all of the USA. Safety & Risk assessment MUST be done first. For example, HPV been taken out of Japan's requirements for 5 years due to many adverse reactions.
<https://www.hpv-yakugai.net/2018/06/29/5years-english/>

Please keep in mind ACIP guidelines where never designed or tested for our unique demographic. There is no one fits all solution.

I oppose Exhibit B

Blanket adoption of the “best practice guidelines for Immunization” as part to our rules and letting go of the freedom and independence as a State to compile our own Guidelines is unacceptable.

Further, I oppose including early-child-hood centers in this rule. There must be consent from the early-child-hood centers themselves and parents. To my knowledge center and parents remain uninformed or have yet to be invited into the process of this proposal. This lack of information creates extra expenses, training, equipment when enrolling new children.

I request the attorney of the DOH to legally verify if this reporting system is in direct conflict with HIPAA & Family Education Protection Act 20 U.S.C. § 1232g. If so, the law will make schools involuntarily break the law by following your

current rule.

I oppose HAR 11-157 for being an incomplete proposal. It fails to offer a draft of the standard medical and religious exemption forms. I am unwilling to accept that DOH has the right to decide without public input what the final form will be. They can make needed medical exemptions unnecessary more complicated or easy. We, the public, are in the dark because these forms are missing.

Informed Choice is already mandated by the State of Hawaii and is failing to be abided by many healthcare practitioners. Healthcare Practitioners must give an informed choice, that includes speaking about the alternatives to the procedure that they are using. Vaccines must by law show both sides.

We all must revisit the safety, health benefit and risk balance here. No vaccine is 100% effective for everyone and not everyone can handle the same amount of vaccination. Additional vaccination needs to stay a choice, a parent guided one. The medical community is urged to offer informed consent.

Parents & Patient MUST be given opportunity to ask questions and clarify all doubts.

The process MUST be free of any kind of coercion.

Consent MUST be voluntary, and patient should have the freedom to revoke the consent.

Consent given under fear of injury/intimidation, misconception or misrepresentation of facts MUST be held invalid.

I respectfully request that the proposed changes to HAR 11-157 be opposed and request that for further changes on immunization a communication link be established between the DOH & DOE to inform all schools, teachers, parents and who ever else will be affected by the change. We MUST be informed as to DOH's intentions. This MUST include a summary of the full implication of the rule change.

From: [REDACTED]
To: [REDACTED]
Subject: Written Testimony for HA 11-157
Date: Wednesday, December 26, 2018 10:51:23 AM
Attachments: [2PageVAXSchoolPrintout FINAL-12232015.pdf](#)
[74769917-Do-Aluminum-Vaccine-Adjuvants-Contribute-to-Rising-Prevalence-of-Autism.pdf](#)
[76789590-Human-virus-HPV-Vaccine-Policy-and-Evidence-based-Medicine-at-Odds.pdf](#)
[Autism-brochure-Color-8.5x11.pdf](#)
[Can HPV Vaccine Cause Injury and Death.docx](#)
[CDC is a Vaccine Company.png](#)
[DNA Contamination in HPV vaccines.docx](#)
[Evidence-statement.pdf](#)
[First Peer Review Study Vaccinated vs. Non Vaccinate.docx](#)
[First Study of Vaccinated versus Unvaccinated Children.docx](#)
[First Study of Vaccinated vs Unvaccinated.docx](#)
[German Vaccination vs. Unvaccinated.docx](#)
[gpub 58635 anti therapeutic action vaccination all.pdf](#)
[HAR-11-157-Exhibits-A-and-B.pdf](#)
[HAR-11-157-Ramseyer-9.6.18.pdf](#)
[ICAN-AluminumAdjuvant-Autism.pdf](#)
[ICAN-HHS-Notice.pdf](#)
[InfectiousDiseaseVaccines copy.pdf](#)
[Lead Developer Of HPV Vaccines Comes Clean.docx](#)
[List of Added Vaccines.docx](#)
[Non-linear-dose-response-of-aluminium-hydroxide-adjuvant-particles-Selective-low-dose-neurotoxicity.pdf](#)
[Research Citations Linking Vaccines To Disease copy.pdf](#)
[State of health of unvaccinated children.docx](#)
[Studies Prove Without Doubt That Unvaccinated Children Are Healthier Than Their Vaccinated Peers.docx](#)
[ten-little-known-facts1.pdf](#)
[Vaccinate vs. Unvaccinated JTS-3-186.pdf](#)
[Vaccine List - Aborted Fetal Cell Lines copy.pdf](#)
[VaccineSafety-Version-1.0-October-2-2017.pdf](#)
[vaccine papers brochure 8.5x11 copy 2.pdf](#)
[VAERS Database Results for 11.14.2018 CHART.docx](#)

To those concerned,

I am writing to include my testimony in opposition to HA 11-157 and the suggested changes to Hawaii's current vaccine requirements. I support anyone who chooses to vaccinate, but I also support those who wish not to vaccinate. Any law that makes vaccines mandatory, even though certain exemptions are allowed, confuses those who are not informed of their rights and the law. If HA 11-157 is enacted Hawaii will be the most vaccinated state in the United States. I am attaching information that I would suggest you consider before adding any of these new vaccines to our children's schedule. Research and scientific studies have shown that vaccines are not 100% safe or effective. I admonish your panel to read and consider the validity of this information for the benefit of our children.

Sincerely,

Robert Abell, N.D.

The contents of this message, together with any attachments, are intended only for the use of the person(s) to which they are addressed and may contain confidential and/or privileged information. Further, any medical information herein is confidential and protected by law. It is unlawful for unauthorized persons to use, review, copy, disclose, or disseminate confidential medical information. If you are not the intended recipient, immediately advise the sender and delete this message and any attachments. Any distribution, or copying of this message, or any attachment, is prohibited.

From: [REDACTED]
To: [REDACTED]
Subject: Opposed to New Immunization Bill
Date: Wednesday, December 26, 2018 11:26:15 AM

To whom it concerns,

My name is Jodee Inouye-Agsalog and I am a mother of 3 beautiful children. I just wanted to Express my opposition to the new Immunization Bill on the table. I believe that it's a very sensitive subject for many families and that ultimately it should be the choice of that family to decide what is best for their children.

Mahalo,
Jodee Inouye-Agsalog

From: [REDACTED]
To: [REDACTED]
Subject: Testimony regarding new vaccine requirements
Date: Wednesday, December 26, 2018 12:26:46 PM

To Whom It May Concern,

I am writing to ask that you not increase the amount/type of vaccines required to attend school. No vaccines should be mandated to receive education. Education is a right that should not be leveraged by mandatory injections, especially when such injections have never been through proper safety studies and the manufacturers are exempt from litigations regarding injuries/death caused by their products. Please allow me to explain.

In 1986, the vaccine manufacturers were bombarded with lawsuits regarding injury/death caused by their product. They threatened to discontinue making vaccines unless they were protected against litigation. President Reagan granted this request even though he recognized that this action would also remove any motivation for the manufacturers to improve and ensure vaccine safety. He instructed the Department of Health and Human Services to work on improving vaccine safety. They were supposed to report on their progress every two years. Robert Kennedy Jr. recently won a lawsuit against the DHS regarding these reports. The DHS settled by signing a declaration that they have no record of studies to improve vaccine safety. So, vaccine manufacturers have been free of legal liability for the past 32 years, and the government department that was supposed to oversee vaccine safety has been doing absolutely nothing.

I have been reading the inserts for the vaccines. Each insert describes the safety studies that were conducted in order to be approved for use. Not one single vaccine currently in use has been tested against an inert placebo. They are all tested against another vaccine, combination of vaccines, or the adjuvant ingredients without the virus. In other words, they are testing toxins against toxins. When there is no significant difference in adverse reactions between the two groups, the new vaccine is deemed safe. If they conducted a true double blind inert placebo study we would have much more accurate data to judge safety. Unfortunately, there has never been a study like this done on any vaccines in use.

The HPV vaccine currently in use, GARDASIL 9, is a very dangerous vaccine that harms more than it protects. It was approved for use without completing thorough studies, and the manufacturer openly admits this in the insert. There are at least four statements in the GARDASIL 9 insert where they say the results were “**Inferred**” based on something other than a test using the GARDASIL 9. Don’t our children deserve better, more rigorous safety testing before a product like this is forced upon them? There are many testimonies from teens that are now living with debilitating conditions as a result of this vaccine. This vaccine should be illegal.

The Whooping Cough vaccines that now use acellular pertussis fail to protect against the disease. Studies have proven that the vaccine only prevents symptoms, it does not prevent infection or spread of infection. In other words, those that are vaccinated with Acellular Pertusis can become silent carriers and put others at greater risk. Please do not mandate a vaccine that does not work.

Our children are experiencing chronic conditions never witnessed in children of previous generations. Autism rates are now 1 in 59 when they were previously 1 in 10,000 in the 1970's. The argument is that they are just diagnosing it better, but we all know this is not the only reason for the stark increase. While it is likely that there are other environmental factors involved, we cannot disregard the correlation between the increase in vaccines and the increase in autism. Studies have come out as recently as this year that are proving a connection between injected aluminum and autistic behavior in animals. I plead with you to wait until further studies are conducted before mandating more vaccines for our children. Please do not subject the children of Hawaii to be used as guinea pigs for these new vaccines. The science is not settled, the truths are still being revealed, and we must protect our children. I urge you to say no to increasing vaccine mandates.

Aloha,

Emi Ayau

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: PLEASE DO NOT Approve mandatory vaccinations for our school children
Date: Wednesday, December 26, 2018 12:56:12 PM

There are places for our government to intercede and help in our lives. This IS NOT one of them. Please reject any attempt to have mandatory vaccinations for our school children or anyone for that matter.

Jason D. Groode

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157
Date: Wednesday, December 26, 2018 1:01:19 PM

Re: HAR 11-157, I STRONGLY OPPOSE these rules. Big Pharmaceutical wins and the people, especially the children, lose.

At the very least, remove the rule that gives s free pass to new vaccines in the pipeline. Do lawmakers realize within a few years approximately 300 new shots will enter the marketplace?

It is malfeasant and without forethought to demand that parents submit their keiki to this kind of chicanery.

I wouldn't want my children subjected to this heresy. Would you?

Chas Mort

Instead of living inside the pitiless confines of a smart phone, engage a child, stranger or friend in face-to-face conversation.

~ Frosty Wooldridge

From: [REDACTED]
To: [REDACTED]
Subject: Re: HAR 11-157 DOH-Proposed Rule Changes Pertaining to Hawai'i Vaccination Policy
Date: Wednesday, December 26, 2018 1:28:35 PM

Aloha, my name is Taur Kiggins and I am in strong opposition to HAR 11-157.

I want to ask that everyone here as a medical professional consider a few questions. Has history ever shown the medical establishment to be wrong about a medical procedure, drug or therapy? True science is willing to question methodical dogma, even when the majority scoff at the idea. I have no doubt most of you are deeply caring individuals who have a desire to heal and protect. That's why you do what you do. That's also why I urge you to reflect on the education you received regarding vaccines. It being the one of the most routine treatments in any pediatrician's office, did you spend countless hours learning all of the ingredients, the adverse reactions, and how to identify them? Or was it mostly about the benefits? Did you learn how to give true fully informed consent? Where are you required by federal law to report reactions (that hopefully you know how to identify)? What is the history of each disease and the huge mortality and incidence decrease in the 20th century prior to the introductions of the vaccines? Brave and learned medical professionals have stepped forward, admitting they didn't learn much about vaccines in school, and now, after reading the literature from both sides for themselves are standing up, concerned about the safety of vaccines. Have you heard what your contemporaries have to say?

A fact I trust you will not lose sight of is that safety testing for vaccines fails the golden standard of every other pharmaceutical drug. Among the failings in vaccine safety studies are adjuvant safety testing individually and when combined as administered on the schedule.

Listed in the Vaccine Excipient & Media Summary (1) some *known* adjuvants include: formaldehyde, blood-brain opening polysorbate 80, phenoxyethanol, ammonium sulfate, human serum albumen, human-diploid fibroblast cell cultures WI-38, human diploid cells MRC-5. Fun fact: vaccine-creator Stanley Plotkin admitted in a deposition earlier 2018 that during said vaccine development, it took 76 aborted fetuses to get the right tissues needed for the culture (2). Also included is fetal bovine serum, monkey kidney cells, african green monkey (VERO) cells, porcine derived gelatin (and porcine circoviruses in Rotarix) as well as egg and yeast proteins. There are 60 or so more metal, chemical, human and animal organisms as adjuvants, including the controversial thimerosal still in multi-dose flu vials. (3) This is what's being mandated into our keiki's muscle tissue.

If that isn't alarming, I trust the *unlisted* contaminants discovered in vaccines in these studies (4, 5) from Italy in 2017 & 2018 will be a surprise. Contaminants found include: Barium, lead, stainless steel, tungsten, gold-zinc, platinum, silver, bismuth, iron, chromium, lead particles, morphologies of red cells (human or animal origin is unknown), and "debris" composed of aluminum, bromine, silicon, potassium and titanium. In some they also could not find the protein antigens that the vaccines were supposed to have. Other independent tests have found glyphosate. (6)

Now for Aluminum. Many childhood vaccines contain it. Aluminum is a known neurotoxin. After learning that many "placebos" used in "safety studies" [including HPV(7)] are either other vaccines or aluminum adjuvant, I was surprised, and I would hope it surprises you too. Placebos are supposed to be inert. Saline is a great placebo. If IA (injected aluminum) placebos were themselves shown to cause damage, would that nullify the study since the control contained this harmful substance?

You may be surprised to hear that they do cause harm. There is one study, known as the Mitkus study that vaccine advocates reference when questioned about the safety of IA. (8) It came under severe scrutiny this year from leading experts in the world on the neurotoxicity of Al. In the paper criticizing the methods of the Mitkus study, the authors also mention other countries who have studies implicating aluminum-containing vaccines in chronic illness:

"The occurrence of *myalgia* and *arthralgia*, *chronic fatigue* and *neurological disorders* following multiple injections of aluminum-containing vaccines against hepatitis B, tetanus and human papilloma virus (HPV) has been reported in many countries: Australia, Canada, Denmark, France, United Kingdom, Italy, Israel, Japan, Mexico, Portugal, and USA." (9)

Recent studies have regarded IA as "poorly biodegradable", with the potential to become "*insidiously unsafe*, especially in the case of *over-immunization* and immature/alterd blood brain barrier..." as well as having potential for neurotoxic effects after long-term accumulation. (10, 11, 12, 13, 14)

To summarize the cited works, here is a summary of what a decade of emerging science on IA toxicity is saying. It can:

- 1) impair brain development,
- 2) remain in the brain much longer than thought,
- 3) is brought into the brain by macrophages that grab the IA from the vaccine injection site and recirculate it,
- 4) may actually be worse when injected in small doses repeatedly (like in vaccination) and,
- 5) remarkably high levels of aluminum have been found in brains of people diagnosed with autism. (15, 16, 17, 19, 20, 21)

IA is also showing to be implicit in damaging motor neurons creating conditions for Parkinson's, Lou Gehrig's and Alzheimers (81)

I realize this hearing is about changes in the already mandatory schedule (unless exempt). But after reviewing the science, please explain how mandating the injections of even more aluminum and other toxic adjuvants into our children will be of benefit to them in the long term? WE HEAR YOU that they can achieve less cases of acute childhood illnesses, I am not saying they are useless. But are they faultless? Emerging science says NO, and it is looking bleak in regard to long-term damage, far worse than the vaccine narrative suggests. Not all children are made the same and forward with more mandates is a mistake. Before making Hawai'i the state with the most mandatory vaccinations for public education... lets wait and see what comes of these aluminum studies. Do the pediatricians and nurses here know this and other information shared? If you do, how could you not inform us of this? And if you don't, then why the hell don't you? DOH you've got about 8-10 hours of hearing videos, a book we all sent you about HPV, and at least a few hundred written testimonies with study links and references to look at. We expect answers to our questions, and knowledgable references to our citations. You have some work to do. Do it, and then honestly weigh the potential consequences of your decisions. How much long term risk will our youth be subjected to because of careless mandates relying on *flawed and outdated science*? You have been given notice.

Where there is scientifically proven risk, there must be choice. Choice that does not take away our children's right to public education. I have faith that the decision makers of the DOH, and also pediatricians and healthcare professionals...you are people of reason, willing to listen, and are big enough to change course when the facts warrant a change. You are leaders and we are depending on you to do more bench research and read more than what is handed to you. Listen. Learn. I have no doubts that there are outside, corporate and other pressures rushing to get these changes stamped and sealed. We compel you to wait until you have updated your knowledge on this subject, as it will affect every child in this state. Mahalo

Citations

- (1) **Vaccine Excipient & Media Summary:** <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf>
- (2) **Partial deposition of Stanley Plotkin (entire deposition available online for reference):** https://www.youtube.com/watch?v=JY_QFlww0dc&list=PL0s8SIHSGQpFPeyXtHQvJJ4KkZ-X9HMNj
- (3) **Package Inserts Listed by Vaccine:** http://www.vaccinesafety.edu/package_inserts.htm
- (4) **New Quality-Control Investigations on Vaccines: Micro and Nanocontamination:** <https://medcraveonline.com/IJVV/IJVV-04-00072.pdf>
- (5) **Initial results on Infanrix Hexa Chemical Composition:** <https://drive.google.com/file/d/128CfYaaJdMwhx5yvCGDRgg15GIKyfWvRc/view>
- (6) **Glyphosate in MMR:** <https://d3n8a8pr07vhm.cloudfront.net/yesmaam/pages/1716/attachments/original/1473534266/FinalGlyphosateinVaccinesPressRelease.pdf?1473534266>
- (7) **HPV Aluminum Control; see pg 17-20 "AAHS – Amorphous Aluminum Hydroxyphosphate Sulfate" :** <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm111263.pdf>
- (8) **Updated aluminum pharmacokinetics following intact exposures through diet and vaccination:** <https://vaccinepapers.org/wp-content/uploads/FDA-aluminum-paper.pdf>
- (9) **Critical analysis of reference studies on the toxicokinetics of aluminum-based adjuvants:** <https://www.ncbi.nlm.nih.gov/pubmed/29307441>
- (10) **Slow CCL2-dependent translocation of biopersistent particles from muscle to brain:** <http://vaccinepapers.org/wp-content/uploads/slow-ccl2-dependent-translocation-of-biopersistent-particles-from-muscle-to-brain.pdf>
- (11) **Non-linear dose-response of aluminium hydroxide adjuvant particles:** Selective low dose neurotoxicity: <http://vaccinepapers.org/wp-content/uploads/Non-linear-dose-response-of-aluminium-hydroxide-adjuvant-particles-Selective-low-dose-neurotoxicity.pdf>
- (12) **Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations:** <http://vaccinesafetycommission.org/pdfs/22-2012-Lupus-Aluminum-Shaw.pdf>
- (13) **Biopersistence and brain translocation of aluminum adjuvants of vaccines:** <http://vaccinepapers.org/wp-content/uploads/Biopersistence-and-brain-translocation-of-aluminum-adjuvants-of-vaccines.pdf>
- (14) **Aluminium in brain tissue in autism:** <https://worldmercuryproject.org/wp-content/uploads/Mold-2017-Aluminum-in-Brain-Tissue-and-Autism.pdf>
- (15) **citations within the article:** <https://jbhandleyblog.com/home/a-lone-fda-scientist-could-end-the-autism-epidemic>
- (16) <https://youtu.be/SmkVv8pcVhc>
- (17) <https://youtu.be/Syabv4Vsrbg>
- (18) <https://youtu.be/HK-93SHnTFk>
- (19) **Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice:** <https://www.ncbi.nlm.nih.gov/pubmed/17114826>
- (20) **Zimmerman Deposition (special attention to pgs. 9-14, 16-24, 25-26.) :** <http://bolenreport.com/wp-content/uploads/2018/09/Andrew-Zimmerman-Deposition.pdf>
- (21) Deposition of Richard Kelley, MD, in the matter of Rolf H. Hazlehurst vs. E. Carlton Hays, November 7, 2016.

Recommended Websites and Books

-Vaccinepapers.org

-*Dissolving Illusions* by Suzanne Humphries

-*How to End the Autism Epidemic* by JB Handley



Virus-free. www.avast.com

From: [REDACTED]
To: [REDACTED]
Subject: RE: Mandatory HPV vaccine
Date: Wednesday, December 26, 2018 2:24:08 PM

Aloha,

It seems like enough HPV vaccinated people have bad reactions that we should proceed with utmost caution. Certainly, mandatory vaccination must be reconsidered. Big Pharma and it's sometimes flawed research in the name of profit, must be put in check. Seems like a lawsuit(s) is likely.

Sincerely,

John Naylor

[REDACTED]

From:

To:

Subject:

Date:

[REDACTED]
[REDACTED]; [REDACTED]; [REDACTED]
Testimony

Wednesday, December 26, 2018 2:43:55 PM

In opposition

Aloha, I am submitting my testimony regarding the increase in required vaccines for Hawaii's children. I strongly oppose this requirement as I see it as a violation of my religious freedom. There are cells from aborted babies in several of the vaccines that are currently used. I believe that abortion is murder and these cells are used without the consent of the person who they belonged to. To force me to inject my child with these cells violates my children's rights religious rights as well.

Mahalo for your consideration.

Rachel Struempf

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Vaccination testimony
Date: Wednesday, December 26, 2018 2:42:54 PM

Dear DOH Hawaii,

I herby email you on the subject of mandatory vaccinations in Hawaii.

I am a mom of a healthy 7 month old boy, to this day he hasn't been sick once. He was born at home at has never seen a pediatrician.

He is growing and developing in the expected way. I refuse to vaccinate him since I believe a little body like his isn't build to deal with the poisonous cocktail that is a vaccination. I believe that IF I wanna give him any vaccinations, I want it to be on our terms.

I am an immigrant to the United States, I am from Germany and when I went through my application process for my green card, I had to get 4 vaccines in one day. I was sick for 5 days after. I was ok with it, but I am a grown woman with a strong immune system.

I am not afraid of autism, I am not afraid the vaccination could change my healthy baby - I simply don't want to put those chemicals into my sons body.

He is raised vegan, local foods, organic and non gmo.

I wanna have my choice. America is all about freedom, the land of the free - tell me sir - where is the freedom of our choices anymore?

I also request another hearing on the subject, I was able to attend the first one, but many families weren't able to make it - on a Friday afternoon (because guess what? Keiki are at school and parents at work).

Mahalo for your time,

Please confirm the receiving of my email,

Kind regards,
Petra Gilmore

From: [REDACTED]
To: [REDACTED]
Subject: Opposition Testimony
Date: Wednesday, December 26, 2018 3:06:53 PM

Aloha,

I am writing to oppose your proposal to change the current vaccination requirements by adding more mandatory vaccines to the list.

I am not attaching any of the many scientific and research based reasons not to vaccinate according to your proposed requirements because I know that many others already have.

However, I will say that it is my right to maintain my own and my children's health as I see fit and it is also our legal right to public education. I also happen to be involved in Hawaii state education as a director of a public charter school board, which gives me first hand experience of families choosing not to vaccinate and using the religious exemption to excuse them. If more vaccines are added, you will see more religious exemptions than before which may jeopardize the validity and allowance of the exemptions. Families will then exit the school system which would burden the schools with reduced per pupil funding.

For families choosing to vaccinate they are doing so under the guidance of their healthcare practitioner who should be the one to make the recommendations if they agree that you think are appropriate. Schools and other places of employment under the thumb of the health department should not be the ones dictating whether those who enter are vaccinated.

Health freedom is an inalienable right.

Mahalo,

A concerned Hawaii resident
Kapaa, HI

Hare Krishna!

From: [REDACTED]
To: [REDACTED]
Subject: Please do not require mandatory vaccinations for school children
Date: Wednesday, December 26, 2018 3:01:54 PM

Please do not require mandatory vaccinations for school children

From: [REDACTED]
To: [REDACTED]
Subject: Oppose mandatory vaccines
Date: Wednesday, December 26, 2018 3:05:44 PM

As a local teacher I strongly oppose HAR 11-157 mandatory vaccines.

Hawaii Revised Statutes 671-3 – Informed consent Current as of: 2016 | Check for updates | Other versions

671-3 Informed consent. (a) The Hawaii medical board may establish standards for health care providers to follow in giving information to a patient, or to a patient's guardian or legal surrogate if the patient lacks the capacity to give an informed consent, to ensure that the patient's consent to treatment is an informed consent. The standards shall be consistent with subsection (b) and may include:

Terms Used In Hawaii Revised Statutes 671-3

Health care provider: means a physician, osteopathic physician, surgeon, or physician assistant licensed under chapter 453, a podiatrist licensed under chapter 463E, a health care facility as defined in section 323D-2, and the employees of any of them. See Hawaii Revised Statutes 671-1

(1) The substantive content of the information to be given;
(2) The manner in which the information is to be given by the health care provider;
and (3) The manner in which consent is to be given by the patient or the patient's guardian or legal surrogate.

(b) The following information shall be supplied to the patient or the patient's guardian or legal surrogate prior to obtaining consent to a proposed medical or surgical treatment or a diagnostic or therapeutic procedure:

(1) The condition to be treated;
(2) A description of the proposed treatment or procedure;
(3) The intended and anticipated results of the proposed treatment or procedure; (4) The recognized alternative treatments or procedures, including the option of not providing these treatments or procedures;
(5) The recognized material risks of serious complications or mortality associated with:
(A) The proposed treatment or procedure;
(B) The recognized alternative treatments or procedures; and (C) Not undergoing any treatment or procedure; and
(6) The recognized benefits of the recognized alternative treatments or procedures.

House Report 106–977
U.S. GOVERNMENT PRINTING OFFICE
WASHINGTON :
67–173 CC
2000
Union Calendar No. 575
106th Congress, 2d Session

House Report 106–977
THE VACCINE INJURY COMPENSATION PROGRAM:
COMMITTEE ON GOVERNMENT REFORM

While the Vaccine Adverse Events Reporting System [VAERS] may be lauded as the “front line” of vaccine safety, the lack of enforcement provisions and effective monitoring of reporting practices preclude accurate assessments of the extent to which adverse events are actually reported. Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events.

The quality of VAERS data has been questioned. Because reports are submitted from a variety of sources, some inexperienced in completing data forms for medical studies, many reports omit important data and contain obvious errors. Assessment is further complicated by the administration of multiple vaccines at the same time, following currently recommended vaccine schedules, because there may be no conclusive way to determine which vaccine or combination of vaccines caused the specific adverse event

Grant Final Report

Grant ID: R18 HS 017045 Submitted to:

The Agency for Healthcare Research and Quality (AHRQ) U.S. Department of Health and Human Services

540 Gaither Road

Rockville, MD 20850

<http://www.ahrq.gov> oppose

Electronic Support for Public Health–
Vaccine Adverse

Event Reporting System (ESP:VAERS)

Inclusive dates: 12/01/07 -09/30/10

Principal Investigator: Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Team members: Michael Klompas, MD, MPH

Performing Organization: Harvard Pilgrim Health Care, Inc. Project Officer: Steve Bernstein

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients,

and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these

doses, 35,570 possible reactions (2.6 percent of vaccinations) were identified. This is an average

of 890 possible events, an average of 1.3 events per clinician, per month. These data were

presented at the 2009 AMIA conference.

Adverse events from drugs and vaccines are common, but underreported.

Although 25% of

ambulatory patients experience an adverse drug event, less than 0.3% of all adverse

drug events

and 1-13% of serious events are reported to the Food and Drug Administration (FDA).

Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of “problem” drugs and vaccines that endanger public health.

New surveillance methods for drug and vaccine adverse effects are needed.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC

contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Child influenza vaccination

Ramifications of adverse events in children in Australia

BMJ 2010; 340 doi: [Ramifications of adverse events in children in Australia](#)



(Published 09 June 2010) Cite this as: BMJ 2010;340:c2994

During the 18-year period from 1990 through 2007 just 88 cases of Kawasaki Disease in children under 5 were reported to VAERS. During the same period about 88 million U.S. children passed through the 0-5 age group; consequently the incidence rate reported to VAERS was 0.10 KD cases per 100,000 person-years. (Pediatr Infect Dis J 28:943, 2009) From 1988 to

2006 the published KD incidence for U.S. children under 5 rose from 11.0 to 20.8 per 100,000 person-years. (Pediatrics 111:448, 2003. Pediatrics 112:495, 2003. Pediatr Infect Dis J 29:483, 2010) Even for infants 3-6 months old, when suspicion for vaccine adverse effects should be especially high, KD incidence as reported to VAERS was 0.11 while published background rates were 23.1 (2000) and 24.6 (2006); fewer than 1 in 200 KD

cases were reported to VAERS.

It is bewildering, therefore, to learn that FDA and CDC officials used VAERS data to dismiss a placebo-controlled trial that found a 5-fold KD risk associated with RotaTeq-RR=4.9; 95% CI

0.6, 239. (Pediatr Infect Dis J 28:943, 2009. 6/15/07.) If confirmed by a larger trial, the KD risk associated with RotaTeq would translate to an extra 4000 U.S. cases annually

(it is worth noting that rotates is Paul Offit's vaccine Offit is an ACIP member and it is my understanding that he did not recuse himself from decision making for this vaccine, but that is heresay)- Joe

HSTA has a committee who also works with the civil rights of students...mandated vaccines are a violation of civil rights...so stating the mandatory informed choice and FERBA is essential in your statement. does not need to be pages...just bring up main concerns and also send it to me when you are done and send to immunization@doh.hawaii.gov gotta be in by 25th....make it simple.

Here are some thoughts cite a reference

House Report 106-977

U.S. GOVERNMENT PRINTING OFFICE

WASHINGTON :

67-173 CC

2000

Union Calendar No. 575

106th Congress, 2d Session

House Report 106-977

THE VACCINE INJURY COMPENSATION PROGRAM: ADDRESSING NEEDS AND IMPROVING PRACTICES

SIXTH REPORT

BY THE

COMMITTEE ON GOVERNMENT REFORM

While the Vaccine Adverse Events Reporting System [VAERS]

may be lauded as the "front line" of vaccine safety, the lack of enforcement provisions and effective monitoring of reporting practices preclude accurate assessments of the extent to which adverse

events are actually reported. Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events.

The quality of VAERS data has been questioned. Because reports are submitted from a variety of sources, some inexperienced in completing data forms for medical studies, many reports omit important data and contain obvious errors. Assessment is further complicated by the administration of multiple vaccines at the same time, following currently recommended vaccine schedules, because there may be no conclusive way to determine which vaccine or combination of vaccines caused the specific adverse event

Grant Final Report

Grant ID: R18 HS 017045 Submitted to:

The Agency for Healthcare Research and Quality (AHRQ) U.S. Department of Health and Human Services

540 Gaither Road

Rockville, MD 20850

<http://www.ahrq.gov>

Electronic Support for Public Health–
Vaccine Adverse

Event Reporting System (ESP:VAERS)

Inclusive dates: 12/01/07 -09/30/10

Principal Investigator: Lazarus, Ross, MBBS, MPH, MMed, GDCompSci

Team members: Michael Klompas, MD, MPH

Performing Organization: Harvard Pilgrim Health Care, Inc. Project Officer: Steve Bernstein

Results

Preliminary data were collected from June 2006 through October 2009 on 715,000 patients,

and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these

doses, 35,570 possible reactions (2.6 percent of vaccinations)

were identified. This is an average

of 890 possible events, an average of 1.3 events per clinician, per month. These data were

presented at the 2009 AMIA conference.

Adverse events from drugs and vaccines are common, but underreported.

Although 25% of

ambulatory patients experience an adverse drug event, less than 0.3% of all adverse drug events

and 1-13% of serious events are reported to the Food and Drug Administration (FDA).

Likewise, fewer than 1% of vaccine adverse events are reported. Low reporting rates preclude or slow the identification of “problem” drugs and vaccines that endanger public health.

New surveillance methods for drug and vaccine adverse effects are needed.

Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC

contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.

Child influenza vaccination

Ramifications of adverse events in children in Australia

BMJ 2010; 340 doi: <https://doi.org/10.1136/bmj.c2994>

(Published 09 June 2010) Cite this as: BMJ 2010;340:c2994

During the 18-year period from 1990 through 2007 just 88 cases of Kawasaki Disease in children under 5 were reported to VAERS. During the same period about 88 million U.S. children passed through the 0-5 age group; consequently the incidence rate reported to VAERS was 0.10 KD cases per 100,000 person-years. (Pediatr Infect Dis J 28:943, 2009) From 1988 to

2006 the published KD incidence for U.S. children under 5 rose from 11.0 to 20.8 per 100,000 person-years. (Pediatrics 111:448, 2003. Pediatrics 112:495, 2003. Pediatr Infect Dis J 29:483, 2010) Even for infants 3-6 months old, when suspicion for vaccine adverse effects should be especially high, KD incidence as reported to VAERS was 0.11 while published background rates were 23.1 (2000) and 24.6 (2006); fewer than 1 in 200 KD

cases were reported to VAERS.

It is bewildering, therefore, to learn that FDA and CDC officials used VAERS data to dismiss a placebo-controlled trial that found a 5-fold KD risk associated with RotaTeq -RR=4.9; 95% CI

0.6, 239. (Pediatr Infect Dis J 28:943, 2009. 6/15/07.) If confirmed by a larger trial, the KD risk associated with RotaTeq would translate to an extra 4000

[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [REDACTED]
Subject: Please do not approve mandatory vaccinations
Date: Wednesday, December 26, 2018 3:07:11 PM

There are places for our government to intercede and help in our lives. This IS NOT one of them. Please reject any attempt to have mandatory vaccinations for our school children or anyone for that matter.

Sincerely,
Lyn Wandell

[REDACTED]

96703

From: [REDACTED]
To: [REDACTED]
Subject: Opposing immunization
Date: Wednesday, December 26, 2018 3:07:14 PM

To whom it may concern,

Re: HAR 11-157, I OPPOSE MANDATORY VACCINATIONS

For many people this would be taking away their freedom to make their own wise Health choices. There are many people who have religious beliefs and or strong convictions that would opposed receiving vaccinations.

It would be seen as a violation of their body, health and morals

There is plenty of anecdotal evidence and research that point to an increase in Autism with vaccinations, as well as triggering autoimmune disorders.

Please do not allow this bill to be passed. We believe this would be a violation of our constitutional right to protect our bodies and our children's bodies from unproven and unsafe Health experimentation.

Vaccination companies are protected from any lawsuit and any type of legal and medical reimbursement for side effects caused by vaccinations.

Please support informed medical consent and freedom of Health choices. Thank you and mahalo,

Nattalia Whalen, R.N.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Re: HAR-11-157
Date: Wednesday, December 26, 2018 3:10:20 PM

Date: 12/26/18 @3pm

To:

Hawaii Dept. of Health

I am writing to submit written testimony (opposing proposed bill HAR-11-157).

From:

Hawaii State citizen-

Corinne Figg-Hoblyn

[Sent from Yahoo Mail on Android](#)

From: [REDACTED]
To: [REDACTED]
Subject: PLEASE DO NOT APPROVE mandatory vaccinations for Hawaii school children
Date: Wednesday, December 26, 2018 3:16:19 PM

To Whom It May Concern:

Aloha, my name is Polli Oliver. I live on [REDACTED] and I am the mother of four children and the grandmother of two. I feel very strongly in opposition to the proposed mandatory vaccinations of our school children. I do not support the idea that additional vaccinations are necessary and I **STRONGLY** oppose the idea that it would be **MANDATORY!** I trust that you will listen to the voices of

the public this matter and will abandon the idea of additional and mandatory vaccinations of the children of Hawaii.

Mahalo nui Loa,
Polli Oliver

From: [REDACTED]
To: [REDACTED]
Subject: Please Do NOT approve mandatory vaccinations for kids
Date: Wednesday, December 26, 2018 3:20:30 PM

Aloha,

The government should not be able to mandate mandatory vaccines for our young. Please reject any attempt to have mandatory vaccinations for our school children or even adults, for that matter.

Thank you,

Regina Floyd (Parent of 2 kids)

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Re:HAR-11-157
Date: Wednesday, December 26, 2018 3:26:48 PM

Date:12/26/18 3:20 Pm

To: Hawaii Dept. Of Health

From:

Thomas Figg-Hoblyn

I'm writing to submit written testimony opposing the proposed bill: HAR-11-157.

Sincerely,

Thomas Figg-Hoblyn

From: [REDACTED]
To: [REDACTED]; [REDACTED]
Cc: [REDACTED]
Subject: TESTIMONY OPPOSING Ch 11-157
Date: Wednesday, December 26, 2018 7:54:58 AM

RE: Testimony STRONGLY OPPOSING the Hawaii DOH's proposed amendments to HAR Ch. 11-157, Examination and Immunization

The Department of Health held several public hearings across the islands, on Honolulu, Maui/Molokai (video conference), Lanai, Kauai, Hilo, and Kona as per the public schedule posted on their website.[\[1\]](#)

Although oral testimony was provided in front of a DOH hearings officer, Steven Jacobsen and Unknown, both publicly stated at every meeting that they had not read or was not familiar with the proposed language and that they were not there to make any decisions.

None of the decision makers were present at any of the hearings, only DOH staffers. The only senior DOH staff seen a couple of hearings was Ron Balajadia of the Immunization Branch, under Dr. Sarah Park, State Epidemiologist.

The DOH recorded over 12 hours of oral testimony from the public on the proposed amendments and requested written testimony. An overwhelming majority of testifiers described personal stories of vaccine injuries, facts and evidence of vaccine injuries and dangers. Only a handful of practitioners testified in support.

The Hearings Officers stated that the DOH would review the audio and written testimonies and would make a decision. Neither Hearings Officer could provide any time frame. When pressed for the names of the decision makers, the Hearings Officers could not provide any names for the record.

This lack of transparency in the administrative process demonstrated that the DOH, specifically the Disease Outbreak Control Division, Immunization Branch under Dr. Sarah Park cannot be allowed to amend, repeal or adopt any administrative rules without additional oversight.

Ch. 11-157 amendments proposes to adopt ACIP guidelines while also mandating several additional vaccines at various school levels, with the additional authority to adopt future amendments as they occur. However, important decisions related to our children cannot be left to individuals who make decisions but are not responsible for the health consequences that may occur from these mandates.

Under the National Childhood Vaccine Injury Act of 1986, specifically 42 USC 300aa-27, the Department of Health and Human Services (DHHS) is required "to improve the safety profile of childhood vaccines, which includes licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on

vaccines, in order to reduce the risks of adverse reactions to vaccines.” These are the same childhood vaccines recommended by the CDC on behalf of the federal government.

However, a recent FOIA request showed that DHHS admitted that it has never conducted any studies or research demonstrating the safety of childhood vaccines recommended by the federal government as required by 42 USC 300aa-27.[2] The federal government was unable to show and continues to be unable to show that childhood vaccines are any safer than they were when they were first introduced onto the market, in some instances, many decades ago.

As the Hawaii DOH attempts to mandate these very same vaccines recommended by the ACIP, a federal advisory committee to the CDC, which falls under DHHS, the issues remain the same. If DHHS has not conducted any studies in the last 30 years on the safety of vaccines, then the ACIP, which has never conducted any clinical studies itself, by default, cannot also claim that its recommendations regarding the CDC recommended childhood vaccines are safe related to adverse reactions.

ACIP guidelines and its vaccine recommendations should not be mandated by the DOH in the proposed Ch. 11-157. These recommendations are intended to only be recommendations where parents and doctors discuss the risks and benefits of vaccines before making an informed decision. To mandate vaccines without evidence of safety is unconscionable and irresponsible by the Hawaii Department of Health, the Director of Health, the State Epidemiologist, the Governor and the State of Hawaii and any other individual involved in making this monumental decision.

Please find included, a link to 50 studies questioning the safety of vaccines published since 2010[3] which I am submitting as evidence for DOH review to OPPOSE Ch. 11-157.

Thank you,

Teresa Chao, RPh, MBA, MJ

[1] <https://health.hawaii.gov/opppd/files/2018/11/11-157-Public-Hearing-Additional-dates.pdf>

[2] <http://www.icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

[3] <http://vaccinesafetycommission.org/pdfs/50-Studies.pdf>

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Submittal
Date: Wednesday, December 26, 2018 3:35:31 PM

Aloha Hawaii Health Department

And thank you for taking comments on the issue of increasing the amount of vaccinations mandated for public school children. The issue of vaccinations sometimes seems so black and white (like many things in our divided society today), and I really do appreciate your openness to a public dialogue on this important matter.

My name is Katie and I'm a Nutritional Therapist in [REDACTED] helping women recover from a debilitating chronic disease called endometriosis. There is no cure, so I help women find symptom management through nutrition, movement, and medical care. This is what holistic care is, a mix of natural, nutritional, lifestyle, *and* medical. Chronic disease sufferers don't have the option to be black or white - all natural versus all western medical - it must be a mix of the two.

And this is exactly how I feel about vaccines. I myself am vaccinated, I grew up believing in vaccines, and I still do. To a degree - as in I can accept the current vaccines mandates by the school system. They have a proven track record of success in mitigating the spread of potentially deadly and quite destructive infectious diseases in our community.

The issue our keiki face today, however, is an onslaught of vaccines for so many more diseases than were available when I was growing up. Although there is, of course, an aim to "save kids" from any sickness at all, I am gravely worried about the efficacy of these newly proposed mandated vaccines and the lack of liability from the global pharmaceutical corporations who make them.

Researchers from Kaiser Permanente Northern California, for example, have recently shown the efficacy of the 2018 flu shot to start waning within weeks of getting it - about 16% for every 2 weeks after vaccination [1]. Another study by Rice University on the 2018 flu vaccine is predicting a measly 20% efficacy [2]. Combine that low efficacy with the amount mercury, polysorbate 80, and formaldehyde being injected directly into the bloodstream of very small humans not just one, but every single year, and it simply doesn't make sense. At all. To mandate this.

As for Gardesil, first of all, mandating a vaccination for a sexually transmitted disease without the consent of the body it's intended for is criminal, in my mind, Second, there's simply no need. The cervical cancer diagnosis rate in the United States is about 8/100,000, which would be near completely avoidable with regular PAP exams as recommended. So why would we mandate a vaccination where even the package insert itself declares a rate of 2.5% serious adverse events within the 15 day trial monitoring period?? That's 2,500 life-altering events per 100,000 women, within 15 days. How about instead we increase education during sex ed on the absolute importance of PAP smears?

On top of that, of course, is the incredible amount of aluminum contained within Gardisil 9 - 1500mcg for the recommended 3 shot dose. The FDA recommended limit for ingested aluminum is 5 mcg per kilogram per day, so for an 80 pound child that would be 180 mcg. To be clear, ingested aluminum is very different than injected aluminum, since very little that's ingested actually makes it into the bloodstream - estimated at .3%. Injected aluminum is a totally different story as it has no barriers to bypass (like your digestive system) and can immediately be stored in muscles, organs, tissues, or the brain.

So back to that 1500 mcg of aluminum, let's do the math. If the FDA's upper limit for that 80 pound kid is 180 mcg of aluminum and we assume they absorb .3%, that means .54 mcg of that into the bloodstream. One Gardisil 9 shot is 500 mcg aluminum straight into the blood stream. That's 925x more aluminum than the upper limit in one day. No thank you, not for my child, nor should that be tolerable for any child. We as adults need to tell the manufacturers to find another way if this is absolutely so necessary,

As for the liability issue, why is there so much aluminum in the vaccines? Because it's a cheap preservative filler and the pharmaceutical companies making these vaccines have absolutely no liability to the consumer they're mandating their ineffective product on. In 2011 the U.S. Supreme Court shielded drug companies from all liability for harm caused by vaccines mandated by government when companies could have made a safer vaccine [3]. That means no vaccine manufacturer is liable for any harm caused by their product.

To put this in perspective, if chicken manufacturers were not liable for E. Coli outbreaks in their processing plants and the State of Hawaii mandated every family eat chicken every week, would you be okay with that? Probably not.

So yes, my baby boy will get his dTap, his MMR, his Polio, and the rest of current mandates. But he won't get Gardesil, nor will he get any flu shot. Although I know I could use the religious exemption - that's not the point. Like vaccines were created to "protect the herd" I think we also need to protect the herd from corporate interests making a LOT of money mandating new vaccines. In fact, in 2012 there were 300 more vaccines in the pipeline [4], all being created without any liability as they move to market. Where will the mandated vaccines stop if not here? Now?

Let's educate our kids about HPV in real ways - teaching safer sex and the importance of annual exams. Let's prevent the transmission of flu through hand washing, mandating sick kids stay home, and focusing on diet and nutrition (which would also really help the diabetes

issue in Hawaii). Let's also mandate in turn that vaccine manufacturers take responsibility for their product, so that we as a community know they actually care about our health and wellbeing.

Thanks so much for your consideration and all you do protecting the future of our keiki

Katie Edmonds
Nutritional Therapy Practitioner



From: [REDACTED]
To: [REDACTED]
Subject: Re: Oppose increased mandatory vaccinations
Date: Wednesday, December 26, 2018 5:10:24 PM

Daer Rep. Onishi -

Thank you so much for your prompt reply! I appreciate it.

Volumes have been written on the topic of vaccine safety and industry corruption. I only briefly touched on the main reasons why it may be dangerous to comply with CDC recommendations. I didn't even include that former CDC Director Frieden prevented a Senior Scientist in the Vaccine agency from testifying before Congress that the CDC threw away data about MMR shots and autism.

In addition, a fortune has been spent on a propaganda campaign trying to convince the public that there is no correlation between autism and vaccinations in any way, yet autism is listed as a side effect on a vaccination package insert, and a special court had to be set up to adjudicate the thousands of cases against the vaccine manufacturers so they wouldn't all go bankrupt - a special court outside of the judicial system that favors the defendants and sets an incredibly high bar of proof for the vaccine-injured victims.

There are no long term studies done on the safety of giving multiple vaccines to children at once. The CDC is content to let the multiple doses be given and watch over the ensuing decades to see how many disabilities are created. Once the manufacturers were given immunity from liability, the vaccine schedule jumped alarmingly, and continues to climb every year. U.S. has highest rate of vaccinations and the worst infant mortality in the developed world.

For the state to deny poor children an education because their parents decide to err on the side of their child's personal safety is discrimination of the most heinous sort. The state forces the poor child to become a guinea pig for corrupt profit-seeking corporations. This partnership of corporations and government is the definition of fascism.

Thank you for your time and attention.

Vicki Vierra
[REDACTED]

On Dec 26, 2018, at 3:46 PM, DOH.Immunization
[REDACTED] wrote:

Your written testimony has been received. Thank you.

Hawaii Department of Health
Immunization Branch
1250 Punchbowl Street, 4th Floor
Honolulu, Hawaii 96813

From: Vicki Vierra [REDACTED]
Sent: Wednesday, December 26, 2018 3:44 PM
To: DOH.Immunization [REDACTED]
Cc: admin Hawaii For Informed Consent [REDACTED]
Subject: Oppose increased mandatory vaccinations

To the Immunization Branch
Hawaii State Department of Health

The very topic of mandatory vaccinations is abhorrent to many people. It reeks of authoritarianism, communism and nazism - virtually every negative "ism" is evoked when the term "mandatory vaccinations" is heard. It assumes that the individual's right to privacy and freedom of choice is non-existent. It strikes at the heart of what it means to be an American living in a Constitutional republic.

Not only Americans are horrified at the thought - in the words Dr. Hiroko Mori, former head of the infectious disease section at the former Institute of Public Health, Japan: "The right to choose should be recognized as a fundamental human right."
<https://www.japantimes.co.jp/life/2014/10/04/lifestyle/vaccination-choice-two-unknowns/>

'Mandatory vaccinations' implies not only that the individual has no such rights, but that they are incapable of deciding, based on the facts, what is best for their own health and the health of their children.

Therein lies the rub - in today's information age, in a climate of medicine for profit, where pharmaceutical corporations wield their billions of dollars like weapons of war and saturate the airwaves with direct-to-consumer advertising, (U.S. being only one of two countries in the world to allow this), and pay their lobbyists to write the legislation that protects them from vaccine liability, in this climate it is exceedingly difficult to find any facts on the topic of vaccines efficacy and safety.

Let's go back in time and look at the early polio vaccines. The original Salk vaccine made of inactivated viruses was replaced by the Sabin oral polio vaccine of three vaccine strain polioviruses cultured from primary cell monkey kidneys. One of the monkeys carried a virus known to cause cancer tumors - SV40. In spite of this fact, public health officials recommended that all children receive this oral polio vaccine. Between 1954 and 1961 over 100 million children and adults received this vaccine. Doctors assumed that the cancer causing virus was removed from the vaccine, however it was discovered that up until 1978 it was still present in the vaccine. (Cutrone r, Lednický J, Dunn G et al. [Some Oral Poliovirus Vaccines Were Contaminated with Infectious SV40 after 1961](#). *Cancer Res* 2005; 65: 10273-10279.)

Of course, the fact that half of all people today will have some kind of cancer must simply be a coincidence...right? "Correlation is not causation" is the mantra we hear so often from those scientists dependent on corporate dollars.

Speaking of which, let's look at the vaccine studies done by scientists funded by the protected class of vaccine manufacturing pharmaceutical corporations, which the CDC relies on. Can we be assured that they present all the pertinent data, free of bias? Hardly.

In the opinion of the Chief Editor of the world's most prestigious medical journal, The Lancet: "The case against science is straightforward: much of the scientific literature, perhaps half, may simply be untrue. Afflicted by studies with small sample sizes, tiny effects, invalid exploratory analyses, and flagrant conflicts of interest, together with an obsession for pursuing fashionable trends of dubious importance, science has taken a turn towards darkness." - "Offline: What is medicine's 5 sigma?" Richard Horton, editor The Lancet
www.thelancet.com vol385 April 11, 2015.

But that's not all. Listen to what the editor at the New England Medical Journal has to say: Marcia Angell: "it is simply no longer possible to believe much of the clinical research that is published, or to rely on the judgment of trusted physicians or authoritative medical guidelines. I take no pleasure in this conclusion, which I reached slowly and reluctantly over my two decades as an editor of *The New England Journal of Medicine*"

So, Hawaii Department of Health now asks us to follow the recommendations made by the CDC for these 'mandatory vaccinations'. Vaccinations are violent, invasive procedures that may result in death, paralysis or permanent disability. And we are asked to do so, because the CDC says it is a good thing.

Let's watch a video as the CDC's "Advisory Committee on Immunization Practices" decides whether to approve the new Hep B vaccine:
<https://thevaccinereaction.org/2018/09/acip-voting-on-a-new-vaccine/>

"Is there any comment on using this vaccine at the same time as other adjuvanted vaccines?"

We have no data to make a recommendation one way or the other. So just to sort of put this in context of other vaccines, while pre-clinical studies were not done using this vaccine simultaneously, our general approach to immunizations is that they can be given at the same time in different limbs.

Are multiple adjuvanted vaccines used in Europe or other markets?

Not to my knowledge. Okay, I think unless there's any further discussion we will take a vote on this recommendation. *So... the voting is completed and it is unanimous to support this recommendation to approve the hepatitis B vaccine."*

In other words, this committee has decided to approve a vaccine known to cause myocardial infarctions and see what happens to the millions of guinea pig people who will unwittingly be testing it.

Is the entire CDC corrupted beyond all repair by pharmaceutical money? Thanks to the efforts of independent journalists we can look at former CDC Director Thomas Frieden for a glimmer of just how bad it could be. Not simply that he was arrested for sexual abuse, but the possible billions in scandals. <https://www.coreysdigs.com/cdc/cdc-thomas-frieden-billions-in-potential-scandals/>

There are too many reasons to list here as to why I oppose mandatory vaccinations. Suffice it to say that not only should the CDC recommendations not be implemented, but the philosophical exemption should be reinstated.

Sincerely,

Vicki Vierra



From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Re: Mandatory vaccinations for HPV and other mandatory vaccinations. (Opposing forced vaccinations)
Date: Wednesday, December 26, 2018 3:50:40 PM

Aloha to the health department and board of education as well as legislators, I am writing this letter in opposition to the new guidelines and proposed rules that will effectively force vaccinations on our children. I can understand a policy like this being implemented in North Korea, but in America? The land of the free? This is beyond comprehension.

I am opposing this also because HPV apparently causes cervical cancer. Preventing cervical cancer requires yearly pap smears and there is no evidence that forced vaccinations will be of service to the public. It will however add to the scheduled list of mandatory vaccinations and be a windfall for the pharmaceutical companies.

Do the math. Crunch the numbers. 72 vaccinations per child attending public schools. How much are the pharmaceutical companies charging per vaccination? How many children attend public schools? How many newborn babies are injected with the vaccinations and accompanying aluminum, formaldehyde and other toxic chemicals? Has the legislature thought just about who is going to pay for this? And what of the damage done to the millions of babies due to exposure to cheaply made vaccinations?

If indeed the public's health was the agenda of these agencies, the pharmaceutical companies would provide these vaccinations for free to the people and not make the government and insurance companies pay for them. I am not opposed to all vaccinations but with our children being exposed to 30 vaccinations within the first year of life, and then by the time they are 18, 72 doses of various vaccinations will be injected directly into the sensitive tissues of our children, this can hardly be called safe, nor integritous on the part of big pharma.

It's very clear that this is about making money for the pharmaceutical companies. With the new proposed rules effectively eliminating parents' rights to protect their children from the proven harmful potential side effects of such an aggressive vaccination schedule through various religious exemptions and such, will only make the pharmaceutical companies richer. And who will pay for this? Who will pay for the damage being done to our keiki? There IS a Vaccine Injury fund for those many children and adults that have been forced to take these toxic chemicals directly into their blood stream.

As a patriotic American citizen, I believe in freedom. The right to choose what happens to our bodies. Vaccinations used to help but now it's clear we have passed the law of diminishing returns. We cannot deny the rates of autism and other debilitating diseases occurring within the vaccinated populations of babies, children and adults.

If the department of health wants to prevent cervical cancer, then stick to the yearly pap smears. Eat organic. Live healthy. That's what prevents cervical and other cancers. There are so many diseases out there, the pharmaceutical companies will never be able to keep up, but they'll keep coercing the public into paying for their injections while our citizens suffer in this allegedly free country via rules and regulations imposed on us by the legislature.

Let's keep America a free country shall we? This is nothing short of fascism disguised in the good will of our lovely pharmaceutical corporations that proclaim to "care" about us. We no longer trust the medical establishment as it exists today. I can understand it necessary to have a few vaccinations, but 30 within the first year of life? I feel like I'm living in the twilight zone and America is fast becoming one of the many nations that no longer fit the description "free".
God Bless America

God Save America from the multi national corporations that care nothing about our health and well being, and put profits over people.

We the people, vigorously oppose this ruling.

Amen.

Melanie.

From: [REDACTED]
To: [REDACTED]
Subject: Vaccine change
Date: Wednesday, December 26, 2018 3:53:03 PM

My name is Cassie DaSilva and I am a [REDACTED] mother of two. I vaccinate my children. The flu vaccine and Hpv vaccine are both choices I have left off our list of recieved vaccines based on research and conversations with my children's pediatricians. Making these mandatory is an infringement on our personal rights. I absolutely oppose this vaccine change and in no way support this being mandatory.

Cassie DaSilva

[REDACTED]

[Sent from Yahoo Mail on Android](#)

From: [REDACTED]
To: [REDACTED]
Subject: Testimony Opposing HAR 11-157
Date: Wednesday, December 26, 2018 3:56:37 PM

To Whom It May Concern at the Department of Health:

Based on a research and after talk to physicians and health care practitioners I have made an informed choice and not vaccinate. I believe it's every parent right to decide about it's child health, and it's decision has to be based on acknowledgment of all the aspects of "pros and cons" of vaccines and not on compulsion.

Mass vaccination of population has started in 1920. That times the child would get only a few vaccines, which were helpful indeed in prevention of a mass epidemics actual for that times. The benefits of that vaccines were greater indeed than it's harm because it was just a small number of it and a risk of epidemic were high. In a last 100 years the situation has changed dramatically. The choice of modern different hygienic and cleaning products minimized the risk of dangerous mass epidemic explosions. That risk is not real and dangerous nowadays compare to the risk of vaccines that every child has to be exposed to. Two or three vaccines became much bigger number, and the danger of some of it's components like mercury, aluminum etc, that accommodates in a humans body is much greater today than 100 years ago.

Many vaccines today are tested on animals, such as rats, and it's benefits are proofed. But the truth is that no one rat does not get the number of vaccines that child does, so the risks from it's components accommodated in a body is still unknown. Why would my child become a "laboratory rabbit"?

Thank You,
Sofia Petrova
Contact:

[REDACTED]

From:

To:

Subject:

Date:

[REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
OPPOSE MANDATORY VACCINATION

Wednesday, December 26, 2018 5:13:31 PM

My name Debra Parzych and I STRONGLY oppose mandatory vaccination! There is a huge list of dangers associated with vaccines and when there are dangers present there MUST be a choice!!

Debra Parzych

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: PLEASE DO NOT Approve mandatory vaccinations for our school children
Date: Wednesday, December 26, 2018 8:50:12 PM

To Whom It May Concern in DOH,

There are places for our government to intercede and help in our lives. This IS NOT one of them. Please reject any attempt to have mandatory vaccinations for our school children or anyone for that matter.

Thank you,

Cindy Williams

From:

To:

Subject:

Date:

[REDACTED]

Vaccines choices

Wednesday, December 26, 2018 11:33:05 PM

Government rule needs to stop at our skin. We should never be forced to inject ourselves or our children with anything, especially something that can have devastating side effects. It's a basic human right to have control over what we allow into our bodies. Please do not pass a law taking that right away.

From: [REDACTED]
To: [REDACTED]
Subject: consent
Date: Wednesday, December 26, 2018 8:42:32 AM

Aloha,
As the mother of a 6th grader, I demand the freedom to choose if my child will be vaccinated in 7th grade.

Be sure that the laws allow this choice.

Julie Ybarra

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: consent
Date: Wednesday, December 26, 2018 7:49:49 AM

Hawaii Law Makers,

I passionately implore you to allow vaccines to be optional. I am an early childhood educator and firmly believe that vaccines have detrimental effects and should be the choice of the parents. Our current schedule is overwhelming to an infant. Let us choose.

Thank you,
Julie Ybarra

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Fw: DOE vaccine recommendations
Date: Wednesday, December 26, 2018 10:03:06 AM

Please add our names to the health care physicians, providers that support the CDC and AAP recommendations for the Department of Education in Hawaii.

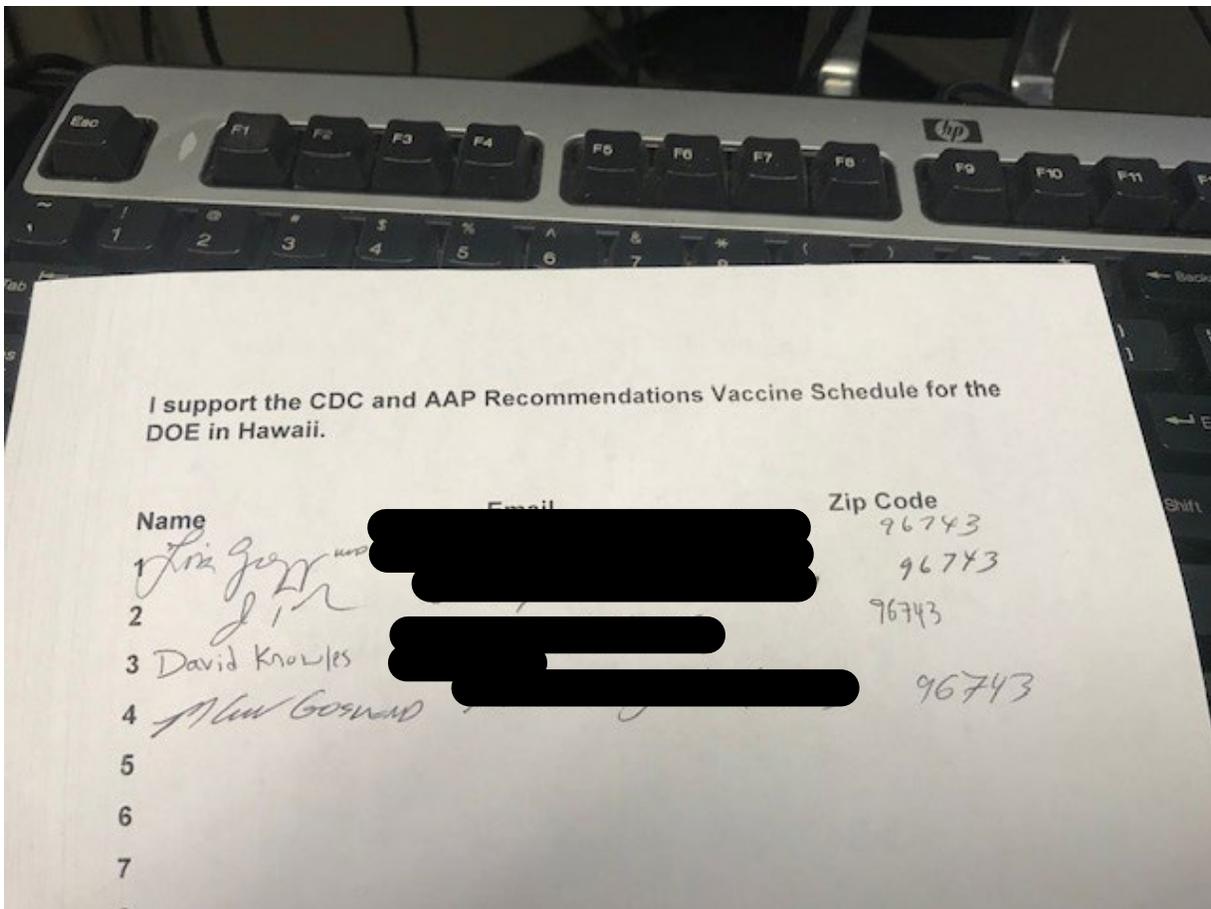
Sincerely,

Lois Gregg MD

Jeffrey Tolan MD

David Knowles PA-C

Melissa Gosland MD



Sent from my iPhone

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by

reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: Fw: HAR 11-157 - I OPPOSE
Date: Wednesday, December 26, 2018 4:02:20 PM

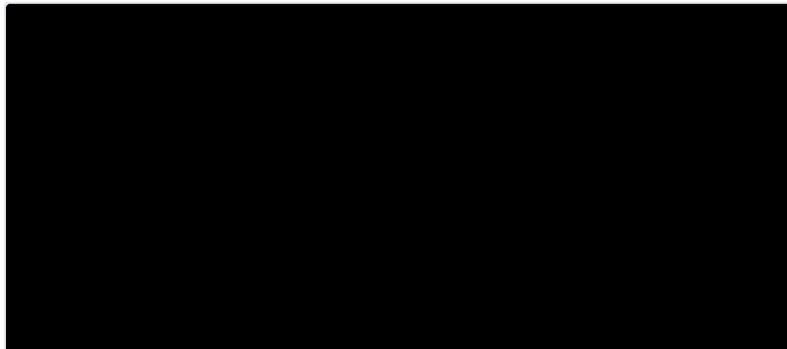
Aloha Hawaii Department of Health,

Thank you for this opportunity to provide testimony.

I Strongly OPPOSE the HAR 11-157 Proposed Rules Update.

I oppose HAR 11-157 for being an incomplete proposal, by not offering the draft of the standard medical and religious exemption forms. I do not accept that DOH assumes power to decide without public input on their final form, and the drafts should have been a part of this proposal. Medical exemptions can be made unnecessary, more complicated or beneficial. We the public simply don't know, because they are missing.

The added six vaccines (baby-college) are NOT tested with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 vaccines to 9 vaccines (k-12) and as one example adds HPV as a requirement, making us one of the most regulated states in all USA. Safety & Risk assessment needs to be done first. For example, HPV been taken out of Japans requirements for 5 years due to many adverse reactions. [Five Years Since the Suspension of Proactive Recommendation of the Human Papillomavirus \(HPV\) Vaccine in Japan](#)



Five Years Since the Suspension of Proactive
Recommendation of the Human...

PDF Download

In addition, the process of the public hearing and your efforts of informing the people of Hawaii been unacceptable. Initially DOH Hawaii planed only one public hearing,

with outside pressure you extended the meeting to the outer islands. The timings often excluded teacher, educators, small business child care center to attend, beside it was already heart for parents in one for many very special holiday times. On top of that no key decision maker was present, you ignored the petition delivered to you before the Maui hearing, a request from the public and we were told that you will review the hours of testimony using the transcript. Please explain this process.

I respectfully request that the proposed changes to HAR 11-157 be opposed and I request that for further changes on immunization a communication link will be established between the DOH & DOE to inform all schools, teachers, parents and who else will be affected by the change, by informing us about the intentions, including a summary of the full implication of the rule change.

Thank you for your time,

Sincerely,
FrancisHertzog, [REDACTED] Decemebr 26, 2018

From: [REDACTED]
To: [REDACTED]
Subject: FW: In strong opposition to HAR 11-157
Date: Wednesday, December 26, 2018 11:34:01 AM

My family is in **STRONG DISSAGREEMENT with the proposed changes to HAR 11-157.**

While the changes might be well intended, they infringe on all Hawaii's residents to determine what is best for their own children, and **will allow the state to do harm to susceptible children.**

Separation of government policies and personal beliefs is ingrained in America's core freedoms, and this separation is codified in our bill of rights and supported in all constitutional amendments.

It is our firm belief that current usage of vaccinations, flu shots, and antibiotics cause more harm than good.

Keep in the front of your minds that the facts have not changed: **All vaccines are not safe for all children.**

And a child's parents know better than the state of their child's health issues and drug allergies.

Ask any local pediatrician: We know how to treat these targeted diseases effectively, but we do not know how to cure a child who reacts negatively to these drugs.

So please educate yourselves on the effectiveness and dangers of many vaccines (<https://thevaccinereaction.org/vaccination/risk-failure-reports/>) ***BEFORE*** approving these proposed rule changes.

The consequences of a severe reaction associated with a forced inoculation of an individual far outweigh the benefits to society.

Please, as a caring parent and firm believer in our individual rights as Americans,

Do the pono thing for our keiki – **DO NOT PASS** these proposed rule

amendments.

- Randy Wolfshagen,



“You may choose to look the other way, but you can never say again that you did not know.”

— *William Wilberforce*

From: [REDACTED]
To: [REDACTED]
Subject: Fw: R.E.: HAR 11-157
Date: Wednesday, December 26, 2018 9:10:52 PM

[Sent from Yahoo Mail for iPhone](#)

Begin forwarded message:

On Wednesday, December 26, 2018, 4:08 PM, zach mccook [REDACTED] wrote:

Re: HAR 11-157, I Strongly Oppose.
For many reasons this is dangerous, we as a community should not be forced to inject our growing children with substances that could harm them. All vaccines have side effects stated in there packaging if there is a risk we should have a choice. By taking away our children's opportunity to go to school with requiring parents to play roulette with there health, you are limiting our freedom. Not to mention other economic and sociological aspects that will change. Please keep our freedoms.

Much Appreciated

Zachary McCook's Ohana

[Sent from Yahoo Mail for iPhone](#)

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Fwd: Mahalo for thoughtful Opinion piece 12-23-18 clarifying the reasons families should have their children vaccinated and that being mandatory is very meaningful public policy.
Date: Wednesday, December 26, 2018 4:10:31 PM

My apology - I am late in conveying my personal support for the proposed revisions to the State of Hawai'i Department of Health rules as spelled out in HEARING DOCKET NO. R-157-18-07.

There are many science-based reasons to support the existing mandatory vaccination requirements and proposed changes. I work at a public school where it is clear that our children, families and community are better off for having been vaccinated.

Thank you for this opportunity to comment and for strengthening the requirements.

I am sure you saw the OPINION piece written by the staff of West Hawai'i Today after reporting on a very one-sided hearing here in Kona. However, in case you missed it, here it is - and I am also grateful for their support for the proposed rule changes.

<http://www.westhawaiiitoday.com/2018/12/23/opinion/our-view-anti-vaccination-message-barely-worth-printing/>

Patti Cook [REDACTED]
[REDACTED]

-----Original Message-----

From: Patti Cook [REDACTED]
To: thasslinger [REDACTED]
Cc: Bruce.S.Anderson [REDACTED] Susan.M.Kim [REDACTED]
[REDACTED] reptarnas [REDACTED] seninouye [REDACTED]

Sent: Wed, Dec 26, 2018 3:56 pm

Subject: Mahalo for thoughtful Opinion piece 12-23-18 clarifying the reasons families should have their children vaccinated and that being mandatory is very meaningful public policy.

Aloha Tom -

I am writing as a community resident, not speaking on behalf of any organization or institution.

I'm not sure if this should be addressed to you, but I want to personally thank West Hawai'i Today for taking a clear, concise, science-based position in support of continuing to vaccinate our children here in Hawai'i against serious,

potentially death-causing diseases for their own well-being and that of their families and the community.

It was alarming to see the news story conveying many false statements several days earlier after a public hearing, but I understand the quandry faced. Your response in the Dec. 23, 2018 Opinion article is spot on. We cannot let "junk science and rhetoric that runs counter to precious medical advancement and science" define our public policy.

Thank you for taking the time and having the courage to support good science and thoughtful public policy. Yours is a powerful voice and I do hope both the general community and our State Department of Health leadership are listening.

<http://www.westhawaii.com/2018/12/23/opinion/our-view-anti-vaccination-message-barely-worth-printing/>

Patti Cook 

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157 - I OPPOSE
Date: Wednesday, December 26, 2018 10:08:51 AM

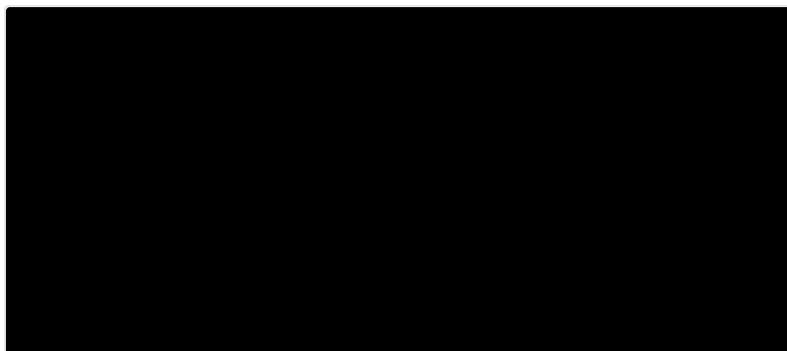
Aloha Hawaii Department of Health,

Thank you for this opportunity to provide testimony.

I Strongly OPPOSE the HAR 11-157 Proposed Rules Update.

I oppose HAR 11-157 for being an incomplete proposal, by not offering the draft of the standard medical and religious exemption forms. I do not accept that DOH assumes power to decide without public input on their final form, and the drafts should have been a part of this proposal. Medical exemptions can be made unnecessary, more complicated or beneficial. We the public simply don't know, because they are missing.

The added six vaccines (baby-college) are NOT tested with the Hawaii diverse demographic in mind and will over regulate our school requirements from 5 vaccines to 9 vaccines (k-12) and as one example adds HPV as a requirement, making us one of the most regulated states in all USA. Safety & Risk assessment needs to be done first. For example, HPV been taken out of Japans requirements for 5 years due to many adverse reactions. [Five Years Since the Suspension of Proactive Recommendation of the Human Papillomavirus \(HPV\) Vaccine in Japan](#)



Five Years Since the Suspension of Proactive Recommendation of the Human...

PDF Download

In addition, the process of the public hearing and your efforts of informing the people of Hawaii been unacceptable. Initially DOH Hawaii planed only one public hearing, with outside pressure you extended the meeting to the outer islands. The timings often excluded teacher, educators, small business child care center to attend, beside

it was already heart for parents in one for many very special holiday times. On top of that no key decision maker was present, you ignored the petition delivered to you before the Maui hearing, a request from the public and we were told that you will review the hours of testimony using the transcript. Please explain this process.

I respectfully request that the proposed changes to HAR 11-157 be opposed and I request that for further changes on immunization a communication link will be established between the DOH & DOE to inform all schools, teachers, parents and who else will be affected by the change, by informing us about the intentions, including a summary of the full implication of the rule change.

Thank you for your time,

Sincerely,

Victoria Holloway, [REDACTED] Decemebr 26, 2018

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: HAR 11-157 - immunization requirement to attend school
Date: Wednesday, December 26, 2018 3:46:52 PM

To DOH Immunization Branch Chief Ronald Balajadia and to whomever else it may concern:

Regarding proposed rule HAR 11-157: I am in opposition. Requirement of any vaccine to attend school or daycare infringes on parental rights.

We are all familiar with the often used mantra, "safe and effective", to describe vaccines and to dismiss any questions or concerns about vaccines. There is evidence that contradicts that description however. If you would like further and more detailed, peer reviewed information please go to the website: Physicians for Informed Consent.

Ultimately what I, and those of us opposing HAR 11-157, want is for all people to have informed consent and be given the choice of whether or not to vaccinate ourselves and/or our children.

Thank you for your time and consideration.

Aloha
Sincerely,
Rocio Bueno

From:

To:

Subject:

Date:

[REDACTED]; HAR 11-157

[REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Wednesday, December 26, 2018 3:03:30 PM

To Whom it may concern:

I am a mother of two sons, a nurse practitioner, and certified nurse midwife and I am against the HAR 11-157 bill requiring mandatory vaccination of all children regardless of parental opposition. With appropriate informed consent all parents should be allowed to make the decisions regarding vaccinations for their families. I take pride in advising my patients of current recommendations by the CDC and WHO but also honor their choices once they have made a decision based on informed consent and education by their providers and pediatricians. There are documented adverse reactions, and I personally know patients who have been victim to vaccine injury. The National Vaccine Injury Compensation Program (VICP) was created for cases such as these and is evidence that vaccine injury does occur.

With the ever increasing list of required vaccines and minimal evidence of safety with newer recommendations. I ask that this bill be dropped or vetoed. Preserve the right of our families to make their choices. It is well studied and document that children that are vaccinated can still contract the disease or be carriers that can infect others.

Mandatory vaccination does not eliminate the problem. As found evident by the EU ASSET project, "the enforcement of mandatory vaccinations does not appear to be relevant in determining childhood immunisation rate in the analysed countries. Those [countries] where a vaccination is mandatory do not usually reach better coverage than neighbour or similar countries where there is no legal obligation." So therefore why take away our rights with this forceful bill. Energy towards efforts for clearer patient-provider informed consent, education around vaccines, and further RCT studies proving the efficacy of vaccines should be the goal.

Thank you for taking the time to accept and consider testimony against this bill.

Mahalo

Colleen Bass

CNM, WHNP

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, December 26, 2018 4:12:53 PM

Aloha,

I am writing to oppose HAR 11-157 for mandatory vaccines. I think there should always be an option of what we are putting into our bodies and our children's bodies.

My father had an adverse reaction from the flu shot 3 years ago where he developed Guillain Barre Syndrome (GBS). He hadn't had a flu shot in almost 20 years and due to traveling for work thought it might be a good idea. The same day he said he felt odd and knew something was not right. The next day he felt really sick and weak, and by the end of the day had double vision, weakness, severe headache and body aches. He went to the ER and when they were doing the routine check in his blood pressure was abnormally high. They initially thought he had a stroke. When the neurologist was involved and did all of the test it was obvious that it was a direct linked to the flu vaccine and not a stroke. The Dr. said my dad was one of the lucky ones all of his other patients at that time would not be walking out of the hospital like he was. For 6 months he had intensive rehabilitation and detoxing of his system to regain strength in his body. He had to wear special glasses to help his eyes correct the severe double vision he was experiencing. Chiropractic and acupuncture appointment after appointment and after a year he was starting to feel like himself again and three years later I feel so blessed that he is fully back to himself.

They cannot pinpoint why it happened to him, if its genetic or not. What I know is I never want anyone I know to go through any of that. I am so grateful that my father has access to the absolute best Dr.'s at the Mayo clinic who gave him the best treatment plan possible.

The 3 vaccines that you are talking about have just awful track records in other countries where they have already stopped requiring them. They are not properly tested and to force that upon people is just wrong. The medical repercussions that they may have in the future are unknown, but why is that even a risk we want to take with our future generations.

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Subject: Statement against changes to mandatory immunizations
Date: Wednesday, December 26, 2018 1:52:46 PM

To Whom It May Concern in the Hawaii DOE, the state legislature, and DOE Immunization Branch Chair Ronald Balajadia:

As a citizen, a father, a medical doctor, and a Big Island resident I believe that your proposed changes to increase immunizations to school children is unconstitutional and inappropriate. For the record, I am not anti-vaccination. Immunizations have saved millions of lives and have been one of the most important public health measures for disease prevention in history, after indoor plumbing and improved hygienic practices. Further, my own children are vaccinated and attend school. Yet, I do not believe that increasing the volume of mandatory vaccinations is appropriate or safe. I am also very concerned about the safety profile of the HPV vaccination and I do not believe that HPV prevention is a necessary public health measure under any circumstance. I am likewise uncertain about the efficacy of the Influenza vaccine and therefore do not think it should be mandatory under any circumstance. The Meningococcal vaccine is a very good vaccine and is appropriate for young people who will be living in close quarters, such as in college dormitories and in military barracks. This vaccine should be mandatory in those scenarios and thus should continue to be optional and administered under the professional guidance of a health care professional, based on sound medical guidelines and not on a mandatory, universal one-size-fits-all public health measure. The immunizations that we already have our children receiving as universal public health and prevention measures are sufficient.

In summary, HPV, Influenza, and Meningococcal immunizations should not become mandatory for school participation. They should continue to be optional. I am pro-vaccine and also pro-american. We cannot mandate immunizations in order for children to receive government sponsored education. This is medical harassment and is an obstruction of our basic rights as americans. I am not suggesting that we go backwards, I am suggesting that we do not continue adding more vaccines to the list of mandatory vaccines. It is irresponsible and unconstitutional. It will force many more children into homeschooling, which will put more kids at risk than any proposed health risk from HPV, Flu, or N. meningitis.

Please reconsider this inappropriate public health recommendation. If you really want to make a public health impact on children then re-appropriate state funds into nutrition and nutrition education.

Sincerely,
Justin Groode, MD
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Stop all Mandatory vaccinations
Date: Wednesday, December 26, 2018 8:34:57 AM

Especially the proposed HPV virus one.

Warmest Mahalo and Aloha,

Susan Douglas

[REDACTED]
(that's spelled [REDACTED])

[REDACTED] (You can call 24/7, if you get my machine leave a long message. NO
texts please.)
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Stop the immunization bill changes due Dec 26 th 2018
Date: Wednesday, December 26, 2018 8:09:45 AM

The Moral Right to Conscientious, Philosophical and Personal Belief Exemption to Vaccination

We have a right to choose what we inject into our bloodstream.

I absolutely oppose the Health Department to make it mandatory vaccine doses for our children. My child has been damaged with severe learning problems and I do believe it was all the heavy amount of vaccines she received to be allowed into the United States after being adopted from Kazakhstan Russia. I took her through a year detox of all these metals and toxins that were in her vaccines with a specialist biochemist after extensive blood work. The change was so dramatic. She began speaking from being mute, increased in learning speed and her movements of her limbs and coordination became soft fluid and normal. It was such a joy to see what getting rid of these vaccines and their poisons did. I had her on rigid health diet for 14 years and I did not want her ever again to have anymore vaccines.

My nutritionist Shannon Nering's letter I have also included as she is more eloquent at explaining the situation. Please read below.

First, our entire mainstream food, supplement and drug supply has become so corrupted, companies we've trusted for decades are committing heinous crimes in the name of profit. Just today, Johnson and Johnson is charged because a three year old was hospitalized due to metal in her intestines from her vitamin gummy bears! This same company also admitted to using asbestos in their baby powders. These companies that rule the market place our ruining lives for the sake of profit.

Daily I read articles on vaccine injury. A new father hospitalized for the flu vaccine with extreme nerve damage, he can not move or open his eyes. He's blinded. Lou Ferigno—aka the Hulk—hospitalized after the pneumonia vaccine. Very sick but recovering. Deaths from the HPV vaccine are climbing now that this is mainstream. And countless other mothers and fathers who claim their once bright lively toddler suddenly turned to stone, days or within weeks of the MMR vaccine. Injuries from DTAP range as the highest—none of this is reported in mainstream news because big pharma controls the media. They also control the government. There are two pharmaceutical lobbyists per one senator in the US government today! Think about that. That means their ears are filled with lies and their pocket books are being filled with money to campaign to make every American take their drugs! They want us sick and dependent for our entire lives.

Now the science behind vaccines might make good sense, but it is the adjuvants and metals they add to preserve [the vaccines](#) that are monumentally damaging to your health. Would you in good conscience inject your children (or yourself) with the following lethal ingredients?

--Mercury -- most toxic substance/metal known to man, they claim to have removed it, however, it continues to show up in the flu vaccine, and others. It's a powerful immunosuppressant amongst myriad other things. When you hear from the vaccine safety

promoters that new studies have shown that ethylmercury (in thimerosal) disappears from the blood within several days. Actually, the mercury leaves the plasma and enters the brain, where it is de-ethylated and remains for a lifetime, wreaking havoc on the brain.

--Aluminum—first added in 1926, another known neurotoxin—DNA damage, cell damage, binds to ATP and affects energy production in all cells. It's linked to dementia, autism, Parkinsons—1 in eight seniors have dementia now (hello flu shot), in less than a decade, it'll be one in four. What's the common thread here?

--Formaldehyde—used to embalm dead bodies. Need we say more? You want that in your kids?

--Peanut oil – why was there a plague of children suddenly with peanut allergies. No one could explain. Well, it was used in vaccines as a preservative for a time. Hmm.

--MSG—a known neurotoxin! You won't eat it, but you'd inject it?

--Also DNA residues, gelatin, antibiotics—like we need more of those!

--And not listed on official ingredient lists are bacterial and viral contaminants, which can include their particulate, fragmented matter.

This is frightening! Connect the dots! They are not saving lives.

In 1983, before the autism epidemic began, children received 10 vaccinations before attending school and the autism incidence was 1 in 10,000. Today, they receive 24+ vaccines before they turn 1, and 36+ by the time they start school and the autism rate is now 1 in 150 births! Do the math!

There are over one million children with autism and the numbers continue to grow. This is a medial disaster of monumental proportions. The link to the vaccine program is scientifically and logically compelling but these same medical elitists refuse to listen. Like smoking and lung cancer, we have enough proof today to call a halt to the present excessive vaccine program and ban any level of mercury in vaccines.

Vaccines are tested for a brief period if at all!!! Three weeks. They have never tested what repeated vaccinations and the current volume/quantity of vaccinations do to animals/humans. We are guinea pigs for big pharma's bottomline—making them BILLIONS of dollars. The vaccine schedule for an infant born in America, before the age of one, is the equivalent of giving an adult one shot a day. Our bodies are so polluted from these toxic injections.

Independent third party studies are vilified and struck from record, almost none are accepted into medical literature. That's what billions of dollars will do.

Lastly -- CHINA -- The Chinese are now the largest vaccine manufacturers in the world, with over 400 biopharmaceutical companies making vaccines and poor quality drugs for the world. The FDA admits that it inspects only 1.8 percent of the 714 drug firms in China and that, according to a GAO study, FDA inspections may be done 13 years apart (In the US it's spaced 2 years apart).

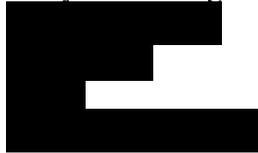
--More frightening is that the inspectors must depend on Chinese translators and US

companies who purchase [the vaccines](#) must have a Chinese communist official serve as its legal representative. One CEO was quoted as saying “every piece of information you get (from the Chinese) is suspect.”

--With thousands of people dying and getting sick, not only in China, but in hundreds of nations receiving China’s tainted pharmaceutical products, future vaccines are an even greater danger.

No thank you. Count my children out of this twisted program that claims to protect our health while destroying bodies and minds. But hey, it does make the ‘elite few’ billions of dollars!

Sincerely,
Shannon Nering ,
Mary Ellen Ringler



From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose
Date: Wednesday, December 26, 2018 3:10:21 PM

To whom it may concern,

I am writing to share that I strongly oppose the HAR 11-157 proposal to require more vaccinations for the children of Hawaii state than any other state in the country.

My name is Erica Bergquist and I have been an educator of young children for 13 years. I hold a Masters degree in Education and have a 10 year old daughter who has never had any vaccinations. She is the healthiest person I've ever met having only ever contracted a cold.

When I was pregnant with my daughter, I wasn't sure about vaccinations. I attended several talks and read many informative books, learning both pros and cons of the realities of vaccines.

I learned much.

It is a common belief that the Polio vaccine saved thousands of families, when in fact studies show that the live-virus polio vaccine is the major cause of polio in the United States today.

In addition, the diphtheria and tetanus vaccines are 'stabilized' with formaldehyde- a known carcinogenic.

Lastly, the measles and pertussis vaccines may cause seizures, brain damage, and death.

If vaccines offered benefits only, the government wouldn't need to mandate them.

Much has changed in recent decades in the ingredients of vaccinations. I recently read that some vaccines still carry mercury as a preservative as well as aborted fetal parts, not to mention animal parts as well.

Please consider these extremely important facts about vaccines when considering requiring them of Hawaii's families. Families need choices when it comes to their children. Many parents are unfortunately brainwashed by mainstream media which portrays the necessity of vaccinations. Most are unaware of the billion dollar medical and insurance companies behind the vaccine industry.

As an educated and informed parent and teacher of young children, I beg you to not only consider the possible damaging effects of vaccines on children, but also the fact that this new law is taking away people's rights to make health choices of their own for their beloved children.

It is a slippery slope when taking away parent's rights and choices concerning their children. What will they take away next? What will they require next?

Please contact me if you have further questions.

Sincerely,
Erica Bergquist

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: Strongly oppose HAR-157
Date: Wednesday, December 26, 2018 6:32:31 AM

My name is Swami Om and I strongly oppose mandated vaccines. I have read how dangerous the vaccines are. Parents should have the right to decide.
This would make Hawaii the most vaccinated state in the United States!

Sent from my iPad
Love & Blessings

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Strongly Oppose Possible Vaccination Changes
Date: Wednesday, December 26, 2018 9:35:14 AM

Hello,

My name is Sonni Dawkins and I live in [REDACTED]. I am a mother of two. I strongly oppose the bill to uphold new vaccine requirements for Hawaii. And I support an informed consent status. If there is a risk, there should be choice.

Because there are no long term efficacy studies required by the FDA or CDC, force vaccination causes our children to be the long term study which is inhumane.

Injecting foreign bodies, chemicals and metals into the tissues and bloodstream completely forgoes the bodies natural defense system, surpassing the skin and mucous membranes. This allows these substances to travel to places like the brain without being broken down first (and wrecking havoc on the myelin sheath and areas of the brain.

We should have a choice and decide as parents what the bigger damage would be for our kids-incurring a vaccine injury or contracting the disease.

If you need more information, you can research Miller's Critical Evaluation of Vaccine studies or visit vaxbook.org.

Mahalo
Sonni Dawkins
[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: support for HAR 11-157 from Hawaii Academy of Family Physicians
Date: Wednesday, December 26, 2018 4:33:17 PM

The Hawaii Academy of Family Physicians representing over 330 family physicians statewide strongly supports the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

We respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration,

Nicole Apoliona, MD, FAAFP
President, Hawaii Academy of Family Physicians

NOTICE TO RECIPIENT: If you are not the intended recipient of this e-mail, you are prohibited from sharing, copying, or otherwise using or disclosing its contents. If you have received this e-mail in error, please notify the sender immediately by reply e-mail and permanently delete this e-mail and any attachments without reading, forwarding or saving them. Thank you.

From: [REDACTED]
To: [REDACTED]
Subject: Support HAR11-157
Date: Wednesday, December 26, 2018 10:41:53 AM

Hello,

I support this bill.

Thank you,

Eric Leeson

From: [REDACTED]
To: [REDACTED]
Subject: Fw: Testimony OPPOSING HAR157 rule changes
Date: Wednesday, December 26, 2018 2:28:43 PM

I never received a response for my testimony. please send me a response to verify you have received this.

----- Forwarded Message -----

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]
Sent: Thursday, November 1, 2018, 10:00:16 AM HAST
Subject: Testimony OPPOSING HAR157 rule changes

November 1, 2018

DOCD, [REDACTED]

(808) 586-8300
Bruce S. Anderson, PhD, Director of Health
Hawaii Department of Health
1250 Punchbowl St.
Honolulu, Hawaii 96813

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

I strongly oppose the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

* I'm requesting that this hearing be held on EVERY island.

My name is Natasha Sky. I am a Hawaii resident, voter, mother, health advocate and member of Hawaii for Informed Consent. I'm writing today with my strong concern on the DOH planned changes on immunization policy.

Currently, 18 states allow philosophical exemptions for those who object to immunizations because of personal, moral or other beliefs. **In Virginia, parents can receive a personal exemption only for the HPV vaccine. If Hawaii mandates HPV for school attendance there should be a philosophical exemption available to opt out of this vaccine for a disease which is non communicable, no long-term safety studies and a higher reported number of incidences of adverse reactions than other vaccines. Please consider in the future to follow policy of these states and support adding a philosophical exemption.

HPV vaccine should not be required for school as it does not have any protection to prevention of an outbreak or being spread in a social setting.

When it comes to the changes on MEDICAL EXEMPTIONS please follow example of Illinois SB1410- "A healthcare provider may consider including without limitation the nationally accepted recommendations from federal agencies such as the Advisory Committee on Immunization Practices, the information outlined in the relevant vaccine information statement, and vaccine package inserts, ALONG WITH THE HEALTHCARE PROVIDERS CLINICAL JUDGEMENT, to determine whether any child may be more susceptible to experiencing an adverse vaccine reaction than the general population, and if so, the healthcare provider may exempt the child from an immunization or adopt an individualized immunization schedule." We cannot remove the practitioners ability to use his/her judgement to issue

medical exemptions. This infringes on the doctor patient relationship and violates a doctors right to do their job.

Mandating Medical exemptions to be filed with the DOH is a HIPPA violation.

Requiring schools to file exemptions with DOH is a FERPA violation.

The current religious exemption policy is fine as it is, there is no need for a form to be provided by DOH, with extra requirements, infringing on our religious rights. We do NOT need to prove our religious beliefs. It is unconstitutional. IF however, a DOH form is required for religious exemption please include "The religious exception stated need not be directed by the tenets of an established religious organization."

"In May 2017, Del Bigtree & Robert F. Kennedy, Jr. suspected that HHS was not fulfilling its critical vaccine safety obligations as required by Congress in The National Childhood Vaccine Injury Act of 1986 of assuring improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. A lawsuit revealed that HHS had never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety." <http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

↑↑Our state shouldn't follow ACIP due to lack of safety studies. The general issue of following the ACIP schedule is that there are no studies on the synergistic affect of each vaccine that keeps getting added to the schedule.

"Adding to public concern about vaccines is the fact that immunization is mandated by many state and local school entry requirements. Because of this widespread use, safety problems with vaccines can have a potential impact on large numbers of persons." – CDC

Anti-choice mandates violate civil liberties. Mandated medical procedures degrade modern medicine and destroy the foundations of our health care system. When you give up the power to choose what can be done to your body — in this case what can be injected into you or your child's body — you are no longer a free, autonomous, sovereign individual.

Please have public hearings held on every island concerning these proposed rule changes that will immensely affect our state. Residents need to ask questions and be made aware of such rule changes before they are made.

Sincerely,
Natasha Sky

[REDACTED]

If there is RISK, there must be choice

November 1, 2018

DOCD, [REDACTED]

(808) 586-8300

Bruce S. Anderson, PhD, Director of Health

Hawaii Department of Health

1250 Punchbowl St.

Honolulu, Hawaii 96813

RE: public hearing for the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

I strongly oppose the proposed amendment and compilation of Hawaii Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization."

* I'm requesting that this hearing be held on EVERY island.

My name is Natasha Sky. I am a Hawaii resident, voter, mother, health advocate and member of Hawaii for Informed Consent. I'm writing today with my strong concern on the DOH planned changes on immunization policy.

Currently, 18 states allow philosophical exemptions for those who object to immunizations because of personal, moral or other beliefs. **In Virginia, parents can receive a personal exemption only for the HPV vaccine. If Hawaii mandates HPV for school attendance there should be a philosophical exemption available to opt out of this vaccine for a disease which is non communicable, no long-term safety studies and a higher reported number of incidences of adverse reactions than other vaccines. Please consider in the future to follow policy of these states and support adding a philosophical exemption. HPV vaccine should not be required for school as it does not have any protection to prevention of an outbreak or being spread in a social setting.

When it comes to the changes on MEDICAL EXEMPTIONS please follow example of Illinois SB1410-

"A healthcare provider may consider including without limitation the nationally accepted recommendations from federal agencies such as the Advisory Committee on Immunization Practices, the information outlined in the relevant vaccine information statement, and vaccine package inserts, **ALONG WITH THE HEALTHCARE PROVIDERS CLINICAL JUDGEMENT**, to determine whether any child may be more susceptible to experiencing an adverse vaccine reaction than the general population, and if so, the healthcare provider may exempt the child from an immunization or adopt an individualized immunization schedule." We cannot remove the practitioners ability to use his/her judgement to issue medical exemptions. This infringes on the doctor patient relationship and violates a doctors right to do their job.

Mandating Medical exemptions to be filed with the DOH is a HIPPA violation.

Requiring schools to file exemptions with DOH is a FERPA violation.

The current religious exemption policy is fine as it is, there is no need for a form to be provided by DOH, with extra requirements, infringing on our religious rights. We do NOT need to prove our religious beliefs. It is unconstitutional. IF however, a DOH form is required for religious exemption please include "The religious exception stated need not be directed by the tenets of an established religious organization."

"In May 2017, Del Bigtree & Robert F. Kennedy, Jr. suspected that HHS was not fulfilling its critical vaccine safety obligations as required by Congress in The National Childhood Vaccine Injury Act of 1986 of assuring improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. A lawsuit revealed that HHS had never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety." <http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

↑↑Our state shouldn't follow ACIP due to lack of safety studies. The general issue of following the ACIP schedule is that there are no studies on the synergistic affect of each vaccine that keeps getting added to the schedule.

"Adding to public concern about vaccines is the fact that immunization is mandated by many state and local school entry requirements. Because of this widespread use, safety problems with vaccines can have a potential impact on large numbers of persons." – CDC

Anti-choice mandates violate civil liberties. Mandated medical procedures degrade modern medicine and destroy the foundations of our health care system. When you give up the power to choose what can be done to your body — in this case what can be injected into you or your child's body — you are no longer a free, autonomous, sovereign individual.

Please have public hearings held on every island concerning these proposed rule changes that will immensely affect our state. Residents need to ask questions and be made aware of such rule changes before they are made.

Sincerely,

Natasha Sky



If there is RISK, there must be choice

From: [REDACTED]
To: [REDACTED]; [REDACTED]; [REDACTED]; [REDACTED]
Subject: Fwd: I oppose HR 11-157
Date: Wednesday, December 26, 2018 3:06:46 PM

Begin forwarded message:

From: Yana Dashevsky [REDACTED]
Subject: I oppose HR 11-157
Date: December 26, 2018 at 3:02:48 PM HST
To: [REDACTED]

Aloha DOH,

Mahalo for the opportunity to submit testimony.

This is Yana. I spoke a couple times so you guys should know who I am. Sorry if I got a little serious during my testimony. I'm not suing anyone anytime soon :).

However I will keep researching this topic and continue to try and find new and innovative SCIENTIFIC information on this topic for you all to consider in your decision making process.

You all have an amazing and unique opportunity to stand for TRUTH AND JUSTICE right now. We all truly want health and happiness for ourselves and our babies.

Lets try and have a mature, healthy happy conversation about this and have a civil question and answer discussion panel as many that have given testimony request.

I very much so, hope that the DOE and everyone making decisions is yearning for truth and information as much as I am and that you find it within yourselves, for the sake of our children to come to the table and have a good discussion with the community about this topic.

A panel where not only do you hear testimony, but also answer our questions and demonstrate that you fully acknowledge and answer our concerns into the matter of mandatory vaccinations.

Just for fun, here is one more study I'd like for you to consider:

Dec 22, 2018 by Richard Harris

Research published in a major medical journal concludes that a parachute is no more effective than an empty backpack at protecting you from harm

if you have to jump from an aircraft.

But before you leap to any rash conclusions, you had better hear the whole story.

The gold standard for medical research is a study that randomly assigns volunteers to try an intervention or to go without one and be part of a control group.

For some reason, nobody has ever done a randomized controlled trial of parachutes. In fact, medical researchers often use the parachute example when they argue they don't need to do a study because they're so sure they already know something works.

Cardiologist Robert Yeh, an associate professor at Harvard Medical School and attending physician at Beth Israel Deaconess Medical Center, got a wicked idea one day. He and his colleagues would actually attempt the parachute study to make a few choice points about the potential pitfalls of research shortcuts.

They started by talking to their seatmates on airliners.

"We'd strike up a conversation and say, 'Would you be willing to be randomized in a study where you had a 50 percent chance of jumping out of this airplane with — versus without — a parachute?' " Yeh says.

Only a few people said yes to this outrageous invitation, and they were excluded for reasons of questionable mental health.

The scientists had much better success asking members of their own research teams from Harvard, University of California, Los Angeles (Where Yeh's brother is a surgery professor), and University of Michigan (where a buddy works) about volunteering to participate in the experiment on other aircraft.

In all, 23 people agreed to be randomly given either a backpack or a parachute and then to jump from a biplane on Martha's Vineyard in Massachusetts or from a helicopter in Michigan.

Relying on two locations and only two kinds of aircraft gave the researchers quite a skewed sample. But this sort of problem crops up frequently in studies, which was part of the point Yeh and his team were trying to make.

Still, photos taken during the experiment show the volunteers were only too happy to take part. "I think people are laughing all of the way to the ground," Yeh says.

Oh, there's one important detail here. The drop in the study was about 2 feet total, because the biplane and helicopter were parked.

Nobody suffered any injuries. Surprise, surprise. So it's technically true that parachutes offered no better protection for these jumpers than the backpacks.

"But, of course, that is a ludicrous result," Yeh says. "The real answer is that that trial did not show a benefit because of the types of patients who were enrolled."

If they had enrolled people at high risk for injury, that is people in *flying aircraft*, the results would have been quite different (not to mention unethical).

But something like this happens in everyday medical research. It's far too easy for scientists who have already anticipated the outcome of their research to cherry-pick patients and circumstances to achieve the results they expect to see. This research paper carried that idea to the ridiculous extreme.

The [study's findings](#) were published in the traditionally lighthearted Christmas issue of the medical journal, *BMJ*.

"It's a little bit of a parable, to say we have to look at the fine print, we have to understand the context in which research is designed and conducted to really properly interpret the results," Yeh says. Scientists often read just the conclusion of a study and then draw their own conclusions that are far more sweeping than are justified by the actual findings.

This is a real problem in science.

"I know that people often don't look detailed enough into what is being investigated to know how to interpret the results of a trial," says [Cecile Janssens](#), an epidemiology professor at Emory University.

Janssens was delighted to come across the paper on Twitter. She says like a lot of research, its results are accurate as far as they go, but "the

results can only be generalized to situations where people jump out of an aircraft within a few feet above the ground."

She plans to give this paper to her students with a straight face and see how long it takes for them to get the deeper points about scientific methodology buried in this absurd experiment.

"It will be unforgettable," she says — far better than assigning a straight-ahead scientific study.

Yeh is pleased to see that the fun he had with his colleagues is turning into a teaching tool. He also savors some of the more subtle lessons buried in the paper.

For example, the scientists attempted to submit it to a government registry of research studies, which is required for many studies involving human subjects. They chose one in Sri Lanka to reduce the risk that it would be discovered in advance, spoiling the joke. It was rejected.

"They thought that a trial conducted in this manner could not lead to scientifically valid evidence," he said.

"They're right!" he adds with a laugh.

In fact, the paper acknowledges that the research team members cracked themselves up so much that "all authors suffered substantial abdominal discomfort from laughter."

"Our greatest accomplishment from all of this was we felt very good that we were able to cite Sir Isaac Newton in the paper," he says. They referred to Newton's classic 1687 paper establishing the law of gravity.

Yes, gravity is a law. Mess with it at your own risk.

You can reach NPR science correspondent Richard Harris by email: rharris@npr.org.

Copyright 2018 NPR. To see more, visit <https://www.npr.org>.

Thank you again for this opportunity to testify and I look forward to hearing good news about your organizations.

Mahalo,

Yana

From: [REDACTED]
To: [REDACTED]
Subject: Fwd: I strongly oppose 11-157 proposed rules
Date: Wednesday, December 26, 2018 4:03:09 PM

I am just adding a reference for the reported vaccine injuries from each vaccine including Gardasil outlined on NVIC.org

Dr. Donna Caplan, ND

[REDACTED]

Sent from my iPhone

Begin forwarded message:

From: "Donna Caplan, ND" <[REDACTED]>
Date: December 26, 2018 at 4:00:08 PM HST
To: [REDACTED]
Subject: I strongly oppose 11-157 proposed rules

Aloha,

I strongly oppose 11-157 proposed rules.

I am a licensed Naturopathic Doctor as well as a mother and grandmother. In my family practice as a primary care doctor in Vermont and Hawaii for 24 years, I have had many vaccine injured babies, children, and adults come to me for treatment.

There are many reasons that I oppose the 11-157 proposed rules. I will mention a few of the important reasons due to time.

It is unlawful to require more vaccinations, especially for a child to be able to enter schools and preschools.

Unfortunately, vaccines are not safe and many children and adults have been injured and often debilitated. Reported vaccine injuries can be seen on the VAERS database.

There have never been proper scientific, double-blind studies done to determine the safety and efficacy of individual vaccines, and no studies have been conducted to evaluate the safety of combining multiple vaccinations in one shot or in one office visit, or the cumulative affects of 48 vaccinations starting from birth through early childhood on the current recommended vaccine schedule (before the added proposed vaccines)!

It is absolutely unlawful to require medical interventions that have a history of causing harm and death, and that have not been studied adequately individually, combined, or cumulative over time.

The vaccines are manufactured with many chemicals and adjuvants that are neurotoxic and

toxic to living beings in general like aluminum, mercury compounds, formaldehyde, phenol, polysorbate 80, to name a few. Some contain material from aborted human fetuses, dog kidneys, genetically modified insects and viruses. How do these interact with a baby or adult's DNA? Do you know? No studies have been done. Animal and aborted human cells can easily be contaminated by other unknown viruses, which may lead to the recipient developing cancer, autoimmune and other conditions. Has this been studied? No.

Gardasil, an hpv vaccine, that is being proposed for requirement, has been shown to have many terrible side effects and reactions, yet hpv is a very slow growing cancer that is easily treated and screamed for.

Due to time I must end here,

Mahalo,

Dr. Donna Caplan, ND



Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, December 26, 2018 8:37:18 AM

I strongly oppose the new mandatory vaccine schedule for Hawaii.

HAR 11-157 requires influenza vaccines, a good friend of mine, Albert Salsedo, acquired Guillain- Barre syndrome after receiving the influenza vaccine. Making this a requirement for all children will increase the incidence of this horrible, paralyzing disease.

Fifty-eight thousand adverse reactions—including *four hundred twenty-seven deaths*—have been reported after HPV vaccine injections in the U.S. alone. (Search the U.S. Government's VAERS Data) <http://www.medalerts.org/>) Insisting that young healthy boys and girls receive this vaccine, when the rates of cervical cancer and penile cancer deaths are so low, and the adverse reactions are so high, is unconscionable.

Thank you for all that you do for the health of this amazing state,
Sammee Albano RN

From: [REDACTED]
To: [REDACTED]
Subject: HAR 11-157
Date: Wednesday, December 26, 2018 4:15:24 PM

Aloha,

I am writing to oppose HAR 11-157 for mandatory vaccines. I think there should always be an option of what we are putting into our bodies and our children's bodies.

My father had an adverse reaction from the flu shot 3 years ago where he developed Guillain Barre Syndrome (GBS). He hadn't had a flu shot in almost 20 years and due to traveling for work thought it might be a good idea. The same day he said he felt odd and knew something was not right. The next day he felt really sick and weak, and by the end of the day had double vision, weakness, severe headache and body aches. He went to the ER and when they were doing the routine check in his blood pressure was abnormally high. They initially thought he had a stroke. When the neurologist was involved and did all of the test it was obvious that it was a direct linked to the flu vaccine and not a stroke. The Dr. said my dad was one of the lucky ones all of his other patients at that time would not be walking out of the hospital like he was. For 6 months he had intensive rehabilitation and detoxing of his system to regain strength in his body. He had to wear special glasses to help his eyes correct the severe double vision he was experiencing. Chiropractic and acupuncture appointment after appointment and after a year he was starting to feel like himself again and three years later I feel so blessed that he is fully back to himself.

They cannot pinpoint why it happened to him, if its genetic or not. What I know is I never want anyone I know to go through any of that. I am so grateful that my father has access to the absolute best Dr.'s at the Mayo clinic who gave him the best treatment plan possible.

The 3 vaccines that you are talking about have just awful track records in other countries where they have already stopped requiring them. They are not properly tested and to force that upon people is just wrong. The medical repercussions that they may have in the future are unknown, but why is that even a risk we want to take with our future generations.

Mahalo,

Kimberley Nagel

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: Im 10 and I OPPOSE Har11-157
Date: Wednesday, December 26, 2018 1:55:52 PM

Dear Department of Health. I am 10 years old and my name is Lily Sky. I OPPOSE Har11-157. I have friends who vaccinate and I dont want the HPV vaccine to be mandated, as I dont want my friends to get this vaccine. There are dangerous side effects from this vaccine you are trying to mandate for thousands of children. Kids do not have sex in school, theres no reason for kids to get this vaccine if theyre not going to have sex. Kids should be taught about safe sex and be able to decide if this is a vaccine they want or need. They should be able to make this choice.

Thankyou, Sincerely Lily Sky
[REDACTED]

From:

To:

Subject:

Date:

[REDACTED]
[REDACTED]; [REDACTED]; [REDACTED]
Testimony

Wednesday, December 26, 2018 2:36:23 PM

Hawaii Midwifery Council
Rachel Curnel Struempf, President

In opposition

Aloha,

Thank you for the opportunity to submit testimony. The Hawaii Midwifery Council strongly opposes the increase in required immunizations for the children of Hawaii. We feel this is not in the best interest of the children who would be subject to this

New policy. Furthermore, we feel the DOH does

Not have the authority to unilaterally make this decision and it should require legislation to be implemented.

Thank you for your time.

Rachel Curnel Struempf, DEM

Hawaii Midwifery Council

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157
Date: Thursday, December 27, 2018 8:03:05 AM

I oppose this bill to make these vaccine and flu shots mandatory. They should be optional.

Sarah Tiritas
Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: I support the bill HAR11-157
Date: Thursday, December 27, 2018 2:50:50 PM

To Whom It May Concern:

The purpose of this email is to support the bill HAR11-157.

Diseases have detrimental consequences to health and well-being. If these diseases can be prevented through evidence-based immunization as part of preventive services, then overall public health promotion and disease prevention may be achieved.

Respectfully,

Melford Lazarte, APRN-Rx, AGACNP-AC, ACNPC-AG, CNOR

From:
To:
Subject:
Date:

[REDACTED]
PLEASE DO NOT Approve mandatory vaccinations for our school children
Thursday, December 27, 2018 12:56:40 AM

There are places for our government to intercede and help in our lives. This IS NOT one of them. Please reject any attempt to have mandatory vaccinations for our school children or anyone for that matter.

Stefan P. Schweitzer

From: [REDACTED]
To: [REDACTED]
Cc: [REDACTED]; [REDACTED]
Subject: REP Bill Posey Calling Investigation CDC's MMR reasearch fraud
Date: Thursday, December 27, 2018 8:52:29 AM

<https://www.c-span.org/video/?c4546421/rep-bill-posey-calling-investigation-cdcs-mmr-reasearch-fraud>

Sent from my iPhone

From: [REDACTED]
To: [REDACTED]
Subject: FW: HAR-11-157 Immunization & Examination Proposed Rule Change
Date: Friday, December 28, 2018 9:05:24 AM

Here's another

From: DOH webmaster
Sent: Friday, December 28, 2018 7:52 AM
To: Ungos-Markham, Jocelyn [REDACTED]
Cc: Yoshiura, Corliss [REDACTED]
Subject: FW: HAR-11-157 Immunization & Examination Proposed Rule Change

Forwarding an inquiry below.

Thank you,
DOH Web Mail (vc)

NOTICE: Individuals should always review or confer with their supervisors about the request and composed responses to ensure it conforms with current DOH position on various policy areas. If a question and or response is current on potential "hot topic" or a "controversial" issue review and approval from the appropriate deputy may be required.

From: Momi Lovell [REDACTED]
Sent: Thursday, December 27, 2018 5:40 PM
To: DOH webmaster [REDACTED]
Cc: Momi Fernandez [REDACTED]
Subject: HAR-11-157 Immunization & Examination Proposed Rule Change

Aloha: This email is submitted as testimony in opposition to the proposed HAR-11-157 immunization and examination rule change by making immunizations mandatory for children. This is especially dangerous for a child/children with (a) compromised immune system(s) and children born with organ disfunction or not fully developed and newborns with spina bifida. Side effects experienced by children too young to communicate their pain and discomfort are especially at risk of being misdiagnosed or their violent reactions minimized.

I am against mandatory immunization for the following reasons:

1. I believe **human rights are violated** when immunizations are mandatory. Human rights to health and health care afford the opportunity to make individual decisions regarding health decisions and to participate in decisions that affect health ... (National Economic & Social Rights Initiative [NESRI], subtitle Participation). At times that means that **we may choose NOT to participate in health initiatives/mandates when we believe our health can be compromised or lessened in any way.**
2. "Health is a fundamental human right", Human Rights Day 2017, one of the World Health Organization (WHO) guiding principles and equal to another WHO guiding principle: "Good health is also clearly determined by other basic human rights including access to safe drinking water and sanitation, nutritious foods, adequate housing, education and safe working conditions." Source: <https://www.who.int/mediacentre/news/statements/fundamental-human-right/en/>.
3. Personal experience with my daughter who suffered **violent reactions to being immunized** on Maui during the

early to mid-1980s. Even half-doses did not alleviate the reactions she suffered for more than a week after being immunized. I am against putting any other child through that misery.

4. After reviewing studies from the US., WHO, UK, Europe, several conclusions are in common. That **there is no vaccine against resistance or refusals that are rooted in social-cultural, religious and political contexts.** That **certain vaccines are promoted more than others based on pharmaceutical companies applying pressure on doctors, hospitals and medical clinics.** In other words, vaccines are promoted because the process allows for pharmaceutical companies to get rich and doctors and hospitals are rewarded for selling the product widely. Source: Dr. Patrick Gentempo research and documentary series: "Vaccines Revealed". The same source shared evidence that vaccines are especially dangerous to people (not just children) diagnosed with autism and in some cases have caused autistic symptoms in children and adults that last for years. It is also dangerous if one has the HIV virus. The quality of life diminishes drastically in those patients.

It is very disappointing that the Department of Health (DOH) doesn't look toward traditional medicine, homeopathic methods that boost the immune system to better protect against disease, whether viral or bacterial infections. Sources and resources are available, however, I don't know of any effort that the DOH has made to bring these valuable and knowledgeable practitioners to the table and within the conversation to listen to viable preventative measures and treatment therapies. These therapies are not expensive and promote health at the highest level by addressing the health of mind, body and spirit.

Instead of immunizing newborns, **babies have a natural protection by leaving the vernix caseosa on their bodies after birth** and allowing it to be absorbed into the skin. This **is the first natural defense babies are born with that protects their immune system.** There are Native Hawaiian la'au lapa'au practices that enhance baby's immune system that have proven to be effective for hundreds of years before and after western contact. I utilize those remedies for my children and grandchildren and teach other mothers upon request. Other native cultures know the same truth and pass down those traditions.

DOH should be promoting more breast feeding. Breast feeding transfers natural defenses that help to nurture a newborn and provide additional defenses that can benefit a child for years to come.

It is interesting that acute flaccid myelitis (AFM) has surfaced during a time when the U.S. suffers from division, unstable stock market, vivid and cruel racism and the worst addiction problems in society supported by doctors and pharmaceutical companies. National leaders demonstrate the lack of respect toward immigrants and homosexuals/trans-gender people, while the middle class is disappearing all while the "national tribe" is losing faith and hope in the political system. The same was true prior to the Great Depression of 1929. Caroline Myss, "Anatomy of the Spirit" (Harmony Books, NY, copyright 1996, 2017) writes of the common "crippling effects" prior to the epidemic of polio in the 1930s. "What adults suffer, children also suffer by becoming weak and susceptible to viral disease similar to the economic dis-ease and social illnesses we are experiencing today. The "tribe", as a nation, took on both physical weakness and resilience by electing Franklin D. Roosevelt as President, as an aligning symbol of much needed hope. Polio and AFM both represent a weakness in the first energy center as it represents tribal power that embraces the "All Is One" tribal energy. Otherwise, what we experience as a nation; both positive and negative. The polio epidemic is viewed as a result of the Great Depression, affecting the entire nation or "tribal energy". It took a physical tribal event and experience of physical strength to "heal" the "tribal spirit". "A sense of heroism and tribal unity, supported by increased jobs, restored pride, power, and honor to each tribal member."

In the United Kingdom, European countries, India and Pakistan where mandatory vaccinations have been proposed, the process has met with protests, marches and resistance. Distrust in government process, policies and processes that diminish the voices of those who demand collaboration and open communication with inclusion rather than exclusion by limiting input and opportunities to decide and express the "tribes" health concerns, remedies, and quality of life that effects life expectancy. "A 2016 ASSET analysis published by Science in Society ... once again did not find evidence of a relationship between national mandatory vaccination policies and increased vaccine uptake in European countries ... "Countries where a vaccination is mandatory do not usually reach better coverage than neighbor or similar countries where there is no legal obligation." Furthermore, a 2015 study revealed "a growing vaccine hesitancy and concern about vaccine safety among healthcare workers and their patients in Europe. Researchers reported healthcare workers had "significant mistrust of pharmaceutical companies who not only had financial interests but also did not communicate sufficient information about side

effects ...”

Respectfully submitted,

Momi Lovell

From: [REDACTED]
To: [REDACTED]
Subject: FW: I oppose HAR 11-157
Date: Thursday, December 27, 2018 8:48:07 AM

We received this in our agency email today.

From: Toadstool Films [REDACTED]
Sent: Wednesday, December 26, 2018 11:26 PM
To: SHPDA Internet [REDACTED]
Subject: I oppose HAR 11-157

Dear DOH officials,

I am writing to express my staunch opposition to HAR 11-157. I was in attendance at the teleconference meeting held in the state building on Maui and I was denied the opportunity to give testimony. I am opposed to the new rules that DOH plans to implement on the grounds of religious freedom, physical sovereignty, and submission to force under duress. You simply cannot tell your constituents that you are going to force them to pay taxes for education and deny their children an education unless they submit to injections which have been proven to be harmful in many events. It's not hard to find the evidence of youth being harmed and even dying as a result of the hpv vaccine.

I have three children who range from full vaccination to partial vaccination that have been harmed in different ways from vaccines. My oldest daughter is 13 and after receiving her latest vaccination has suffered multiple bouts of angioedema that cause her to miss school. My second daughter is 6 and has permanent nerve damage in her legs. My youngest almost died from fever and dehydration the week of her last vaccination. Please, I am begging you not to mandate me to further harm them so that they can attend school.

Not only would this be a clear violation of our rights, it is legalized theft to take my tax dollars for something that I would be denied access to. Further, this is the equivalent of taxation without representation. If I am forced to take this to court then I suppose I will do what I must to ensure my children are not denied their right to an education. I am willing to defend them and all of the other children you plan to inject with harmful toxins if I must.

I appreciate you at the Department of Health taking the time to understand the reasons why I am not willing to follow the proposed guidelines of HAR 11-157. I humbly ask you to please reconsider the use of force and coercion in reaching your objectives.

Sincerely, Brandi Chanthathep

[REDACTED]

From: [REDACTED]
To: [REDACTED]
Subject: Ha11-157
Date: Thursday, December 27, 2018 1:50:41 AM

Dear Health Department officials,

It is please imperative that we continue to vaccinate children according to our current public health standards. The opposition to this bill is not thinking on a scientific basis and it will adversely affect our community as these diseases can be lethal.

We need to continue to vaccinate and prevent a medical and moral travesty. Measles almost wiped out the Hawaiian population in the past when an unvaccinated population was exposed by sailors bringing in the virus. History should not repeat itself due to ignorance nor should we drop our standards.

Sincerely,

Bridget S. Bongaard MD, FACP, HCMD



HAWAII
FOR
INFORMED
CONSENT

Disease Outbreak Control Division (DOCD)
1250 Punchbowl Street
Room 443
Honolulu, HI 96813

via email

December 28, 2018

RE: STRONG OPPOSITION TO HAR 11-157 PROPOSED RULE CHANGES

Dear Disease Outbreak Control Division:

Hawaii for Informed Consent (HFIC) is a non-partisan group of ordinary people with over 1600 members whose mission is to defend the basic human right of freedom to make informed, voluntary, healthcare choices for ourselves and our minor children. We advocate for a more accurate and complete informed consent for vaccine consumers through continued research, education, and empowerment of our citizens, legislators, and health care professionals. Our legislative goals aim to preserve flexible medical, religious, and conscientious vaccine exemptions for all human beings, free from coercion, harassment, or penalty, as we bring respect, compassion, and awareness to the fact that vaccine injury is real and becoming more prevalent every day.

The Hawai'i Department of Health (DOH) is proposing an amendment and compilation of Hawai'i Administrative Rules (HAR) Title 11, Chapter 157, "Examination and Immunization." The proposed rule changes seek to:

- ▶ increase the vaccine *requirements* for Hawai'i's children ([Exhibit A](#)) by adding multiple doses of seven recommended vaccines by the Advisory Committee on Immunization Practices (ACIP) of the Department of Health and Human Services .
- ▶ update and clarify the immunization and examination procedures for school, post-secondary school, and child care facility attendance in Hawai'i by adopting as *requirements* ACIP's "General Best Practice Guidelines for Immunization" ([Exhibit B: page 3](#)).

HAWAII FOR INFORMED CONSENT

[Redacted signature block]

[Redacted footer text]

First do no harm

HFIC opposes the DOH-proposed rule changes for the following reasons:

1. The vaccine **recommendations** and administration **guidelines** put forth by ACIP are not intended to be **requirements**, or blanket state mandates for school entry.

The ACIP develops recommendations on how to use vaccines to control disease in the United States. The Committee's recommendations are forwarded to CDC's Director for approval," who then publishes and creates "the final and official CDC recommendations for immunization of the U.S. population."

<https://www.cdc.gov/vaccines/acip/recommendations.html>

In its online document, "General Best Practice Guidelines for Immunization," the ACIP clarifies its advisory function "for clinicians and other health care providers who vaccinate patients" to "help vaccination providers to assess vaccine benefits and risks." These **general recommendations and guidelines** are intended to **guide** providers' discussions and decision-making process with unique, individual patients. <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/intro.html>

ACIP members publicly have demonstrated questionable judgment and negligence to protect Americans from harm; watch [this video \[hyperlinked here\]](#) as they unanimously approve a new vaccine and **subsequently** discuss the myocardial infarction "signal" discovered in preliminary and incomplete testing of that vaccine. They resolve to track future occurrences of myocardial infarction in the **post-marketing** period for a few years, rendering the people who receive the vaccine as **human guinea-pigs**. ACIP members' also demonstrated remarkable unresponsiveness to public testimony presented, including personal vaccine injuries, professional experiences in the healthcare environment, as can be observed [here](#).

Vaccination is a **medical procedure** that carries risk of serious injury, death, and risk of failure to prevent infection and transmission for some individuals. Physicians must be free to utilize their best judgment and intimate patient knowledge in weighing the genetic, biological, and environmental risk factors which could render some patients more susceptible to vaccine reactions than others.

Physicians must consider the four core universal values defined in medical ethics:

- **Autonomy: The rights of the individual to self-determination**
- **Beneficence: Taking actions that serve the best interest of the patient**
- **Non-maleficence: "First Do No Harm"**
- **Respect for Human Rights: The inalienable, fundamental rights to which a person is inherently entitled simply because she or he is a human being**

https://en.wikipedia.org/wiki/Medical_ethics

Neither ACIP nor the CDC has any regulatory authority to force vaccines onto the public by law. Furthermore, unelected, career individuals of an administrative agency such as the DOH should not have any statutory authority to promulgate federal vaccine recommendations and individual practitioner use guidelines into state law as a one-size fits all requirement for entry into Hawaii schools and daycare facilities.

HAR 11-157 has not been updated since July 2002, therefore the DOH's desire to have Hawaii's vaccine policy conform with national recommendations and recognized standard medical practices is understandable. Most physicians in the state of Hawai'i already consider CDC recommendations and guidelines. *There is a significant difference, however, between vaccine recommendations and vaccine requirements.* Currently, Rhode Island is the only state to require the entire list of ACIP-recommended children's vaccines for school eligibility. Rhode Island's exemptions to vaccination, notably, are more broad than Hawaii's. ***Therefore, if these rules were to be adopted, Hawaii would have the most stringent childhood vaccination requirements for school eligibility in the US.***

HFIC respectfully urges the Hawai'i Department of Health to modify its language in the proposed amendment to replace the word "requirements" with the word "recommendations," in accordance with the verbiage of the US Department of Health and Human Services' Centers For Disease Control and Prevention (CDC).

- 2.** HFIC discourages the DOH from expanding the list of vaccines required for school entry, since the current requirements *already* conform with the national standard.

Please consider the following statements of fact:

- Congress passed *The National Childhood Vaccine Injury Act of 1986* to shield vaccine manufacturers from civil product liability

lawsuits for all harm caused by vaccines, including permanent disability and death (Public Law 99-660).

<https://www.ncbi.nlm.nih.gov/books/NBK220067/>

- Since the 1986 Act sheltered vaccine manufacturers from liability, the recommended childhood vaccination schedule has exploded to a current **74 doses of 17 different vaccines** (commencing in pregnancy, on the first day of birth, and continuing until 18 years old). See the CDC normal childhood schedule [here](#) (as well as the recommended CDC schedule for the immunocompromised....whom, contrary to what we are lead to believe, also receive most vaccinations.
- Both Tdap and Influenza vaccine package inserts state that neither safety nor effectiveness have been established in pregnant women; yet both vaccines are routinely recommended by ACIP for this specific population. Doctors are merely “encouraged to register [their patients] in a pregnancy registry” which later, without patient consent, becomes the manufacturer’s post-marketing data or “research.”—a [violation of the spirit of the Nuremberg Code](#) that individuals must expressly and voluntarily offer their informed consent to participate in medical research. <https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm142764.pdf> [Please refer to section 8.1 in this link]
- The US administers 2-3 times more childhood vaccines than any other developed nation, and yet we have the highest infant mortality rate in that category. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3170075/?tool=pubmed>
- According to CDC statistics, we now have the *sickest generation* of children in the history of mankind: <https://www.ncbi.nlm.nih.gov/pubmed/21570014>
 - 54% of children suffer from chronic illness such as autoimmune and/or neurological disease, allergies, and asthma
 - 1 in 6 are diagnosed with neurodevelopmental disorders such as ADHD/ADD, autistic spectrum disorder, tics, speech delays
 - 1 in 36 have autism <https://www.cdc.gov/mmwr/volumes/67/ss/ss6706a1.htm>
 - 13-25% of children require special education learning environments
- The HPV vaccine (Gardasil) is supposed to counter the effects of a sexually transmitted disease which is not communicable in the school setting. It is a highly controversial vaccine that has proven to be neither safe nor effective. (Please see both the detailed and heavily referenced article recently published in the [Maui Independent](#) and [Mary Holland’s book, The HPV Vaccine On Trial](#)).
- *The potentially dangerous, synergistic and long-term effects of the ever-growing childhood vaccination schedule has NEVER been evaluated for safety.*
 - A 2013 study by the prestigious Institute of Medicine (IOM)

concluded that:

"The key elements of the entire [childhood vaccine] schedule: the number, frequency, timing, order, and age of administration of vaccination have not been systematically examined in research studies."

- In May 2017, Robert F. Kennedy, Jr. (childrenshealthdefense.org) & Del Bigtree (icandecide.org) filed a lawsuit against the US Department of Health and Human Services, suspecting it was not fulfilling its critical vaccine safety obligations.

DHHS is required by Congress as per the NCVIA of 1986 to assure "improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions". ***The lawsuit revealed that DHHS had never—not even once—submitted a single biennial report to Congress detailing any improvements in vaccine safety.***

<http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

It is evident that increasing vaccination requirements via rule changes is supported by neither the public nor the Legislature. In 2016 the Hawai'i State Legislature, with checks and balances of the full complement of legislators and formal public input, opted not to proceed with vaccine mandates such as: HPV for all seventh graders (SB2316/HB1910), Influenza vaccine for all healthcare workers (SB2394/HB1945), and a bill for Hawai'i to automatically adopt ACIP guidelines and recommendations *without* this public hearings process (SB2393/HB1946); each bill failed when submitted through the rightful legislative process.

3. Requiring Healthcare Providers to adhere to the ACIP's Best Practices Guidelines for Immunization (Exhibit B) may interfere with the sacred doctor-patient relationship on many levels, but especially as it pertains to writing **medical exemptions**. It is worth stating again that the proposed practice guidelines should remain just that: guidelines— not requirements.

The proposed amendment requires medical exemptions to vaccination to be written "in a form or format specified by the department,"... "due to a stated cause, in conformance with recognized medical practices."... "Issuing physicians [shall] forward a copy of the

form to the department.” This language is too vague and too restrictive at the same time, and there are three inherent problems with this proposed change:

- A. If requiring a medical exemption to vaccination were to be based solely on ACIP’s (“recognized medical practices”) table of contraindications, *this would be a deliberate act denying individual rights to informed consent to medical risk-taking, as well as a breach of Medical Ethics by the physician. ACIP’s Guidelines and CDC handouts, Vaccine Information Statements (VISs), do not contain the same detailed adverse events (possible side effects) as the vaccine manufacturer’s package inserts.* In fact, the primary condition that qualifies as a contraindication to most vaccines according to ACIP (exhibit B , Table 4-2) is “severe allergic reaction (e.g., anaphylaxis) after a previous dose”. Most autoimmune and neurological disorders, as well as collapse or shock-like state, seizure ≤ 3 days, family history of seizures, or even Sudden Infant Death Syndrome (SIDS) are not considered contraindications by ACIP for giving vaccines. We contend that physicians ought to consider these conditions as contraindications, based on the body of independent peer reviewed medical literature linking acknowledged vaccine components to neurological system effects. [see [here](#), [here](#), [here](#)]
- B. Physicians who otherwise might be uncertain of the safety of vaccination might feel more compelled to recommend vaccines versus not recommend vaccines if vaccines were required by law (HRS 302A-1162 Rules) to follow ACIP guidelines, since all providers are also indemnified under the 1986 NCVIA—protecting providers from vaccine injury lawsuits. This potentially would not be in the best interest of those individual patients’ well-being.
- C. The proposed rule changes would require physicians to submit copies of medical exemptions directly to the DOH. This opens the door for the health department to scrutinize those medical exemptions, try to deny them and harass physicians who are writing them (which has been ongoing in California since SB277 passed there).

Physicians’ best professional judgements, utilizing their intimate patient-specific, as well as family history knowledge, should be the sole determining factor in whether a medical exemption is warranted....period. The “Precautionary Principle of Medicine” must be upheld and not be restricted by bureaucratic over-reach. No children should be forced to risk their lives, supposedly to protect others.

- **The recognized alternative treatments or procedures, including the option of not providing these treatments or procedures;**
 - **The recognized material risks of serious complications or mortality associated with:**
 - a. **The proposed treatment or procedure;**
 - b. **The recognized alternative treatments or procedures; and**
 - c. **Not undergoing any treatment or procedure;...and**
 - **The recognized benefits of the recognized alternative treatments or procedures**
- https://www.capitol.hawaii.gov/hrscurrent/Vol13_Ch0601-0676/HRS0671/HRS_0671-0003.htm

4. Finally, HFIC opposes the existing AND the proposed rules which violate both Federal privacy law [Family Educational Rights and Privacy Act (FERPA)], as well as Hawaii's HAR 8-34 [pertaining to the Department of Education (DOE)] by requiring schools to report the names of children with medical and religious exemptions to the DOH.

<https://www2.ed.gov/policy/gen/guid/fpco/ferpa/index.html>
<http://boe.hawaii.gov/policies/AdminRules/Pages/Admin-Rule34.aspx>

The DOH may gather and report aggregate numbers of students in non-compliance with vaccine requirements, but should not be allowed to report personally identifiable information (PII). Current

- QUESTIONS HFIC WOULD LIKE TO SUBMIT FOR THE RECORD:**
1. How will these new requirements financially impact schools, private daycare centers, and private healthcare practitioners?

- state law* does not require schools to violate federal privacy laws.
2. Has there been a detailed cost/benefit analysis on exactly what costs to DOH to put out the training materials for educating public to implement this mandate? What would be the costs to taxpayers to purchase Vaccines For Children (VFC) for DOH's new requirements? What would be the costs to DOE to implement the administrative and operational requirements of this mandate? Have costs been analyzed for small businesses to implement this new mandate?
 3. If healthcare providers were not to strictly adhere to the ACIP's Best Practice Guidelines for Immunization procedures and/or abide by the list of vaccines in Exhibit A, Table 1, would there be fines and penalties? If so, how would compliance be enforced? Who will determine and how would penalties and fines be determined and assessed? For whom--doctors? Parents? Schools? Principals?
 4. There are almost 300 vaccines currently in development. How many will ACIP approve and is there any limit to the number and nature of vaccine recommendations DOH will convert to requirements for the people of Hawai'i?
 5. What would be the process for medical exemption approval, and who will be in charge of approvals/rejections?
 6. The members of HFIC *were shocked to learn* that PII regarding our children's religious and medical vaccination exemptions were being reported to the DOH by the DOE, *without* our express consent. How will the DOH handle multiple lawsuits in regard to this violation of privacy laws? Will these intentional violations of FERPA jeopardize Federal funds to Hawai'i's public schools, as well as funding for special education from the Office of Special Education Programs? If not, what kind of assurances have been secured?
 7. Does the DOH take adequate action to safeguard privacy of the records it currently maintains, and can people reasonably expect that private medical information will remain private? Where is the database of student vaccination records being stored and to whom distributed once the DOH has acquired this information?
 8. ***Are the current proposed rules in violation of Hawai'i Revised Statute 671-3 re: Informed Consent?*** Is information

regarding the following required to be discussed, in an accurate and complete fashion, with each patient, in regards to each vaccine?

HFIC appreciates the mission statement of the Hawai'i Department of Health as stated to "protect and improve the health and environment for all people of Hawai'i", yet we are concerned that the proposed amendments to HAR 11-157 may present unforeseen individual-, family-, and society-wide health, financial and legal burdens on our ohana. Preventing the spread of infectious disease is important; however, establishing *true health*, in both individuals and the community, is incumbent upon so many factors beyond simply increasing antibody levels to just 17 of the hundreds of known and unknown infectious agents.

We are experiencing an *absolute epidemic of chronic childhood neurological and autoimmune illnesses*. If we are to protect and improve the health and environment of *all people—not just immunocompromised people for whom mass vaccination policies are nominally intended to protect*—then every health department, including Hawai'i State DOH and federal health agencies, *MUST* begin focusing on this alarming crisis, which will have grave impact on us socially and economically. Public health agencies cannot myopically focus merely on increasing vaccine uptake, "thereby" eradicating infectious diseases—a notion which independent scientific studies have and continue to challenge. The ***ever-unsettled***, larger body of industry-independent scientific research is pointing more and more toward vaccination and [*acknowledged vaccine components and contaminants*](#) as possible culprits in neurological and autoimmune disorders (see [here](#) and [here](#)).

We thank you for your time and consideration of this critical issue regarding children's health.

Hawaii For Informed Consent

cc:

[Redacted]

Governor Ige
DOH Director Anderson

From: [REDACTED]
To: [REDACTED]
Subject: Testimony in Favor of HAR 11-157
Date: Monday, December 31, 2018 2:12:34 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Trudy K. Murakami

From:
To:
Subject:
Date:

[REDACTED]
Testimony for Hawaii Administrative Rules Chapter 157
Monday, December 31, 2018 2:41:42 PM

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Lurena Engel

From: [REDACTED]
To: [REDACTED]
Subject: Endorsement of updated Hawaii Administrative Rules, Chapter 157
Date: Tuesday, January 01, 2019 8:30:49 AM
Importance: High

Thank you for this opportunity to provide testimony. I am writing to strongly support the proposed update to the Chapter 11-157 administrative rules as a community member and strong advocate for public health and safety in Hawaii. The proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP), the officially accepted professional organization that makes recommendations regarding immunizations. ACIP voting members have professional expertise in vaccinology, immunology, pediatrics, internal medicine, nursing, family medicine, virology, public health, infectious diseases, and preventive medicine. A consumer representative also provides perspectives on the social and community aspects of vaccination. ACIP provides evidence-base recommendations that take into account disease epidemiology and burden of disease, vaccine efficacy and effectiveness, vaccine safety, the quality of evidence reviewed, economic analyses, and implementation issues. ACIP has consistently made prudent recommendations that take into consideration possible adverse effects, costs, and other concerns.

Public health research clearly shows that communities with more vaccine exemptions have a greater risk for vaccine-preventable disease outbreaks. Ideally, limiting exemptions to those that are medically indicated, improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders. Without vaccinations, ongoing cases and outbreaks of measles, mumps, rubella, diphtheria, pertussis (whooping cough), tetanus, meningococcal meningitis, and *Hemophilus influenza* septicemia and meningitis would continue as they had 100 years ago, causing death, disability and severe illness that affected the lives of individuals and communities. These micro-organisms still exist. Within the past few years alone, we have had mumps, measles, rubella, pertussis and hepatitis A outbreaks in Hawaii as well as ongoing cases of hepatitis B, and cancers caused by human papilloma virus (HPV). Vaccines today are as important as law enforcement is to crime. They are an essential part of a morally responsible society.

I wholeheartedly endorse, and respectfully request that the proposed changes to Hawaii Administrative Rules, Chapter 11-157 be passed for the ongoing protection of the health and safety of the people and community in Hawaii.

Thank you for your consideration.

Glenn M. Wasserman, MD, MPH
Chief, Communicable Disease and

Public Health Nursing Division
State of Hawaii Department of Health



Testimony of
Hawaii Immunization Coalition (HIC)

Before:
Department of Health
State of Hawaii

Re: Hawaii Administrative Rules (HAR) Title 11, Chapter 157, “Examination and Immunization”

Dr. Bruce Anderson, thank you for this opportunity to provide testimony on the proposed rules.

The Hawaii Immunization Coalition (HIC) **strongly supports the HAR11-157 proposed rules.** This update of the Administrative Rules would establish immunization and requirements for school, post-secondary school, and child care facility attendance in Hawaii and to provide for the immunization of indigents and other high-risk individuals. Mandatory vaccination required set by the State of Hawaii, and specifically the Department of Health, are selected to protect those most vulnerable.

- More than 732,000 American lives were saved by childhood vaccination in the past 20 years.
- School health requirements for attendance/registration that include vaccination are a valuable strategy for keeping our schools safe for children who **can** get vaccinated and for those who **cannot** because of medical reasons.
- School immunization regulations rely on **herd immunity** – that at least 93% of the school population is vaccinated - to protect students.

These immunization updates will bring much needed, up-to-date Advisory Committee on Immunization Practices (ACIP) requirements to our current rules. This update is especially important to require students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels, especially for the HPV vaccine.

The reality is that no vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and persons with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, these vulnerable groups will stay protected. The vaccinated students protect those who cannot be immunized.

The Centers for Disease Control and Prevention (CDC) clearly states:

- State and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases (VPDs).
- Studies have shown that vaccine exemptions tend to cluster geographically, making communities with more vaccine exemptions at greater risk for disease outbreaks.

The Hawaii Immunization Coalition (HIC) is a state-wide, community-based non-profit 501(c) 3 coalition of public and private organizations and concerned individuals whose mission is to promote effective strategies to ensure that all of Hawaii’s families are appropriately vaccinated against vaccine-preventable diseases. Focus: Immunizations across the lifespan. The coalition has been active in Hawaii since 1979 and has more than four hundred immunization supporters.

We respectfully request that the Hawaii Administrative Rule 11-157 be supported and passed for the reasons noted above.

Thank you for your consideration.

The Hawaii Immunization Coalition (HIC) is a statewide, community-based 501C (3) non-profit organization working to ensure all of Hawaii’s families are appropriately vaccinated against vaccine-preventable diseases

Tax ID

Dear Sir or Madam,

I am appalled that the Hawaii Department of Health is considering mandatory vaccinations for children for the human papilloma virus. How can anyone who oversees the health of Hawaii's children seek to force a vaccination which may potential have serious side effects. Is the department so in bed with the pharmaceutical industry that it is ignoring safety issues?

While U.S. citizens are prohibited from suing vaccine manufacturers, lawsuits have been launched in Japan, France, Ireland, Spain, and Columbia claiming HPV vaccine harm.

It is beyond question that some children are permanently disabled or die from their vaccine exposures. A broad spectrum of suspected and confirmed adverse vaccine events has grown in the decades from the beginning of mass vaccination. (U.S. Dep't of Health Res. & Human Servs. Admin., National Vaccine Injury Compensation Program Monthly Statistics Report (2017)).

In the U.S. the NVICP has paid affected families approximately \$3.7 billion since it began taking claims in 1989. <http://law.emory.edu/elj/content/volume-67/issue-3/articles/liability-vaccine-injury-united-european-world.html>.

The Vigibase database of the World Health Organization has compiled more than 86,000 serious adverse event reports for Merck's HPV vaccine. They include nervous system disorders (39,092), respiratory, thoracic and mediastinal disorders (6060), vascular disorders (5766), nervous system disorders (39,092), reproductive system and breast disorders (3267), cardiac disorders (2604), and blood and lymphatic system disorders (2035). <http://www.vigiaccess.org/>

Among 12 - 17 year olds, 45,000 adverse events have been reported.

The number of AE's reported for HPV vaccines, in each country, are overwhelmingly higher than that for other vaccines. But national health authorities and medical professionals continue to deny any causal relationship between HPV vaccines and AE's.

Under the Freedom of Information Act, in 2013 Judicial Watch received documents from the Department of Health and Human Services (HHS) revealing that its National Vaccine Injury Compensation Program has awarded more than \$5 million to 49 victims in claims made against the HPV vaccine. <https://www.judicialwatch.org/press-room/press-releases/hpv-vaccine-injuries-and-deaths-is-the-government-compensating/>

Judicial Watch also received documents, under the Freedom of Information Act, from the U.S. Food and Drug Administration (FDA) detailing reports of adverse reactions to Gardasil. The adverse reaction reports detail 26 deaths reported between September 1, 2010 and September 15, 2011 as well as incidents of seizures, paralysis, blindness, pancreatitis, speech problems, short term memory loss and Guillain-Barré Syndrome.

The conservative watchdog points out, "Merck has waged an aggressive lobbying campaign with state governments to mandate this HPV vaccine for young girls."

It's fascinating that Dr. Julie Gerberding, who approved Gardasil when she was director of the C.D.C., was subsequently hired by Merck in 2010 as president of Merck Vaccines. In 2015 she made more than \$2 million selling Merck shares.

https://en.wikipedia.org/wiki/Julie_Gerberding

While the CDC and international government bodies promote the vaccine's safety, there is compelling evidence that Merck conducted shoddy, questionable clinical trials; and that a number of individuals around the world have suffered drastic health consequences post vaccination.

According to a 2015 Atlantic magazine article, Merck's top selling vaccine is Gardasil, which brings in \$1.7 billion in sales. With such massive sales is it any wonder any attempts to raise safety issues are routinely dismissed, contrary to evidence.

<https://www.theatlantic.com/business/archive/2015/02/vaccines-are-profitable-so-what/385214/>

There is widespread concern about adverse effects caused by the Gardasil vaccination. They include paralysis, narcolepsy, respiratory dysfunction, cognitive impairment, involuntary movements, blood clots, and a rapid heartbeat.

A 2016 Canadian study looked at over 195,000 girls who had received HPV vaccines. Within forty-two days of HPV vaccination, the girls experienced over 20,000 emergency room visits or hospitalizations. But only 198 adverse events were reported. Liu XC, Bell CA, Simmonds KA, Svenson LW, Russell ML. Adverse events following HPV vaccination, Alberta 2006–2014. Vaccine 2016;34(15):1800-1805.

In 2012 Canadian researchers looked at whether or not some serious autoimmune and neurological ADRs followed HPV vaccinations are causal or merely coincidental. They analyzed post-mortem brain tissue specimens from two young women who suffered from cerebral vasculitistype symptoms following vaccination with Gardasil. They conceded “our study suggests that HPV vaccines containing HPV-16L1 antigens pose an inherent risk for triggering potentially fatal autoimmune vasculopathies.”

“The fact that many of the symptoms reported to vaccine safety surveillance databases following HPV vaccination are indicative of cerebral vasculitis, but are unrecognized as such (i.e., intense persistent migraines, syncope, seizures, tremors and tingling, myalgia, locomotor abnormalities, psychotic symptoms and cognitive deficits), is a serious concern.”

“It thus appears that in some cases vaccination may be the triggering factor of fatal autoimmune/neurological events.” <https://www.omicsonline.org/open-access/death-after-quadrivalent-human-papillomavirus-hpv-vaccination-causal-or-coincidental-2167-7689.S12-001.php?aid=9036>

The basis for HPV vaccination is its ability to prevent precancerous lesions related to HPV type 16 and 18 infections and the idea that preventing those lesions would prevent cervical cancer. According to University of Louisville researcher Dr. Diane Harper who led clinical trials of HPV vaccination, HPV infection can take years to result in cervical cancer. That leaves plenty of time for screening, treatment and prevention. Furthermore, 90% of HPV infections are removed from the body by its own immune system and related processes

without medical or other consequences within three years. Only a tiny minority leads to cancer.

The FDA licensed Merck's vaccine as a result of trials that were just three years long.

Dr. Kelly Brogan notes: “In the marketing and licensure of the HPV vaccine, changes to cervical cells have been equated with death. This is called using a “surrogate marker” and in vaccine research, this is considered acceptable because we can’t otherwise prove a non-event is attributable to an intervention. There are leaps in logic and in science inherent in this practice that render conclusions nothing more than false marketing.”

<https://kellybroganmd.com/new-gardasil/>

Former neurosurgeon Dr. Russell Blaylock claimed in 2013: “It has never been proven that the HPV vaccine prevents cervical cancer.”

A study by researchers at the University of Texas looked at HPV vaccination data from 2007–2012. The results showed that young women 20 to 26 years of age who received the four-strain Gardasil vaccine were actually more likely than non-HPV-vaccinated women to be infected with high-risk nonvaccine strains of HPV ten years later. Guo F, Hirth JM, Berenson AB. Comparison of HPV prevalence between HPV-vaccinated and non-vaccinated young adult women (20-26 years). *Hum Vaccin Immunother* 2015;11(10):2337-2344.

A review published in 2014 in *Autoimmunity Reviews*, “On the relationship between human papilloma virus vaccine and autoimmune disease,” pointed out: “Along with the introduction of the HPV vaccines, several cases of onset or exacerbations of autoimmune diseases following the vaccine shot have been reported in the literature and pharmacovigilance databases, triggering concerns about its safety.”

The authors caution that, “the decision to vaccinate with HPV vaccine is a personal decision, not one that must be made for public health. HPV is not a lethal disease in 95% of the infections; and the other 5% are detectable and treatable in the precancerous stage.” <http://www.ncbi.nlm.nih.gov/pubmed/24468416>

In a July 2016 lawsuit against Gardasil’s manufacture Merck, in the Superior Court of the State of California, Los Angeles County, evidence was presented questioning the safety of adjuvantes in vaccines that can produce autoimmune disorders, such as the addition of aluminum salts. <http://www.greenmedinfo.com/blog/merck-accused-fraud-deceit-and-negligence-us-gardasil-case>

“It is medically and scientifically accepted that aluminum salts are toxic to and damage the human cells at the injection site. In addition, the aluminum salts cause inflammation at the site. These aluminum salts may bind with the free DNA released from the damaged and dying cells at the injection site. The combination of the Aluminum salt bound by the human DNA is effective in activating Toll Like Receptors (“TLR”), whose function in the immune system is highly complex.”

Lawsuits internationally include one against the French manufacturer of Gardasil in 2013, where the court found 50% of the blame for a teenager’s subsequent multiple sclerosis on

Gardasil. Two weeks after the first injection, she experienced sensory and motor problems in the upper limbs. Three months after the second injection she was hospitalized.

<https://www.reuters.com/article/us-sanofi-lawsuit/sanofi-sued-in-france-over-gardasil-vaccine-idUSBRE9AN0FX20131124>

In Japan, an injury lawsuit in 2017 against the state and the HPV vaccine drug makers prompted the Japanese health ministry to withdraw their official recommendation for the HPV vaccination.

Twenty eight girls and women suffering what they say are side effects from cervical cancer vaccines that were recommended by the government, demanded compensation from the state and drug makers at the Tokyo District Court.

<https://www.japantimes.co.jp/news/2017/02/13/national/crime-legal/suit-opens-tokyo-court-cervical-cancer-vaccine-side-effects/#.XBg7OCx7ILM>

The plaintiffs, ranging in age from 15 to 22, said they have experienced a wide range of health problems, including pain all over their bodies and impaired mobility, after receiving HPV vaccines between 2010 and 2013.

Erina Sonoda, a 20-year-old college student, reported she started to suffer strong menstrual pain after receiving the second of three recommended shots of the Cervarix vaccine, and the pain spread to other parts of her body after the third vaccination. Due to agonizing pain, Sonoda said she has difficulty walking without a cane and often must use a wheelchair.

According to the health ministry, 2,945 people out of the 3.39 million women who had received the shots by the end of April 2017 reported side effects.

In Columbia anthropological researcher Mario Lamo-Jiménez, has raised concerns about the side effects of Gardasil, and is assisting attorneys prosecuting the collective action lawsuit filed by 700 women in that country demanding some \$160 million in compensation from Merck. <https://hetq.am/en/article/84400>

She reported Columbian girls suffering from ASIA syndrome after vaccination, as well as onset of early menopause, where there is a premature ovarian failure and they become sterile, as well as Guillain Barré Syndrome.

In Ireland around 650 girls reported requiring medical intervention or treatment after receiving the HPV vaccine, according to data collected by the State's medicines watchdog. Ireland accounts for one in five of all reports of suspected adverse reactions against Gardasil in Europe. At this time there are eight cases filed in Ireland's High Court that relate to the HPV vaccine.

At least 6 Danish women have report they developed chronic health problems during an HPV clinical trial. At Aalborg University Hospital, one of the trial sites in Denmark, Miam Donslund began to experience persistent flu-like symptoms as well as two infections, one of which required hospitalization, shortly after immunization. Stine Sørensen began to experience general discomfort, headaches, and a profound fatigue that often made her miss

school after she got her first shot of Gardasil. All the women have one or more agonistic autoantibodies in their bodies.

German scientist Gerd Wallukat noted about the autoantibodies, they reveal “the classical pattern I’ve seen in patients after vaccination.”

In Spain in 2017, the High Court of Justice of Asturias condemned the Asturian Health System for the death of Andrea, a young Spanish girl who died in September 2012 after getting the second shot of the HPV vaccine. The Court admonished the hospitals of Jove and Cabueñes, since they did not diagnose the patient’s pathology before the second shot of the vaccine was supplied which caused the death of the young woman.

<https://healthimpactnews.com/2017/spain-high-court-rules-hpv-vaccine-caused-death-of-young-woman/>

When she got the first shot of the HPV vaccine on July 23, 2012, the woman had a headache and breathing difficulty. Although, she suffered from severe asthmatic exacerbation, she got the second shot on August 23, 2012, and worsened. As a result she suffered severe dyspnea and seizures only 12 hours after receiving the vaccine, and died.

This year India’s Ministry of Health and Family Welfare indicated that it was unlikely to include HPV vaccines in the national immunization program.

In 2009, an HPV vaccine trial in the Indian states of Gujarat and Andhra Pradesh conducted by the Program for Appropriate Technology in Health, came under scrutiny for endangering the lives of participants. The study involved vaccinating 13,000 girls in Andhra Pradesh and 10,000 girls in Gujarat aged 10–14. The government halted the trial in March 2010 after seven girls who had received the vaccines reportedly died during the trial. Though a government inquiry later concluded that the deaths were unrelated to the vaccines.

Last year an empirical study confirmed that the inability to sue vaccine manufacturers in U.S. civil courts since 1986 is associated with a decrease in vaccine safety in FDA-approved vaccines after 1986. Gayle DeLong, Is “Delitigation” Associated with a Change in Product Safety? The Case of Vaccines, Rev. Ind. Org. (June 14, 2017),

<https://link.springer.com/article/10.1007/s11151-017-9579-7>.

DeLong found that vaccines licensed after 1986 are associated with approximately 5.2 more reported adverse events per 100,000 vaccine doses than the vaccines that were licensed before the passage of Vaccine Act.

A 2017 investigation by Slate revealed problems with the clinical trials for Gardasil, which was supposed to establish the vaccine’s efficacy and safety before it was approved. The article raises questions about why regulators knowingly accepted the company’s flawed data. <https://slate.com/health-and-science/2017/12/flaws-in-the-clinical-trials-for-gardasil-made-it-harder-to-properly-assess-safety.html>

“Interviews with five clinical trial study participants and more than 2,300 pages of documents obtained through freedom-of-information requests from hospitals and health authorities suggest inadequacies built into Merck’s major clinical tests of Gardasil.”

“European health regulators worried about Merck’s methods during a review of the company’s marketing application for Gardasil 9, the latest version of the vaccine, but have not made their concerns public. In an internal 2014 EMA report about Gardasil 9 obtained through a freedom-of-information request, senior experts called the company’s approach “unconventional and suboptimal” and said it left some “uncertainty” about the safety results.

“If I were a research subject, I would feel betrayed,” said Trudo Lemmens, a bioethicist and professor of health law and policy at the University of Toronto.

It’s worth remembering that former Merck virologists Stephen A. Krahling and Joan A. Wlochowski, filed a lawsuit against Merck in 2010. The scientists alleged that the efficacy tests for the measles, mumps, rubella vaccine (MMR) were faked. They claimed that over the years the effectiveness of the mumps vaccine declined. In 2014 a federal judge rejected Merck’s motion to dismiss. The lawsuit is still active with the court ruling class certification is due by 2/15/2019. <http://ahrp.org/former-merck-scientists-sue-merck-alleging-mmr-vaccine-efficacy-fraud/>

Slate reported when Dr. Rebecca Chandler, at Läkemedelsverket, the Swedish Medical Products Agency began analyzing Merck’s safety data for Gardasil 9, three girls vaccinated with Gardasil 9 had been diagnosed with POTS (postural orthostatic tachycardia syndrome), and one with CRPS (Complex regional pain syndrome). There were also several cases of neurological disorders. But none of them had been reported by the company as adverse events.

The suspicion that postural orthostatic tachycardia syndrome is related the HPV vaccine comes from a 2015 study by Danish researchers who provided some observational evidence about POTS occurrence after HPV vaccines. The authors stated that they “found a close chronologic association to the vaccination. The study found that the average number of days between vaccination and diagnosing POTS was around 11 days.

POTS normally occurs in approximately 1% of adolescents.

The Norwegian press has reported on the case of a 12 years old Norwegian girl, Maria Lysaker Wenersberg, who received the HPV vaccine at school. In April 2015 she was diagnosed with Postural Orthostatic Tachycardia Syndrome which is suspected to be a serious side effect from the vaccine. Most of the time she is now bedridden. Sometimes she faints daily. She has not been able to attend school for the past four and a half years. She has to be pushed in a wheelchair from her bed into the living room. <http://www.vg.no/nyheter/innenriks/maria-18-har-vaert-alvorlig-syk-i-fem-aar/a/23517356/>

In May 2016, Professor Peter C. Gøtzsche and Cochran Nordic Deputy Director Karsten Juhl Jørgensen, along with others, filed an official complaint about how the European Medicines Agency (EMA) handled the HPV safety issue.

In 2014, Australian doctors published in the Journal of Investigative Medicine a case study of a series of teens who had entered premature menopause after vaccination - a phenomenon Dr. Little and Dr. Ward described as ordinarily “so rare as to be also unknown.”

They noted – “Long-term follow-up data after HPV vaccination has not surveyed ovarian function, recorded, measured, or analyzed symptoms or signs of dysfunction. Principles of informed consent, population health, and vaccine confidence require careful, rigorous and independent research to establish ovarian safety following HPV vaccination.”

In a public forum Dr. Little spoke about the poor quality of research being performed on HPV vaccines. She noted a September 2018 article published in Paediatrics which found that women in the USA who received Gardasil were no more likely than those who did not receive Gardasil to have premature ovarian insufficiency meaning that their ovaries were no longer functioning. Little suggest the effect of HPV vaccines on the female ovary needs further study.

The American College of Pediatricians in 2016 released a health warning about the HPV vaccine – “It has recently come to the attention of the College that one of the recommended vaccines could possibly be associated with the very rare but serious condition of premature ovarian failure (POF), also known as premature menopause.”

In January 2016, pathologist Dr. Sin Hang Lee, MD, Director of Milford Medical Laboratory, sent an open letter of complaint to the Director-General of the World Health Organization (WHO), Dr. Margaret Chan, in which he challenged the integrity of the GACVS (Global Advisory Committee on Vaccine Safety) Statement on the Continued Safety of HPV Vaccination.

He wrote: “A series of emails recently uncovered via a Freedom of Information request submitted in New Zealand revealed evidence that Dr. Robert Pless, the chairperson of the Global Advisory Committee on Vaccine Safety (GACVS), Dr. Nabae Koji of the Ministry of Health of Japan, Dr. Melinda Wharton of the CDC, Dr. Helen Petousis-Harris of Auckland University, New Zealand, and others may have been actively involved in a scheme to deliberately mislead the Japanese Expert Inquiry on human papillomavirus (HPV) vaccine safety.” <https://sanevax.org/wp-content/uploads/2016/01/Allegations-of-Scientific-Misconduct-by-GACVS.pdf>

In 2011, Dr. Lee found that every one of the 13 Gardasil samples that he examined contained HPV L1 gene DNA fragments. He also found that the HPV DNA fragments were not only bound to Merck’s proprietary aluminum adjuvant but also adopted a non-B conformation, thereby creating a new chemical compound of unknown toxicity.

This non-B conformation, Dr. Lee believes, is responsible for the array of autoimmune illnesses experienced by children and young women following vaccination with Gardasil.

In 2012, he testified at a coroner’s inquest of the death of a New Zealand teenager, 6 months after receiving 3 Gardasil vaccine injections.

During the inquest neuroscientist Professor Christopher Shaw of the University of Columbia in Vancouver told the New Zealand inquest that he was sent the teenager’s brain tissue to test. He said there was aluminium in all the samples he tested and there were some abnormalities in the samples. The human papillomavirus (HPV16) was found in her brain, which could have only got there through the vaccine, Prof Shaw said. He said there was a

"biological plausibility" that vaccine likely caused her death. He could not say conclusively that was the cause of her death.

Finally, a new study, published in the Journal of Toxicology and Environmental Health, suggests a link between the HPV vaccine and declining fertility. It examined the childbearing capacity of women who received the HPV vaccine – compared to those who didn't, and discovered an alarming correlation. Approximately 60% of women who did not receive the HPV vaccine had been pregnant at least once compared to 35% of women who had had an HPV shot had ever conceived. For married women, 75% who did not receive the shot were found to have conceived, while only 50% who received the vaccine had ever been pregnant.

Considering all this relevant information I would hope that that the Department of Health in all good conscience would not try to force the HPV vaccine on Hawaii's children, when it is known that harm might occur in those more susceptible to injury.

Any decision to vaccinate or not to vaccinate against the sexually transmitted HPV virus is a private medical matter, and not the responsibility of the state.

Jon Woodhouse, M.Ed.



Michelle Kwik R.N., B.S.N., P.H.N, M.Ed. School Nurse

I Strongly Oppose HAR 11-157 (Mandatory Vaccines throughout Hawaii)

I began working as a Neonatal Intensive Care Nurse in the late 1980's; I worked with many premature infants as well as infants that were born with anomalies, infections, and addiction. From there I worked as a Public Health Nurse for mothers and their children ages newborn to 5 years. I was also a Triage Nurse in a Pediatric Office for six Pediatricians. My most recent job was working as a Certified School Nurse in Southern California caring for more than 9,000, 3-13 year olds over a course of 13 years.

Over the past 30 years I have seen the significant increase in children with autism, allergies, mental health illness, learning disabilities, and other chronic illnesses such as asthma. This increase has been dramatic. As a school nurse I kept logs in Southern California which included all health concerns noted by parents and physicians; I also wrote up more than 200 yearly health and developmentals for children receiving Special Education Services. For example, reviewing records our district went from 13 children with epipens for life threatening allergies to over 200 children in a course of 15 years. The cases of children on the Autism Spectrum has risen immensely in the same time period and has put a strain on society especially the families who have minimal coping resources as well as the educational system who must pay for special services.

It does not take a professional, to see so many insults to the welfare of our children is directly related to the toxins in our environment and what we put in our children's bodies. Each child is a unique individual with a genetically diverse make-up. As a School Nurse, Neonatal Nurse, Pediatric Nurse, Childhood Triage Nurse, Public Health Nurse, I can tell you a parent is their child's first line of defense and they know their child and their child's health more than anyone else. They are their child's first and foremost advocate. When it comes to their child's health, no physician can know a child like a parent does. As a nurse, I have always been a patient advocate, when it comes to children I advocate for them and their parents because I know they know their child and Pediatricians do not always have time, energy, and accessibility to follow through with a patient's critical needs and it is up to the parent to pursue their child's wellness.

Immunizations were first introduced in recorded history as early on as 1500's. There is some evidence the first immunizations were actually done as early on as 200 BC. Immunizations were originally created to prevent the spread of a specific disease that was deemed detrimental to society and the well-being of life. As like many things, money has taken place of what is best for our world and its children. The immunizations today are laden with so many chemicals that make them an insult to immature bodies struggling in a toxic environment already. For example the aluminum in each vaccination today is 1.47 to 49 times higher than the U.S. Food and Drug Administration safety limits allow. Aluminum is added to potentiate the effects of the inoculation so less virus can be used and it is cheaper. In the HPV inoculation there has been no evidence that the Aluminum helps to potentiate the virus and it is questionable if it is the cause of the aversive reactions including death that has been seen after giving this shot (Please review Dr. Mercola under immunizations benefits and detriments).

Each child is a unique individual. I have first handedly seen young healthy children given the MMR, have

seizures, go into a coma and loose language and be diagnosed with Severe Autism. Dr. Sears, one of the most highly regarded Pediatricians in America was the Pediatrician in one case. He directly linked this case to the immunization. He has two sons, both are now Pediatricians. One is pro vaccine the other is opposed due to what they have learned and seen. On the other side of the debate, I had a child who at one years old, contracted chicken pox. During this time his body attacked his pancreas causing him to require insulin for the rest of his life with a diagnosis of Type I Diabetese. It is unknown if a cold or flu could have done the same thing his body attacked itself in response to an illness (This is not uncommon in children who acquire type 1 Diabetes). It could of happened after a vaccination, if his body attacked itself in response to the vaccination. I knew a 23 year old healthy, vital, young man who had a flu shot in my district; within 48 hours of the flu shot his body attacked itself and his vital organs bled out and he died. Another child who was severly allergic to many things, had severe asthma and given a flu shot to prevent a bad flu, this boy ended up getting petechiae which is a severe reaction and one of the first signs of the body attacking itself before it fully attacks the organs. This child was not allergic to eggs. He survived but will never be immunized again. Each person, each body is unique in its response to viruses as well as vaccinations . I have had numerous friends children have seizures from immunizations because their bodies reacted violently to the vaccine. Unless they do more studies to find a genetic link and this can be tested prior to an immunization no one knows how a child will react until they are given the vaccination. Many parents are waiting to vaccinate until their children are 3 when there language is intact and there bodies are stronger than the infant stage in case they were to have a reaction, or they vaccinate 3 months prior to daycare.

Children who are born today are at a greater risk of developing a reaction to an immunization because their bodies and genetic make up is being altered by all of the contaminants in our environment. Adding the huge load of aluminum and other perservatives to an already sensitive system, is detremental and dangerous. My son at one years old was given the MMR, one week later he got Rotovirus was hospitalized, lost 5 lbs., and ended up with double pneumoniae. His body was not immunologically strong enough for the MMR and it made him vulnerable. When I got an MMR vaccine at 28 years old, I got the measles. I got a rash covering my entire body and I got arthritis in all of my joints lasting two weeks. My nursing supervisor at the time did not believe me and told me to go to my clinical which was working with children with Cystic Fibrosis in the hospital. I was wise enough to stay home knowing if they came in physical contact with my rash they could have acquired measles if their titers were not high enough (titers meaning their immune response measured in a blood test). The same adverse reactions happened when I got a DPT and a flu shot. With both I acquired bronchitis and asthma for close to 6 months. Myself and my son were/are genetically sensitive.

There are rules in a school district, if their is an outbreak and your child is not vaccinated they must stay home. If a parent wants to they can immunize at that time. If your child contracted the illness previously and has immunity their blood test (i.e. titer will show an adequate level), this counts as an immunization. When we had children from other countries, especially children adopted from overseas, who came to school without records, we had parents acquire their titers to show immunity so the children did not need the vaccination again and if they had the disease it would show as immunity. Some people actually do not acquire immunity from certain vaccines even if the vaccine is given

numerous times. It is unknown why this happens.

I can not say children with autism are autistic because of mercury in their vaccines, I can say I do know some children who are, and I can definitely say most children with autism have an increased sensitivity to food allergens and environmental toxins and immunizing them is not wise unless the risk of getting the disease out weighs the benefits of the immunization. Thus, if there is an outbreak parents must keep their unimmunized children home and they can immunize at that time if they feel it is important.

I can probably write you a thesis on the importance of allowing parents to make a judgement call on their own child's health. Parents are there to decide what is best for their own child; I have seen children die when parents did not listen to their own instincts or the signs and symptoms of their child when pediatricians were left to solely diagnosis their children with a short office visit and phone calls. I believe immunizations save many lives and also take some lives. I have seen them weaken further an already weakened system. Who are we to decide for a parent. It is best if we as citizens and health care workers advocate for more efficient and healthy vaccines that do not have preservatives and activators that are toxic and we advocate for more blood titers (if a specific titer is reached with one dose a child does not need more; titers can be checked every few years easily and as needed for at risk children). We also need to advocate for a clean environment with safe food and drinking water since this is where many of the insults have started. If you pay attention the same companies who make weed killer, insecticides, etc. are the companies making the preservatives and compounds added to the vaccines. This is where we need to put up boundaries. The health of our children is more important than the profits of some companies. Even if vaccines are like they were in 200 BC or 1500's without added chemicals, our environment is much different now. If there is an outbreak we can immunize and check titers before a child returns to school or the family can home school until there is no evidence of illness. We can not take away parents rights. We can educate and encourage families in options such as immunizing in summer when children tend to be healthier so their immune system does not get an extra load during flu season, or get titers so you can see if your child has enough immunity rather than over immunizing. Maybe they can make an expensive brand of immunization for children more at risk to the preservatives, which are all children really but those with autism, asthma, mental illness etc..

My sister is a nurse practitioner who gives the HPV vaccine often, she stated she gives about 1000 doses a year, has had one anaphylactic reaction requiring resuscitation, and otherwise she believes the problems associated with HPV far outweigh the risk of the vaccine. That saying, we need to educate parents, not in a doctor's office there is never time. If anything could be mandated it could be a class discussing immunizations for people opting out and this, I believe, should be in a school setting with actual facts including the pros and cons. The amount of aluminum, the chemicals, children's reactions to the vaccines, cases involving no vaccines and what has happened due to contracting measles and other illnesses. People must make their own choices and people should be fully educated.

I will never be immunized again due to my sensitivities. My children were given the least immunizations required to reach normal titers. They were not given immunizations which were not necessary due to their sexual activities such as Hep B, which is a blood born contaminant until they were teens and they opted for them. They were educated on Blood and Body Fluid precautions. I only immunized in the

summer due to my sons vulnerabilities to seasonal illness, he still got pneumonia even in the summer but less often. I spread out the immunizations since there was no active illness at the time and due to my sons vulnerabilities. I do believe in social responsibility and if my child had an illness another child contracted and that child had a severe reaction to that illness I would feel at fault. That is why I ended up immunizing, also because I was in the Pediatric field and I was in contact with illnesses of every kind. Which actually most do not have a vaccine for like Epstein Barr Virus, Toxoplasmosis, Cytomegalovirus, to name a few. We need more research and parents need more education. If we do not let parents know the ugly truth about immunizations when they find it out on their own they are even more inclined to say no because we hid the truth. We need to tell them the whole truth so they can decide for themselves. They need videos, power point presentations, other parents comments from both sides, naturopathic doctor responses as well as pediatricians. Honestly if vaccines were a less contaminated and people were better educated I believe that would increase the declining vaccination rate by about 25% but until that happens people will put their children in home school programs whatever it takes to prevent them from being immunized. I know I worked in California and I have talked to thousands of parents and I know why they refuse to vaccinate. Sometimes it is the lazy secretaries at the schools who try to make it easy on their book keeping so they can just not follow through on children who need updated immunizations, they have the parents decline all of them, this gives a sense of people not immunizing. I have been audited numerous times at one or more of the schools I looked after in California and we had to document why parents did not complete the vaccinations. Most of them actually do complete the vaccinations just not on the schedule the documentation requires.

I have covered why people do not vaccinate and I have given options in to what can be done to increase the vaccination rates and why I strongly oppose the mandate that requires vaccination. Like I said I would mandate a two sided debate and educational review on the pros and cons of immunizations at each grade level K, 6, 9 for those parents who wish to opt out of immunizations. That way if the levels of chemical additives decreases in the immunizations or the level of illness increases in the community, or if the immunizations have caused more fatalities people know and they can change their minds. Parents whose children have contracted an illness who were not immunized can speak, mothers who were pregnant and contracted an illness that caused a birth defect can talk, the person who has cancer from HPV can talk, parents whose children got violently ill or passed away from a vaccine can talk. That's what a health care provider does they give facts and let the public decide that way it is informed consent and a person can choose.

Mahalo for Your Time and attention to this matter, Michelle Kwik

Please contact me if you need further information [REDACTED]

My name is Jennifer Bonifacio, a mother, teacher, Permaculturist, farmer, entrepreneur, and an advocate for the 'aina and the people's rights. I strongly oppose the changes to HAR 11-157, especially those in HAR 11-157-3 a and b. Where there is risk, there must be choice. Everyone has the right to informed consent. We should know everything about a drug, vaccination, or procedure so that we can make a good decision on what is best for us and our families. I do not appreciate being made to feel like I am stupid for even asking to see a vaccine insert or asking for a second opinion.

The recommended requirements in table 3-1 in Exhibit A List of Required Vaccines (July 1, 2020) is ridiculous. How can anyone believe that injecting a child with all those vaccines with all the various ingredients be safe especially at birth? The list of ingredients can be found on the CDC's website.

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/excipient-table-2.pdf>

A good number of those ingredients can be harmful to the human body. Please take a look at the list. There are three pages of it. Do you want even a small dose of formaldehyde in your system? The CDC provides a VIS or Vaccine Information Statement and these are what doctors or immunization clinics provide the patients. VIS do NOT list the ingredients as a vaccine package insert does.

I once (Oct 2013) calculated the amount of mercury in a flu vaccine and it was more than the number the EPA reported as safe for consumption. My calculation compared the EPA's recommendation for a 130lbs woman. For a child, the amount of mercury is even more than that which is considered safe by the EPA.

Here is my calculations:

According to NRDC who used the EPA's recommendation for a 130 lbs woman, more than 0.5 ppm of mercury in fish is considered highest and should be avoided. High mercury in fish is considered to be 0.3 to 0.49 ppm and recommendation is at most eating three times a month or less. According to one of the flu vaccine's website: "Multidose vial, 5-mL. Contains thimerosal, a mercury derivative (25 mcg mercury per 0.5-mL dose). Thimerosal is added as a preservative."

$1\text{mcg/ml} = 1\text{ppm}$

Converting to ppm, this vial contains 50 ppm of thimerosal.

"Prefilled syringe, 0.5-mL. Thimerosal, a mercury derivative used during manufacture, is removed by subsequent purification steps to a trace amount (≤ 1 mcg mercury per 0.5-mL dose)."

So basically it's ≤ 2 ppm in the prefilled syringe.

But this is Thimerosal, organomercury compound, a compound that contains mercury.

From the FDA's website:

"A vaccine containing 0.01% thimerosal as a preservative contains 50 micrograms of thimerosal per 0.5 mL dose or approximately 25 micrograms of mercury per 0.5 mL dose."

So basically it's saying that the amount of mercury is half that of thimerosal. So in this case, the multidose vial contains 25 ppm of mercury and the prefilled syringe contains ≤ 1 ppm of mercury. Isn't that still a lot?

According to the EPA's Fact Sheet Mercury Update: Impact on Fish Advisories, the multidose vial of this flu vaccine company contains more mercury than some of the fish sampled in their report at the highest range.

Now let's think logically. Does this make sense?

Hep B at birth. That infant will not be engaging in sex or use drug needles. If the mom may have Hep B, shouldn't her physician have determined that during pregnancy? Not only that, the brain of a child is undergoing continual development until about the age of 12. How can anyone think it's safe to inject all those ingredients in a child from birth? How can anyone think that this is safe?!

HPV around middle school. The act of sex is NOT a class in school so why is it recommended? The message in school should be abstinence and not just safe sex.

Flu every year. A healthy body does not need to have a flu vaccine. Nature has made the body perfect and able to fight off disease as long as one has enough nutrients. Working with plants, I observed this perfectly. When the plant is sick or being attacked by pests, I just give it more nutrients such as worm casting tea (compost tea) or inputs from Korean Natural Farming practices. A few days later, the plant has shown significant improvement or is better as it's stronger to fight off even pests like aphids. I do not use synthetic fertilizers nor do I use synthetic herbicides or pesticides like Roundup.

It's the same with my child. When my child is sick, all I do is give my child extra nutrients in the form of very good natural supplements and is better in usually 24 hours while my child's friends are still out a week or two.

Vaccines have never been proven safe as many of my friends who've submitted testimonials have brought up and provided links to. There have been NO studies between vaccinated or unvaccinated populations. All sides should be allowed to be heard without the witch hunt that the medical community or media advertises.

The chances of vaccine injury over the chances of a complication from a childhood disease are too high. We cannot and should not compare ourselves (the United States) to places like Africa and India where sanitation is pretty non-existent. Polio, for example can be spread by fecal matter. It is not common practice anymore in the US to use the bathroom in the river upstream from where children are playing. Yes, complication can and do occur when someone gets a disease but the chances of that are minimal in the US today. The media will report a case where someone's child died over not getting a shot but will not report how many have died from

receiving that shot. The Vaccine Adverse Event Reporting System (VAERS) have reports on death but only a very small fraction of reactions are reported so the true numbers are basically unknown.

We have the best doctors and medicine in the world and I believe they can help a person who develops a complication from a disease. Vaccine injury however is first of all discounted/dismissed.

Why is it that the government of Japan actually stopped recommending the HPV vaccine and called for research because of the high reporting of adverse reactions where the US government just calls for more vaccination? Here is a paper done on the lessons learned in Japan. Read especially III. Structural flaws: an ethics viewpoint

<http://ijme.in/articles/lessons-learnt-in-japan-from-adverse-reactions-to-the-hpv-vaccine-a-medical-ethics-perspective/?galley=html>

Why is it in the US, the government is actively trying to keep us clueless about these. Where is the ethics of the American Medical community and Department of Health?

I am a mother and I will not stand for this. My child was vaccine injured and sickly for the first four and a half years of her life. Thankfully I found a doctor who figured it out. He wasn't her pediatrician, dermatologist, or allergist, all of whom kept prescribing more drugs (that she'd have to be on 24 hours a day) and steroids. This doctor was able to determine the cause and clear her. She has been healthy ever since and as mentioned above, if she gets sick, only for max 48 hours.

The Department of Health is so focused on immunizing the population with vaccines instead of preventive health measures such as exercising and eating organic and non-genetically modified nutritious foods. The focus should be on working with the Department on Agriculture to make sure everyone has access to good foods. Instead, the focus is making sure everyone is vaccinated against diseases that a person can fight off with the right nutrients.

I strongly oppose the changes in HAR 11-157-3 a and b.

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Sheree Loui

Print Name

 , Hawaii, 
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii’s rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Print Name

_____, Hawaii, _____
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Tiana Gervacio

Print Name

_____, Hawaii, _____
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

[Redacted Name]
Print Name

[Redacted City], Hawaii, [Redacted Zip Code]
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii’s rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Dikki Ho

Print Name

_____, Hawaii, _____
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



Print Name

 , Hawaii, 
City  Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

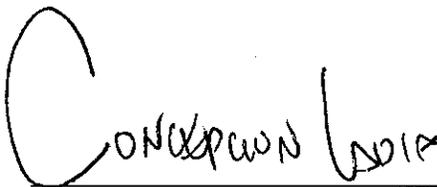
The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

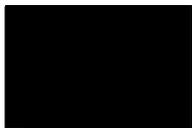
Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

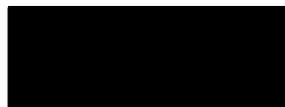


Print Name



City

, Hawaii,



Zip Code

I am writing to strongly support the HAR 11-157 proposed rules update.

Across the country and within the state there has been an increase in vaccine preventable disease. The proposed rules update would bring the state rules into compliance with the recommendations of the Advisory Committee on Immunization Practices (ACIP). It is important that students receive HPV, MCV, and Tdap shots because they have the ability to protect individuals against life threatening illness and can provide protection against cancer.

Certain segments of the population including newborns and individuals with suppressed immune systems are not able to receive immunizations, however they are protected from these life threatening diseases when around 93% of the population is immunized. Research has shown that communities with low vaccination rates are most at risk for outbreaks of vaccine preventable diseases. Vaccine exemptions should be limited to individuals who are medically unable to receive immunizations, so these members of the community will still remain protected by herd immunity.

In recent years, Hawaii has been hit with outbreaks of preventable diseases. Last year nearly a thousand people in Hawaii were infected with Mumps, a disease that usually affects less than ten people in the state. This was a case of an outbreak of a vaccine preventable disease spread through the school system by infected students. HAR 11-157 would help prevent events like that from occurring in the future.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed to help ensure that all segments of the population remain healthy.

Thank you for your consideration,

Sienna Ogawa

From: [REDACTED]
To: [DOH.Immunization](#)
Subject: HAR 11-157, I OPPOSE
Date: Monday, November 19, 2018 9:57:31 AM

Aloha Hawaii Department of Health,

Thank you for this opportunity to provide testimony.

I STRONGLY OPPOSE THE HAR 11-157 PROPOSED RULES UPDATE!

I OPPOSE INCREASING VACCINE REQUIREMENTS. The risks of adverse reactions include autism, infertility, autoimmune disorders, seizures, paralysis, and death. Over 59,000 adverse effects from the HPV vaccine have been reported to VAERS, including 425 deaths.

I OPPOSE INCREASING REQUIREMENTS FOR MEDICAL AND RELIGIOUS EXEMPTION. Complicating the exemption process would contribute to more allergic reactions and adverse reactions for susceptible genetic types. We must be allowed to refuse the injections of toxic metals, harmful chemicals, allergens, and xeno-biological agents such as animal and fetal derived DNA.

I OPPOSE ADOPTING THE ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES (ACIP) RECOMENDATIONS. These recommendations have not been proven safe and pose risks of severe adverse reactions. The FDA admits that only 1-10% of adverse reactions are even reported.

The HAR 11-157 proposed rule changes increase vaccine requirements and complicate the acquiring of vaccine exemptions, which would cause an increase in adverse reactions.

HEALTH FREEDOM AND INFORMED CONSENT ARE BASIC HUMAN RIGHTS! Everybody must be allowed the right to chose or refuse what is put into the body. Vaccination is a medical intervention that carries a risk of injury or death. The right to informed consent to any medical intervention that can kill or injure you or your child is a human right.

Please consider the health concerns of everyone susceptible to adverse reactions to immunizations.

Thank you again for the opportunity to provide testimony opposing the HAR 11-157 proposed rules update and the adverse consequences it would cause.

Mahalo,
JANELLE MARTIN and TALLY WINTER

[REDACTED]

[REDACTED]

From: [REDACTED]
To: [DOH.Immunization](#); [REDACTED]
Subject: HAR 11-157 Testimony
Date: Tuesday, October 30, 2018 8:03:23 PM

Aloha,

Thank you for this opportunity to provide testimony. We live on the island of [REDACTED] and we strongly OPPOSE the HAR 11-157 proposed rules update. We oppose the proposed rule changes for the following reasons:

1. It takes away our civil rights, our freedom, the whole point of being American. Please stop encroaching on our civil liberties. The idea that you believe you have the right to mandate anything being injected into our bloodstreams without consent is appalling/uncivil/tyrannous, what right and liberty will you be taking away next? I am literally terrified of living in a country who thinks it is ok to inject whatever they deem necessary into their civilian's bloodstreams. No government body or health department should have this kind of power, ever.
2. The safety obligations from the 1986 National Childhood Vaccine Injury Act are supposed to be in place to protect our children. However, as I am sure you have heard, that those safety obligations have never been upheld. We cannot trust the government/system to follow through with their promises when it comes to the health and safety of our children—so parents must. The GOVERNMENT/SYSTEM HAS FAILED US REPEATEDLY even with the supposed checks and balances in place, except this time the lives of our children are on the line. Stop making it harder for us to protect our children. Do not take my right to protect my child/children away from me. Common sense knows that where there are humans completing anything there is human error. There is a margin of human error in these vaccines hence the list of side effects, but common sense would know it is not just limited to side effects. There have been no studies showing the effects of the suggested vaccine schedule as a whole, let alone as how they are currently dosed, NOR detailed enough studies on people with different genetics in this incredibly diverse country and state. Attempting to mandate a medical procedure when there are no adequate safety studies in place is a BLATANT DISREGARD FOR PUBLIC SAFETY. There are no check and balances in the vaccine program, as vaccines are classified differently than any other medications and are not subject to the rigorous scrutiny or the liability that comes along with putting new drugs on the market. And as common sense would have it, I do not trust the "goodwill" of a company who has no repercussions to any of the vaccine products administered to the public since the vaccine companies can not be sued for any damage caused by the vaccines and as the Supreme Court ruled the are unavoidably unsafe. I am not sure how you can trust the "goodwill" of a company or person with your childs' life on the line when there are billions of dollars that could be theres instead.
3. Where there is risk, there MUST be a choice. Vaccines carry risk. Read the vaccine insert/prescribing information ---the actual, lengthy, detailed insert that comes in the vaccine box. Each vaccine administered to children was never evaluated for its ability to cause cancer, genetic mutation, or infertility. The studies lack important details that are needed, THAT ARE NECESSARY, in order for them to make claims that the vaccines are for everyone. A simple example of their lack of detail for genetic differences for a injection directly into the bloodstream, which can have incredibly serious consequences if there is anything harmful--- there have never been studies regarding the effectiveness and safety for use of vaccines for people with autoimmune issues and/or MFTHR gene. We have an incredibly diverse genetic country and state. This lack of detail or care for the population as a whole matters when making this decision. Vaccines are not safe for everyone and children should be given the chance to lead a normal life before our society makes the decision without their consent to take that from them before we even know for EXACT certainty that they will not have an adverse reaction, which is humanly impossible with the margin of human error. It is wrong to mandate a medical procedure that is known to cause harm and carries risk, without informed consent. Just an example, the MMR vaccine insert contains 42 paragraphs of warnings and adverse reactions, including seizures, encephalitis, pneumonia, deafness, and death. DTaP lists SIDS as a side effect. The inserts on live virus vaccines state that recipients should avoid close contact with susceptible high-risk individuals for up to 6-weeks following vaccination. <- Common sense again, would have you

wondering if the outbreaks are from the vaccines themselves, which is hardly ever reported with honesty. Also, the government does not know and can not control which individuals would be included in this group and would be forcing individuals that fall into those categories (immunocompromised, pregnant women, new infants, etc.) who work and attend the schools to exposure to those illnesses. Will the schools be accepting doctor's notes with paid leave for up to 6-week post vaccine absences? And, how come when the break outs of these diseases occur the vaccines are never investigated for possibly being the contaminate?

4. I disagree with the HPV vaccine being a requirement for every child to attend school. There have been numerous lawsuits across the world, including Spain, France, Japan, Colombia, India and right here in the US. Why are you recommending a vaccine that has never been proven effective at the prevention of cancer? Because as all vaccines go, the studies are inadequate for suggesting them for the whole public. The HPV vaccine has been linked to including but not limited to: lesion development, ovarian failure, autoimmune disease, pancreatitis, infertility, silent seizures and disseminated encephalomyelitis, and death following vaccination. The median age for cervical cancer diagnosis is age 49. Why are we taking away or damaging young children's lives before they have even started? Not all children fall under this blanket, there are still more people without HPV than with HPV that this vaccine would be harming. How about responsibility for your own sexual conduct and when of age making the choice to take on the risks of the HPV vaccine if you believe you are at higher risk of contracting the disease?<---- this is called informed consent and having rights and liberties as a citizen.

5. Requiring the flu vaccine is inappropriate. Again, taking away our rights and liberties. I am literally terrified of living in a country who thinks it is ok to inject whatever they deem necessary into their civilian's bloodstreams. No government body or health department should have this kind of power.

6. According to the CDC's publication "Vaccine Excipient & Media Summary", "In addition to weakened or killed disease antigens (viruses or bacteria), vaccines contain very small amounts of other ingredients – excipients or media." These excipients include thimerosal (a form of mercury), aluminum (as amorphous aluminum hydroxyphosphate sulfate p/k/a aluminum hydroxide), aborted fetal cells (injecting fetal cells has shown to permanently change our DNA), bovine extract, formaldehyde, monkey kidney cells, calf serum, chicken cells and polysorbate80 (breaks down the blood brain barrier). This is disgusting, we should have the right to decide if these items are put into our bodies or our children's especially with the different side effects that each of these substances can cause. Our children should have the right to decide if this is put into their bodies. How is rape not ok, but you making the decision to inject your civilians bodies with these disgusting substances against our will is ok? Again, the decision should not be the government's, but the individual and when it comes to minors, their parents' decision, till they are of age.

6. I also question why the state epidemiologist, Dr. Park, who used to work for the CDC, isn't being investigated for the conflict of interest. She has stated that "giving parents full informed consent would hurt her flu shot program in the schools." How about the harm her program inflicts on the families that have adverse reactions?

I ALSO REQUEST FOR THE DOH TO HOST PUBLIC HEARINGS STATEWIDE.

Thank you & Sincerely,
Tanner & Matt Brittan



Reply

Forward

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

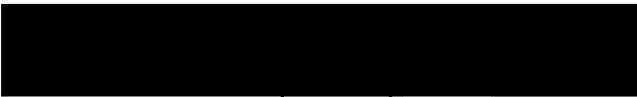
Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Jonna Gomes

Print Name



City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Angie Mizushima
Print Name

 , Hawaii, 
City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Asia Gosnell

Print Name

City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Joana Garcia

Print Name



City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

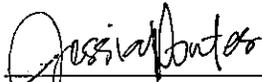
The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.


Print Name _____


City


Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

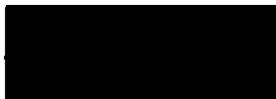
Aida Hinosa

Print Name



City

, Hawaii,



Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



Print Name

 , Hawaii, 
City Zip Code

To Legislators and Administrators Granted Power to Make Decisions Affecting Public Health:

I vehemently OPPOSE HAR 11-157 and any legislation that would prevent me from exercising my human and civil right to freedom of thought, speech, and belief under the Constitution of the United States to make informed voluntary choices regarding my health and the health of those whom God has entrusted into my care.

Nobody should be forced to use pharmaceuticals that carry the risk of harm or failure, especially those made with toxic substances or derived from unethical sources such as aborted human fetuses.

It is religious discrimination to accept exemptions from specific religious organizations and not others. Every individual has the right to exercise their religious beliefs as they so chose. It is my belief that God created our bodies with the power and ability to build and maintain a strong immune system by making healthy choices. Compromising the immune system from birth through the administration of vaccines alters natural immunity for life and is contrary to God's design for the body.

As consumers of anything, we are voting for whatever we put into or on our bodies. Forced vaccinations denies us our "right to vote" against drug and chemical companies, immune from accountability and liability, whose interest is in profit and not our health and well-being.

I strongly encourage you to educate yourself by watching the Youtube video with Del Bigtree called THE IRREFUTABLE ARGUMENT AGAINST VACCINE SAFETY before you attempt to make any more mistakes regarding mandatory vaccinations.

I will pray for each of you to have wisdom to do what is right and for God's mercy when you stand before him accountable for the damage and death that may result from the decisions you make.

Sincerely and respectfully,

Sue Pantano-Saldana

██████████

██████████████████

Kamala Galletes

Aloha, my name is Kamala Galletes. I am a parent, and have been a DOE educator for over ten years. Thank you for your CAREFUL review of this, and ANY vaccination issue! NO vaccinations should be mandatory, let alone for the entrance into school.

I oppose HAR 11-157, and cannot believe I need to defend children against proposed mandatory vaccines!

YES, defend children from vaccinations that are a RISK to them, can HURT them, and can even KILL them! In all actuality, I need to defend children against pharmaceutical companies that intentionally poison our children for a profit! These companies DO NOT care about the welfare of our children, and if injured from a vaccine parents are stuck dealing with much more than the Vaccine Injury Compensation Program (VICP). Injury compensation; I believe many parents DENY the scheduled vaccines because there is INJURY/RISKS involved.

In 1986 the vaccine-manufacturing pharmaceutical companies were freed from all liability related to vaccine injuries and death via the National Childhood Vaccine Injury Act (NCVIA). Clearing the way for these companies to mass produce poison and make a profit off of children.

Vaccines contain TOXIC chemicals that DO NOT belong in anyone's body! For example, aluminum is KNOWN to cause brain and developmental damage even in small amounts. Formaldehyde is KNOWN to cause cancer in humans. These ingredients and several others are documented in vaccines.

Parents who DO NOT vaccinate ARE making sound, conscious choices for THEIR children. We feel strongly against poisoning them, and do understand that this poison is made for a PROFIT! There is RISK that can result in injury, that IS documented by many cases around the world!

Parents will choose to keep their children safe verses sending them to school if a mandatory vaccine schedule is forced on them! How with the state handle those circumstances?

Mahalo nui loa,

Kamala Galletes

Aloha DOH,

These references were in my talks and this is a written documentation of them and the topics that embraced them. It is essential that mandatory vaccines do not happen in Kona or any part of Hawaii for a multiple of reasons, some of which are stated below and part of my testimony.

Clare Loprinzi, Traditional Midwife, MCH (Maternal/Child Healthcare, CPM

1. **Premature birth weight Primary immunization of premature infants with gestational age <35 weeks: cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. CRP level is expected to be elevated in the 48 hours following immunization. In a minority of infants immunized, cardiorespiratory events were associated with presumed need for intervention. Underlying medical conditions and possibly multiple injections are associated with cardiorespiratory events. Precautionary monitoring following immunizations is warranted multiple separate vaccines simultaneously.**
<https://www.ncbi.nlm.nih.gov/pubmed/17643770>

2. **premature birth weight. We evaluated the tolerance to immunization of 64 very low birth weight preterm infants. Thirty-three of the infants experienced a cardiorespiratory event after the first vaccination, and 6 of these 33 (18%) had a recurrence after the second vaccination, including 2 infants previously discharged to home. A cardiorespiratory event associated with the first vaccination was the sole risk factor for recurrence identified.**
<https://www.ncbi.nlm.nih.gov/pubmed/17643770>

3. CHANGING DNA

To assess the public health consequences of fetal cell line manufactured vaccines that contain residual human fetal DNA fragments utilizing laboratory and ecological approaches including statistics, molecular biology and genomics. Vaccines manufactured in human fetal cell lines contain unacceptably high levels of fetal DNA fragment contaminants. The human genome naturally contains regions that are susceptible to double strand break formation and DNA insertional mutagenesis. The "Wakefield Scare" created a natural experiment that may demonstrate a causal relationship between fetal cell-line manufactured vaccines and ASD prevalence. Kingdom of Hawaii and Indigenous Rights are being violated.

<https://www.ncbi.nlm.nih.gov/pubmed/26103708>

2. Cancer and Immune systems

Fever are important to build the immune system. Herd immunity will never happen as the vaccines do not last forever and many consequences from them with no studies. Building resistance is a natural healthy process. Epidemiological research into the connection between fever and protection against cancer Other interesting studies describe the same connection between the growing number of cancer cases and the decrease of febrile childhood diseases as a result of vaccinations (!), antibiotics and antipyretics over the last few decades importance of febrile disease in preventing cancer.
https://www.wanttoknow.info/health/cancer_link_vaccination_fever_research.pdf

6. Autism in our children

<https://www.ncbi.nlm.nih.gov/pubmed/23609067>

<https://www.ncbi.nlm.nih.gov/pubmed/25428645>

Epidemiologic and Molecular Relationship Between Vaccine Manufacture and Autism Spectrum Disorder Prevalence. [Deisher TA](#), [Doan NV](#), [Koyama K](#), [Bwabye S](#).

5. Informed Choice is already mandated by the State of Hawaii and is failing to be abided by many healthcare practitioners.

Healthcare Practitioners must give an informed choice, that includes speaking about the alternatives to the procedure that they are using. Vaccines need to by law show both sides.

Hawaii Revised Statutes 671-3 – Informed consent

6. FERPA Family Educational Rights and Privacy Act (FERPA)

DOH violation of demanding at a DOE school for the list of students not vaccinated for the Flu Vaccine in 2018.

FERPA Family Educational Rights and Privacy Act (FERPA)

7. VAERS While the Vaccine Adverse Events Reporting System [VAERS]

may be lauded as the “front line” of vaccine safety, the lack of enforcement provisions and effective monitoring of reporting practices preclude accurate assessments of the extent to which adverse events are actually reported. Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events. The quality of VAERS data has been questioned. Because reports are submitted from a variety of sources, some inexperienced in completing data forms for medical studies, many reports omit important data and contain obvious errors. Assessment is further complicated by the administration of multiple vaccines at the same time, following currently recommended vaccine schedules, because there may be no conclusive way to determine which vaccine or combination of vaccines caused the specific adverse event.

Pediatr Infect Dis J 28:943, 2009

8. Blood Money

The taking of STEM Cells from cord blood is a war crime in Hawaii under occupation as the baby needs them and they contain DNA.

AIMS Journal Vol. 16, NO 4 2005 pg 6,7

AIM Journal Vol. 17 pg 25, 26

*MCH 789 Case Stud/Research/MCH Program 2008 Clare Loprinzi Portfolio Dr. Horowitz ,
Professon Lorreta Fuddy Statistics , Birth Studies MCH JABSON Degree 2008 Clare Loprinzi*

9. Flu Vaccination and Exposure and Effects on Children.

*MCH 789 Case Stud/Research/MCH Program 2008 Clare Loprinzi Portfolio
Violation of Hawaii Revised Statutes 671-3 – Informed consent*

To Department of Health- Disease Outbreak Control Division,

I am writing to oppose the proposed rule changes to Hawai'i's vaccine requirement for children. It is a human right to have access to informed consent regarding any medical procedure that may have adverse affects on our children.

Deciding whether to vaccinate, like any medical procedure with inherent risks, is a choice that each individual should have the right to make. Vaccination is a medical procedure performed on otherwise healthy individuals that carries inherent risks, such as seizures and for some vaccines death. As parents, we have a responsibility and a right to examine the advantages and risks of a procedure before having it performed on our children.

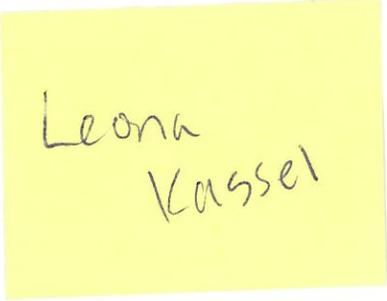
I ask you to consider your stance on informed consent. Specifically:

- Do you acknowledge that there are inherent risks associated with vaccinations?
- Do you affirm that informed consent is a basic human right?
- Do you endorse an informed consent for vaccinations?

We do not want to be forced to give our children all vaccines. Many of us parents believe that certain vaccines have risks that outweigh their benefit, such as the HPV and influenza vaccines. I strongly urge you to affirm our basic human right to informed consent regarding all medical procedures that may have adverse affects, including vaccines.

Thank you,

Leona Kassel



Leona
Kassel

Testimony of Dr. Joseph Kassel N.D., L.Ac.

I am testifying against the expansion of the mandatory vaccine schedule put forth by the DOH. The 1986 vaccine injury act protects the Pharmaceutical industry from lawsuits for vaccine injury. The U.S. government was played by the pharmaceutical industry to protect and now enhance their profits.

They now are promoting what will be a never ending expansion of vaccine mandates with impunity and inadequate supportive research on safety. I must note that this violates the favorite principal of the colonial occupying power that the free market will sort everything out. In point of fact the U.S. government has betrayed this principal as it has become a corporate oligarchy, a revolving door of conflicts of interest, the handmaiden to Pharmaceutical fossil fuel, tech and other interests. The interests of the people, colonized and otherwise will go unrecognized until they refuse to cooperate. The Hawaii state DOH marches in lockstep (or should I say goosetstep) serving these corporate interests under the guise of protecting human health. The aforementioned 1986 vaccine injury act also created VAERS to sort out reports of vaccine injury, however the vast majority of vaccine injuries go unreported, one calculation printed in the BMJ, estimated underreporting for one condition to be less than 1 report per 200 cases.

Autoimmune disease secondary to vaccination adjuvants now have their own acronym, ASIA Auto Immune Syndrome Induced by Adjuvants

The most commonly used adjuvant, Aluminum is a heavy metal with known neurotoxic effects on human and animal nervous systems. It can be found in the following childhood vaccines – DTaP, Pediarix (DTaP-Hepatitis B-Polio combination), Pentacel (DTaP-HIB-Polio combination), Hepatitis A, Hepatitis B, Haemophilus influenzae B (HIB), Human Papilloma Virus (HPV), and Pneumococcal vaccines.[2]

In 1996, the American Academy of Pediatrics issued a position paper on Aluminum Toxicity in Infants and Children which stated in the first paragraph, "Aluminum is now being implicated as interfering with a variety of cellular and metabolic processes in the nervous system and in other tissues.[3]

Many current vaccines including the Gardasil HPV vaccine utilize the most toxic aluminum adjuvant, the same form used in the notorious DPT vaccine that gave rise to the 1986 vaccine injury act.

My primary concerns about current vaccination protocols relate to disruption of normal immune function and likely potential for neurotoxicity from adjuvants preservatives and other components of vaccines.

It's important for those impacted to know that the hallmark of a healthy, mature immune system in children is demonstrated by an equal and balanced TH1, TH2 and TH3 immune response to the natural environment. TH1, TH2 & TH3 do not work independently, and require a very important synergistic relationship to function properly in our bodies. As soon as one or more of these three arms begins to over or under work in relation to the other, chronic illness begins to express itself.

More on Aluminum

Aluminum is placed in the vaccines to selectively target the up-regulation of the humoral arm (TH2 cells) of children's immune systems, to drive the production of antibodies. The medical community leads us to believe that this production of antibodies is what imparts for children a protective nature against vaccine-preventable illnesses. Yet, this outcome may come at a cost. I want to raise a concern that I haven't heard mentioned yet, I want to present the fact that a number of studies have shown that experiencing febrile illnesses both in childhood and adulthood, results in reduced cancer rates, an association recognized by Hippocrates, who admonished us as Physicians to first do no harm.

It is becoming quite evident to those of us looking at all available evidence, that modern science's mercenary tunnel vision is failing to explore the total impacts of vaccinations on human health thereby disrupting the natural development and balance between the 3 main arms of the immune system, it is increasing rates of atopic diseases such as asthma eczema, allergic rhinitis, and autoimmune diseases, while reducing the ability of naturally acquired illnesses to cultivate a vigorous healthy and balanced immune system. Modern vaccination schedules are doing harm, in violation of the hippocratic oath.

5 Hawaii Revised Statutes 671-3

Hawaii Board of Medical Examiners requires a thorough informed consent

- (1) The condition to be treated;
- (2) A description of the proposed treatment or procedure;
- (3) The intended and anticipated results of the proposed treatment or procedure;
- (4) The recognized alternative treatments or procedures, including the option of not providing these treatments or procedures;
- (5) The recognized material risks of serious complications or mortality associated with:
 - (A) The proposed treatment or procedure;
 - (B) The recognized alternative treatments or procedures; and
 - (C) Not undergoing any treatment or procedure; and
- (6) The recognized benefits of the recognized alternative treatments or procedures.

Are Medical Doctors associated with the DOH advocating for adherence or violation of this statute?

The Childhood IMMUNIZATION SCHEDULE and Safety

STAKEHOLDER CONCERNS, SCIENTIFIC EVIDENCE, AND FUTURE STUDIES

Committee on the Assessment of Studies of Health Outcomes Related to the Recommended Childhood Immunization Schedule

Board on Population Health and Public Health Practice

INSTITUTE OF MEDICINE

OF THE NATIONAL ACADEMIES. 2013 this is a seriously cautious and conservative institution

In summary, few studies have comprehensively assessed the association between the entire immunization schedule or variations in the overall schedule and categories of health outcomes, and no study has directly examined health outcomes and stakeholder concerns in precisely the way that the committee was charged to address in its statement of task. No studies have compared the differences in health outcomes that some stakeholders questioned between entirely unimmunized populations of children and fully immunized children. Experts who addressed the committee pointed not to a body of evidence that had been overlooked but rather to the fact that existing research has not been designed to test the entire immunization schedule.

In summary, to consider whether and how to study the safety and health outcomes of the entire childhood immunization schedule, the field needs valid and accepted metrics of the entire schedule (the "exposure") and clearer definitions of health outcomes linked to stakeholder concerns (the "outcomes") in rigorous research that will ensure validity and generalizability.

Is this acknowledgement of the unknown impacts of vaccination schedules shared in DOH recommended informed consents for vaccination?

Does the DOH have examples of vaccination informed consents that the DOH endorses?

Do they meet the requirements set forth in HRS 671-3?

Is the DOH encouraging Health Care Providers to share these conclusions with Vaccine recipients?

Please provide the examples of unbiased balanced informed consents for vaccinations provided by M.D.'s associated with the DOH or the DOH itself.

Is the DOH expected to or required to support/adhere to HRS 671-3?

Is the acknowledgement of the unknown impacts of vaccination schedules shared in DOH recommended informed consents for vaccination?

Are or would the vaccines cultured in fetal tissue cell lines and containing residual fetal DNA (Varicella, Rubella, Hepatitis A, Rabies and Shingles) identified in DOH endorsed informed consent?

Are or would the various animal cell lines, antibiotics, adjuvants including known toxicities, additives, history and possibility of viral contamination of vaccines be included in vaccine informed consents?

Where does the leap from ACIP recommendations to DOH/DOE mandates come from?

Has it resulted in alterations to DOH endorsed informed consent for vaccination schedules?

Does the DOH support informing parents/patients that vaccination creates an imperfect immune response that can predispose to the vaccinated to becoming carriers when exposed to the illness, as well as becoming vulnerable to illness or asymptomatic carrier later in life?

Will the DOH agree to the formation of a committee including skilled members (both advocates and opponents of universal vaccination) to write comprehensive informed consents for affected individuals and parents?

Several years ago I had a 4th year medical student observe in my clinic. She noted how healthy the children were. I shared that those were the sick ones, but they were born at home, breast fed and unvaccinated. Later I pointed out that many of the parents I work with follow my suggestion to give the children moderate amounts of vitamin c, which has been used for 7 decades to treat virtually all of the childhood illnesses which are now vaccinated for including 100% successful treatment of polio by Dr Klenner. I.V. vitamin c is finally beginning to be recognized as a crucial treatment increasing survival in sepsis significantly. So that will probably trigger multiple alarm bells of conventional dogma, and my intention today is not to convince you of anything, but I do want to state the following

1 There is significant scientific evidence of negative impacts of vaccination and a paucity of data supporting multiple vaccination schedule safety, failure to use genuine placebos in most safety studies and therefore there is a basis for a scientific as well as religious exemptions to vaccination schedules. That scientific exemptions are not recognized is a violation of civil rights and the bodily integrity of all those impacted by these rules.

2 unlike what is promulgated by the advocates of current expanding vaccination regimes, the science supporting vaccine safety is not conclusive, in fact there are not only significant volumes of contradictory research, but much of the requisite research to confirm safety has not been done.

3 People in positions of influence such as the DOH, are violating a sacred public trust by turning CDC recommendations into mandates and failing to honestly convey to parents what is known and unknown about vaccine effectiveness and safety.

4 the mandatory vaccination policy may well reduce vaccination rates by forcing parents who would have opted for selective vaccination to choose none on religious grounds since they are left no other option.

5 There is some serious cynicism afoot with some of the required vaccines in this expansion of the vaccine schedule. The annual flu vaccine is worse than a bad joke.

Over 75% of annual flu like illnesses are not influenza, the vaccination will not protect against these illnesses, yet the cdc will include morbidity and mortality from these illnesses in their scare tactics. One annual study showed 19% of flu like illnesses were in fact the flu and 57% of those with the flu were vaccinated. Meanwhile adults receiving the flu vaccine 5 years in a row demonstrate a 10 fold increase in Alzheimers disease. The HPV vaccines are another nightmare with limited if any advantage over routine screening in impacting cervical cancer and extremely serious neurological and reproductive consequences.

6The inclusion of Naturopathic Physicians as providers capable of assessing Medical exemptions, while imposing stringent adherence to an alien allopathic Medical paradigm for making such assessments is a hollow and patronizing inclusion.

7 finally, Imposing vaccination schedules originating from the Federal agency of the occupying power, the CDC, is in fact a War Crime, since no such vaccination schedule exists for the occupied Hawaiian Kingdom

The Childhood
IMMUNIZATION SCHEDULE
and Safety

STAKEHOLDER CONCERNS, SCIENTIFIC EVIDENCE, AND FUTURE STUDIES
Committee on the Assessment of Studies of Health Outcomes Related to the Recommended
Childhood Immunization Schedule
Board on Population Health and Public Health Practice
INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Lupus. 2012 Feb;21(2):223-30. doi: 10.1177/0961203311430221.
Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations.
Tomljenovic L1, Shaw CA.

J Autoimmun. 2013 Dec;47:1-16. doi: 10.1016/j.jaut.2013.10.004. Epub 2013 Nov 13.
Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the
pathogenic, clinical and diagnostic aspects.
Perricone C1, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y.

Am J Public Health. 2012 May; 102(5): 893-898.
Published online 2012 May. doi: [10.2105/AJPH.2011.300576]
PMCID: PMC3483914
PMID: 22420796
Pharmaceutical Companies' Role in State Vaccination Policymaking: The Case of Human
Papillomavirus Vaccination
Michelle M. Mello, JD, PhD, Sara Abiola, JD, PhD, and James Colgrove, PhD

Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination: A
Case Series Seen in General Practice
Deirdre Therese Little, Harvey Rodrick Grenville Ward
J Investig Med High Impact Case Rep. 2014 Oct-Dec; 2(4): 2324709614556129. Published
online 2014 Oct 28. doi: 10.1177/2324709614556129

Association of measles and mumps with cardiovascular disease: The Japan Collaborative
Cohort (JACC) study.
Kubota Y, et al. Atherosclerosis. 2015.
Atherosclerosis. 2015 Aug;241(2):682-6. doi: 10.1016/j.atherosclerosis.2015.06.026. Epub 2015
Jun 18.

Allergic Disease and Atopic Sensitization in Children
in Relation to Measles Vaccination and
Measles Infection
Helen Rosenlund, MSc, Anna Bergström, PhD, et al.

PEDIATRICS Volume 123, Number 3, March 2009

The Risk of Seizures after Receipt of Whole-Cell Pertussis or Measles, Mumps, and Rubella
Vaccine
William E. Barlow, Ph.D., Robert L. Davis, M.D., M.P.H., et. al.
N Engl J Med 2001; 345:656-661

BMJ. 1999 Oct 23; 319(7217): 1133.

PMCID: PMC1116914
PMID: 10531116
Association between type 1 diabetes and Hib vaccine
Causal relation is likely
J Barthelow Classen,
BMJ. 1999 Oct 23; 319(7217): 1133.

Ann N Y Acad Sci. 2003 Nov;1005:404-8.
Vaccinations may induce diabetes-related autoantibodies in one-year-old children.
Wahlberg J1, Fredriksson J, Vaarala O, Ludvigsson J; Abis Study Gröu

Arch Dis Child. 2001 Mar; 84(3): 227-229.
doi: [10.1136/adc.84.3.227]
PMCID: PMC1718684
PMID: 11207170
Idiopathic thrombocytopenic purpura and MMR vaccine
E Miller, P Waight, C Farrington, N Andrews, J Stowe, and B Taylor

Immunol Res. 2013 Jul;56(2-3):304-16. doi: 10.1007/s12026-013-8403-1.
Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine
adjuvants, and autoimmunity.
Shaw CA1, Tomljenovic L

Immunotherapy. 2014;6(10):1055-71. doi: 10.2217/imt.14.81.
Are there negative CNS impacts of aluminum adjuvants used in vaccines and immunotherapy?
Shaw CA1, Li D, Tomljenovic

**Issues Law Med. 2015 Spring;30(1):47-70.Epidemiologic and Molecular
Relationship Between Vaccine Manufacture and Autism Spectrum Disorder
Prevalence.Deisher TA, Doan NV, Koyama K, Bwabye**

**J Inorg Biochem. 2018 Apr;181:87-95. doi: 10.1016/j.jinorgbio.2017.12.015.
Epub 2017 Dec 28.Critical analysis of reference studies on the toxicokinetics of
aluminum-based adjuvants.Masson JD1, Crépeaux G2, Authier FJ1, Exley
C3, Gherardi RK**

**Medical Hypotheses Volume 51, Issue 4, October 1998, Pages 315-320Febrile
infectious childhood diseases in the history of cancer patients and matched
controlAuthor links open overlay panelH.U.AlbonicoH.U.Bräker*aJ.Hüsler*a**

**Cancer Detect Prev. 2006;30(1):83-93. Epub 2006 Feb 21.Acute infections as a
means of cancer prevention: opposing effects to chronic infections?Hopton
Cann SA1, van Netten JP, van Netten C.**

Victoria, J., Wang, C., Jones, M., Jaing, C., McLoughlin, K., Gardner, S., & Delwart, E. (2010). Viral nucleic acids in live-attenuated vaccines: detection of minority variants and an adventitious virus. *Journal of Virology* DOI: [10.1128/JVI.02690-09](https://doi.org/10.1128/JVI.02690-09)

Measles Outbreak Traced to Fully Vaccinated Patient for First Time By
Nsikan Akpan Apr. 11, 2014 , 12:00 PM. Science.

Waning Protection after Fifth Dose of Acellular Pertussis Vaccine in Children Nicola P. Klein, M.D., Ph.D., Joan Bartlett, M.P.H., M.P.P., Ali Rowhani-Rahbar, M.D., M.P.H., Ph.D., Bruce Fireman, M.A., and Roger Baxter, M.D. September 13, 2012 *N Engl J Med* 2012; 367:1012-1019 DOI: [10.1056/NEJMoa1200850](https://doi.org/10.1056/NEJMoa1200850)

Klenner FR. The treatment of poliomyelitis and other virus diseases with vitamin C. *Southern Medicine and Surgery*, July, 1949, p 209.

Biofactors. 2009 Jan–Feb; 35(1): 5–13.

doi: [10.1002/biof.7]

PMCID: PMC2767105

NIHMSID: NIHMS151756

PMID: 19319840

Mechanism of action of vitamin C in sepsis: Ascorbate modulates redox signaling in endothelium

John X. Wilson*

Phase I safety trial of intravenous ascorbic acid in patients ...

Fowler AA, Fisher BJ, DeWilde C, Priday A, Syed A, Farthing CA, Larus TL, Knowlson S, Natarajan R. Parenteral vitamin C attenuates markers of organ injury and inflammation in severe sepsis [abstract] *Am J Respir Crit Care Med*. 2012; 185 (2012):A6718.

J Exp Med. 1939 Aug 31; 70(3): 315–332.

A FURTHER CONTRIBUTION TO VITAMIN C THERAPY IN EXPERIMENTAL POLIOMYELITIS

Claus W. Jungeblut

Ramifications of adverse events in children in Australia *BMJ* 2010; 340 doi:

<https://doi.org/10.1136/bmj.c2994> (Published 09 June 2010) Cite this as: *BMJ* 2010;340:c2994

Is this acknowledgement of the unknown impacts of vaccination schedules shared in DOH recommended informed consents for vaccination?
Does the DOH have examples of vaccination informed consents that the DOH endorses?
Do they meet the requirements set forth in HRS 671-3?
Is the DOH encouraging Health Care Providers to share these conclusions with Vaccine recipients?

Please provide the examples of unbiased balanced informed consents for vaccinations provided by M.D.'s associated with the DOH or the DOH itself.
Is the DOH expected to or required to support/adhere to HRS 671-3?
Is the acknowledgement of the unknown impacts of vaccination schedules shared in DOH recommended informed consents for vaccination?
Are or would the vaccines cultured in fetal tissue cell lines and containing residual fetal DNA (Varicella, Rubella, Hepatitis A, Rabies and Shingles) identified in DOH endorsed informed consent?

Are or would the various animal cell lines, antibiotics, adjuvants, additives, history and possibility of viral contamination of vaccines be included in vaccine informed consents?

Where does the leap from ACIP recommendations to DOH/DOE mandates come from?
Has it resulted in alterations to DOH endorsed informed consent for vaccination schedules?
Will the DOH agree to the formation of a committee including skilled members (both advocates and opponents of universal vaccination) to write comprehensive informed consents for affected individuals and parents?

Does the DOH support informing parents/patients that vaccination creates an imperfect immune response that can predispose to the vaccinated to becoming carriers when exposed to the illness, as well as becoming vulnerable to illness or asymptomatic carrier later in life?

Hi my name is Nayeva Pajot Gendron.
I oppose HR 11 157

And Specifically Point 6 Enhanced reporting requirements for medical and religious exemptions

We currently have exemptions for medical and religious and we don't want that to change at all.
And I feel that we should also add philosophical exemptions to the state of Hawaii.

I would like to submit Exhibit a.

"President Trump promised the American people that his administration would vigorously uphold the rights of conscience and religious freedom. That promise is being kept today. The Founding Fathers knew that a nation that respects conscience rights is more diverse and more free, and OCR's new division will help make that vision a reality."

<https://www.hhs.gov/about/news/2018/01/18/hhs-ocr-announces-new-conscience-and-religious-freedom-division.html?language=en>

also President Trump commissioned Robert Kennedy to investigate the pharmaceutical immunizations.

It is against our constitutional rights to force American citizens to inject poisons with unknown side effects into our bodies against our will or without the right to choose.

The Universal Declaration of Human Rights adopted in 1948 after World War II states that, "Everyone has the right to freedom of thought, conscience and religion; this right includes freedom to change his religion or belief, and freedom, either alone or in community with others and in public or private, to manifest his religion or belief in teaching, practice, worship and observance."

U.S. Supreme Court: Vaccines are "Unavoidably Unsafe"

In 2011, the U.S. Supreme Court agreed with what Congress said in 1986, and that is: government licensed vaccines are "unavoidably unsafe" and pharmaceutical corporations should not be liable for vaccine injuries and deaths. 30 31 Today, when your child dies or is permanently brain injured after vaccination or the vaccine fails to protect your child, you cannot hold the vaccine manufacturer or the doctor who gave the vaccine accountable in court in front of a jury of your peers.

With this free pass, in 2011 and 2012 the multi-billion dollar vaccine machine powered by medical trade, industry and government rolled into the legislatures of Washington, Vermont and other states with the goal of eliminating religious and conscience vaccine exemptions that have been in place in the U.S. for more than half a century. 32 NVIC has worked with families and other grassroots organizations to protect vaccine exemptions in 15 states but, in 2015, Vermont lost the conscience exemption and California lost the personal belief exemption protecting both exercise of conscience and religious beliefs. 33

There are three general statements about vaccination in the U.S. that cannot be disputed, which are:

1. Like prescription drugs, vaccines are pharmaceutical products that carry a risk of injury, death and failure. 46 47 48 49
2. There are genetic, biological and environmental high risk factors that make some individuals more susceptible to vaccine reactions, but doctors cannot predict who will be harmed. 50
3. The U.S. Congress and Supreme Court have declared government licensed and mandated vaccines to be “unavoidably unsafe” and more than \$3 billion dollars in federal vaccine injury compensation has been awarded to children and adults under the National Childhood Vaccine Injury Act of 1986.

These three basic facts about vaccination affect your human right to exercise freedom of thought, conscience and religious belief:

Because vaccines can injure or kill and doctors cannot predict who will be harmed, and the U.S. government has acknowledged that fact and indemnified pharmaceutical corporations and doctors, while awarding financial compensation to children and adults who have been injured or died from government licensed vaccines, 52 you have the human right to exercise informed consent, freedom of conscience and religious belief when making a decision about vaccination for yourself or your minor. Whatever your sincere religious beliefs, you do not have to be a member of an organized religion or church to hold them and defend your human right to exercise freedom of conscience. In America, you should not have to live in fear that you will be judged and punished for exercising freedom of thought, conscience and religious belief.

Thank you for doing the right thing and protecting our right to choose.

~ Nayeva Pajot Gendron

HHS Announces New Conscience and Religious Freedom Division

Today, the U.S. Department of Health and Human Services (HHS) is pleased to announce the formation of a new Conscience and Religious Freedom Division in the HHS Office for Civil Rights (OCR). The announcement will take place at an event at HHS headquarters from 10:30 a.m. to noon. It will be livestreamed [here](#). Speakers will include Acting Secretary Eric D. Hargan, House Majority Leader Kevin McCarthy, Representative Vicky Hartzler, Senator James Lankford, OCR Director Roger Severino, and special guests.

The Conscience and Religious Freedom Division has been established to restore federal enforcement of our nation's laws that protect the fundamental and unalienable rights of conscience and religious freedom. OCR is the law enforcement agency within HHS that enforces federal laws protecting civil rights and conscience in health and human services, and the security and privacy of people's health information. The creation of the new division will provide HHS with the focus it needs to more vigorously and effectively enforce existing laws protecting the rights of conscience and religious freedom, the first freedom protected in the Bill of Rights.

OCR already has enforcement authority over federal conscience protection statutes, such as the Church, Coats-Snowe, and Weldon Amendments; Section 1553 of the Affordable Care Act (on assisted suicide); and certain federal nondiscrimination laws that prohibit discrimination on the basis of religion in a variety of HHS programs.

OCR Director Severino said, "Laws protecting religious freedom and conscience rights are just empty words on paper if they aren't enforced. No one should be forced to choose between helping sick people and living by one's deepest moral or religious convictions, and the new division will help guarantee that victims of unlawful discrimination find justice. For too long, governments big and small have treated conscience claims with hostility instead of protection, but change is coming and it begins here and now."

Acting HHS Secretary Hargan said, "President Trump promised the American people that his administration would vigorously uphold the rights of conscience and religious freedom. That promise is being kept today. The Founding Fathers knew that a nation that respects conscience rights is more diverse and more free, and OCR's new division will help make that vision a reality."

To learn more about the new Conscience and Religious Freedom Division, visit us at www.hhs.gov/conscience.

To file a complaint with OCR based on a violation of civil rights, conscience or religious freedom, or health information privacy, visit us at <https://www.hhs.gov/ocr/complaints>.

VACCINATION EXEMPTION PURSUANT TO THE
Hawaii Administrative Rules §11-157-5 & OFFICIAL CODE OF Haw. Rev. Stat. § 325-34

§11-157-5 Exemptions. (b) *A religious exemption shall be granted to a student whose parent, custodian, guardian, or other person in loco parentis certifies that the person's religious beliefs prohibit the practice of immunization. Requests for religious exemptions based on objections to specific immunizing agents will not be granted. Students who have reached the age of majority shall apply on their own behalf. The certification shall be retained in the student's health record. Reports of such exemptions shall be submitted to the department by each school.*

§ 325-34 *No person shall be subjected to vaccination, revaccination or immunization, who shall in writing object thereto on the grounds that the requirements are not in accordance with the religious tenets of an established church of which the person is a member or adherent, or, if the person is a minor or under guardianship, whose parent or guardian shall in writing object thereto on such grounds, but no objection shall be recognized when, in the opinion of the director of health, there is danger of an epidemic from any communicable disease.*

VACCINE EXEMPTION FORM

I, _____, as the parent, guardian or person in
(insert your name)
loco parentis of the child _____, hereby certify that the
(insert your child's name)
administration of any vaccine or other immunizing agents is contrary to our personal
religious beliefs.

- | | | |
|--------------------------------------|--|--------------------------------|
| <input type="checkbox"/> Diphtheria | <input type="checkbox"/> Measles | <input type="checkbox"/> Other |
| <input type="checkbox"/> Tetanus | <input type="checkbox"/> Mumps | <input type="checkbox"/> ALL |
| <input type="checkbox"/> Pertussis | <input type="checkbox"/> Rubella | |
| <input type="checkbox"/> Polio | <input type="checkbox"/> Haemophilus influenzae type b | |
| <input type="checkbox"/> Hepatitis B | <input type="checkbox"/> Varicella | |
| <input type="checkbox"/> Smallpox | <input type="checkbox"/> Anthrax | |

This is pursuant to my right to refuse vaccination on the grounds that vaccinations conflict with my religious beliefs. Pursuant to Hawaii statute I am providing a copy of this statement to our child's school administrator or operator of the group program pursuant to Hawaii Administrative Rules §11-157-5 and Haw. Rev. Stat. § 325-34.

Parent _____ Date _____

Parent _____ Date _____

Subscribed and Sworn before me this _____ day of _____, 20_____.

Notary's Signature and Seal

Making Informed Decisions

Your decision to vaccinate or not should be an informed decision. Vaccines can cause severe injuries such as seizures, death, anaphylaxis, brain damage and other reactions. The type and severity of reactions may vary from vaccine to vaccine and child to child. The effects of a vaccine injury may be temporary or permanent. If you notice any changes in your child's condition after receiving a vaccine, you should contact your doctor immediately or go to a hospital. Vaccines have never been proven to be safe or effective and your child may contract the disease even if he is vaccinated. What has been proven is that you can get the disease from the vaccine or from coming into contact with a recently vaccinated person. The polio vaccine is just one example. It is a known fact that most healthcare providers do not fully inform patients of the side effects a vaccine can have on the body, brain and immune system. Because of the highly toxic ingredients all vaccines contain, you should thoroughly research vaccines for yourself before making such an important decision. DO NOT allow someone else, even your healthcare provider, scare or force you into making this decision without being fully informed. Many healthcare providers have not researched vaccine history or toxicology and are not fully informed.

Always provide a detailed history of your child's health to your doctor. Make sure they know of allergies, neurological problems, nutritional deficiencies, any immune system disorder and skin diseases such as eczema. Most physicians and nurses do not warn parents that if their child's health is compromised in any way, such as having a common cold or previous reaction to a vaccine, they should not receive vaccines.

Benefits of Non-Vaccination

When you choose to not vaccinate your child, you have the responsibility to educate yourself on how to maintain the well-being of not only their body but also their mind and spirit as well. Childhood diseases can result in minor symptoms to severe complication or death depending on the child's immune system and treatment protocols followed. The stronger the immune system, the less severe are the symptoms of the disease. A child that goes through the full expression of the disease (i.e. fever and skin eruptions, without suppressing any of these symptoms) usually acquires immunity from that disease for life. Good nutrition and cleanliness play a major role. The risk of contracting various diseases can vary over time or locality. Symptoms or complications of these diseases may be treatable by alternative methods or may resolve without treatment. Educate yourself on childhood diseases from informed alternative sources. Fear of these diseases comes from not being properly informed.

For More Information

To make a truly informed decision there are numerous sources of information on the risks of vaccines and the risks and benefits of childhood diseases. Sources of information to determine if the risks associated with vaccines outweigh any perceived benefits include: vaccine package inserts, the Physicians Desk Reference, the U.S. Center for Disease Control and Prevention, public and medical libraries or state and local health agencies. (NOTE: These sources do not give complete and total information on vaccine ingredients and their toxicity, nor do they provide accurate statistics.)
Vaccination Liberation – www.vaclib.org or (888) 249-1421
National Vaccine Information Center – www.909shot.com or (800) 909-SHOT / (703) 938-0324
(NOTE: The two websites above, Vaccination Liberation and the National Vaccine Information Center, have proven to be excellent sources for extensive vaccine information.)

Reporting Reactions

If you do decide to vaccinate, report vaccine reactions to the Vaccine Adverse Event Reporting System (800) 822-7969. Always get the vaccine name, vaccine manufacturer and lot number. Keep records of day to day reactions from the time of vaccination for at least 6 months to 2 years, no matter how slight the reactions. Long-term effects of vaccines have not been well documented by the allopathic community and are just now being researched. If your child has been injured by a vaccine, he may be eligible for compensation under the National Vaccine Injury Compensation Program.

State Vaccination Exemptions: Medical, Religious, and Philosophical



medical
 medical and religious
 medical, religious, and philosophical

States (and DC) Click on the state to view its statutes on vaccine regulations and exemptions in PDF format	Allows Medical Exemption	Allows Religious Exemption	Allows Philosophical Exemption
	(50 states and DC)	(47 states and DC)	(17 states and DC)
Alabama	✓	✓	✗
Alaska	✓	✓	✗
Arizona	✓	✓	✓
Arkansas	✓	✓	✓
California	✓	✗	✗
Colorado	✓	✓	✓
Connecticut	✓	✓	✗
Delaware	✓	✓	✗

Washington, DC	✓	✓	✗
Florida	✓	✓	✗
Georgia	✓	✓	✗
Hawaii	✓	✓	✗
Idaho	✓	✓	✓
Illinois	✓	✓	✗
Indiana	✓	✓	✗
Iowa	✓	✓	✗
Kansas	✓	✓	✗
Kentucky	✓	✓	✗
Louisiana	✓	✓	✓
Maine	✓	✓	✓
Maryland	✓	✓	✗
Massachusetts	✓	✓	✗
Michigan	✓	✓	✓
Minnesota	✓	✓	✓
Mississippi	✓	✗	✗
Missouri	✓	✓	✗
Montana	✓	✓	✗
Nebraska	✓	✓	✗
Nevada	✓	✓	✗
New Hampshire	✓	✓	✗
New Jersey	✓	✓	✗
New Mexico	✓	✓	✗
New York	✓	✓	✗
North Carolina	✓	✓	✗
North Dakota	✓	✓	✓
Ohio	✓	✓	✓
Oklahoma	✓	✓	✓

Oregon	✓	✓	✓
Pennsylvania	✓	✓	✓
Rhode Island	✓	✓	✗
South Carolina	✓	✓	✗
South Dakota	✓	✓	✗
Tennessee	✓	✓	✗
Texas	✓	✓	✓
Utah	✓	✓	✓
Vermont	✓	✓	✗
Virginia	✓	✓	✗
Washington	✓	✓	✓
West Virginia	✓	✗	✗
Wisconsin	✓	✓	✓
Wyoming	✓	✓	✗

For an example of what a vaccination exemption form looks like, see Wyoming's medical and religious vaccination exemption forms.

Sources:

Pat Bradley, "Vermont Governor Signs Bill Removing Philosophical Exemption from Vaccine Choice," wamc.org, May 29, 2015

Centers for Disease Control and Prevention (CDC), "Childcare and School Immunization Requirements," www.2a.cdc.gov, June 23, 2008

Centers for Disease Control and Prevention (CDC), "School Vaccination Requirements, Exemptions and Web Links," www.cdc.gov, July 21, 2011

National Conference of State Legislators (NCSL), "States with Religious and Philosophical Exemptions from School Immunization Requirements," www.ncsl.org, Dec. 2009

National Vaccine Information Center (NVIC), "State Vaccine Requirements," www.nvic.org (accessed Jan. 22, 2010)

Vaccingate: Initial results on Infanrix Hexa chemical composition

When we started these analysis, from the metagenomics to the chemical ones, we had a lot of questions and we were only looking for answers...
After these first results, more questions have arisen and so did the concerns!

The quali-quantitative analysis of organic compound is of great importance in the pharmacological field, as potential safety problems arise from the new production processes of biological drugs and from the complex structural and biological characteristics of these products.

In Infanrix Hexa we found

- chemical contamination from the manufacturing process or cross-contamination with other manufacturing lines;
- chemical toxins;
- bacterial peptide toxins;
- insoluble and indigestible macromolecule that reacts to the protein assay, but cannot be recognized by any protein databases.

We have not found:

- Protein antigens of diphtheria toxoids, tetanus, pertussis, hepatitis B, haemophilus influenzae B, Poliomyelitis 1-2-3;
- Formaldehyde and glutaraldehyde, phenoxyethanol, antibiotic residues indicated in the composition;

In Infanrix Hexa there are six antigens

Tetanus, diphtheria and pertussis toxoids, D antigens of Poliomyelitis 1-2-3, hepatitis B proteins obtained with genetic engineering and Haemophilus polysaccharides chemically linked to tetanus toxoid as carrier. Toxoids are created by treatments with formaldehyde and glutaraldehyde that should remove toxicity keeping intact their ability to stimulate protective antibodies against original toxins.

We were expecting to find the three toxoids and the other antigens not modified by treatment with formaldehyde and glutaraldehyde, to separate the antigens from each other and to be digestible by the enzyme specific for proteins (trypsin). **We have found instead a real polymer, insoluble and indigestible, that we supposed to be the set of antigens chemically bound together (has to be defined if this is present as an aggregate of the individual antigens or a single macromolecule), on which we can find in literature partial information regarding the single antigens.**

This macromolecule could not be recognized in any way by the protein databases, and in fact it turned out to be a solid compound of an unknown chemical structure.

Proteins solubility and their digestion (i.e. the capacity to divide them into small peptide fragments) are two typical proteins characteristics that not only makes it possible to study them through some specific analysis methods **but are also fundamental for the interaction with the immune system to create protective antibodies**, because if the protein structure is heavily altered from the original one, the new antibodies result completely different from those that are able to attack the original antibodies causing illnesses.】

Since this polymer we have encountered, derived from the antigenic mix, is not only different for its spatial conformation but it's chemically different, so **we can state that we are not facing antigens similar to the original ones but in the form of a compound with an unknown and unpredictable toxicity and efficacy.**

Not only vaccine antigens have been not detected, there were also 65 signs of chemical contaminants of which only 35% is known, there are among these various processing residues and cross-contaminations from other manufacturing lines, and their identification will be checked during the second level of the analytical study (i.e. with standard controls).

7 chemical toxins among these signals have also been identified, probably deriving from chemical contaminants of the manufacturing process or other manufacturing lines at the vaccine manufacturing site; these toxins have a structure that could probably be partially derived from the formaldehyde, glutaraldehyde and cyanogen bromide reaction with other chemical contaminants in the vaccine. We'd like to point out that the toxicity of many of these toxins have been confirmed and published in Pubchem or Toxnet and this poses important safety problems, issues and concerns.

From the protein and peptide fraction study, various free peptides of bacterial origin have been obtained probably coming from the bacterial culture cells used for the antigen extraction. Literature reports bacterial peptides as potential allergens ⁵ and also as capable of inducing autoimmune reactions ⁶ and these too put a safety issue that needs to be further clarified with the regulatory bodies.

Coming back to the two basic principles that have been our topic on this analysis path, we reaffirm what we have said in the recent interview on the scientific journal Nature: we are inquiring the vaccines efficacy and safety and we can't quite understand how it is possible to claim that this vaccine is even able to generate the 6 protective antibodies - reason why it is designed for - and furthermore to understand how this cluster made of 6 neurotoxic antigens bound together can be claimed as not toxic for newborns.

Infanrix Hexa hexavalent, as for the method we have commissioned, casts major doubts on both its effectiveness and on its safety...

One thing is for sure: we will not stop to proceed.

Study on the chemical composition profile of Infanrix Hexa

Introduction and description of the need

The quali-quantitative analysis of organic compounds is of great importance in the pharmacological field¹, as potential safety problems arise from the new production processes of biological drugs and from the complex structural and biological characteristics of these products.²

The review of the registration dossiers for military vaccines that we find in the final report³ of the Parliamentary Commission of Inquiry "Depleted Uranium"⁴ revealed the presence of protein-chemical contaminants and impurities, which required further analytical study. Our association has decided to take charge of it, as far as possible.

This project is part of the above-mentioned insights. It has been therefore necessary to develop a technology capable of analyzing a wide spectrum of molecules of chemical, metabolic and protein origin in order to evaluate the quality of the obtained results.

A method has been therefore developed, based on SANIST technology to test vaccines for purity and safety (further information below).

Results and Discussion

1. Analysis of the composition declared in the vaccine leaflet

Compound	Presence	Ionic species
Amino acids	YES	[M+H] ⁺
Formaldehyde ⁵	Not detected	-
Lactose anhydrous	YES	[M+H-H ₂ O] ⁺
Vitamins	Not detectable	-
Water	YES	[M+H] ⁺
Neomycin	Weak signal	[M+2H] ²⁺
Diphtheria Toxoid ⁶	Not detected	[M+nH] ⁿ⁺
Tetanus Toxoid ⁷	Not detected	[M+nH] ⁿ⁺
Pertussis Toxoid ⁸	Not detected	[M+nH] ⁿ⁺
Filamentous Haemagglutinin Adhesin (FHA)	Not detected	[M+nH] ⁿ⁺
Pertactin (PRN)	Not detected	[M+nH] ⁿ⁺
Haemophilus Influenzae B polysaccharide ⁹	Not detected	[M+nH] ⁿ⁺
Polyribosylribitol Phosphate (PRP) ¹⁰	Not detectable	-
Polymyxin ¹⁰	Non rilevabile	-

¹ Lett Appl Microbiol. 2015 Feb;60(2):174-80. doi: 10.1111/lam.12355 - <https://www.ncbi.nlm.nih.gov/pubmed/25376111>

² Fuchs F, Biochimie. 2002 Nov;84(11):1173-9 - <https://www.ncbi.nlm.nih.gov/pubmed/12595146>

³ <http://www.camera.it/leg17/491?idLegislatura=17&categoria=022bis&tipologiaDoc=documento&numero=023&doc=pdfel>

⁴ http://www.camera.it/leg17/436?shadow_organo_parlamentare=2588

⁵ <https://pubchem.ncbi.nlm.nih.gov/compound/formaldehyde>

⁶ <https://www.who.int/biologicals/vaccines/diphtheria/en/>

⁷ <https://www.who.int/ith/vaccines/tetanus/en/>

⁸ <http://www.who.int/biologicals/vaccines/pertussis/en/>

⁹ https://www.who.int/biologicals/areas/vaccines/haemophilus/haemophilus_influenzae_typeb_Hib/en/

¹⁰ <https://www.sciencedirect.com/topics/neuroscience/polymyxin>

2. Protein fraction analysis

According to the manufacturer, Infanrix Hexa vaccine contains some proteins. The sample has been analyzed for the identification of these proteins. At a visual analysis, the sample appears milky.

Different analysis have been conducted on the sample:

2.1 - 1st analysis: Digestion as it is

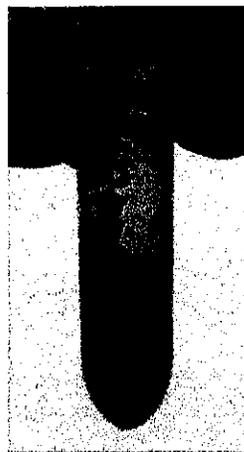
To start with, the sample has been subjected to an enzymatic digestion process: 10 μL of a raw sample has been treated with 50 μL Trypsin, left overnight in thermoblock at 37 ° C. A 1 mg / mL hemoglobin control has been prepared and treated as the sample. **This analysis revealed the absence of any proteins in the sample.**

2.2 - 2nd Analysis: Digestion of Precipitate

The sample has been then subjected to further analysis by separating, by centrifugation, the liquid part from the solid part of the milky suspension. All the supernatant has been taken. The remaining precipitate has been treated with 30 μL Trypsin and left overnight in thermoblock at 37 ° C. A 1 mg / mL hemoglobin control has been prepared and treated as the sample. After digestion, the sample and the control have been centrifuged. The supernatant has been taken and placed in vials for analysis. 20 μL osmotized H_2O have been added in order to give enough volume for injection. **This analysis revealed the absence of any proteins in the sample.**

2.3 - 3rd analysis: Bradford assay

To identify the actual presence of proteins, Infanrix Hexa vaccine has been subjected to the Bradford assay. 200 μL of the raw sample has been treated with 300 μL osmotic H_2O to obtain volume. Then 500 μL of Bradford reagent have been added. After a visual analysis, we can confirm the presence of proteins or peptide sequences given by the blue color (see Figure below):



Based on the calibration line, a protein concentration of 1.099 mg/mL was detected.

2.4 - 4th analysis: Digestion as it is at 57 ° C

After Bradford's assay, 20 μL of the raw sample has been treated with 80 μL of Trypsin. A 1 mg / mL hemoglobin control has been prepared and treated as the sample. They have been left in thermoblock at 37 ° C for 4 hours and then at 57 ° C for 30 minutes. The sample and the control have

then been subjected to centrifugation and the supernatant has been taken and placed in vial for analysis.

In order to process the data thus obtained, the Mascot¹¹ database has been initially used but **nothing has been found**. Therefore, the GMP has been used but also in this case **no protein sequences have been detected**. By the DeNovo research, the following peptide sequences that do not meet the trypsin cutting criteria and therefore potentially belong to free peptides have been identified. Below is the detected sequences list:

YLSA	YLSA	SLGS	HNLPT
QLYTCC	CHFAHD	WRASST	SYLPFT
SAGE	HLLNMT	YSDDQC	NMAWW
DEV	CHPPYL	TDTENW	GPFRVW
AEYHW	TLAPRF	ALAPWF	RWGPH
DEV	GSAAG	MNFHR	DSYWH
VLYACPP	DEV	NSNWW	WGC
	SNCGYY	VFHRE	

These sequences have been filed into the MS-BLAST¹² search engine obtaining the characterizations reported in Table 1. As can be seen, they have been potentially attributed by structural similarity to proteins of the bacterial world. **The proteins relating to the antigens present in the vaccine have not been detected**. This may be due to its extensive structural modification, introduced by formaldehyde and glutaraldehyde. In fact, the database research has been carried out Without considering the m/z variation introduced by the above-mentioned compounds

It is important to verify whether these changes have led to cross-linked macromolecular complexes shaping. In this regard, we will ask for further analysis using MALDI-TOF-MS¹³ technology widely acknowledged in clinical practice for the study of high weight macromolecules,

Table 1 - Batch #1 (A21CD072D)

Name of Protein	Organism	Total Score
Hypothetical protein CALCODRAFT_501505	Calocera cornea HHB 12733	159
Erg4/erg24 family protein	Dictyostelium lacteum	154
3-phenylpropionic acid transporter	Rhodospirillum rubrum	154
Hypothetical protein LAESUDRAFT_731137	Chaetium sulphureum 93-53	149
Aldehyde ferredoxin oxidoreductase	Alkaliphilus oremlandii	138
Aldehyde ferredoxin oxidoreductase	Alkaliphilus oremlandii OhLAs	138
Hypothetical protein KAFR_OH02570	Kazachstania africana CBS 2517	136
Hypothetical protein	Pseudoxanthomonas mexicana	136
Hypothetical protein	Endozoicomonas elysicola	135
Homeodomain-like DNA binding domain-containing transcription factor	Phycomyces blakesleeianus NRRL 1555(-)	110
Transcriptional regulator	Streptomyces clavuligerus	109
DNA-binding protein	Streptomyces clavuligerus ATCC 27064	109
Glycosyl hydrolase family 3 N-terminal domain protein	Thermotoga bacterium CAG:56	108
PREDICTED: zinc finger CCCH domain-containing protein 69-like	Pyru x bretscheideri	108
Hypothetical protein CC1G_06886	Coprinopsis cinerea okayama7#130	108
Hypothetical protein FIBSPDRAFT_917685	Bulborhizoctonia sp. CBS 109695	107
Uncharacterized protein	Blastocystis hominis	104
Unnamed protein product	Blastocystis hominis	104
Hypothetical protein J132_09024	Termitomyces ssp. J132	104

3. Metabolic fraction Analysis

¹¹ http://www.matrixscience.com/help/seq_db_setup_db_gui.html

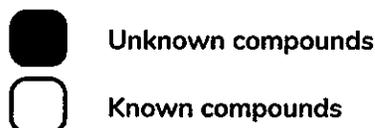
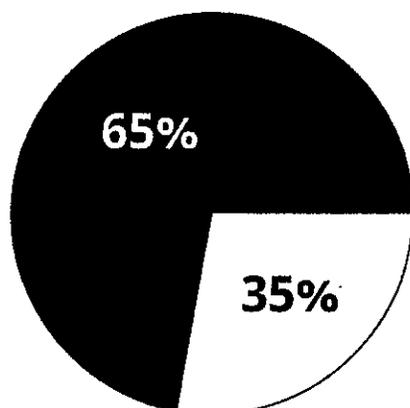
¹² <http://genetics.bwh.harvard.edu/msblast/>

¹³ <https://it.wikipedia.org/wiki/MALDI>

It should be emphasized that this screening study provides a semi-quantitative data which correspond to a range from nanograms to micrograms as an indicative order of magnitude. To obtain accurate quantitative data, it will be necessary to proceed using certified analytical standards of known strength.

Below, we report the identification screening results obtained in the two batches under examination:

Batch #1 (A21CD072D)



In Batch # 1 we have 65 signals of which only 35% are known

It has not been possible to carry out the analyzes on different batches because since all the Infanrix Hexa we have purchased for more than a year on the national territory, in different regions and in different periods, belong to batch A21CD072D.



NOTES FOR UNDERSTANDING: this is a first level analysis, that is an identification based on molecular weight. If the result is univocal, (ie at a measured molecular weight only one compound is associated as a structure) it is more likely the right one, but absolute certainty is not possible in this phase. As you will notice, as far as a certain number of compounds is concerned, different substances correspond to a particular molecular weight.

3.1. Infanrix Hexa Vaccine - Batch # 1 (A21CD072D)

65 signals were detected, among which only the 35% gave a potential classification (Table 2).

It must be specified that compound identity is not certain and it should be confirmed by a second level screening carried out with certified analytical standards.

In fact, during screening level, the device measures a particular data by its accurate molecular weight (measurement error <10 ppm). The empirical formula is calculated on the basis of these measures. Some formulas might correspond to several compounds having the same molecular weight but different chemical identity.



NOTES FOR UNDERSTANDING: in essence, the certain data is that we have 65 chemically different substances among which only 35% is known.

Molecules potentially belonging to toxin category have been researched. They have been suggested on the basis of accurate m / z mode research (error <10 ppm) using the toxic compounds database in the Metlin search engine. Table 3 shows the candidates obtained.

It is emphasized that different detected compounds have a candidate empirical formula containing sulfur compounds or sulfur in the form of various functional groups. Furthermore, the presence of formic acid in the form of sodium salt and a polymer deriving from contaminations of Poly Ethylene Glycol (PEG)¹⁴ with an average molecular weight equal to 1340 Da have been detected.

¹⁴ <https://www.sciencedirect.com/topics/materials-science/polyethylene-glycol>

5. Final considerations

Most of the contaminants and impurities detected were not characterized using the metabolic and protein reference databases (KEGG, NCBI-Protein SwissProt).⁸⁻⁹

There is a critical issue in the contamination of various compounds potentially or definitely harmful to human health.

In short, the first questions we asked ourselves, and the relative answers obtained, are the following:

- | | |
|--|---|
| 1. Are the chemical substances listed in the data sheet present? | in part |
| 2. Are there any chemical and protein contaminations? | YES |
| 3. How many contaminating compounds are there? | From 65 |
| 4. What are they? | Chemical toxins, chemical compounds, peptides |

Next analysis

1. First of all, it is necessary to identify with certainty the most interesting probable compounds
2. Then to determine the exact amount of each contaminant
3. Finally to determine the structure of the macromolecule constituted by the set of antigens

6. Future research developments

Confirmation and identity analysis will be performed using the "Tandem Mass Spectrometry (MS / MS)" technique associated with the aid of certified analytical standards. The analysis will be performed in compliance with the European directives (EU directive 2002/657 / EC) useful for the identification of compounds.

In particular, the investigation will have the objective of confirming those substances whose toxicity and allergenicity is known and the 7 toxins identified will be an element of careful study.

7. Description of the SANIST technology

The innovative internationally renowned SANIST platform, through publications in peer-reviewed scientific journals¹⁵⁻¹⁶ - was used to perform a first identification screening on the vaccines of interest.

8. Details related to the analytical method

SANIST technology consists of:

- a) a kit for the extraction of analytes (the unknown substances to be determined);
- b) the LC-SACI / ESI-MS analysis system which allows to reduce the chemical noise of mass spectrometers and obtain a better detection of instrumental signals;

¹⁵ Albinì A. et al., Rapid Commun Mass Spectrom. 2015 Oct 15;29(19):1703-10. doi: 20.1002/rcm.7270. (<https://onlinelibrary.wiley.com/doi/full/10.1002/rcm.7270>)

¹⁶ Cristoni S. et al., J Mass Spectrom. 2017 Jan;52(1):16-21. doi:10.1002/jms.3895. (<https://www.ncbi.nlm.nih.gov/pubmed/27776380>)

- c) the **SANIST data processing system** consisting of a local bioinformatics and network platform capable of processing data using dedicated databases and customized algorithms. It is specified that, during the screening phase, the recognition is made in the context of scientific research and through research in official banks (KEGG, NCBI-Prot and SwissProt)^{17,18} without the aid of certified analytical standards. It is therefore necessary to perform a second level analysis with certified analytical standards to confirm their identity.

9. Areas of application of SANIST technology

To date, the **SANIST platform** is applicable in the following fields:

- In **clinical research** of disease markers and their direct application in the diagnostic field.
- Food services**, food traceability. Comparative studies to determine the quality of products based on their complex molecular composition. Control of food counterfeiting.
- Nutraceutical sector**, development of the nutritional value of a food supplement based on its molecular composition. Forged search (for example: added drugs).
- Pharmaceutical sector**, drug control and research of active biomolecules.
- Cosmetic industry**: the molecular composition of cosmetic products can be carefully monitored and correlated with the quality of the product.

10. How to read the tables

This is a screening phase; the instrument measures a particular data by its accurate molecular weight (measurement error <10 ppm). On the basis of these measures a brute formula is calculated. Some formulas can correspond to several compounds having the same molecular weight but different chemical identity.

Example of a single associated component:

Atovaquone Medication for the treatment of malaria

In this example, the instrument detected a signal with a certain molecular weight. By inserting the brute formula in the databases, it was possible to associate a **probable component**.

Example of a number of associated components:

Tetracenomycin F2
 Decaketide tricyclic intermediate
 1-hydroxyversicolorone
 Monocarboxylic hydroxy acid
 Member of the anthracenes
 Antrafuran

In this example, the instrument detected a signal with a certain molecular weight. By inserting the brute formula in the databases, it was possible to associate **three probable components**.

11. Tables of contaminants

Table 2 - Batch #1 (A21CD072D)

Tungsten carbide
 Inorganic carbide industrially used to synthesize cemented carbides.

¹⁷ Kanehisa M. et al., Nucleic Acids Res. 2017 Jan 4;45(D1):D353-D361. doi:10.1093/nar/gkw1092. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5210567/>)

¹⁸ Cristoni S. et al., Expert Rev Proteomics. 2004 Dec; 1(4):469-83. (<https://www.ncbi.nlm.nih.gov/pubmed/15966842>)

[T]Tetracenomycin F2	[M]Monocarboxylic hydroxy acid
[D]Decaketide tricyclic intermediate	[M]Member of the anthracenes
[I]1-hydroxyversicolorone	[A]Antrafuran
[L]Lactose	[A]Added as a stabilizer.
[S]Sodium methallylsulfonate	[M]Monomer used in the polymer industry.
[S]Salicin 6-phosphate	[G]Glycoside phosphate derived from salicin (anti-inflammatory agent)
[P]Pachyrhizone	[M]Member of the Rotenoni
[A]Arnottin II	[M]Member of 2-benzofurans
[T]Tetracenomycin F1	[M]Monocarboxylic hydroxy acid
[O]Octadecanamide	[A]Amide of stearic acid
[L]-Leucine	[A]Amino acid
[L]Lichenin (altri 19 possibili candidati)	[G]Glucan. Study to use glucans as vaccine adjuvants
[U]Usticidin B	[L]Lignan
[D]Dihydrochelirubine	[D]Dihydrobenzophenantridinico Alkaloid
[O]6-oxochelerythrine	[A]Alkaloid
[7,8-Didemethyl-8-hydroxy-5-deazariboflavin	[R]Riboflavin
[D]Deamino-alpha-keto-demethylphosphinothricin	[E]
[C]Cassythine	[A]Alkaloid
[6-alpha-D-glucosaminy]-1D-myo inositol	[A] derivative of a D-glucosaminide and a monosaccharide.
[C]Carbenicillin sodium	[B]Bactericidal antibiotic
[B]bis-D-fructose 2', 1:2, 1'-dianhydride	[D]Dianhydride sugar
[D]-Fructofuranose 1,2':2,3'-dianhydride	[D]Dianhydride sugar
[P]Prazepam	[B]Benzodiazepine derivative /
[2,3-Dehydro-UWM6 /	[M]Member of the phenanthrenes
[L]Levofuraltadone	[A]Antibiotic that can be used in combination with a vaccine consisting of hybrid cells for cancer treatment
[S]Mycocyclosin	[C]Heterotetracyclic compound
[A]Atovaquone	[M]Medication for the treatment of malaria
[A]Amoxicillin	[A]Antibiotic
[C]Cephalexin monohydrate	[A]Antibiotic that decreases the effectiveness of vaccines
[C]Cefroxadine	[C]Cephalosporin antibiotic
[CGP 28-392	[A]Aromatic ether
[7-deoxyloganate	[M]Metabolite of plants
[9-epideoxyloganic acid	[M]Metabolite of plants
[LY395153	[M]Member of the benzamides
[AL-294	[A]Alkylbenzene
[3-Chloro-orto-phenylenediamine	[M]Member of the monochlorobenzene
[12-N, 6-N-Bis(2,3-dihydroxy benzoyl)-L-Lysine amide	[E]
[2-Iodo-6-methoxyphenol	[M]Member of the phenols
[T]Tungstate	[C]Compound containing a tungsten oxoanion
[2-amino-5-chloromuconate-6-semialdehyde	[S]Semialdehyde
[2,5-Dichloro-4-oxohex-2-enedioate	[M]Member of the family of medium-chain keto acids
[1-Palmitoyl-2-(5-hydroxy-8-oxo-6-octenoyl)-sn-glycero-3-phosphatidylcholine	[1,2-diacyl-sn-glicero-3-fosfocolina

Table 3 - Batch #1 (A21CD072D)

Candidate compound

[S]Sodium formate

Empirical Formula

CHNaO2

[7]Hepta-2,3,4,5,6-pentaenenitrile	C7H3N
[10](Methanesulfonyl)(dioxo)-lambda-5--azane [10]oxaziridine-2-sulfonic acid	CH3NO4S
[13]4-Dihydro-3-thioxo-1,2,4-triazin-5(2H)-one [15]Thioxo-4,5-dihydro-1,2,4-triazin-3(2H)-one [11]2,4-oxadiazole-3-carbothioamide [11]2,3-Thiadiazole-4-carboxamide [15]-amino-1,3,4-thiadiazole-2-carbaldehyde [11]1,1-Difluoro-1-isocyanatoethane [11]1,1-Difluoro-2-isocyanatoethane	C3H3N3OS
[13]-(methylsulfonyl)-1H-1,2,4-triazole [11]H-Imidazole-2-sulfonamide [15]-(4,5-Dihydro-1,3-thiazol-2-yl)nitramide [11]H-Imidazole-5-sulfonamide [11]H-Pyrazole-4-sulfonamide [11]Undeca-2,4,6,8,10-pentaynenitrile	C3H3F2NO
[12]-Aminobenzenethiol [14]-Methyl-5-vinylthiazole [12]-Pyridinemethanethiol [12]-Isopropenylthiazole [15]5,6-Dihydro-4H-cyclopenta[d][1,3]thiazole [14]-Aminothiophenol 3-Pyridinemethanethiol [15]Pyridine, 2-(methylthio) [15]Pyridine, 3-(methylthio)-	C6H7NS
[13]Phenthiазamine	C9H8N2S
[14]-Chloro-N-hydroxybenzene-1-sulfonamide	C6H6ClNO3S
[15]Carbamodithioic acid, (4-hydroxyphenyl)-	C7H7NOS2

New Quality-Control Investigations on Vaccines: Micro- and Nanocontamination

Research Article

Abstract

Vaccines are being under investigation for the possible side effects they can cause. In order to supply new information, an electron-microscopy investigation method was applied to the study of vaccines, aimed at verifying the presence of solid contaminants by means of an Environmental Scanning Electron Microscope equipped with an X-ray microprobe. The results of this new investigation show the presence of micro- and nanosized particulate matter composed of inorganic elements in vaccines' samples which is not declared among the components and whose unduly presence is, for the time being, inexplicable. A considerable part of those particulate contaminants have already been verified in other matrices and reported in literature as non biodegradable and non biocompatible. The evidence collected is suggestive of some hypotheses correlated to diseases that are mentioned and briefly discussed.

Keywords: Vaccine; Disease; Contamination; Protein corona; Biocompatibility; Toxicity; Nanoparticle; Immunogenicity; Foreign body; Environment; Industrial process; Quality control

Volume 4 Issue 1 - 2017

Antonietta M Gatti^{1,2*} and Stefano Montanari³

¹National Council of Research of Italy, Institute for the Science and Technology of Ceramics, Italy

²International Clean Water Institute, USA

³Nanodiagnosics srl, Italy

*Corresponding author: Dr. Antonietta Gatti, National Council of Research of Italy, c/o Nanodiagnosics Via E. Fermi, 1/L, 41057 San Vito (MO), Italy, Tel: 059798778; Email: gatti@nanodiagnosics.it

Received: November 30, 2016 | Published: January 23, 2017

Introduction

Vaccines are one of the most notable inventions meant to protect people from infectious diseases. The practice of variolation is century-old and is mentioned in Chinese and Indian documents dated around 1000 A.D. Over time, variolation has been replaced by vaccination, vaccines have been enhanced as to technology, and the vaccination practice is now standardized worldwide.

Side effects have always been reported but in the latest years it seems that they have increased in number and seriousness, particularly in children as the American Academy of pediatrics reports [1,2]. For instance, the diphtheria-tetanus-pertussis (DTaP) vaccine was linked to cases of sudden infant death syndrome (SIDS) [3]; measles-mumps-rubella vaccine with autism [4,5]; multiple immunizations with immune disorders [6]; hepatitis B vaccines with multiple sclerosis, etc.

The notice of Tripedia DTaP by Sanofi Pasteur reports "Adverse events reported during post-approval use of Tripedia vaccine include idiopathic thrombocytopenic purpura, SIDS, anaphylactic reaction, cellulitis, autism, convulsion/grand mal convulsion, encephalopathy, hypotonia, neuropathy, somnolence and apnea". The epidemiological studies carried out did not show a clear evidence of those associations, even if in 2011 the National Academy of Medicine (formerly, IOM) admitted: "Vaccines are not free from side effects, or adverse effects" [7].

Specific researches on components of the vaccines like adjuvants (in most instances, Aluminum salts) are already indicated as possible responsible of neurological symptoms [8-10] and in some cases, in-vivo tests and epidemiological studies demonstrated a possible correlation with neurological

diseases [10,11]. Neurological damages induced in patients under hemodialysis treated with water containing Aluminum are reported in literature [12].

Recently, with the worldwide-adopted vaccines against Human Papillomavirus (HPV), the debate was reawaken due to some adverse effects reported by some young subjects.

Specific studies communicated the existence of symptoms related to never-described-before syndromes developed after the vaccine was administered. For instance, Complex Regional Pain Syndrome (CRPS), Postural Orthostatic Tachycardia Syndrome (POTS), and Chronic Fatigue Syndrome (CFS) [13]. The side-effects that can arise within a relatively short time can be local or systemic.

Pain at the site of injection, swelling and uncontrollable movement of the hands (though this last symptom can also be considered systemic) are described. Among the systemic effects, fever, headache, irritability, epileptic seizures, temporary speech loss, lower limbs dysaesthesia and paresis, hot flashes, sleep disorders, hypersensitivity reactions, muscle pain, recurrent syncope, constant hunger, significant gait impairment, incapacity to maintain the orthostatic posture are reported [14].

It is a matter of fact that every day millions of vaccine doses are administered and nothing notable happens, but it is also irrefutable that, regardless of the amount of side effects that are not recorded and the percentage of which remains in fact unknown, in a limited number cases something wrong occurs. No satisfactory explanation or, in many cases, no explanation at all has been given and it seems that those adverse effects happen on a random and stochastic basis.

Those situations induced us to verify the safety of vaccines from a point of view which was never adopted before: not a biological, but a physical approach. So, we developed a new analysis method based on the use of a Field Emission Gun Environmental Scanning Electron Microscope investigations to detect possible physical contamination in those products.

Materials and Methods

44 types of vaccines coming from 2 countries (Italy and France) were analyzed. Table 1 groups them in terms of name, brand and purpose.

Table 1: List of vaccines analyzed, according to their purpose.

N	Name	Brand Name, Country of Distribution	Description	Production Batch, Expiry Date
1	Vivotif Berna	Berna Biotech SA, Italy	Anti-Thyphoid Vaccine (Live), group Ty21a	3000336 [2004]
2	Typhim Vi	Aventis Pasteur MSD, Italy	Anti-Salmonella typhi Vaccine	U1510-2 [2004]
3	Typherix	GlaxoSmithKline S.p.a., Italy	Anti-Thyphoid Vaccine (polysaccharide Vi)	ATYPB061BB [2009]
4	Anatetall	Chiron (now Novartis) Italy	Adsorbed anti-Tetanus Vaccine	030106 [2004]
5	Anatetall	Novartis Vaccines and Diagnostics, Italy	Adsorbed anti-Tetanus Vaccine	060510 [2009]
6	Tetabulin	Baxter AG, Italy	Adsorbed anti-Tetanus Vaccine	VNG2G006A [2009]
7	Dif-Tet-All	Novartis Vaccines and Diagnostics, Italy	Adsorbed anti-Tetanus and diphtheria Vaccine	070501 [2009]
8	Infanrix	GlaxoSmithKline S.p.a., Italy	Anti-Diphtheria, tetanus and pertussis vaccine	AC14B071A] [2009]
9	Infanrix hexa	GlaxoSmithKline Biologicals s, Italy	Anti-diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by Haemophilus influenzae type b	A21CC512A [2017]
10	Infanrix hexa	GlaxoSmithKline Biologicals s. a. France	Anti-diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by Haemophilus influenzae type b	A21CC421A [2017]
11	M-M-R vaxPro	Sanofi Pasteur MSD, Italy	M-M-R vaxPro (measles, mumps, and rubella) analyzed in Cambridge	L012437 [2017]
12	Repevax	Sanofi Pasteur MSD, France	Anti-diphtheria-tetanus-pertussis-polio-vaccine	L0362-1 [2017]
13	Repevax	Sanofi Pasteur MSD SNC France	Anti-diphtheria-tetanus-pertussis-polio-vaccine	L0033-1 [2016]
14	Priorix	GlaxoSmithKline S.p.a., Italy	Anti--measles-mumps, and rubella (MMR) vaccine	A69CB550A [2009]
15	Morupar	Chiron (now Novartis,), Italy	Anti-measles- mumps, and rubella (MMR) vaccine	7601 [2004]
16	Varilrix	GlaxoSmithKline S.p.a., Italy	Anti-Chicken pox vaccine (group OKA)	A70CA567A [2009]
17	Stamaril Pasteur	Sanofi Pasteur MSD, Italy	anti-yellow fever vaccine	A5329-6 [2009]
18	Allergoid-Adsorbat 6-Graser Starke B.	Allergopharma, Germany	Antiallergic vaccine	Ch-B.:30005999-B [2006]
19	Engerix-B	GlaxoSmithKline S.p.a., Italy	Adsorbed anti-hepatitis B vaccine	AHBVB468BD [2009]
20	Prenevar 13	Pfizer, Italy	Antipneumococcal vaccine	G79324 [2013]
21	Prevenar 13	Pfizer, France	Antipneumococcal vaccine	N27430 [2018]
22	Mencevax Acwy	GlaxoSmithKline, Italy	anti-Neisseria meningococcal group A, C, W135 and Y vaccine	N402A47B 12 [2004]
23	Meningitec	Pfizer, Italy	(group C 10) (adsorbed on Al-Phosphate)	H92709 [2015]
24	Meningitec	Pfizer-Italy	Anti-meningococcus (group C 10) vaccine (adsorbed on Al-Phosphate)	H20500 [2014]

25	Meningitec	Pfizer-Italy	Anti-meningococcus vaccine sequestred by Procura della Repubblica	G76673 [2014]
26	Meningitec	Pfizer-Italy	Anti-meningococcus vaccine sequestred by Procura della Repubblica	H99459 [2015]
27	Meningitec	Pfizer-Italy	Anti-meningococcus vaccine sequestred by Procura della Repubblica	H52269 [2015]
28	Menjugate	Novartis Vaccines and Diagnostics	Anti-meningococcus group C	YA0163AB [2010]
29	Menveo	Novartis Vaccines and Diagnostics	Antimeningococcus groups A, C, W135, Y	A15083 [2017]
30	Meningitec	Wyeth Pharmaceutical - France	Anti-meningococcus group C vaccine	E83920 [2011]
31	Inflexal V	Berna Biotech	Anti-flu vaccine 2008/2009	3001463-01 [2009]
32	Vaxigrip	Sanofi Pasteur MSD	Anti-flu vaccine 2008/2009	D9703-1 [2009]
33	Vaxigrip	Sanofi Pasteur	Anti-flu vaccine 2012/2013	J8401-1 [2013]
34	Vaxigrip	Sanofi Pasteur, Italy	Anti-flu vaccine, with inactivated and split virus	M7319-1 [2016]
35	Focetria	Novartis Vaccines and Diagnostics	Anti-pandemic flu H1N1 vaccine	0902401 [2010]
36	Agrippal	Novartis	Anti-flu vaccine 2012/2013	127002A [2013]
37	Agrippal	Novartis vaccines, Italy	Anti-flu vaccine with inactivated and split virus 2015/2016 -	152803 [2016]
38	Agrippal S1	Novartis Vaccines and Diagnostics	Anti-flu inactivated/superficial antigene v - 2014/2015	147302A [2015]
39	Fluarix	GlaxoSmithKline - GSK	Anti-flu vaccine 2013	AFLUA789AA [2014]
40	Fluad	Novartis Vaccines and Diagnostics	Anti-flu inactivated/superficial antigene vaccine - 2014/2015	142502 [2015]
41	Gardasil	Sanofi Pasteur MSD, Italy	Anti-HPV types 6,11,16,18 vaccine	NP01250 [2012]
42	Gardasil	Sanofi Pasteur MSD, Italy	Anti-HPV (types 6,11,16,18) vaccine	K023804 [2016]
43	Cervarix	GlaxoSmithKline Biological, Italy	Anti-HPV (type 16,18)	AHPVA238AX [2017]
44	Feligen CRP	Virbac S.A. - Carros - Italy	anti-panleucopenia, infectious rhinotracheitis and infections by Calciavirus, veterinary Vaccine for cats	3R4R [2013]

Some vaccines, in fact a minority, are meant to deal with a single bacterium or virus, while others are multi-valent. The list of vaccines we analyzed may contain repeated names, because we considered different batches and years of production of the same vaccine: the ones against influenza in particular.

The study was aimed at verifying a possible physical contamination. To do that, we performed a new kind of investigation based on observations under a Field Emission Gun Environmental Electron Scanning Microscope (FEG-ESEM, Quanta 200, FEI, The Netherlands) equipped with the X-ray microprobe of an Energy Dispersive Spectroscopy (EDS, EDAX, Mahwah, NJ, USA) to detect the possible presence of inorganic, particulate contaminants and identify their chemical composition.

A drop of about 20 microliter of vaccine is released from the syringe on a 25-mm-diameter cellulose filter (Millipore, USA), inside a flow cabinet. The filter is then deposited on an Aluminum stub covered with an adhesive carbon disc. The sample is immediately put inside a clean box in order to avoid any contamination and the box is re-opened only for the sample to be inserted inside the FEG-ESEM chamber. We selected that particular type of microscope as it allows to analyse watery and oily samples in low vacuum (from 10 to 130 Pa) at a high sensitivity.

When the water and saline the vaccine contains are evaporated, the biological/physical components emerge on the filter and it is then possible to observe them. This type of microscope

(low-vacuum observations) prevents the possible sample contamination and the creation of artefacts. The observations are made with different sensors (SE: secondary-electron sensor and BSE: backscattered-electron sensor), and are performed at a pressure of 8.9×10^{-1} mbar, at energies ranging from 10 to 30kV to detect the particulate matter's size, morphology and its elemental composition. The method identifies clearly inorganic bodies with a higher atomic density (looking whiter) than the biological substrate. So, organic entities are visible and easy to distinguish from inorganic ones. The method cannot distinguish between proteins and organic adjuvants (e.g. squalene, glutamate, proteins, etc.) or viruses, bacteria, bacteria's DNA, endo-toxins and bacteria's waste, but their comparatively low atomic density allows us to identify these entities as organic matter. In some vaccines, the organic matter contains white-looking debris named aggregates, while a high concentration of inorganic debris is called a cluster.

Single inorganic particles or organic-inorganic aggregates are identified, evaluated and counted. The counting procedure is repeated three times by three different operators, with an error lower than 10%. When a layer of salts (Sodium chloride or Aluminum) is detected, we record the situation but we do not do body count.

Results

The investigations verified the physical-chemical composition of the vaccines considered according to the inorganic component as declared by the Producer. In detail, we verified the presence of saline and Aluminum salts, but further presence of micro-, sub-micro- and nanosized, inorganic, foreign bodies (ranging from 100nm to about ten microns) was identified in all cases, whose presence was not declared in the leaflets delivered in the package of the product (Table 2).

Table 2: List of the vaccines according to their manufacturers with the chemical composition of the debris identified in each sample. The elements most represented are reported.

N	Company	Name	Alluminum	Elements Identified
1	Allergopharma - Germany	Allergoid	yes	Al
2	Aventis Pasteur MSD Lyon - France	Typhim Vi	no	BrKP, PbSi, FeCr, PbCISiTi
3	Baxter AG	Tetabulin	no	SiMg, Fe, SiTiAl, Sba, Zn
4	Berna Biotech	Vivotif Berna	no	FeAl, ZrAlHf, SrAl, BiAlCl
5	Berna Biotech	Inflexal V	no	CuSnPbZn, Fe, CaSiAl, SiAl, NaPZn, ZnP, AlSiTi
6	Chiron	Anatetall	Al(OH) ₃	FeAl, SZnBaAl
7	Chiron	Morupar	no	/
8	GlaxoSmithKline- Belgium	Mencevax ACWY	no	FeCrNi, ZrAl, FeCrNiZrAlSi
9	GlaxoSmithKline	Infanrix	Al(OH) ₃	Al, AlTi, AlSi
10	GlaxoSmithKline Biologicals	Infanrix hexa	Al(OH) ₃	Sba, FeCu, SiAl, FeSi, CaMgSi, AlCaSi, Ti, Au, Sca, SiAlFeSnCuCrZn, CaAlSi
11	GlaxoSmithKline Biologicals	Infanrix hexa	Al(OH) ₃ , AlPO ₄ ·2H ₂ O	W, FeCrNi, Ti
12	GlaxoSmithKline	Typherix	no	Ti, TiW, AlSiTiWCr, Sba, W, SiAl, AlSiTi
13	GlaxoSmithKline	Priorix	no	WCa, WFeCu, SiAl, SiMg, PbFe, Ti, WNiFe
14	GlaxoSmithKline	Engerix-B	no	Al (precipitates)
15	GlaxoSmithKline	Varilrix	no	FeZn, FeSi, AlSiFe, SiAlTiFe, MgSi, Ti, Zr, Bi
16	GlaxoSmithKline	Fluarix	no	AlCu, Fe, AlBi, Si, SiZn, AlCuFe, SiMg, Sba, AlCuBi, FeCrNi, SPZn
17	GlaxoSmithKline Biologicals	Cervarix	Al(OH) ₃	AlSi, FeAl, SiMg, CaSiAl, CaZn, FeAlSi, FeCr, CuSnPb
18	Novartis Vaccines and Diagnostics	Anatetall	Al(OH) ₃	Al, FeCrNi, AlCr, AlFe, BaS, ZnAl
19	Novartis Vaccines and Diagnostics	DiF-Tet-All	Al(OH) ₃	Fe, Sba, SiSba, AlZnCu, AlZnFeCr
20	Novartis Vaccines and Diagnostics	Menjugate kit	Al(OH) ₃	SiAl, Ti, FeZn, Fe, Sb, SiAlFeTi, W, Zr
21	Novartis Vaccines and Diagnostics	Focetria	no	Fe, FeCrNiCu, FeCrNi, SiFeCrNi, Cr, SiAlFe, AlSiTiFe, AlSi, SiMgFe, Si, FeZn

22	Novartis	Agrippal S1	no	Ca, Fe, SBa, SBaZn, Cr, Si, Pb, Bi, e FeSiAlCr, SiAlSBaFe, CaAlSi, Zn, CeFeTiNi, FeCrNi
23	Novartis Vaccines and Diagnostics	Agrippal S1	no	SiAlK, Si, SiMgFe, CaSiAl, SBaZn
24	Novartis vaccines	Agrippal	no	Cr, Ca, SiCaAl, ZrSi, SBa, CuZn, SCA
25	Novartis Vaccines and Diagnostics S	Fluad	no	CaSiAl, FeSiTi, SiMgAlFe, SBa
26	Novartis Vaccines and Diagnostics	Menveo	no	CaSiAl, SiAlFe, FeCrNi, Fe, Al, SBa
27	Pfizer	Prenevar 13	no	FeCr
28	Pfizer	Prevenar 13	no	W, CaAlSi, Al, CaSiAlFe, FeS, FeCr; FeCrNi, Fe, , CaP, FeTiMn, Ba, SiMgAlFe
29	Pfizer	Meningitec - ctrl	no	Cr, Si
30	Pfizer	Meningitec - ctrl	no	FeCrNi, W
31	Pfizer	Meningitec	no	CaSiAl, CaSi, SiAlFeTi, FeCrNi, W, Fe, Pb
32	Pfizer	Meningitec	no	Cr (precipitates), Ca, AlSi
33	Pfizer	Meningitec	no	W, SiCa, CaSi, Pb, FeCrNi, Cr
34	Wyeth Pharmaceutical - UK	Meningitec	no	SiAlFe, SiAlTi, SiMgFe, W, Fe, Zr, Pb, Ca, Zn, FeCrNi
35	Sanofi Pasteur MSD-France	Vaxigrip	no	Fe, FeCrNi, SiAlFe, AlSi, SiAlFeCr
36	Sanofi Pasteur MSD	Stamaril Pasteur	no	CaSiAl, AlSi, Fe, SiMgFe, SiMgAlFe, CrSiFeCr, CrSiCuFe
37	Sanofi Pasteur MSD	Gardasil	AlPO ₄ · 2H ₂ O	AlCuFe, PbBi, Pb, Bi, Fe
38	Sanofi Pasteur MSD	Gardasil	AlPO ₄ · 2H ₂ O	CaAlSi, AlSi, SiMgFe, AlFe, AlCuFe, FeSiAl, BiBaS, Ti, TiAlSi
39	Sanofi Pasteur	Vaxigrip	no	Ca, CrFe, FeCrNi, CaSZn, CaSiAlTiFe, Ag, Fe
40	Sanofi Pasteur	Vaxigrip	no	SiMgFe, CaSiAl, AlSiFe, AlSi, FeCr, FeZn, Fe
41	Sanofi Pasteur MSD	Repevax	AlPO ₄ · 2H ₂ O	Bi, Fe, AlSiFe, SiMg, SBa, Ca
42	Sanofi Pasteur MSD S	Repevax	AlPO ₄ · 2H ₂ O	Ti, Br, AuCuZn, Ca, SiZn, SiAuAgCu, SiMgFe, FeCrNi, AlSiMgTiMnCrFe, SiFeCrNi, FeAl
43	Sanofi Pasteur MSD	M-M-R vaxPro	no	Si, SiFeCrNi, FeCrNi, FeNi, Fe, SCA, AlSiCa, CaAlSiFeV, SBa, Pt, PtAgBiFeCr
44	Virbac S.A. - Carros - France	Feligen CRP	no	Ca, SiAl

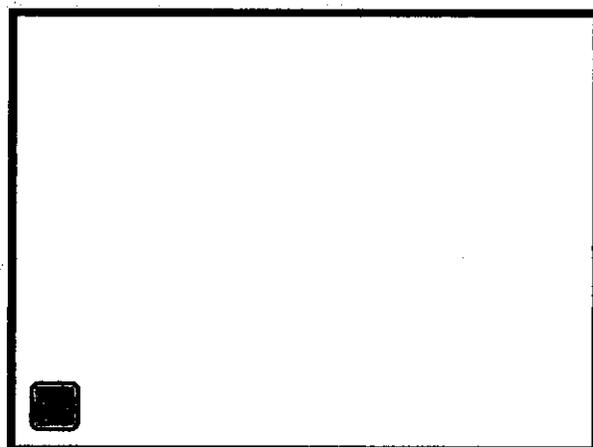


Figure 1a shows a layer of crystals of Sodium chloride (NaCl) embedding salts of Aluminum phosphate ($AlPO_4$) in a drop of Gardasil (anti-HPV vaccine by Merck) as the EDS spectrum (Figure 1b) shows. Saline is the fluid base to any vaccine preparation and Aluminum salts or Aluminum hydroxide [$Al(OH)_3$] are the adjuvants which are usually added.

Looking at the area outside these precipitates but inside the liquid drop, we identified other things: single particles, clusters of particles and aggregates (organic-inorganic composites) that are due to an interaction of the inorganic particulate matter with the organic part of the vaccine.

Figure 2a-2f shows the different typology of entities identified in the vaccines (Repevax, Prevenar and Gardasil); single particles, cluster of micro- and nanoparticles (<100nm) and aggregates with their EDS spectra (Figure 2d-2f). The images (Figure 2a & 2d) show debris of Aluminum, Silicon, Magnesium and Titanium; of Iron, Chromium, Silicon and Calcium particles (Figure 2b & 2e) arranged in a cluster, and Aluminum -Copper debris (Figure 2c & 2f) in an aggregate.

As can be seen, the particles are surrounded and embedded in a biological substrate. In all the samples analyzed, we identified particles containing: Lead (Typhym, Cervarix, Agrippal S1, Meningitec, Gardasil) or stainless steel (Mencevax, Infarix Hexa, Cervarix, Anateall, Focetria, Agrippal S1, Menveo, Prevenar 13, Meningitec, Vaxigrip, Stamaril Pasteur, Repevax and MMRvaxPro).

Figure 3a-3d show particles of Tungsten identified in drops of Prevenar and Infarix (Aluminum, Tungsten, Calcium chloride).

Figure 4a-4d present singular debris found in Repevax (Silicon, Gold, Silver) and Gardasil (Zirconium).

Some metallic particles made of Tungsten or stainless steel were also identified. Other particles containing Zirconium, Hafnium, Strontium and Aluminum (Vivotif, Meningetec); Tungsten, Nickel, Iron (Priorix, Meningetec); Antimony (Menjugate kit); Chromium (Meningetec); Gold or Zinc (Infarix Hexa, Repevax), or Platinum, Silver, Bismuth, Iron, Chromium (MMRvaxPro) or Lead, Bismuth (Gardasil) or Cerium (Agrippal S1) were also found. The only Tungsten appears in 8/44 vaccines, while Chromium (alone or in alloy with Iron and Nickel) in 25/44. The investigations revealed that some particles are embedded in a biological substrate, probably proteins, endo-toxins and residues of bacteria. As soon as a particle comes in contact with proteic

fluids, a nano-bio-interaction [6] occurs and a "protein corona" is formed [7-10]. The nano-bio-interaction generates a bigger-sized compound that is not biodegradable and can induce adverse effects, since it is not recognized as self by the body.

Figure 5a-5f show examples of these nano-bio-interactions. Aggregates can be seen (stable composite entities) containing particles of Lead in Meningitec, (Figure 5a & 5b) of stainless steel (Iron, Chromium and Nickel, Figure 5c & 5d) and of Copper, Zinc and Lead in Cervarix (Figure 5e & 5f). Similar aggregates, though in different situations (patients suffering from leukemia or cryoglobulinemia), have already been described in literature.

The link between these two entities generates an unfolding of the proteins that can induce an autoimmune effect once those proteins are injected into humans.

Figure 6a & 6b show one of the foreign bodies identified in Agrippal. The particle is composed of Cerium, Iron, Titanium and Nickel. (Figure 7a & 7b) present an area of Repevax where the morphology of red cells - we cannot tell whether they are human or animal- is clearly visible.

Table 3 summarizes the number and morphology of the debris identified, in term of single particles, clusters of particles or aggregates (organic-inorganic compounds), while Figure 8 shows the graph obtained calculating the total number of particles (particles plus clusters plus aggregates) identified for 20 microl of every vaccine.

Similar aggregates were already described by other scientists who identified them in the blood e.g. in leukemic patients [15] and in subjects affected by cryoglobulinemia [16].

Not all the vaccines analyzed contain the same contamination, though the same vaccine belonging to different batches and, in some cases, coming from different countries can contain a similar contamination (e.g. the vaccines by Glaxo Infarix, Typherix and Priorix contain Tungsten. Tungsten was also identified in Menjugate kit by Novartis, and Prevenar, Meningitec by Pfizer and Meningitec by Wyeth.)

Feligen, the only veterinary vaccine tested, proved to be the only sample free from inorganic contamination, while Allergoid generates a layer of inorganic salts so thick that it does not allow to detect other particulate contaminants.

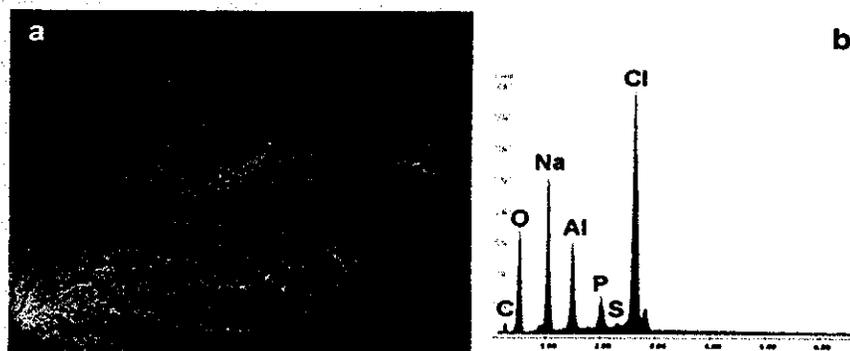


Figure 1: Crystals of saline solution and Aluminum Phosphate and corresponding EDS spectra.

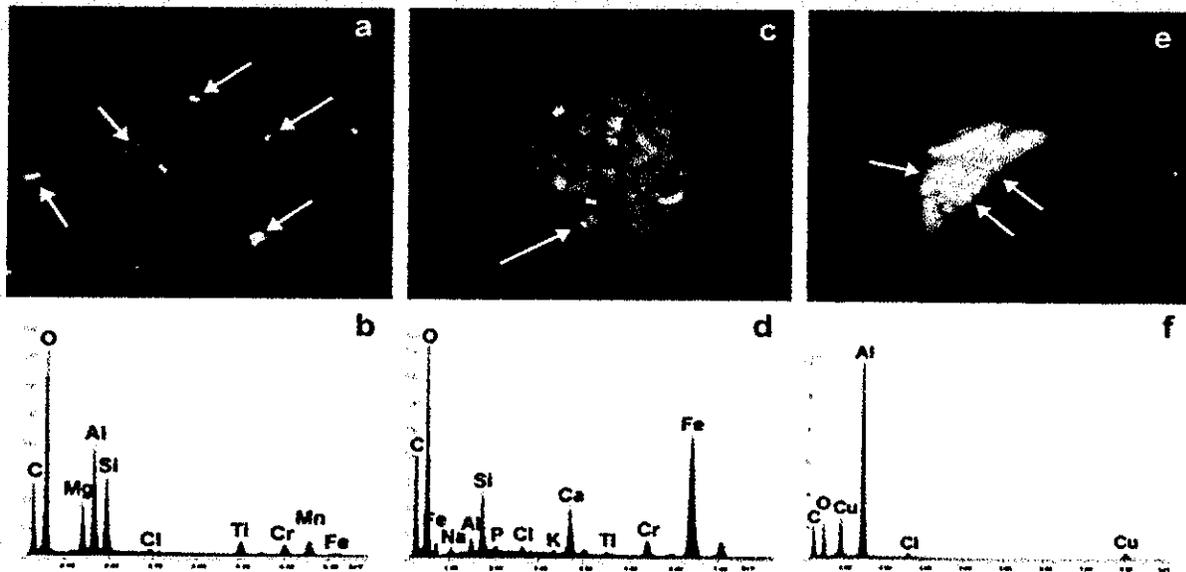


Figure 2: Images of single particles, cluster of micro- and nanoparticles (<100nm) and aggregates with their EDS spectra. They are respectively composed of (a,b) Aluminum, Silicon, Magnesium, Titanium, Chromium, Manganese, Iron, (c,d) Iron, Silicon, Calcium Titanium, Chromium, (e,f) Aluminum, Copper. The arrows show the points where EDS spectra were taken.

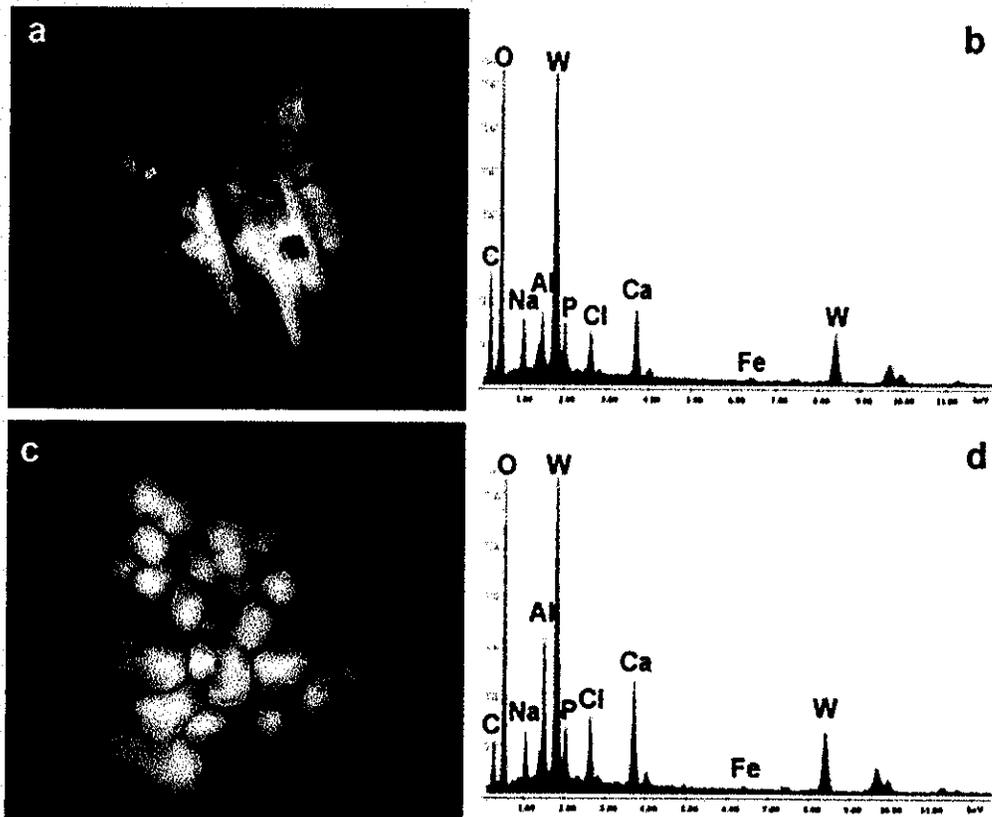


Figure 3: Images of Tungsten particles identified in drops of Prevenar and Infarix. They are composed respectively of Tungsten, Aluminum, Iron but in different concentrations. The arrows show the points where EDS spectra were taken.

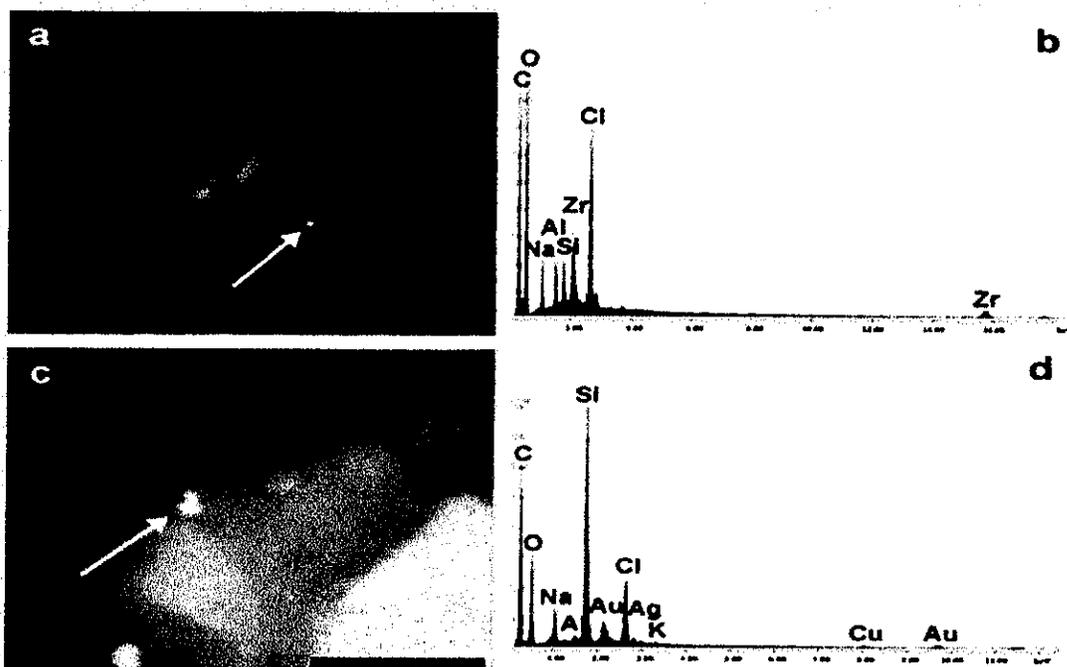


Figure 4: Images show examples of nano biointeraction. The aggregate (a,b) identified in Gardasil contains nanoparticles of Chlorine, Silicon, Aluminum, Zirconium, while the debris found in Repevax contains Silicon, Gold, Silver (c,d). The arrows show the points where EDS spectra were taken.

Table 3: List of the debris' number identified in each vaccine as single particle, clusters and aggregates. Characterization is made by shape, size range and variability of the number of particles counted in each aggregate [in brackets].

Name	Total Debris n.	Size Range in μm	Cluster n.	Size Range in μm	Aggregate n.(Range of Particles)	Size Range μm
Allergoid	NaCl precipitates	/	/	/	/	/
Typhim Vi	394	0,1-2,5			3[9-350]	2-35
Tetabulin	519	0,1-15			3[100-180]	25-60
Vivotif Berna	4	1,5-15				
Inflexal V	103	0,1-17	1	20	3[35-45]	10-25
Anatetall	2	1-3				
Morupar	/		/		/	
Mencevax ACWY	13	0,2-5				
Infanrix	3	1-5	1	25		
Infanrix hexa	1821	0,1-15			15[1820]	20-140
Infanrix hexa	162	0,3-7	12	60	2[7 debris]	3.5-44
Typherix	8	0,2-8	1	15		
Priorix	641	0,05-30	1	10	3[600]	20-70
Engerix-B	precipitates			/		
Varilrix	2723	0,1-4			36 [120-2000]	15-40

Fluarix	1317	0,1-40			3[83]	7-30
Cervarix	1569	0,2-3	2	5-10	4[1400]	8-30
Anatetall	47	0,05-40				
Dif-Tet-All	111	0,2-3				
Menjugate	73	0,1-5				
Focetria	35	0,7-10				
Agrippal S1	430	0,2-6	13	0.2-80	5[410]	20
Agrippal S1	1029	0,1-12			9[1025]	35-80
Agrippal	480	0,1-6			11[460]	2-80
Fluad	605	0,2-15	4	12-25	6[600]	70
Menveo	452	0,1-13			4[430]	30-110
Prenevar 13	precipitates + 5 debris	1-7				
Prevenar 13	precipitates + 81 debris	0,2-50	3	5-40	1 [60]	25
Meningitec	3	10-20				
Meningitec	24	8-60				
Meningitec	673	0,1-20	1	7	9[624]	5-110
Meningitec	precipitates + 40	0,1-3,5			2[40]	25-70
Meningitec	177	0,2-10			3[165]	15-100
Meningitec	241	0,1-15	1	50	2[230]	50
Vaxigrip	86	0,1-7			2[50]	2-2,5
Stamaril Pasteur	152	0,1-7	2	5-7	3[145]	4-20
Gardasil	304	0,05-3			1[300]	15
Gardasil	454	0,1-30	2	7-20	9[445]	5-60
Vaxigrip	304	0,1-10	1	13	2[300]	35
Vaxigrip	674	0,3-25	2	2-12	10[660]	9-150
Repevax	137	0,1-20			2[130]	40-50
Repevax	214	0,1-10			6[150]	5-30
M-M-R vaxPro	93	0,1-15			2[50]	Oct-15
Feligen CRP	92	0,1-12	1	12	1 (40 debris)	25

Discussion

The quantity of foreign bodies detected and, in some cases, their unusual chemical compositions baffled us. The inorganic particles identified are neither biocompatible nor biodegradable, that means that they are biopersistent and can induce effects that can become evident either immediately close to injection time or after a certain time from administration. It is important to remember that particles (crystals and not molecules) are bodies foreign to the organism and they behave as such. More in particular, their toxicity is in some respects different from that of the chemical elements composing them, adding to that toxicity which, in any case, is still there, that typical of foreign bodies. For that reason, they induce an inflammatory reaction.

After being injected, those microparticles, nanoparticles and

aggregates can stay around the injection site forming swellings and granulomas [17]. But they can also be carried by the blood circulation, escaping any attempt to guess what will be their final destination. We believe that in many cases they get distributed throughout the body without causing any visible reaction, but it is also likely that, in some circumstances, they reach some organ, none excluded and including the microbiota, in a fair quantity. As happens with all foreign bodies, particularly that small, they induce an inflammatory reaction that is chronic because most of those particles cannot be degraded. Furthermore, the protein-corona effect (due to a nano-bio-interaction [18]) can produce organic/inorganic composite particles capable of stimulating the immune system in an undesirable way [19-22]. It is impossible not to add that particles the size often observed in vaccines can enter cell nuclei and interact with the DNA [23].

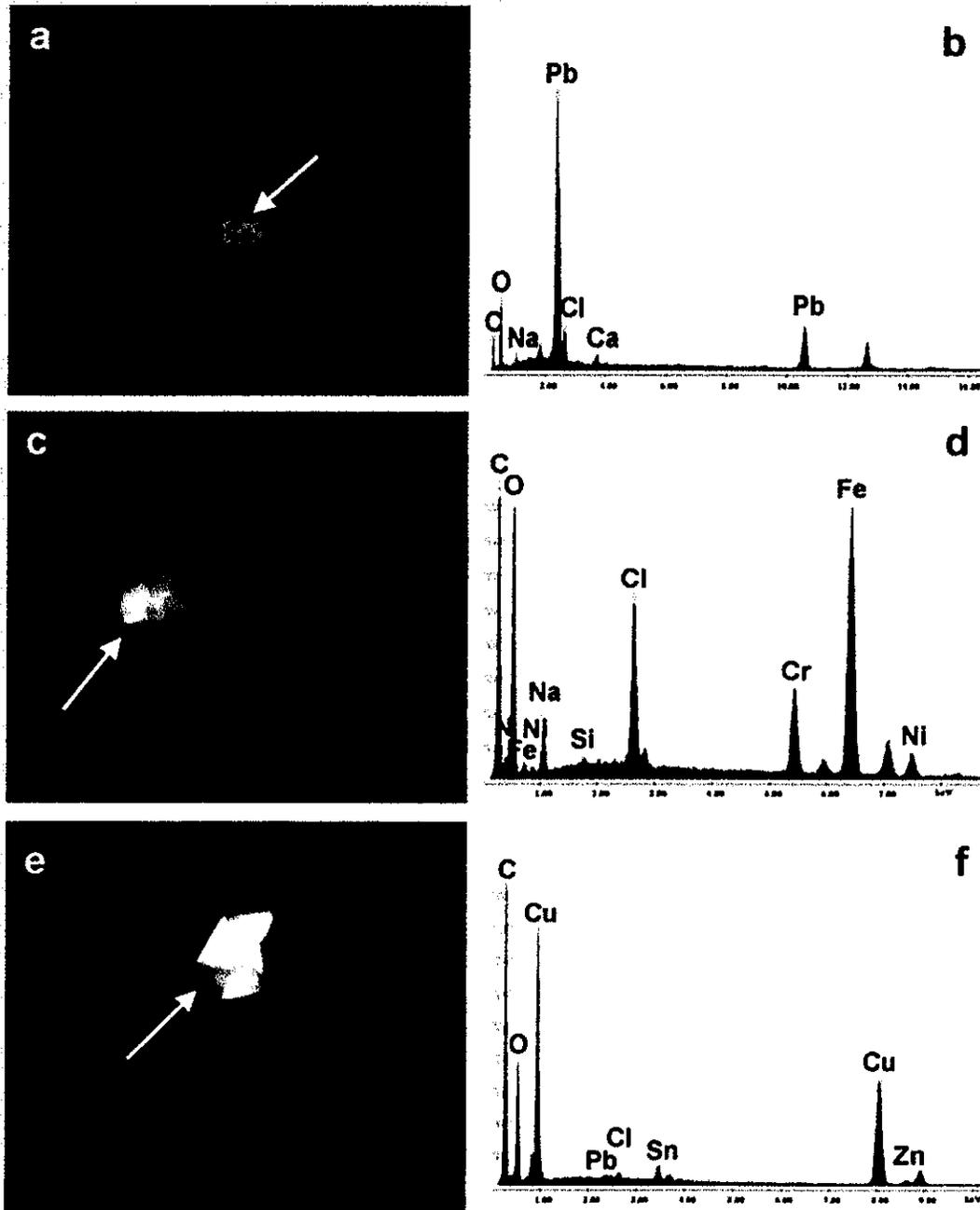


Figure 5: show particles surrounded by an organic compound. They are composed of Lead (a,b), Iron, Chromium, Nickel (stainless steel; c,d), Copper, Tin, Lead (e,f). The arrows show the points where EDS spectra were taken.

In some cases, e.g. as occurs with Iron and some Iron alloys, they can corrode and the corrosion products exert a toxicity affecting the tissues [24-26].

The detection of presence of Aluminum and NaCl salts is obvious as they are substances used by the Producers and declared as components, but other materials are not supposed to be in the vaccine or in any other injectable drug, at that, and, in any case, Aluminum has already been linked with neurological diseases [27-29].

Given the contaminations we observed in all samples of human-use vaccines, adverse effects after the injection of those vaccines are possible and credible and have the character of randomness, since they depend on where the contaminants are carried by the blood circulation. It is only obvious that similar quantities of these foreign bodies can have a more serious impact on very small organisms like those of children. Their presence in the muscles, due an extravasation from the blood, could heavily impair the muscle functionality [30,31].

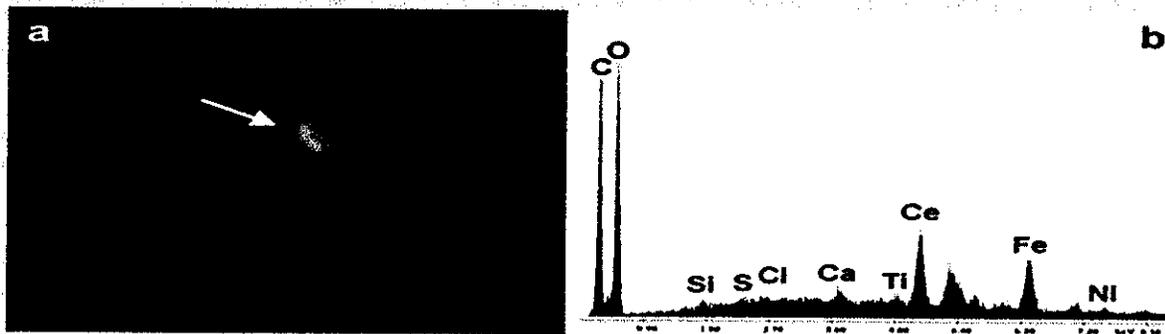


Figure 6: show an organic aggregate containing a debris made of Cerium, Iron, Nickel, Titanium. The red arrow indicates the organic layer (less atomically dense) that covers the Cerium particle.

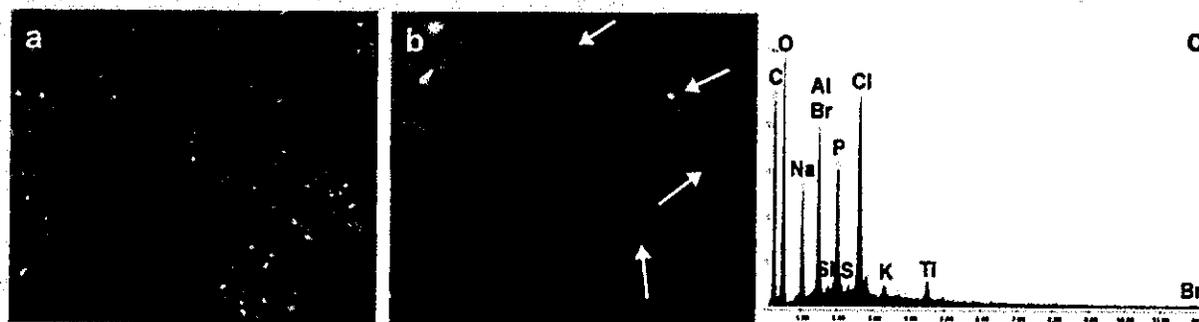


Figure 7: Image of an area in a Repevax drop where the morphology of red cells (red arrows) were identified. It is impossible to know whether they are human or animal origin. Among the debris of saline and Aluminum phosphate, there is the presence of debris (white arrows) composed of Aluminum, Bromine, Silicon, Potassium, Titanium.

We come across particles with chemical compositions, similar to those found in the vaccines we analyzed, when we study cases of environmental contamination caused by different pollution sources. In most circumstances, the combinations detected are very odd as they have no technical use, cannot be found in any material handbook and look like the result of the random formation occurring, for example, when waste is burnt. In any case, whatever their origin, they should not be present in any injectable medicament, let alone in vaccines, more in particular those meant for infants.

Other forms of so-far unknown contaminations have recently been observed and, in any case, vaccines contain components that could themselves be the cause of adverse effects. It is a well-known fact in toxicology that contaminants exert a mutual, synergic effect, and as the number of contaminants increases, the effects grow less and less predictable. The more so when some substances are unknown.

As a matter of fact, no exhaustive and reliable official data exist on the side-effects induced by vaccines. The episodic evidence reported by people allegedly damaged by vaccines is twofold: some say the damage occurred and became visible within a few hours from administration, and some maintain that it was a matter of some weeks. Though we have no indisputable evidence as to the reliability of those attestations, we can put forward a hypothesis to explain the different phenomena. In the former

case, the pollutants contained in the drug have reached the brain and, depending on the anatomical site interested, have induced a reaction. If that is the case, the whole phenomenon is very rapid. In the latter circumstance, the pollutants reached the microbiota, thus interfering with the production of enzymes necessary to carry out neurological functions [32-35]. That possibility takes time, as it involves the production of chemical compounds in a sufficient quantity, and an elapse of some weeks between injection and clinical evidence is reasonable. Of course, ours is no more than a hypothesis open to discussion and in need of proof, hoping that a chance of further investigation is allowed.

Conclusion

The analyses carried out show that in all samples checked vaccines contain non biocompatible and bio-persistent foreign bodies which are not declared by the Producers, against which the body reacts in any case. This new investigation represents a new quality control that can be adopted to assess the safety of a vaccine. Our hypothesis is that this contamination is unintentional, since it is probably due to polluted components or procedures of industrial processes (e.g. filtrations) used to produce vaccines, not investigated and not detected by the Producers. If our hypothesis is actually the case, a close inspection of the working places and the full knowledge of the whole procedure of vaccine preparation would probably allow to eliminate the problem.

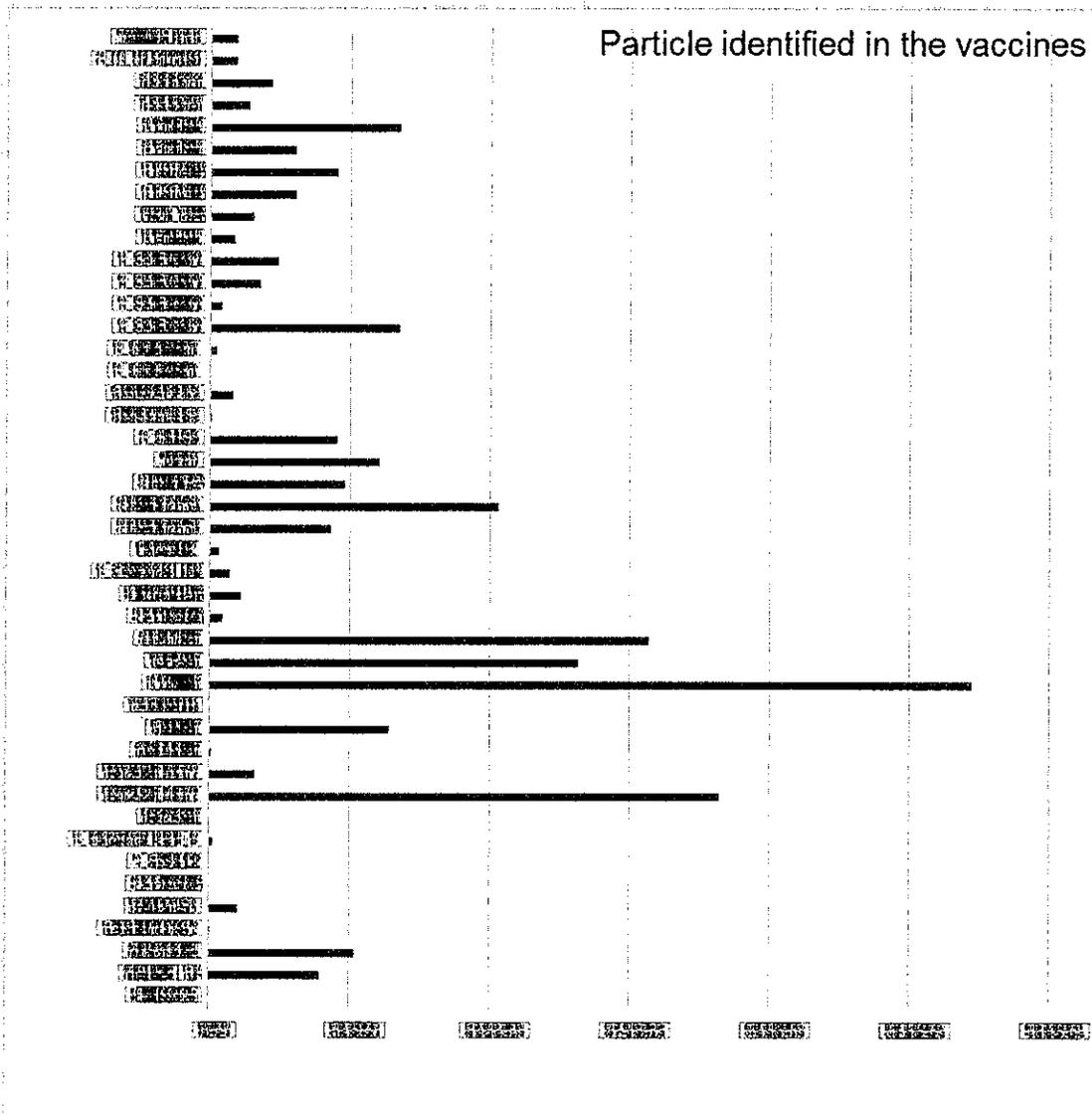


Figure 8: Graph of the debris' quantities identified in a 20 microl drop of every vaccine.

A further purification of the vaccines could improve their quality and could probably decrease the number and seriousness of the adverse incidental effects.

Acknowledgment

The Authors are indebted to Dr. Federico Capitani, Dr. Laura Valentini and Ms. Lavinia Nitu for their technical assistance. The opinions and conclusions are not necessarily those of the Institution.

References

Healthy Children.org

- [1] US Dpt of health and human services (1996) Report Update: Vaccine Side Effects, Adverse Reactions, Contraindications, and Precautions. CDC 45(RR-12): 1-35.
- [2] Ottaviani G, Lavezzi AM, Maturri L (2006) Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination: pathology in suspected SIDS? Virchows Arch 448(1): 100-104.
- [3] Taylor B, Miller E, Farrington CP, Petropoulos MC, Favot-Mayaud I, et al. (1999) Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. Lancet 353(9169): 2026-2029.
- [4] Demicheli V, Rivetti A, Debalini MG, Di Pietrantonj C (2012) Vaccines for measles, mumps and rubella in children. Cochrane Database Syst Rev 15(2): CD004407.

- [1] Carola Bardage, Ingemar Persson, Åke Örtqvist, Ulf Bergman, Jonas F Ludvigsson, et al. (2011) Neurological and autoimmune disorders after vaccination against pandemic influenza A (H1N1) with a monovalent adjuvanted vaccine: population based cohort study in Stockholm, Sweden. *BMJ* 343: d5956.
- [2] Johann Liang R (2012) Updating the Vaccine Injury Table following the 2011 IOM Report on Adverse Effects of vaccines. *HRSA*, pp. 1-27.
- [3] L Tomljenovic, CA Shaw (2011) Aluminum Vaccine Adjuvants: Are they Safe? *Current Medicinal Chemistry* 18(17): 2630-2637.
- [4] Shaw CA, Petrik MS (2009) Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. *J Inorg Biochem* 103(11): 1555-1562.
- [5] Authier FJ, Sauvat S, Christov C, Chariot P, Raisbeck G, et al. (2006) AIOH3-adjuvanted vaccine-induced macrophagic myofasciitis in rats is influenced by the genetic background. *Neuromuscul Disord* 16(5): 347-352.
- [6] Exley C, Esiri MM (2006) Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall, UK. *J Neurol Neurosurg Psychiatry* 77(7): 877-879.
- [7] Wills MR, Savory J (1985) Water content of aluminium, dialysis dementia, and osteomalacia. *Environ Health Perspect* 63: 141-147.
- [8] Brinth L, Pors K, Theibel AC, Mehlsen J (2015) Suspected side effects to the quadrivalent human papilloma vaccine. *Danish Medical J* 62(4): 1-12.
- [9] Palmieri B, Poddighe D, Vadalà M, Laurino C, Carnovale C, et al. (2016) Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature. *Immunol Res*.
- [10] Visani G, Manti A, Valentini L, Canonico B, Loscocco F, et al. (2016) Environmental nanoparticles are significantly over-expressed in acute myeloid leukemia. *Leuk Res* 50: 50-56.
- [11] Artoni E, Sighinolfi GL, Gatti AM, Sebastiani M, Colaci M, et al. (2016) Micro and nanoparticles as possible pathogenetic co-factors in mixed cryoglobulinemia. *Occupational Medicine*.
- [12] Hansen, L Klimek, F Bittinger, I Hansen, A Gatti, et al. (2008) Mast cell reiches Aluminium granuloma *Pathologie* 29(4): 311-313.
- [13] Gatti AM, Manti A, Valentini L, Montanari S, Gobbi P, et al. (2016) Nano biointeraction of particulate matter in the blood circulation. *Frontiers* 30: 3.
- [14] Tenzer S, Docter D, Rosfa S, Wlodarski A, Kuharev J, et al. (2011) Nanoparticle size is a critical physicochemical determinant of the human blood plasma corona: a comprehensive quantitative proteomic analysis. *ACS Nano* 5(9): 7155-167.
- [15] Radauer Preiml, Andosch A, Hawranek T, Luetz-Meindl U, Wiederstein M, et al. (2015) Nanoparticle-allergen interactions mediate human allergic responses: protein corona characterization and cellular responses. *Fibre toxicology* 13: 3.
- [16] Cedervall T, Lynch I, Lindman S, Berggård T, Thulin E, et al. (2016) Understanding the nanoparticle-protein corona using methods to quantify exchange rates and affinities of proteins for nanoparticles. *PNAS* 104 (7): 2050-2055.
- [17] Lynch I, Cedervall T, Lundqvist M, Cabaleiro-Lago C, Linse S, et al. (2007) The nanoparticle-protein complex as a biological entity; a complex fluids and surface science challenge for the 21st century. *Advances in Colloid and Interface Science* 134-135: 167-174.
- [18] Gatti AM, Quagliano D, Sighinolfi GL (2009) A Morphological Approach to Monitor the Nanoparticle-Cell Interaction. *International Journal of Imaging and Robotics* 2: 2-21.
- [19] Urban RM, Jacobs JJ, Gilbert JL, Galante JO (1994) Migration of corrosion products from modular hip prostheses. Particle microanalysis and histopathological findings. *The Journal of Bone and Joint Surgery* 76(9): 1345-1359.
- [20] Kirkpatrick CJ, Barth S, Gerdes T, Krump-Konvalinkova V, Peters (K 2002) Pathomechanisms of impaired wound healing by metallic corrosion products. *Mund Kiefer Gesichtschir* 6(3): 183-190.
- [21] Lee SH, Brennan FR, Jacobs JJ, Urban RM, Ragasa DR, et al. (1997) Human monocyte/macrophage response to cobalt-chromium corrosion products and titanium particles in patients with total joint replacements. *J Orthop Res* 15(1): 40-49.
- [22] Shaw CA, Seneff S, Kette SD, Tomljenovic L, Oller Jr JW, et al. (2014) Aluminum-Induced Entropy in Biological Systems: Implications for Neurological Disease. *Journal of Toxicology* 2014: 491316.
- [23] Shaw CA, Kette SD, Davidson RM, Seneff S (2013) Aluminum™s Role in CNS-immune System Interactions leading to Neurological Disorders. *Immunome Research* 9: 069.
- [24] Seneff S, Swanson N, Chen Li (2015) Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease. *Agricultural Sciences* 6(1): 42-70.
- [25] Pegaz B, Debeve E, Ballini JP, Konan-Kouakou YN, van den Bergh HJ (2006) Effect of nanoparticle size on the extravasations and the photothrombic activity of meso(p-tetracarboxyphenyl)porphyrin. *J Photochem Photobiol B* 85(3): 216-222.
- [26] Brinth LS, Pors K, Hoppe AG, Badreldin I, Mehlsen J (2015) Is Chronic Fatigue Syndrome/Myalgic Encephalomyelitis a Relevant Diagnosis in Patients with Suspected Side Effects to Human Papilloma Virus Vaccine? *International Journal of Vaccines and Vaccination* 1(1):1-5.
- [27] Moos WH, Faller DV, Harpp DN, Kanara I, Pernokas J, et al. (2016) Microbiota and Neurological Disorders: A Gut Feeling. *Biores Open Access* 5(1): 137-145.
- [28] Sekirov I, Russell SL, Caetano L, Antunes M, Brett (2010) Gut Microbiota in Health and Disease. *Physiological Rev* 90(3): 859-904.
- [29] Umbrello G, Esposito S (2016) Microbiota and neurologic diseases: potential effects of probiotics. *J Transl Med* 14(1): 298.
- [30] Kinoshita T, Abe RT, Hineno A, Tsunekawa K, Nakane S, et al. (2014) Peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine. *Intern Med* 53(19): 2185-2200.

HPV testimony to DOH

I would like to start off my testimony with questions for the decision makers at the Dept of Health as well as any State Legislators that may read or hear this testimony regarding the potential addition of the HPV vaccine to the mandatory list of vaccines needed for children to go to public school

Why is the HPV vaccine so heavily marketed for starters? Why make a vaccine for a disease that afflicts way less than 1% of people in their lifetime? Why include ingredients that are toxic, especially high doses of ingredients that scientists have objected to, and with documented toxicity to reproductive organs? Why use "placebos" in the testing that has been done by Pharmaceutical companies that contained both the high doses of aluminium as well as polysorbate 80 ? These are serious questions and need thoughtful deliberation.

When the U.S. introduced the human papilloma virus (HPV) vaccine in 2006, cervical cancer rates had been steadily declining for several decades This was due largely to successful and routine cervical cancer screening. HPV is an illness women have a lifetime risk of being diagnosed with 0.6%. Usually diagnosed most frequently at age 47 yrs old in the US, it is now targeting girls aged 11 to 26. Since then it is being marketed to boys as young as nine to prevent very rare anal and penile cancers — a disease that afflicts 0.2 % of men in their lifetime.

. Recent letters published in the *British Medical Journal* (BMJ) have brought forward some stark numbers that illustrate the vaccine's **appalling** record:

- A serious adverse event rate of 1 in 15 (7%) and a death rate among the vaccinated (14 per 10,000) that far exceeds the risk of dying from cervical cancer (.23 per 10,000) (*BMJ letter*, May 2018).
- Reports to the World Health Organization's global adverse drug reactions database—conservatively estimated to represent 10% of actual reactions—of over 305,000 adverse reactions where the HPV vaccine "is believed to have been the cause," including 445 deaths (23 of which were sudden) and over 1,000 cancerous tumors (including 168 cervical cancers), among other serious reactions (*BMJ letter*, December 2017).

HPV vaccines have a high number of reported adverse events: 45,277 in the US alone from its introduction in 2006 to May, 2018 (and these are considered to be vastly under-reported).

These hundreds of thousands of reported and unreported case reports can no longer be discarded simply as 'anecdotes' or 'coincidence,'. OUR CHILDREN AND GRANDCHILDREN ARE NOT ANECDOTES TO US !

It is argued that a healthy 16-year-old is at zero immediate risk of dying from cervical cancer but is faced with a small but real risk of death or serious disability from this vaccine. Cervical screening will always detect more pre-cancers and cancers than vaccination can prevent.

There is now reason to believe that there is a lowered probability of pregnancy in females in the US between 25 and 29 who received the HPV vaccine. The HPV vaccine may just be the common denominator behind the growing infertility link. I submit a link to a study, published in the current Journal of Toxicology and Environmental Health, which examines the childbearing capacity of women who received the human papilloma virus (HPV) vaccine – compared to those who didn't.

Both HPV vaccines contain aluminum, a toxic metal with documented potential to induce autoimmune self-attack, including on reproductive organs. HPV vaccines are loaded with aluminum: Merck's original Gardasil vaccine contained 225 micrograms of aluminum in each of three shots; the "new improved" Gardasil 9 shots contain a total of 1500 micrograms – a tremendous stimulant for the immune system that might just be "a tipping point" for youths who have had so many previous injections of aluminum in the schedule of 50 vaccines before school age.

Vaccine believers must accept that, like all drugs, vaccines can and do have thousands of documented long-term adverse reactions. Because these responses are mediated by the individual's unique immune system, they are diverse, unpredictable and profound.

Why does the CDC, and our Dept of Health brush off 45,277 reports of adverse events – including neurological and reproductive symptoms — among young women of childbearing age?

More studies must be done. The precautionary rule must apply so that our children do not needlessly suffer from the mistake by the CDC, and our own Dept of Health of making HPV a MANDATORY VACCINE !

Links to information in this testimony:

<https://childrenshealthdefense.org/news/vaccine-safety/vaccine-boom-population-bust-study-queries-the-link-between-hpv-vaccine-and-soaring-infertility/>

Journal of Toxicology & Environmental Health -

<https://www.tandfonline.com/doi/full/10.1080/15287394.2018.1477640>

Aloha, my name is Stasia Estep and I am in opposition to HAR 11-157. Thank you everyone who rearranged their schedule to get here. Your voices matter. I know everyone here is striving for the same end which is keeping our keiki as healthy and safe as possible.

Before I begin I want to ask that everyone here as a medical professional consider a few questions. Has history ever shown the medical establishment to be wrong about a medical procedure, drug or therapy? True science is willing to question methodical dogma, even when the majority scoff at the idea. I have no doubt most of you are deeply caring individuals who have a desire to heal and protect. That's why you do what you do. That's also why I urge you to reflect on the education you received regarding vaccines. It being the one of the most routine treatments in any pediatrician's office, did you spend countless hours learning all of the ingredients, the adverse reactions, and how to identify them? Or was it mostly about the benefits? Did you learn how to give true fully informed consent? Where are you required by federal law to report reactions (that hopefully you know how to identify)? What is the history of each disease and the huge mortality and incidence decrease in the 20th century prior to the introductions of the vaccines? Brave and learned medical professionals have stepped forward, admitting they didn't learn much about vaccines in school, and now, after reading the literature from both sides for themselves are standing up, concerned about the safety of vaccines. Have you heard what your contemporaries have to say?

A fact I trust you will not lose sight of is that safety testing for vaccines fails the golden standard of every other pharmaceutical drug. Among the failings in vaccine safety studies are adjuvant safety testing individually and when combined as administered on the schedule.

Listed in the Vaccine Excipient & Media Summary (1) some *known* adjuvants include: formaldehyde, blood-brain opening polysorbate 80, phenoxyethanol, ammonium sulfate, human serum albumen, human-diploid fibroblast cell cultures WI-38, human diploid cells MRC-5. Fun fact: vaccine-creator Stanley Plotkin admitted in a deposition earlier 2018 that during said vaccine development, it took 76 aborted fetuses to get the right tissues needed for the culture (2). Also included is fetal bovine serum, monkey kidney cells, african green monkey (VERO) cells, porcine derived gelatin (and porcine circoviruses in Rotarix) as well as egg and yeast proteins. There are 60 or so more metal, chemical, human and animal organisms as adjuvants, including the controversial thimerosal still in multi-dose flu vials. (3) This is what's being mandated into our keiki's muscle tissue.

If that isn't alarming, I trust the *unlisted* contaminants discovered in vaccines in these studies (4, 5) from Italy in 2017 & 2018 will be a surprise. Contaminants found include: Barium, lead, stainless steel, tungsten, gold-zinc, platinum, silver, bismuth, iron, chromium, lead particles, morphologies of red cells (human or animal origin is unknown), and "debris" composed of aluminum, bromine, silicon, potassium and titanium. In some they also could not find the protein antigens that the vaccines were supposed to have. Other independent tests have found glyphosate. (6)

Now for Aluminum. Many childhood vaccines contain it. Aluminum is a known neurotoxin. After learning that many "placebos" used in "safety studies" [including HPV(7)] are either other vaccines or aluminum adjuvant, I was surprised, and I would hope it surprises you too. Placebos are supposed to be inert. Saline is a great placebo. If IA (injected aluminum) placebos were themselves shown to cause damage, would that nullify the study since the control contained this harmful substance?

You may be surprised to hear that they do cause harm. There is one study, known as the Mitkus study that vaccine advocates reference when questioned about the safety of IA. (8) It came under severe scrutiny this year from leading experts in the world on the neurotoxicity of Al. In the paper criticizing the methods of the Mitkus study, the authors also mention other countries who have studies implicating aluminum-containing vaccines in chronic illness: "The occurrence of *myalgia* and *arthralgia*, *chronic fatigue* and *neurological disorders* following multiple injections of aluminum-containing vaccines against hepatitis B, tetanus and human papilloma virus (HPV) has been reported in many countries: Australia, Canada, Denmark, France, United Kingdom, Italy, Israel, Japan, Mexico, Portugal, and USA." (9)

Recent studies have regarded IA as "poorly biodegradable", with the potential to become "*insidiously unsafe*, especially in the case of *over-immunization* and immature/altered blood brain barrier..." as well as having potential for neurotoxic effects after long-term accumulation. (10, 11, 12, 13, 14)

To summarize the cited works, here is a summary of what a decade of emerging science on IA toxicity is saying. It can:

- 1) impair brain development,
- 2) remain in the brain much longer than thought,
- 3) is brought into the brain by macrophages that grab the IA from the vaccine injection site and recirculate it,
- 4) may actually be worse when injected in small doses repeatedly (like in vaccination) and,
- 5) remarkably high levels of aluminum have been found in brains of people diagnosed with autism. (15, 16, 17, 19, 20, 21)

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GARDASIL safely and effectively. See full prescribing information for GARDASIL.

GARDASIL[®]

[Human Papillomavirus Quadrivalent (Types 16, 18, 6, and 11) Vaccine, Recombinant]

Suspension for intramuscular injection

Initial U.S. Approval: 2006

INDICATIONS AND USAGE

GARDASIL is a vaccine indicated in girls and women 9 through 26 years of age for the prevention of the following diseases caused by Human Papillomavirus (HPV) types included in the vaccine:

- Cervical, vulvar, vaginal, and anal cancer caused by HPV types 16 and 18 (1.1)
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11 (1.1)

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and Cervical adenocarcinoma *in situ* (AIS) (1.1)
- Cervical intraepithelial neoplasia (CIN) grade 1 (1.1)
- Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3 (1.1)
- Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3 (1.1)
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3 (1.1)

GARDASIL is indicated in boys and men 9 through 26 years of age for the prevention of the following diseases caused by HPV types included in the vaccine:

- Anal cancer caused by HPV types 16 and 18 (1.2)
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11 (1.2)

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18:

- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3. (1.2)

Limitations of GARDASIL Use and Effectiveness:

- GARDASIL does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. (1.3, 17)
- Recipients of GARDASIL should not discontinue anal cancer screening if it has been recommended by a health care provider. (1.3, 17)
- GARDASIL has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a person has previously been exposed through sexual activity. (1.3, 14.4, 14.5)
- GARDASIL is not intended to be used for treatment of active external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN, or AIN. (1.3)
- GARDASIL has not been demonstrated to protect against diseases due to HPV types not contained in the vaccine. (1.3, 14.4, 14.5)

- Not all vulvar, vaginal, and anal cancers are caused by HPV, and GARDASIL protects only against those vulvar, vaginal, and anal cancers caused by HPV 16 and 18. (1.3)
- GARDASIL does not protect against genital diseases not caused by HPV. (1.3)
- Vaccination with GARDASIL may not result in protection in all vaccine recipients. (1.3)
- GARDASIL has not been demonstrated to prevent HPV-related CIN 2/3 or worse in women older than 26 years of age. (14.7)

DOSAGE AND ADMINISTRATION

0.5-mL suspension for intramuscular injection at the following schedule: 0, 2 months, 6 months. (2.1)

DOSAGE FORMS AND STRENGTHS

- 0.5-mL suspension for injection as a single-dose vial and prefilled syringe. (3, 11)

CONTRAINDICATIONS

- Hypersensitivity, including severe allergic reactions to yeast (a vaccine component), or after a previous dose of GARDASIL. (4, 11)

WARNINGS AND PRECAUTIONS

- Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position. (5.1)

ADVERSE REACTIONS

The most common adverse reaction was headache. Common adverse reactions (frequency of at least 1.0% and greater than AAHS control or saline placebo) are fever, nausea, dizziness; and injection-site pain, swelling, erythema, pruritus, and bruising. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

DRUG INTERACTIONS

GARDASIL may be administered concomitantly with RECOMBIVAX HB[®] (7.1) or with MenaCTra and Adacel. (7.2)

USE IN SPECIFIC POPULATIONS

Safety and effectiveness of GARDASIL have not been established in the following populations:

- Pregnant women. Women who receive GARDASIL during pregnancy are encouraged to contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231. (8.1)
- Children below the age of 9 years. (8.4)
- Immunocompromised individuals. Response to GARDASIL may be diminished. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

- 1.1 Girls and Women
- 1.2 Boys and Men
- 1.3 Limitations of GARDASIL Use and Effectiveness

2 DOSAGE AND ADMINISTRATION

- 2.1 Dosage
- 2.2 Method of Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Syncope
- 5.2 Managing Allergic Reactions

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Use with RECOMBIVAX HB
- 7.2 Use with MenaCTra and Adacel
- 7.3 Use with Hormonal Contraceptives
- 7.4 Use with Systemic Immunosuppressive Medications

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Immunocompromised Individuals

- 10 OVERDOSAGE
- 11 DESCRIPTION
- 12 CLINICAL PHARMACOLOGY
 - 12.1 Mechanism of Action
- 13 NONCLINICAL TOXICOLOGY
 - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 14 CLINICAL STUDIES
 - 14.1 Prophylactic Efficacy – HPV Types 6, 11, 16, and 18 in Girls and Women 16 through 26 Years of Age
 - 14.2 Prophylactic Efficacy – HPV Types 6, 11, 16, and 18 in Boys and Men 16 through 26 Years of Age
 - 14.3 Prophylactic Efficacy – Anal Disease Caused by HPV Types 6, 11, 16, and 18 in Boys and Men 16 through 26 Years of Age in the MSM Sub-study
 - 14.4 Population Impact in Girls and Women 16 through 26 Years of Age

- 14.5 Population Impact in Boys and Men 16 through 26 Years of Age
- 14.6 Overall Population Impact
- 14.7 Studies in Women 27 through 45 Years of Age
- 14.8 Immunogenicity
- 14.9 Long-Term Follow-Up Studies
- 14.10 Studies with RECOMBIVAX HB [hepatitis B vaccine (recombinant)]
- 14.11 Studies with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)]
- 16 HOW SUPPLIED/STORAGE AND HANDLING
- 17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Girls and Women

GARDASIL® is a vaccine indicated in girls and women 9 through 26 years of age for the prevention of the following diseases caused by Human Papillomavirus (HPV) types included in the vaccine:

- Cervical, vulvar, vaginal, and anal cancer caused by HPV types 16 and 18
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and Cervical adenocarcinoma *in situ* (AIS)
- Cervical intraepithelial neoplasia (CIN) grade 1
- Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3
- Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

1.2 Boys and Men

GARDASIL is indicated in boys and men 9 through 26 years of age for the prevention of the following diseases caused by HPV types included in the vaccine:

- Anal cancer caused by HPV types 16 and 18
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, and 18:

- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

1.3 Limitations of GARDASIL Use and Effectiveness

The health care provider should inform the patient, parent, or guardian that vaccination does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Women who receive GARDASIL should continue to undergo cervical cancer screening per standard of care. [See Patient Counseling Information (17).]

Recipients of GARDASIL should not discontinue anal cancer screening if it has been recommended by a health care provider. [See Patient Counseling Information (17).]

GARDASIL has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a person has previously been exposed through sexual activity. [See Clinical Studies (14.4, 14.5).]

GARDASIL is not intended to be used for treatment of active external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN; or AIN.

GARDASIL has not been demonstrated to protect against diseases due to HPV types not contained in the vaccine. [See Clinical Studies (14.4, 14.5).]

Not all vulvar, vaginal, and anal cancers are caused by HPV, and GARDASIL protects only against those vulvar, vaginal, and anal cancers caused by HPV 16 and 18.

GARDASIL does not protect against genital diseases not caused by HPV.

Vaccination with GARDASIL may not result in protection in all vaccine recipients.

GARDASIL has not been demonstrated to prevent HPV-related CIN 2/3 or worse in women older than 26 years of age. [See Clinical Studies (14.7).]

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

GARDASIL should be administered intramuscularly as a 0.5-mL dose at the following schedule: 0, 2 months, 6 months. [See *Clinical Studies (14.8).*]

2.2 Method of Administration

For intramuscular use only.

Shake well before use. Thorough agitation immediately before administration is necessary to maintain suspension of the vaccine. GARDASIL should not be diluted or mixed with other vaccines. After thorough agitation, GARDASIL is a white, cloudy liquid. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Do not use the product if particulates are present or if it appears discolored.

GARDASIL should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.

Syncope has been reported following vaccination with GARDASIL and may result in falling with injury; observation for 15 minutes after administration is recommended. [See *Warnings and Precautions (5.1).*]

Single-Dose Vial Use

Withdraw the 0.5-mL dose of vaccine from the single-dose vial using a sterile needle and syringe and use promptly.

Prefilled Syringe Use

This package does not contain a needle. Shake well before use. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Administer the entire dose as per standard protocol.

3 DOSAGE FORMS AND STRENGTHS

GARDASIL is a suspension for intramuscular administration available in 0.5-mL single dose vials and prefilled syringes. See *Description (11)* for the complete listing of ingredients.

4 CONTRAINDICATIONS

Hypersensitivity, including severe allergic reactions to yeast (a vaccine component), or after a previous dose of GARDASIL. [See *Description (11).*]

5 WARNINGS AND PRECAUTIONS

5.1 Syncope

Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position.

5.2 Managing Allergic Reactions

Appropriate medical treatment and supervision must be readily available in case of anaphylactic reactions following the administration of GARDASIL.

6 ADVERSE REACTIONS

Overall Summary of Adverse Reactions

Headache, fever, nausea, and dizziness; and local injection site reactions (pain, swelling, erythema, pruritus, and bruising) occurred after administration with GARDASIL.

Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following vaccination with GARDASIL and may result in falling with injury; observation for 15 minutes after administration is recommended. [See *Warnings and Precautions (5.1).*]

Anaphylaxis has been reported following vaccination with GARDASIL.

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

Studies in Girls and Women (9 Through 45 Years of Age) and Boys and Men (9 Through 26 Years of Age)

In 7 clinical trials (5 Amorphous Aluminum Hydroxyphosphate Sulfate [AAHS]-controlled, 1 saline placebo-controlled, and 1 uncontrolled), 18,083 individuals were administered GARDASIL or AAHS control or saline placebo on the day of enrollment, and approximately 2 and 6 months thereafter, and safety was evaluated using vaccination report cards (VRC)-aided surveillance for 14 days after each injection of GARDASIL or AAHS control or saline placebo in these individuals. The individuals who were monitored using VRC-aided surveillance included 10,088 individuals 9 through 45 years of age at enrollment who received GARDASIL and 7,995 individuals who received AAHS control or saline placebo. Few individuals (0.2%) discontinued due to adverse reactions. The race distribution of the 9- through 26-year-old girls and women in the safety population was as follows: 62.3% White; 17.6% Hispanic (Black and White); 6.8% Asian; 6.7% Other; 6.4% Black; and 0.3% American Indian. The race distribution of the 24- through 45-year-old women in the safety population of Study 6 was as follows: 20.6% White; 43.2% Hispanic (Black and White); 0.2% Other; 4.8% Black; 31.2% Asian; and 0.1% American Indian. The race distribution of the 9- through 26-year-old boys and men in the safety population was as follows: 42.0% White; 19.7% Hispanic (Black and White); 11.0% Asian; 11.2% Other; 15.9% Black; and 0.1% American Indian.

Common Injection-Site Adverse Reactions in Girls and Women 9 Through 26 Years of Age

The injection site adverse reactions that were observed among recipients of GARDASIL at a frequency of at least 1.0% and also at a greater frequency than that observed among AAHS control or saline placebo recipients are shown in Table 1.

Table 1: Injection-Site Adverse Reactions in Girls and Women 9 Through 26 Years of Age*

Adverse Reaction (1 to 5 Days Postvaccination)	GARDASIL (N = 5088) %	AAHS Control[†] (N = 3470) %	Saline Placebo (N = 320) %
<i>Injection Site</i>			
Pain	83.9	75.4	48.6
Swelling	25.4	15.8	7.3
Erythema	24.7	18.4	12.1
Pruritus	3.2	2.8	0.6
Bruising	2.8	3.2	1.6

*The injection-site adverse reactions that were observed among recipients of GARDASIL were at a frequency of at least 1.0% and also at a greater frequency than that observed among AAHS control or saline placebo recipients.

[†]AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Common Injection-Site Adverse Reactions in Boys and Men 9 Through 26 Years of Age

The injection site adverse reactions that were observed among recipients of GARDASIL at a frequency of at least 1.0% and also at a greater frequency than that observed among AAHS control or saline placebo recipients are shown in Table 2.

Table 2: Injection-Site Adverse Reactions in Boys and Men 9 Through 26 Years of Age*

Adverse Reaction (1 to 5 Days Postvaccination)	GARDASIL (N = 3093) %	AAHS Control[†] (N = 2029) %	Saline Placebo (N = 274) %
<i>Injection Site</i>			
Pain	61.4	50.8	41.6
Erythema	16.7	14.1	14.5
Swelling	13.9	9.6	8.2
Hematoma	1.0	0.3	3.3

*The injection-site adverse reactions that were observed among recipients of GARDASIL were at a frequency of at least 1.0% and also at a greater frequency than that observed among AAHS control or saline placebo recipients.

†AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Evaluation of Injection-Site Adverse Reactions by Dose in Girls and Women 9 Through 26 Years of Age

An analysis of injection-site adverse reactions in girls and women by dose is shown in Table 3. Of those girls and women who reported an injection-site reaction, 94.3% judged their injection-site adverse reaction to be mild or moderate in intensity.

Table 3: Postdose Evaluation of Injection-Site Adverse Reactions in Girls and Women 9 Through 26 Years of Age (1 to 5 Days Postvaccination)

Adverse Reaction	GARDASIL (% occurrence)			AAHS Control* (% occurrence)			Saline Placebo (% occurrence)		
	Post-dose 1 N [†] = 5011	Post-dose 2 N = 4924	Post-dose 3 N = 4818	Post-dose 1 N = 3410	Post-dose 2 N = 3351	Post-dose 3 N = 3295	Post-dose 1 N = 315	Post-dose 2 N = 301	Post-dose 3 N = 300
Pain	63.4	60.7	62.7	57.0	47.8	49.6	33.7	20.3	27.3
Mild/Moderate	62.5	59.7	61.2	56.6	47.3	48.9	33.3	20.3	27.0
Severe	0.9	1.0	1.5	0.4	0.5	0.6	0.3	0.0	0.3
Swelling[‡]	10.2	12.8	15.1	8.2	7.5	7.6	4.4	3.0	3.3
Mild/Moderate	9.6	11.9	14.2	8.1	7.2	7.3	4.4	3.0	3.3
Severe	0.6	0.8	0.9	0.2	0.2	0.2	0.0	0.0	0.0
Erythema[‡]	9.2	12.1	14.7	9.8	8.4	8.9	7.3	5.3	5.7
Mild/Moderate	9.0	11.7	14.3	9.5	8.4	8.8	7.3	5.3	5.7
Severe	0.2	0.3	0.4	0.3	0.1	0.1	0.0	0.0	0.0

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

†N = Number of individuals with follow-up

‡Intensity of swelling and erythema was measured by size (inches): Mild = 0 to ≤1; Moderate = >1 to ≤2; Severe = >2.

Evaluation of Injection-Site Adverse Reactions by Dose in Boys and Men 9 Through 26 Years of Age

An analysis of injection-site adverse reactions in boys and men by dose is shown in Table 4. Of those boys and men who reported an injection-site reaction, 96.4% judged their injection-site adverse reaction to be mild or moderate in intensity.

Table 4: Postdose Evaluation of Injection-Site Adverse Reactions in Boys and Men 9 Through 26 Years of Age (1 to 5 Days Postvaccination)

Adverse Reaction	GARDASIL (% occurrence)			AAHS Control* (% occurrence)			Saline Placebo (% occurrence)		
	Post-dose 1 N [†] = 3003	Post-dose 2 N = 2898	Post-dose 3 N = 2826	Post-dose 1 N = 1950	Post-dose 2 N = 1854	Post-dose 3 N = 1799	Post-dose 1 N = 269	Post-dose 2 N = 263	Post-dose 3 N = 259
Pain	44.7	36.9	34.4	38.4	28.2	25.8	27.5	20.5	16.2
Mild/Moderate	44.5	36.4	34.1	37.9	28.2	25.5	27.5	20.2	16.2
Severe	0.2	0.5	0.3	0.4	0.1	0.3	0.0	0.4	0.0
Swelling[‡]	5.6	6.6	7.7	5.6	4.5	4.1	4.8	1.5	3.5
Mild/Moderate	5.3	6.2	7.1	5.4	4.5	4.0	4.8	1.5	3.1
Severe	0.2	0.3	0.5	0.2	0.0	0.1	0.0	0.0	0.4
Erythema[‡]	7.2	8.0	8.7	8.3	6.3	5.7	7.1	5.7	5.0
Mild/Moderate	6.8	7.7	8.3	8.0	6.2	5.6	7.1	5.7	5.0
Severe	0.3	0.2	0.3	0.2	0.1	0.1	0.0	0.0	0.0

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

†N = Number of individuals with follow-up

‡Intensity of swelling and erythema was measured by size (inches): Mild = 0 to ≤1; Moderate = >1 to ≤2; Severe = >2.

Common Systemic Adverse Reactions in Girls and Women 9 Through 26 Years of Age

Headache was the most commonly reported systemic adverse reaction in both treatment groups (GARDASIL = 28.2% and AAHS control or saline placebo = 28.4%). Fever was the next most commonly

reported systemic adverse reaction in both treatment groups (GARDASIL = 13.0% and AAHS control or saline placebo = 11.2%).

Adverse reactions that were observed among recipients of GARDASIL, at a frequency of greater than or equal to 1.0% where the incidence in the GARDASIL group was greater than or equal to the incidence in the AAHS control or saline placebo group, are shown in Table 5.

Table 5: Common Systemic Adverse Reactions in Girls and Women 9 Through 26 Years of Age (GARDASIL ≥Control)*

Adverse Reactions (1 to 15 Days Postvaccination)	GARDASIL (N = 5088) %	AAHS Control [†] or Saline Placebo (N = 3790) %
Pyrexia	13.0	11.2
Nausea	6.7	6.5
Dizziness	4.0	3.7
Diarrhea	3.6	3.5
Vomiting	2.4	1.9
Cough	2.0	1.5
Toothache	1.5	1.4
Upper respiratory tract infection	1.5	1.5
Malaise	1.4	1.2
Arthralgia	1.2	0.9
Insomnia	1.2	0.9
Nasal congestion	1.1	0.9

*The adverse reactions in this table are those that were observed among recipients of GARDASIL at a frequency of at least 1.0% and greater than or equal to those observed among AAHS control or saline placebo recipients.

[†]AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Common Systemic Adverse Reactions in Boys and Men 9 Through 26 Years of Age

Headache was the most commonly reported systemic adverse reaction in both treatment groups (GARDASIL = 12.3% and AAHS control or saline placebo = 11.2%). Fever was the next most commonly reported systemic adverse reaction in both treatment groups (GARDASIL = 8.3% and AAHS control or saline placebo = 6.5%).

Adverse reactions that were observed among recipients of GARDASIL, at a frequency of greater than or equal to 1.0% where the incidence in the group that received GARDASIL was greater than or equal to the incidence in the AAHS control or saline placebo group, are shown in Table 6.

Table 6: Common Systemic Adverse Reactions in Boys and Men 9 Through 26 Years of Age (GARDASIL ≥Control)*

Adverse Reactions (1 to 15 Days Postvaccination)	GARDASIL (N = 3093) %	AAHS Control [†] or Saline Placebo (N = 2303) %
Headache	12.3	11.2
Pyrexia	8.3	6.5
Oropharyngeal pain	2.8	2.1
Diarrhea	2.7	2.2
Nasopharyngitis	2.6	2.6
Nausea	2.0	1.0
Upper respiratory tract infection	1.5	1.0
Abdominal pain upper	1.4	1.4
Myalgia	1.3	0.7
Dizziness	1.2	0.9
Vomiting	1.0	0.8

*The adverse reactions in this table are those that were observed among recipients of GARDASIL at a frequency of at least 1.0% and greater than or equal to those observed among AAHS control or saline placebo recipients.

[†]AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Evaluation of Fever by Dose in Girls and Women 9 Through 26 Years of Age

An analysis of fever in girls and women by dose is shown in Table 7.

Table 7: Postdose Evaluation of Fever in Girls and Women 9 Through 26 Years of Age (1 to 5 Days Postvaccination)

Temperature (°F)	GARDASIL (% occurrence)			AAHS Control* or Saline Placebo (% occurrence)		
	Postdose 1 N [†] = 4945	Postdose 2 N = 4804	Postdose 3 N = 4671	Postdose 1 N = 3681	Postdose 2 N = 3564	Postdose 3 N = 3467
≥100 to <102	3.7	4.1	4.4	3.1	3.8	3.6
≥102	0.3	0.5	0.5	0.2	0.4	0.5

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate
[†]N = Number of individuals with follow-up

Evaluation of Fever by Dose in Boys and Men 9 Through 26 Years of Age

An analysis of fever in boys and men by dose is shown in Table 8.

Table 8: Postdose Evaluation of Fever in Boys and Men 9 Through 26 Years of Age (1 to 5 Days Postvaccination)

Temperature (°F)	GARDASIL (% occurrence)			AAHS Control* or Saline Placebo (% occurrence)		
	Postdose 1 N [†] = 2972	Postdose 2 N = 2849	Postdose 3 N = 2792	Postdose 1 N = 2194	Postdose 2 N = 2079	Postdose 3 N = 2046
≥100 to <102	2.4	2.5	2.3	2.1	2.2	1.6
≥102	0.6	0.5	0.5	0.5	0.3	0.3

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate
[†]N = Number of individuals with follow-up

Serious Adverse Reactions in the Entire Study Population

Across the clinical studies, 26 serious adverse reactions (GARDASIL N = 128 or 0.8%; placebo N = 130 or 1.0%) out of 29,323 (GARDASIL N = 15,706; AAHS control N = 13,023; or saline placebo N = 594) individuals (9- through 45-year-old girls and women; and 9- through 26-year-old boys and men) reported a serious systemic adverse reaction.

Of the entire study population (29,323 individuals), 0.04% of the reported serious systemic adverse reactions were judged to be vaccine related by the study investigator. The most frequently (frequency of 4 cases or greater with either GARDASIL, AAHS control, saline placebo, or the total of all three) reported serious systemic adverse reactions, regardless of causality, were:

- Headache [0.02% GARDASIL (3 cases) vs. 0.02% AAHS control (2 cases)],
- Gastroenteritis [0.02% GARDASIL (3 cases) vs. 0.02% AAHS control (2 cases)],
- Appendicitis [0.03% GARDASIL (5 cases) vs. 0.01% AAHS control (1 case)],
- Pelvic inflammatory disease [0.02% GARDASIL (3 cases) vs. 0.03% AAHS control (4 cases)],
- Urinary tract infection [0.01% GARDASIL (2 cases) vs. 0.02% AAHS control (2 cases)],
- Pneumonia [0.01% GARDASIL (2 cases) vs. 0.02% AAHS control (2 cases)],
- Pyelonephritis [0.01% GARDASIL (2 cases) vs. 0.02% AAHS control (3 cases)],
- Pulmonary embolism [0.01% GARDASIL (2 cases) vs. 0.02% AAHS control (2 cases)].

One case (0.006% GARDASIL; 0.0% AAHS control or saline placebo) of bronchospasm; and 2 cases (0.01% GARDASIL; 0.0% AAHS control or saline placebo) of asthma were reported as serious systemic adverse reactions that occurred following any vaccination visit.

In addition, there was 1 individual in the clinical trials, in the group that received GARDASIL, who reported two injection-site serious adverse reactions (injection-site pain and injection-site joint movement impairment).

Deaths in the Entire Study Population

Across the clinical studies, 40 deaths (GARDASIL N = 21 or 0.1%; placebo N = 19 or 0.1%) were reported in 29,323 (GARDASIL N = 15,706; AAHS control N = 13,023, saline placebo N = 594) individuals (9- through 45-year-old girls and women; and 9- through 26-year-old boys and men). The events reported were consistent with events expected in healthy adolescent and adult populations. The most common cause of death was motor vehicle accident (5 individuals who received GARDASIL and 4 individuals who received AAHS control), followed by drug overdose/suicide (2 individuals who received GARDASIL and 6 individuals who received AAHS control), gunshot wound (1 individual who received GARDASIL and 3 individuals who received AAHS control), and pulmonary embolus/deep vein thrombosis (1 individual who

received GARDASIL and 1 individual who received AAHS control). In addition, there were 2 cases of sepsis, 1 case of pancreatic cancer, 1 case of arrhythmia, 1 case of pulmonary tuberculosis, 1 case of hyperthyroidism, 1 case of post-operative pulmonary embolism and acute renal failure, 1 case of traumatic brain injury/cardiac arrest, 1 case of systemic lupus erythematosus, 1 case of cerebrovascular accident, 1 case of breast cancer, and 1 case of nasopharyngeal cancer in the group that received GARDASIL; 1 case of asphyxia, 1 case of acute lymphocytic leukemia, 1 case of chemical poisoning, and 1 case of myocardial ischemia in the AAHS control group; and 1 case of medulloblastoma in the saline placebo group.

Systemic Autoimmune Disorders in Girls and Women 9 Through 26 Years of Age

In the clinical studies, 9- through 26-year-old girls and women were evaluated for new medical conditions that occurred over the course of follow-up. New medical conditions potentially indicative of a systemic autoimmune disorder seen in the group that received GARDASIL or AAHS control or saline placebo are shown in Table 9. This population includes all girls and women who received at least one dose of GARDASIL or AAHS control or saline placebo, and had safety data available.

Table 9: Summary of Girls and Women 9 Through 26 Years of Age Who Reported an Incident Condition Potentially Indicative of a Systemic Autoimmune Disorder After Enrollment in Clinical Trials of GARDASIL, Regardless of Causality

Conditions	GARDASIL (N = 10,706)	AAHS Control* or Saline Placebo (N = 9412)
	n (%)	n (%)
Arthralgia/Arthritis/Arthropathy ¹	120 (1.1)	98 (1.0)
Autoimmune Thyroiditis	4 (0.0)	1 (0.0)
Celiac Disease	10 (0.1)	6 (0.1)
Diabetes Mellitus Insulin-dependent	2 (0.0)	2 (0.0)
Erythema Nodosum	2 (0.0)	4 (0.0)
Hyperthyroidism ³	27 (0.3)	21 (0.2)
Hypothyroidism ⁵	35 (0.3)	38 (0.4)
Inflammatory Bowel Disease ⁴	7 (0.1)	10 (0.1)
Multiple Sclerosis	2 (0.0)	4 (0.0)
Nephritis ⁶	2 (0.0)	5 (0.1)
Optic Neuritis	2 (0.0)	0 (0.0)
Pigmentation Disorder ⁷	4 (0.0)	3 (0.0)
Psoriasis ⁸	13 (0.1)	15 (0.2)
Raynaud's Phenomenon	3 (0.0)	4 (0.0)
Rheumatoid Arthritis ⁹	6 (0.1)	2 (0.0)
Scleroderma/Morphea	2 (0.0)	1 (0.0)
Stevens-Johnson Syndrome	1 (0.0)	0 (0.0)
Systemic Lupus Erythematosus	1 (0.0)	3 (0.0)
Uveitis	3 (0.0)	1 (0.0)
All Conditions	245 (2.3)	218 (2.3)

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

¹Arthralgia/Arthritis/Arthropathy includes the following terms: Arthralgia, Arthritis, Arthritis reactive, and Arthropathy

³Hyperthyroidism includes the following terms: Basedow's disease, Goiter, Toxic nodular goiter, and Hyperthyroidism

⁵Hypothyroidism includes the following terms: Hypothyroidism and thyroiditis

⁴Inflammatory bowel disease includes the following terms: Colitis ulcerative, Crohn's disease, and Inflammatory bowel disease

⁶Nephritis includes the following terms: Nephritis, Glomerulonephritis minimal lesion, Glomerulonephritis proliferative

⁷Pigmentation disorder includes the following terms: Pigmentation disorder, Skin depigmentation, and Vitiligo

⁸Psoriasis includes the following terms: Psoriasis, Pustular psoriasis, and Psoriatic arthropathy

⁹Rheumatoid arthritis includes juvenile rheumatoid arthritis. One woman counted in the rheumatoid arthritis group reported rheumatoid arthritis as an adverse experience at Day 130.

N = Number of individuals enrolled

n = Number of individuals with specific new Medical Conditions

NOTE: Although an individual may have had two or more new Medical Conditions, the individual is counted only once within a category. The same individual may appear in different categories.

Systemic Autoimmune Disorders in Boys and Men 9 Through 26 Years of Age

In the clinical studies, 9- through 26-year-old boys and men were evaluated for new medical conditions that occurred over the course of follow-up. New medical conditions potentially indicative of a systemic autoimmune disorder seen in the group that received GARDASIL or AAHS control or saline placebo are

shown in Table 10. This population includes all boys and men who received at least one dose of GARDASIL or AAHS control or saline placebo, and had safety data available.

Table 10: Summary of Boys and Men 9 Through 26 Years of Age Who Reported an Incident Condition Potentially Indicative of a Systemic Autoimmune Disorder After Enrollment in Clinical Trials of GARDASIL, Regardless of Causality

Conditions	GARDASIL (N = 3093)	AAHS Control* or Saline Placebo (N = 2303)
	n (%)	n (%)
Alopecia Areata	2 (0.1)	0 (0.0)
Ankylosing Spondylitis	1 (0.0)	2 (0.1)
Arthralgia/Arthritis/Reactive Arthritis	30 (1.0)	17 (0.7)
Autoimmune Thrombocytopenia	1 (0.0)	0 (0.0)
Diabetes Mellitus Type 1	3 (0.1)	2 (0.1)
Hyperthyroidism	0 (0.0)	1 (0.0)
Hypothyroidism [†]	3 (0.1)	0 (0.0)
Inflammatory Bowel Disease [‡]	1 (0.0)	2 (0.1)
Myocarditis	1 (0.0)	1 (0.0)
Proteinuria	1 (0.0)	0 (0.0)
Psoriasis	0 (0.0)	4 (0.2)
Skin Depigmentation	1 (0.0)	0 (0.0)
Vitiligo	2 (0.1)	5 (0.2)
All Conditions	46 (1.5)	34 (1.5)

*AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

[†]Hypothyroidism includes the following terms: Hypothyroidism and Autoimmune thyroiditis

[‡]Inflammatory bowel disease includes the following terms: Colitis ulcerative and Crohn's disease

N = Number of individuals who received at least one dose of either vaccine or placebo

n = Number of individuals with specific new Medical Conditions

NOTE: Although an individual may have had two or more new Medical Conditions, the individual is counted only once within a category. The same individual may appear in different categories.

Safety in Concomitant Use with RECOMBIVAX HB[®] [hepatitis B vaccine (recombinant)] in Girls and Women 16 Through 23 Years of Age

The safety of GARDASIL when administered concomitantly with RECOMBIVAX HB[®] [hepatitis B vaccine (recombinant)] was evaluated in an AAHS-controlled study of 1871 girls and women with a mean age of 20.4 years [see *Clinical Studies (14.10)*]. The race distribution of the study individuals was as follows: 61.6% White; 23.8% Other; 11.9% Black; 1.6% Hispanic (Black and White); 0.8% Asian; and 0.3% American Indian. The rates of systemic and injection-site adverse reactions were similar among girls and women who received concomitant vaccination as compared with those who received GARDASIL or RECOMBIVAX HB [hepatitis B vaccine (recombinant)].

Safety in Concomitant Use with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)]

The safety of GARDASIL when administered concomitantly with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] was evaluated in a randomized study of 1040 boys and girls with a mean age of 12.6 years [see *Clinical Studies (14.11)*]. The race distribution of the study subjects was as follows: 77.7% White; 1.4% Multi-racial; 12.3% Black; 6.8% Hispanic (Black and White); 1.2% Asian; 0.4% American Indian, and 0.2% Indian.

There was an increase in injection-site swelling reported at the injection site for GARDASIL (concomitant = 10.9%, non-concomitant = 6.9%) when GARDASIL was administered concomitantly with Menactra and Adacel as compared to non-concomitant (separated by 1 month) vaccination. The majority of injection-site swelling adverse experiences were reported as being mild to moderate in intensity.

Safety in Women 27 Through 45 Years of Age

The adverse reaction profile in women 27 through 45 years of age was comparable to the profile seen in girls and women 9 through 26 years of age.

6.2 Postmarketing Experience

The following adverse events have been spontaneously reported during post-approval use of GARDASIL. Because these events were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to vaccine exposure.

Blood and lymphatic system disorders: Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, lymphadenopathy.

Respiratory, thoracic and mediastinal disorders: Pulmonary embolus.

Gastrointestinal disorders: Nausea, pancreatitis, vomiting.

General disorders and administration site conditions: Asthenia, chills, death, fatigue, malaise.

Immune system disorders: Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.

Musculoskeletal and connective tissue disorders: Arthralgia, myalgia.

Nervous system disorders: Acute disseminated encephalomyelitis, dizziness, Guillain-Barré syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonic-clonic movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis.

Infections and infestations: cellulitis.

Vascular disorders: Deep venous thrombosis.

7 DRUG INTERACTIONS

7.1 Use with RECOMBIVAX HB

Results from clinical studies indicate that GARDASIL may be administered concomitantly (at a separate injection site) with RECOMBIVAX HB [hepatitis B vaccine (recombinant)] [see *Clinical Studies (14.10)*].

7.2 Use with Menactra and Adacel

Results from clinical studies indicate that GARDASIL may be administered concomitantly (at a separate injection site) with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] [see *Clinical Studies (14.11)*].

7.3 Use with Hormonal Contraceptives

In clinical studies of 16- through 26-year-old women, 13,912 (GARDASIL N = 6952; AAHS control or saline placebo N = 6960) who had post-Month 7 follow-up used hormonal contraceptives for a total of 33,859 person-years (65.8% of the total follow-up time in the studies).

In one clinical study of 24- through 45-year-old women, 1357 (GARDASIL N = 690; AAHS control N = 667) who had post-Month 7 follow-up used hormonal contraceptives for a total of 3400 person-years (31.5% of the total follow-up time in the study). Use of hormonal contraceptives or lack of use of hormonal contraceptives among study participants did not impair the immune response in the per protocol immunogenicity (PPI) population.

7.4 Use with Systemic Immunosuppressive Medications

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune responses to vaccines [see *Use in Specific Populations (8.6)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B:

Reproduction studies have been performed in female rats at doses equivalent to the recommended human dose and have revealed no evidence of impaired female fertility or harm to the fetus due to GARDASIL. There are, however, no adequate and well-controlled studies in pregnant women. Because

animal reproduction studies are not always predictive of human responses, GARDASIL should be used during pregnancy only if clearly needed.

An evaluation of the effect of GARDASIL on embryo-fetal, pre- and postweaning development was conducted using rats. One group of rats was administered GARDASIL twice prior to gestation, during the period of organogenesis (gestation Day 6) and on lactation Day 7. A second group of pregnant rats was administered GARDASIL during the period of organogenesis (gestation Day 6) and on lactation Day 7 only. GARDASIL was administered at 0.5 mL/rat/occasion (120 mcg total protein which is equivalent to the recommended human dose) by intramuscular injection. No adverse effects on mating, fertility, pregnancy, parturition, lactation, embryo-fetal or pre- and postweaning development were observed. There were no vaccine-related fetal malformations or other evidence of teratogenesis noted in this study. In addition, there were no treatment-related effects on developmental signs, behavior, reproductive performance, or fertility of the offspring.

Clinical Studies in Humans

In clinical studies, women underwent urine pregnancy testing prior to administration of each dose of GARDASIL. Women who were found to be pregnant before completion of a 3-dose regimen of GARDASIL were instructed to defer completion of their vaccination regimen until resolution of the pregnancy.

GARDASIL is not indicated for women 27 years of age or older. However, safety data in women 16 through 45 years of age was collected, and 3819 women (GARDASIL N = 1894 vs. AAHS control or saline placebo N = 1925) reported at least 1 pregnancy each.

The overall proportions of pregnancies that resulted in an adverse outcome, defined as the combined numbers of spontaneous abortion, late fetal death, and congenital anomaly cases out of the total number of pregnancy outcomes for which an outcome was known (and excluding elective terminations), were 22.6% (446/1973) in women who received GARDASIL and 23.1% (460/1994) in women who received AAHS control or saline placebo.

Overall, 55 and 65 women in the group that received GARDASIL or AAHS control or saline placebo, respectively (2.9% and 3.4% of all women who reported a pregnancy in the respective vaccination groups), experienced a serious adverse reaction during pregnancy. The most common events reported were conditions that can result in Caesarean section (e.g., failure of labor, malpresentation, cephalopelvic disproportion), premature onset of labor (e.g., threatened abortions, premature rupture of membranes), and pregnancy-related medical problems (e.g., pre-eclampsia, hyperemesis). The proportions of pregnant women who experienced such events were comparable between the groups receiving GARDASIL and AAHS control or saline placebo.

There were 45 cases of congenital anomaly in pregnancies that occurred in women who received GARDASIL and 34 cases of congenital anomaly in pregnancies that occurred in women who received AAHS control or saline placebo.

Further sub-analyses were conducted to evaluate pregnancies with estimated onset within 30 days or more than 30 days from administration of a dose of GARDASIL or AAHS control or saline placebo. For pregnancies with estimated onset within 30 days of vaccination, 5 cases of congenital anomaly were observed in the group that received GARDASIL compared to 1 case of congenital anomaly in the group that received AAHS control or saline placebo. The congenital anomalies seen in pregnancies with estimated onset within 30 days of vaccination included pyloric stenosis, congenital megacolon, congenital hydronephrosis, hip dysplasia, and club foot. Conversely, in pregnancies with onset more than 30 days following vaccination, 40 cases of congenital anomaly were observed in the group that received GARDASIL compared with 33 cases of congenital anomaly in the group that received AAHS control or saline placebo.

Women who receive GARDASIL during pregnancy are encouraged to contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

8.3 Nursing Mothers

Women 16 Through 45 Years of Age

It is not known whether GARDASIL is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when GARDASIL is administered to a nursing woman.

GARDASIL or AAHS control were given to a total of 1133 women (vaccine N = 582, AAHS control N = 551) during the relevant Phase 3 clinical studies.

Overall, 27 and 13 infants of women who received GARDASIL or AAHS control, respectively (representing 4.6% and 2.4% of the total number of women who were breast-feeding during the period in which they received GARDASIL or AAHS control, respectively), experienced a serious adverse reaction.

In a post-hoc analysis of clinical studies, a higher number of breast-feeding infants (n = 7) whose mothers received GARDASIL had acute respiratory illnesses within 30 days post vaccination of the mother as compared to infants (n = 2) whose mothers received AAHS control.

8.4 Pediatric Use

Safety and effectiveness have not been established in pediatric patients below 9 years of age.

8.5 Geriatric Use

The safety and effectiveness of GARDASIL have not been evaluated in a geriatric population, defined as individuals aged 65 years and over.

8.6 Immunocompromised Individuals

The immunologic response to GARDASIL may be diminished in immunocompromised individuals [see *Drug Interactions (7.4)*].

10 OVERDOSAGE

There have been reports of administration of higher than recommended doses of GARDASIL.

In general, the adverse event profile reported with overdose was comparable to recommended single doses of GARDASIL.

11 DESCRIPTION

GARDASIL, Human Papillomavirus Quadrivalent (Types 6, 11, 16, and 18) Vaccine, Recombinant, is a non-infectious recombinant quadrivalent vaccine prepared from the purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, and 18. The L1 proteins are produced by separate fermentations in recombinant *Saccharomyces cerevisiae* and self-assembled into VLPs. The fermentation process involves growth of *S. cerevisiae* on chemically-defined fermentation media which include vitamins, amino acids, mineral salts, and carbohydrates. The VLPs are released from the yeast cells by cell disruption and purified by a series of chemical and physical methods. The purified VLPs are adsorbed on preformed aluminum-containing adjuvant (Amorphous Aluminum Hydroxyphosphate Sulfate). The quadrivalent HPV VLP vaccine is a sterile liquid suspension that is prepared by combining the adsorbed VLPs of each HPV type and additional amounts of the aluminum-containing adjuvant and the final purification buffer.

GARDASIL is a sterile suspension for intramuscular administration. Each 0.5-mL dose contains approximately 20 mcg of HPV 6 L1 protein, 40 mcg of HPV 11 L1 protein, 40 mcg of HPV 16 L1 protein, and 20 mcg of HPV 18 L1 protein.

Each 0.5-mL dose of the vaccine contains approximately 225 mcg of aluminum (as Amorphous Aluminum Hydroxyphosphate Sulfate adjuvant), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, <7 mcg yeast protein/dose, and water for injection. The product does not contain a preservative or antibiotics.

After thorough agitation, GARDASIL is a white, cloudy liquid.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

HPV only infects human beings. Animal studies with analogous animal papillomaviruses suggest that the efficacy of L1 VLP vaccines may involve the development of humoral immune responses. Human beings develop a humoral immune response to the vaccine, although the exact mechanism of protection is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

GARDASIL has not been evaluated for the potential to cause carcinogenicity or genotoxicity.

GARDASIL administered to female rats at a dose of 120 mcg total protein, which is equivalent to the recommended human dose, had no effects on mating performance, fertility, or embryonic/fetal survival.

The effect of GARDASIL on male fertility has been studied in male rats at an intramuscular dose of 0.5 mL/rat/occasion (120 mcg total protein which is equivalent to the recommended human dose). One group of male rats was administered GARDASIL once, 3 days prior to cohabitation, and a second group of male rats was administered GARDASIL three times, at 6 weeks, 3 weeks, and 3 days prior to cohabitation. There were no treatment-related effects on reproductive performance including fertility, sperm count, and sperm motility. There were no treatment-related gross or histomorphologic and weight changes on the testes.

14 CLINICAL STUDIES

CIN 2/3 and AIS are the immediate and necessary precursors of squamous cell carcinoma and adenocarcinoma of the cervix, respectively. Their detection and removal has been shown to prevent cancer; thus, they serve as surrogate markers for prevention of cervical cancer. In the clinical studies in girls and women aged 16 through 26 years, cases of CIN 2/3 and AIS were the efficacy endpoints to assess prevention of cervical cancer. In addition, cases of VIN 2/3 and VaIN 2/3 were the efficacy endpoints to assess prevention of HPV-related vulvar and vaginal cancers, and observations of external genital lesions were the efficacy endpoints for the prevention of genital warts.

In clinical studies in boys and men aged 16 through 26 years, efficacy was evaluated using the following endpoints: external genital warts and penile/perineal/perianal intraepithelial neoplasia (PIN) grades 1/2/3 or penile/perineal/perianal cancer. In addition, cases of AIN grades 1/2/3 and anal cancer made up the composite efficacy endpoint used to assess prevention of HPV-related anal cancer.

Anal HPV infection, AIN, and anal cancer were not endpoints in the studies conducted in women. The similarity of HPV-related anal disease in men and women supports bridging the indication of prevention of AIN and anal cancer to women.

Efficacy was assessed in 6 AAHS-controlled, double-blind, randomized Phase 2 and 3 clinical studies. The first Phase 2 study evaluated the HPV 16 component of GARDASIL (Study 1, N = 2391 16- through 26-year-old girls and women) and the second evaluated all components of GARDASIL (Study 2, N = 551 16- through 26-year-old girls and women). Two Phase 3 studies evaluated GARDASIL in 5442 (Study 3) and 12,157 (Study 4) 16- through 26-year-old girls and women. A third Phase 3 study, Study 5, evaluated GARDASIL in 4055 16- through 26-year-old boys and men, including a subset of 598 (GARDASIL = 299; placebo = 299) men who self-identified as having sex with men (MSM population). A fourth Phase 3 study, Study 6, evaluated GARDASIL in 3817 24- through 45-year-old women. Together, these six studies evaluated 28,413 individuals (20,541 girls and women 16 through 26 years of age at enrollment with a mean age of 20.0 years, 4055 boys and men 16 through 26 years of age at enrollment with a mean age of 20.5 years, and 3817 women 24 through 45 years of age at enrollment with a mean age of 34.3 years). The race distribution of the 16- through 26-year-old girls and women in the clinical trials was as follows: 70.4% White; 12.2% Hispanic (Black and White); 8.8% Other; 4.6% Black; 3.8% Asian; and 0.2% American Indian. The race distribution of the 16- through 26-year-old boys and men in the clinical trials was as follows: 35.2% White; 20.5% Hispanic (Black and White); 14.4% Other; 19.8% Black; 10.0% Asian; and 0.1% American Indian. The race distribution of the 24- through 45-year-old women in the clinical trials was as follows: 20.6% White; 43.2% Hispanic (Black and White); 0.2% Other; 4.8% Black; 31.2% Asian; and 0.1% American Indian.

The median duration of follow-up was 4.0, 3.0, 3.0, 3.0, 2.3, and 4.0 years for Study 1, Study 2, Study 3, Study 4, Study 5, and Study 6, respectively. Individuals received vaccine or AAHS control on the day of enrollment and 2 and 6 months thereafter. Efficacy was analyzed for each study individually and for all studies in girls and women combined according to a prospective clinical plan.

Overall, 73% of 16- through 26-year-old girls and women, 67% of 24- through 45-year-old women, and 83% of 16- through 26-year-old boys and men were naïve (i.e., PCR [Polymerase Chain Reaction] negative and seronegative for all 4 vaccine HPV types) to all 4 vaccine HPV types at enrollment.

A total of 27% of 16- through 26-year-old girls and women, 33% of 24- through 45-year-old women, and 17% of 16- through 26-year-old boys and men had evidence of prior exposure to or ongoing infection with at least 1 of the 4 vaccine HPV types. Among these individuals, 74% of 16- through 26-year-old girls and women, 71% of 24- through 45-year-old women, and 78% of 16- through 26-year-old boys and men had evidence of prior exposure to or ongoing infection with only 1 of the 4 vaccine HPV types and were naïve (PCR negative and seronegative) to the remaining 3 types.

In 24- through 45-year-old individuals, 0.4% had been exposed to all 4 vaccine HPV types.

In individuals who were naïve (PCR negative and seronegative) to all 4 vaccine HPV types, CIN, genital warts, VIN, VaIN, PIN, and persistent infection caused by any of the 4 vaccine HPV types were counted as endpoints.

Among individuals who were positive (PCR positive and/or seropositive) for a vaccine HPV type at Day 1, endpoints related to that type were not included in the analyses of prophylactic efficacy. Endpoints related to the remaining types for which the individual was naïve (PCR negative and seronegative) were counted.

For example, in individuals who were HPV 18 positive (PCR positive and/or seropositive) at Day 1, lesions caused by HPV 18 were not counted in the prophylactic efficacy evaluations. Lesions caused by HPV 6, 11, and 16 were included in the prophylactic efficacy evaluations. The same approach was used for the other types.

14.1 Prophylactic Efficacy – HPV Types 6, 11, 16, and 18 in Girls and Women 16 through 26 Years of Age

GARDASIL was administered without prescreening for presence of HPV infection and the efficacy trials allowed enrollment of girls and women regardless of baseline HPV status (i.e., PCR status or serostatus). Girls and women with current or prior HPV infection with an HPV type contained in the vaccine were not eligible for prophylactic efficacy evaluations for that type.

The primary analyses of efficacy with respect to HPV types 6, 11, 16, and 18 were conducted in the per-protocol efficacy (PPE) population, consisting of girls and women who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, and were naïve (PCR negative in cervicovaginal specimens and seronegative) to the relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and through 1 month Postdose 3 (Month 7). Efficacy was measured starting after the Month 7 visit.

GARDASIL was efficacious in reducing the incidence of CIN (any grade including CIN 2/3); AIS; genital warts; VIN (any grade); and VaIN (any grade) related to vaccine HPV types 6, 11, 16, or 18 in those who were PCR negative and seronegative at baseline (Table 11).

In addition, girls and women who were already infected with 1 or more vaccine-related HPV types prior to vaccination were protected from precancerous cervical lesions and external genital lesions caused by the other vaccine HPV types.

Table 11: Analysis of Efficacy of GARDASIL in the PPE* Population¹ of 16- Through 26-Year-Old Girls and Women for Vaccine HPV Types

Population	GARDASIL		AAHS Control		% Efficacy (95% CI)
	N	Number of cases	N	Number of cases	
HPV 16- or 18-related CIN 2/3 or AIS					
Study 1 [†]	755	0	750	12	100.0 (65.1, 100.0)
Study 2	231	0	230	1	100.0 (-3744.9, 100.0)
Study 3	2201	0	2222	36	100.0 (89.2, 100.0)
Study 4	5306	2	5262	63	96.9 (88.2, 99.6)
Combined Protocols [§]	8493	2	8464	112	98.2 (93.5, 99.8)
HPV 16-related CIN 2/3 or AIS					
Combined Protocols [§]	7402	2	7205	93	97.9 (92.3, 99.8)
HPV 18-related CIN 2/3 or AIS					
Combined Protocols [§]	7382	0	7316	29	100.0 (86.6, 100.0)
HPV 16- or 18-related VIN 2/3					
Study 2	231	0	230	0	Not calculated
Study 3	2219	0	2239	6	100.0 (14.4, 100.0)
Study 4	5322	0	5275	4	100.0 (-50.3, 100.0)
Combined Protocols [§]	7772	0	7744	10	100.0 (55.5, 100.0)
HPV 16- or 18-related VaIN 2/3					
Study 2	231	0	230	0	Not calculated
Study 3	2219	0	2239	5	100.0 (-10.1, 100.0)
Study 4	5322	0	5275	4	100.0 (-50.3, 100.0)
Combined Protocols [§]	7772	0	7744	9	100.0 (49.5, 100.0)
HPV 6-, 11-, 16-, or 18-related CIN (CIN 1, CIN 2/3) or AIS					
Study 2	235	0	233	3	100.0 (-138.4, 100.0)
Study 3	2241	0	2258	77	100.0 (95.1, 100.0)
Study 4	5388	9	5374	145	93.8 (88.0, 97.2)
Combined Protocols [§]	7864	9	7865	225	96.0 (92.3, 98.2)
HPV 6-, 11-, 16-, or 18-related Genital Warts					
Study 2	235	0	233	3	100.0 (-139.5, 100.0)
Study 3	2261	0	2279	58	100.0 (93.5, 100.0)
Study 4	5404	2	5390	132	98.5 (94.5, 99.8)
Combined Protocols [§]	7900	2	7902	193	99.0 (96.2, 99.9)
HPV 6- and 11-related Genital Warts					
Combined Protocols [§]	6932	2	6856	189	99.0 (96.2, 99.9)

*The PPE population consisted of individuals who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, and were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and through 1 month postdose 3 (Month 7).

[†]See Table 14 for analysis of vaccine impact in the general population.

[‡]Evaluated only the HPV 16 L1 VLP vaccine component of GARDASIL

[§]Analyses of the combined trials were prospectively planned and included the use of similar study entry criteria.

N = Number of individuals with at least 1 follow-up visit after Month 7

CI = Confidence Interval

Note 1: Point estimates and confidence intervals are adjusted for person-time of follow-up.

Note 2: The first analysis in the table (i.e., HPV 16- or 18-related CIN 2/3, AIS or worse) was the primary endpoint of the vaccine development plan.

Note 3: Table 11 does not include cases due to non-vaccine HPV types.

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Prophylactic efficacy against overall cervical and genital disease related to HPV 6, 11, 16, and 18 in an extension phase of Study 2, that included data through Month 60, was noted to be 100% (95% CI: 12.3%, 100.0%) among girls and women in the per protocol population naïve to the relevant HPV types.

GARDASIL was efficacious against HPV disease caused by HPV types 6, 11, 16, and 18 in girls and women who were naïve for those specific HPV types at baseline.

14.2 Prophylactic Efficacy – HPV Types 6, 11, 16, and 18 in Boys and Men 16 through 26 Years of Age

The primary analyses of efficacy were conducted in the per-protocol efficacy (PPE) population. This population consisted of boys and men who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, and were naïve (PCR negative and seronegative) to the

relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and through 1 month postdose 3 (Month 7). Efficacy was measured starting after the Month 7 visit.

GARDASIL was efficacious in reducing the incidence of genital warts related to vaccine HPV types 6 and 11 in those boys and men who were PCR negative and seronegative at baseline (Table 12). Efficacy against penile/perineal/perianal intraepithelial neoplasia (PIN) grades 1/2/3 or penile/perineal/perianal cancer was not demonstrated as the number of cases was too limited to reach statistical significance.

Table 12: Analysis of Efficacy of GARDASIL in the PPE* Population of 16- Through 26-Year-Old Boys and Men for Vaccine HPV Types

Endpoint	GARDASIL		AAHS Control		% Efficacy (95% CI)
	N [†]	Number of cases	N	Number of cases	
External Genital Lesions HPV 6-, 11-, 16-, or 18- related					
External Genital Lesions	1394	3	1404	32	90.6 (70.1, 98.2)
Condyloma	1394	3	1404	28	89.3 (65.3, 97.9)
PIN 1/2/3	1394	0	1404	4	100.0 (-52.1, 100.0)

*The PPE population consisted of individuals who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, and were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and through 1 month postdose 3 (Month 7).

[†]N = Number of individuals with at least 1 follow-up visit after Month 7

CI = Confidence Interval

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

14.3 Prophylactic Efficacy – Anal Disease Caused by HPV Types 6, 11, 16, and 18 in Boys and Men 16 through 26 Years of Age in the MSM Sub-study

A sub-study of Study 5 evaluated the efficacy of GARDASIL against anal disease (anal intraepithelial neoplasia and anal cancer) in a population of 598 MSM. The primary analyses of efficacy were conducted in the per-protocol efficacy (PPE) population of Study 5.

GARDASIL was efficacious in reducing the incidence of anal intraepithelial neoplasia (AIN) grades 1 (both condyloma and non-acuminate), 2, and 3 related to vaccine HPV types 6, 11, 16, and 18 in those boys and men who were PCR negative and seronegative at baseline (Table 13).

Table 13: Analysis of Efficacy of GARDASIL for Anal Disease in the PPE* Population of 16- Through 26-Year-Old Boys and Men in the MSM Sub-study for Vaccine HPV Types

HPV 6-, 11-, 16-, or 18- related Endpoint	GARDASIL		AAHS Control		% Efficacy (95% CI)
	N [†]	Number of cases	N	Number of cases	
AIN 1/2/3	194	5	208	24	77.5 (39.6, 93.3)
AIN 2/3	194	3	208	13	74.9 (8.8, 95.4)
AIN 1	194	4	208	16	73.0 (16.3, 93.4)
Condyloma Acuminatum	194	0	208	6	100.0 (8.2, 100.0)
Non-acuminate	194	4	208	11	60.4 (-33.5, 90.8)

*The PPE population consisted of individuals who received all 3 vaccinations within 1 year of enrollment, did not have major deviations from the study protocol, and were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and through 1 month postdose 3 (month 7).

[†]N = Number of individuals with at least 1 follow-up visit after Month 7

CI = Confidence Interval

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

14.4 Population Impact in Girls and Women 16 through 26 Years of Age

Effectiveness of GARDASIL in Prevention of HPV Types 6-, 11-, 16-, or 18-Related Genital Disease in Girls and Women 16 Through 26 Years of Age, Regardless of Current or Prior Exposure to Vaccine HPV Types

The clinical trials included girls and women regardless of current or prior exposure to vaccine HPV types, and additional analyses were conducted to evaluate the impact of GARDASIL with respect to HPV 6-, 11-, 16-, and 18-related cervical and genital disease in these girls and women. Here, analyses included events arising among girls and women regardless of baseline PCR status and serostatus, including HPV infections that were present at the start of vaccination as well as events that arose from infections that were acquired after the start of vaccination.

The impact of GARDASIL in girls and women regardless of current or prior exposure to a vaccine HPV type is shown in Table 14. Impact was measured starting 1 month Postdose 1. Prophylactic efficacy denotes the vaccine's efficacy in girls and women who are naïve (PCR negative and seronegative) to the relevant HPV types at Day 1. Vaccine impact in girls and women who were positive for vaccine HPV infection, as well as vaccine impact among girls and women regardless of baseline vaccine HPV PCR status and serostatus are also presented. The majority of CIN and genital warts, VIN, and VaIN related to a vaccine HPV type detected in the group that received GARDASIL occurred as a consequence of HPV infection with the relevant HPV type that was already present at Day 1.

There was no clear evidence of protection from disease caused by HPV types for which girls and women were PCR positive regardless of serostatus at baseline.

Table 14: Effectiveness of GARDASIL in Prevention of HPV 6, 11, 16, or 18-Related Genital Disease in Girls and Women 16 Through 26 Years of Age, Regardless of Current or Prior Exposure to Vaccine HPV Types

Endpoint	Analysis	GARDASIL or HPV 16 L1 VLP Vaccine		AAHS Control		% Reduction (95% CI)
		N	Cases	N	Cases	
HPV 16- or 18-related CIN 2/3 or AIS	Prophylactic Efficacy*	9346	4	9407	155	97.4 (93.3, 99.3)
	HPV 16 and/or HPV 18 Positive at Day 1 [†]	2870	142	2898	148 [‡]	-- [§]
	Girls and Women Regardless of Current or Prior Exposure to HPV 16 or 18 [¶]	9836	146	9904	303	51.8 (41.1, 60.7)
HPV 16- or 18-related VIN 2/3 or VaIN 2/3	Prophylactic Efficacy*	8642	1	8673	34	97.0 (82.4, 99.9)
	HPV 16 and/or HPV 18 Positive at Day 1 [†]	1880	8	1876	4	-- [§]
	Girls and Women Regardless of Current or Prior Exposure to HPV 16 or 18 [¶]	8955	9	8968	38	76.3 (50.0, 89.9)
HPV 6-, 11-, 16-, 18-related CIN (CIN 1, CIN 2/3) or AIS	Prophylactic Efficacy*	8630	16	8680	309	94.8 (91.5, 97.1)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	2466	186 [¶]	2437	213 [¶]	-- [§]
	Girls and Women Regardless of Current or Prior Exposure to Vaccine HPV Types [¶]	8819	202	8854	522	61.5 (54.6, 67.4)
HPV 6-, 11-, 16-, or 18-related Genital Warts	Prophylactic Efficacy*	8761	10	8792	252	96.0 (92.6, 98.1)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	2501	51 [¶]	2475	55 [¶]	-- [§]
	Girls and Women Regardless of Current or Prior Exposure to Vaccine HPV Types [¶]	8955	61	8968	307	80.3 (73.9, 85.3)
HPV 6- or 11-related Genital Warts	Prophylactic Efficacy*	7769	9	7792	246	96.4 (93.0, 98.4)
	HPV 6 and/or HPV 11 Positive at Day 1 [†]	1186	51	1176	54	-- [§]
	Girls and Women Regardless of Current or Prior Exposure to Vaccine HPV Types [¶]	8955	60	8968	300	80.1 (73.7, 85.2)

*Includes all individuals who received at least 1 vaccination and who were HPV-naïve (i.e., seronegative and PCR negative) at Day 1 to the vaccine HPV type being analyzed. Case counting started at 1 month postdose 1.

[†]Includes all individuals who received at least 1 vaccination and who were HPV positive or had unknown HPV status at Day 1, to at least one vaccine HPV type. Case counting started at Day 1.

[‡]Out of the 148 AAHS control cases of 16/18 CIN 2/3, 2 women were missing serology or PCR results for Day 1.

[§]There is no expected efficacy since GARDASIL has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity.

[¶]Includes all individuals who received at least 1 vaccination (regardless of baseline HPV status at Day 1). Case counting started at 1 month postdose 1.

[¶]Includes 2 AAHS control women with missing serology/PCR data at Day 1.

[¶]Includes 1 woman with missing serology/PCR data at Day 1.

CI = Confidence Interval

N = Number of individuals who have at least one follow-up visit after Day 1

Note 1: The 16- and 18-related CIN 2/3 or AIS composite endpoint included data from studies 1, 2, 3, and 4. All other endpoints only included data from studies 2, 3, and 4.

Note 2: Positive status at Day 1 denotes PCR positive and/or seropositive for the respective type at Day 1.

Note 3: Table 14 does not include disease due to non-vaccine HPV types.

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Effectiveness of GARDASIL in Prevention of Any HPV Type Related Genital Disease in Girls and Women 16 Through 26 Years of Age, Regardless of Current or Prior Infection with Vaccine or Non-Vaccine HPV Types

The impact of GARDASIL against the overall burden of dysplastic or papillomatous cervical, vulvar, and vaginal disease regardless of HPV detection, results from a combination of prophylactic efficacy

against vaccine HPV types, disease contribution from vaccine HPV types present at time of vaccination, the disease contribution from HPV types not contained in the vaccine, and disease in which HPV was not detected.

Additional efficacy analyses were conducted in 2 populations: (1) a generally HPV-naïve population (negative to 14 common HPV types and had a Pap test that was negative for SIL [Squamous Intraepithelial Lesion] at Day 1), approximating a population of sexually-naïve girls and women and (2) the general study population of girls and women regardless of baseline HPV status, some of whom had HPV-related disease at Day 1.

Among generally HPV-naïve girls and women and among all girls and women in the study population (including girls and women with HPV infection at Day 1), GARDASIL reduced the overall incidence of CIN 2/3 or AIS; of VIN 2/3 or VaIN 2/3; of CIN (any grade) or AIS; and of Genital Warts (Table 15). These reductions were primarily due to reductions in lesions caused by HPV types 6, 11, 16, and 18 in girls and women naïve (seronegative and PCR negative) for the specific relevant vaccine HPV type. Infected girls and women may already have CIN 2/3 or AIS at Day 1 and some will develop CIN 2/3 or AIS during follow-up, either related to a vaccine or non-vaccine HPV type present at the time of vaccination or related to a non-vaccine HPV type not present at the time of vaccination.

Table 15: Effectiveness of GARDASIL in Prevention of Any HPV Type Related Genital Disease in Girls and Women 16 Through 26 Years of Age, Regardless of Current or Prior Infection with Vaccine or Non-Vaccine HPV Types

Endpoints Caused by Vaccine or Non-vaccine HPV Types	Analysis	GARDASIL		AAHS Control		% Reduction (95% CI)
		N	Cases	N	Cases	
CIN 2/3 or AIS	Prophylactic Efficacy*	4616	77	4680	136	42.7 (23.7, 57.3)
	Girls and Women Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	8559	421	8592	516	18.4 (7.0, 28.4)
VIN 2/3 and VaIN 2/3	Prophylactic Efficacy*	4688	7	4735	31	77.1 (47.1, 91.5)
	Girls and Women Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	8688	30	8701	61	50.7 (22.5, 69.3)
CIN (Any Grade) or AIS	Prophylactic Efficacy*	4616	272	4680	390	29.7 (17.7, 40.0)
	Girls and Women Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	8559	967	8592	1189	19.1 (11.9, 25.8)
Genital Warts	Prophylactic Efficacy*	4688	29	4735	169	82.8 (74.3, 88.8)
	Girls and Women Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	8688	132	8701	350	62.5 (54.0, 69.5)

*Includes all individuals who received at least 1 vaccination and who had a Pap test that was negative for SIL [Squamous Intraepithelial Lesion] at Day 1 and were naïve to 14 common HPV types at Day 1. Case counting started at 1 month postdose 1.

[†]Includes all individuals who received at least 1 vaccination (regardless of baseline HPV status or Pap test result at Day 1). Case counting started at 1 month postdose 1.

CI = Confidence Interval

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

14.5 Population Impact in Boys and Men 16 through 26 Years of Age

Effectiveness of GARDASIL in Prevention of HPV Types 6-, 11-, 16-, or 18-Related Anogenital Disease in Boys and Men 16 Through 26 Years of Age, Regardless of Current or Prior Exposure to Vaccine HPV Types

Study 5 included boys and men regardless of current or prior exposure to vaccine HPV types, and additional analyses were conducted to evaluate the impact of GARDASIL with respect to HPV 6-, 11-, 16-,

and 18-related anogenital disease in these boys and men. Here, analyses included events arising among boys and men regardless of baseline PCR status and serostatus, including HPV infections that were present at the start of vaccination as well as events that arose from infections that were acquired after the start of vaccination.

The impact of GARDASIL in boys and men regardless of current or prior exposure to a vaccine HPV type is shown in Table 16. Impact was measured starting at Day 1. Prophylactic efficacy denotes the vaccine's efficacy in boys and men who are naive (PCR negative and seronegative) to the relevant HPV types at Day 1. Vaccine impact in boys and men who were positive for vaccine HPV infection, as well as vaccine impact among boys and men regardless of baseline vaccine HPV PCR status and serostatus are also presented. The majority of anogenital disease related to a vaccine HPV type detected in the group that received GARDASIL occurred as a consequence of HPV infection with the relevant HPV type that was already present at Day 1.

There was no clear evidence of protection from disease caused by HPV types for which boys and men were PCR positive regardless of serostatus at baseline.

Table 16: Effectiveness of GARDASIL in Prevention of HPV Types 6-, 11-, 16-, or 18-Related Anogenital Disease in Boys and Men 16 Through 26 Years of Age, Regardless of Current or Prior Exposure to Vaccine HPV Types

Endpoint	Analysis	GARDASIL		AAHS Control		% Reduction (95% CI)
		N	Cases	N	Cases	
External Genital Lesions	Prophylactic Efficacy*	1775	13	1770	54	76.3 (56.0, 88.1)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	460	14	453	26	-- [‡]
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [§]	1943	27	1937	80	66.7 (48.0, 79.3)
Condyloma	Prophylactic Efficacy*	1775	10	1770	49	80.0 (59.9, 90.9)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	460	14	453	25	-- [‡]
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [§]	1943	24	1937	74	68.1 (48.8, 80.7)
PIN 1/2/3	Prophylactic Efficacy*	1775	4	1770	5	20.7 (-268.4, 84.3)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	460	2	453	1	-- [‡]
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [§]	1943	6	1937	6	0.3 (-272.8, 73.4)
AIN 1/2/3	Prophylactic Efficacy*	259	9	261	39	76.9 (51.4, 90.1)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	103	29	116	38	-- [‡]
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [§]	275	38	276	77	50.3 (25.7, 67.2)
AIN 2/3	Prophylactic Efficacy*	259	7	261	19	62.5 (6.9, 86.7)
	HPV 6, HPV 11, HPV 16, and/or HPV 18 Positive at Day 1 [†]	103	11	116	20	-- [‡]
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [§]	275	18	276	39	54.2 (18.0, 75.3)

*Includes all individuals who received at least 1 vaccination and who were HPV-naïve (i.e., seronegative and PCR negative) at Day 1 to the vaccine HPV type being analyzed. Case counting started at Day 1.

[†]Includes all individuals who received at least 1 vaccination and who were HPV positive or had unknown HPV status at Day 1, to at least one vaccine HPV type. Case counting started at Day 1.

[‡]There is no expected efficacy since GARDASIL has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity.

[§]Includes all individuals who received at least 1 vaccination. Case counting started at Day 1.

CI = Confidence Interval

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

Effectiveness of GARDASIL in Prevention of Any HPV Type Related Anogenital Disease in Boys and Men 16 Through 26 Years of Age, Regardless of Current or Prior Infection with Vaccine or Non-Vaccine HPV Types

The impact of GARDASIL against the overall burden of dysplastic or papillomatous anogenital disease regardless of HPV detection, results from a combination of prophylactic efficacy against vaccine HPV types, disease contribution from vaccine HPV types present at time of vaccination, the disease contribution from HPV types not contained in the vaccine, and disease in which HPV was not detected.

Additional efficacy analyses from Study 5 were conducted in 2 populations: (1) a generally HPV-naïve population that consisted of boys and men who are seronegative and PCR negative to HPV 6, 11, 16, and 18 and PCR negative to HPV 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 at Day 1, approximating a population of sexually-naïve boys and men and (2) the general study population of boys and men regardless of baseline HPV status, some of whom had HPV-related disease at Day 1.

Among generally HPV-naïve boys and men and among all boys and men in Study 5 (including boys and men with HPV infection at Day 1), GARDASIL reduced the overall incidence of anogenital disease (Table 17). These reductions were primarily due to reductions in lesions caused by HPV types 6, 11, 16, and 18 in boys and men naïve (seronegative and PCR negative) for the specific relevant vaccine HPV type. Infected boys and men may already have anogenital disease at Day 1 and some will develop anogenital disease during follow-up, either related to a vaccine or non-vaccine HPV type present at the time of vaccination or related to a non-vaccine HPV type not present at the time of vaccination.

Table 17: Effectiveness of GARDASIL in Prevention of Any HPV Type Related Anogenital Disease in Boys and Men 16 Through 26 Years of Age, Regardless of Current or Prior Infection with Vaccine or Non-Vaccine HPV Types

Endpoint	Analysis	GARDASIL		AAHS Control		% Reduction (95% CI)
		N	Cases	N	Cases	
External Genital Lesions	Prophylactic Efficacy*	1275	7	1270	37	81.5 (58.0, 93.0)
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	1943	38	1937	92	59.3 (40.0, 72.9)
Condyloma	Prophylactic Efficacy*	1275	5	1270	33	85.2 (61.8, 95.5)
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	1943	33	1937	85	61.8 (42.3, 75.3)
PIN 1/2/3	Prophylactic Efficacy*	1275	2	1270	4	50.7 (-244.3, 95.5)
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	1943	8	1937	7	-13.9 (-269.0, 63.9)
AIN 1/2/3	Prophylactic Efficacy*	129	12	126	28	54.9 (8.4, 79.1)
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	275	74	276	103	25.7 (-1.1, 45.6)
AIN 2/3	Prophylactic Efficacy*	129	8	126	18	52.5 (-14.8, 82.1)
	Boys and Men Regardless of Current or Prior Exposure to Vaccine or Non-Vaccine HPV Types [†]	275	44	276	59	24.3 (-13.8, 50.0)

*Includes all individuals who received at least 1 vaccination and who were seronegative and PCR negative at enrollment to HPV 6, 11, 16 and 18, and PCR negative at enrollment to HPV 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59. Case counting started at Day 1.

[†]Includes all individuals who received at least 1 vaccination. Case counting started at Day 1.

CI = Confidence Interval

AAHS Control = Amorphous Aluminum Hydroxyphosphate Sulfate

14.6 Overall Population Impact

The subject characteristics (e.g. lifetime sex partners, geographic distribution of the subjects) influence the HPV prevalence of the population and therefore the population benefit can vary widely.

The overall efficacy of GARDASIL will vary with the baseline prevalence of HPV infection and disease, the incidence of infections against which GARDASIL has shown protection, and those infections against which GARDASIL has not been shown to protect.

The efficacy of GARDASIL for HPV types not included in the vaccine (i.e., cross-protective efficacy) is a component of the overall impact of the vaccine on rates of disease caused by HPV. Cross-protective efficacy was not demonstrated against disease caused by non-vaccine HPV types in the combined database of the Study 3 and Study 4 trials.

GARDASIL does not protect against genital disease not related to HPV. One woman who received GARDASIL in Study 3 developed an external genital well-differentiated squamous cell carcinoma at Month 24. No HPV DNA was detected in the lesion or in any other samples taken throughout the study.

In 18,150 girls and women enrolled in Study 2, Study 3, and Study 4, GARDASIL reduced definitive cervical therapy procedures by 23.9% (95% CI: 15.2%, 31.7%).

14.7 Studies in Women 27 through 45 Years of Age

Study 6 evaluated efficacy in 3253 women 27 through 45 years of age based on a combined endpoint of HPV 6-, 11-, 16- or 18-related persistent infection, genital warts, vulvar and vaginal dysplastic lesions of any grade, CIN of any grade, AIS, and cervical cancer. These women were randomized 1:1 to receive either GARDASIL or AAHS control. The efficacy for the combined endpoint was driven primarily by prevention of persistent infection. There was no statistically significant efficacy demonstrated for CIN 2/3, AIS, or cervical cancer. In post hoc analyses conducted to assess the impact of GARDASIL on the individual components of the combined endpoint, the results in the population of women naïve to the relevant HPV type at baseline were as follows: prevention of HPV 6-, 11-, 16- or 18-related persistent infection (80.5% [95% CI: 68.3, 88.6]), prevention of HPV 6-, 11-, 16- or 18-related CIN (any grade) (85.8% [95% CI: 52.4, 97.3]), and prevention of HPV 6-, 11-, 16- or 18-related genital warts (87.6% [95% CI: 7.3, 99.7]).

Efficacy for disease endpoints was diminished in a population impact assessment of women who were vaccinated regardless of baseline HPV status (full analysis set). In the full analysis set (FAS), efficacy was not demonstrated for the following endpoints: prevention of HPV 16- and 18-related CIN 2/3, AIS, or cervical cancer and prevention of HPV 6- and 11-related condyloma. No efficacy was demonstrated against CIN 2/3, AIS, or cervical cancer in the general population irrespective of HPV type (FAS any type analysis).

14.8 Immunogenicity

Assays to Measure Immune Response

The minimum anti-HPV titer that confers protective efficacy has not been determined.

Because there were few disease cases in individuals naïve (PCR negative and seronegative) to vaccine HPV types at baseline in the group that received GARDASIL, it has not been possible to establish minimum anti-HPV 6, anti-HPV 11, anti-HPV 16, and anti-HPV 18 antibody levels that protect against clinical disease caused by HPV 6, 11, 16, and/or 18.

The immunogenicity of GARDASIL was assessed in 23,951 9- through 45-year-old girls and women (GARDASIL N = 12,634; AAHS control or saline placebo N = 11,317) and 5417 9- through 26-year-old boys and men (GARDASIL N = 3109; AAHS control or saline placebo N = 2308).

Type-specific immunoassays with type-specific standards were used to assess immunogenicity to each vaccine HPV type. These assays measured antibodies against neutralizing epitopes for each HPV type. The scales for these assays are unique to each HPV type; thus, comparisons across types and to other assays are not appropriate.

Immune Response to GARDASIL

The primary immunogenicity analyses were conducted in a per-protocol immunogenicity (PPI) population. This population consisted of individuals who were seronegative and PCR negative to the relevant HPV type(s) at enrollment, remained HPV PCR negative to the relevant HPV type(s) through 1 month postdose 3 (Month 7), received all 3 vaccinations, and did not deviate from the study protocol in ways that could interfere with the effects of the vaccine.

Immunogenicity was measured by (1) the percentage of individuals who were seropositive for antibodies against the relevant vaccine HPV type, and (2) the Geometric Mean Titer (GMT).

In clinical studies in 16- through 26-year-old girls and women, 99.8%, 99.8%, 99.8%, and 99.4% who received GARDASIL became anti-HPV 6, anti-HPV 11, anti-HPV 16, and anti-HPV 18 seropositive, respectively, by 1 month postdose 3 across all age groups tested.

In clinical studies in 27- through 45-year-old women, 98.2%, 97.9%, 98.6%, and 97.1% who received GARDASIL became anti-HPV 6, anti-HPV 11, anti-HPV 16, and anti-HPV 18 seropositive, respectively, by 1 month postdose 3 across all age groups tested.

In clinical studies in 16- through 26-year-old boys and men, 98.9%, 99.2%, 98.8%, and 97.4% who received GARDASIL became anti-HPV 6, anti-HPV 11, anti-HPV 16, and anti-HPV 18 seropositive, respectively, by 1 month postdose 3 across all age groups tested.

Across all populations, anti-HPV 6, anti-HPV 11, anti-HPV 16, and anti-HPV 18 GMTs peaked at Month 7 (Table 18 and Table 19). GMTs declined through Month 24 and then stabilized through Month 36 at levels above baseline. Tables 20 and 21 display the persistence of anti-HPV cLIA geometric mean titers by gender and age group. The duration of immunity following a complete schedule of immunization with GARDASIL has not been established.

Table 18: Summary of Month 7 Anti-HPV cLIA Geometric Mean Titers in the PPI* Population of Girls and Women

Population	N [†]	n [‡]	% Seropositive (95% CI)	GMT (95% CI) mMU [§] /mL
Anti-HPV 6				
9- through 15-year-old girls	1122	917	99.9 (99.4, 100.0)	929.2 (874.6, 987.3)
16- through 26-year-old girls and women	9859	3329	99.8 (99.6, 99.9)	545.0 (530.1, 560.4)
27- through 34-year-old women	667	439	98.4 (96.7, 99.4)	435.6 (393.4, 482.4)
35- through 45-year-old women	957	644	98.1 (96.8, 99.0)	397.3 (365.2, 432.2)
Anti-HPV 11				
9- through 15-year-old girls	1122	917	99.9 (99.4, 100.0)	1304.6 (1224.7, 1389.7)
16- through 26-year-old girls and women	9859	3353	99.8 (99.5, 99.9)	748.9 (726.0, 772.6)
27- through 34-year-old women	667	439	98.2 (96.4, 99.2)	577.9 (523.8, 637.5)
35- through 45-year-old women	957	644	97.7 (96.2, 98.7)	512.8 (472.9, 556.1)
Anti-HPV 16				
9- through 15-year-old girls	1122	915	99.9 (99.4, 100.0)	4918.5 (4556.6, 5309.1)
16- through 26-year-old girls and women	9859	3249	99.8 (99.6, 100.0)	2409.2 (2309.0, 2513.8)
27- through 34-year-old women	667	435	99.3 (98.0, 99.9)	2342.5 (2119.1, 2589.6)
35- through 45-year-old women	957	657	98.2 (96.8, 99.1)	2129.5 (1962.7, 2310.5)
Anti-HPV 18				
9- through 15-year-old girls	1122	922	99.8 (99.2, 100.0)	1042.6 (967.6, 1123.3)
16- through 26-year-old girls and women	9859	3566	99.4 (99.1, 99.7)	475.2 (458.8, 492.1)
27- through 34-year-old women	667	501	98.0 (96.4, 99.0)	385.8 (347.6, 428.1)
35- through 45-year-old women	957	722	96.4 (94.8, 97.6)	324.6 (297.6, 354.0)

*The PPI population consisted of individuals who received all 3 vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the Month 6 and Month 7 visit, and were naive (PCR negative and seronegative) to the relevant HPV type(s) (types 6, 11, 16, and 18) prior to dose 1 and through 1 month Postdose 3 (Month 7).

[†]Number of individuals randomized to the respective vaccination group who received at least 1 injection.

[‡]Number of individuals contributing to the analysis.

cLIA = Competitive Luminex Immunoassay

CI = Confidence Interval

GMT = Geometric Mean Titers

[§]mMU = milli-Merck Units

Table 19: Summary of Month 7 Anti-HPV cLIA Geometric Mean Titers in the PPI* Population of Boys and Men

Population	N [†]	n [‡]	% Seropositive (95% CI)	GMT (95% CI) mMU [§] /mL
Anti-HPV 6				
9- through 15-year-old boys	1072	884	99.9 (99.4, 100.0)	1037.5 (963.5, 1117.3)
16- through 26-year-old boys and men	2026	1093	98.9 (98.1, 99.4)	447.8 (418.9, 478.6)
Anti-HPV 11				
9- through 15-year-old boys	1072	885	99.9 (99.4, 100.0)	1386.8 (1298.5, 1481.0)
16- through 26-year-old boys and men	2026	1093	99.2 (98.4, 99.6)	624.3 (588.4, 662.3)
Anti-HPV 16				
9- through 15-year-old boys	1072	882	99.8 (99.2, 100.0)	6056.5 (5601.3, 6548.7)
16- through 26-year-old boys and men	2026	1136	98.8 (97.9, 99.3)	2403.3 (2243.4, 2574.6)
Anti-HPV 18				
9- through 15-year-old boys	1072	887	99.8 (99.2, 100)	1357.4 (1249.4, 1474.7)
16- through 26-year-old boys and men	2026	1175	97.4 (96.3, 98.2)	402.6 (374.6, 432.7)

*The PPI population consisted of individuals who received all 3 vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the Month 6 and Month 7 visit, and were naïve (PCR negative and seronegative) to the relevant HPV type(s) (types 6, 11, 16, and 18) prior to dose 1 and through 1 month Postdose 3 (Month 7).

[†]Number of individuals randomized to the respective vaccination group who received at least 1 injection.

[‡]Number of individuals contributing to the analysis.

cLIA = Competitive Luminex Immunoassay

CI = Confidence Interval

GMT = Geometric Mean Titers

[§]mMU = milli-Merck Units

Table 20: Persistence of Anti-HPV cLIA Geometric Mean Titers in 9- Through 45-Year-Old Girls and Women

Assay (cLIA)/ Time Point	9- to 15-Year-Old Girls (N* = 1122)		16- to 26-Year-Old Girls and Women (N* = 9859)		27- to 34-Year-Old Women (N* = 667)		35- to 45-Year-Old Women (N* = 957)	
	n [†]	GMT (95% CI) mMU [‡] /mL	n [†]	GMT (95% CI) mMU [‡] /mL	n [†]	GMT (95% CI) mMU [‡] /mL	n [†]	GMT (95% CI) mMU [‡] /mL
Anti-HPV 6								
Month 07	917	929.2 (874.6, 987.3)	3329	545.0 (530.1, 560.4)	439	435.6 (393.4, 482.4)	644	397.3 (365.2, 432.2)
Month 24	214	156.1 (135.6, 179.6)	2788	109.1 (105.2, 113.1)	421	70.7 (63.8, 78.5)	628	69.3 (63.7, 75.4)
Month 36 [§]	356	129.4 (115.6, 144.8)	-	-	399	79.5 (72.0, 87.7)	618	81.1 (75.0, 87.8)
Month 48 [¶]	-	-	2514	73.8 (70.9, 76.8)	391	58.8 (52.9, 65.3)	616	62.0 (57.0, 67.5)
Anti-HPV 11								
Month 07	917	1304.6 (1224.7, 1389.7)	3353	748.9 (726.0, 772.6)	439	577.9 (523.8, 637.5)	644	512.8 (472.9, 556.1)
Month 24	214	218.0 (188.3, 252.4)	2817	137.1 (132.1, 142.3)	421	79.3 (71.5, 87.8)	628	73.4 (67.4, 79.8)
Month 36 [§]	356	148.0 (131.1, 167.1)	-	-	399	81.8 (74.3, 90.1)	618	77.4 (71.6, 83.6)
Month 48 [¶]	-	-	2538	89.4 (85.9, 93.1)	391	67.4 (60.9, 74.7)	616	62.7 (57.8, 68.0)
Anti-HPV 16								
Month 07	915	4918.5 (4556.6, 5309.1)	3249	2409.2 (2309.0, 2513.8)	435	2342.5 (2119.1, 2589.6)	657	2129.5 (1962.7, 2310.5)
Month 24	211	944.2 (804.4, 1108.3)	2721	442.6 (425.0, 460.9)	416	285.9 (254.4, 321.2)	642	271.4 (247.1, 298.1)
Month 36 [§]	353	642.2 (562.8, 732.8)	-	-	399	291.5 (262.5, 323.8)	631	276.7 (254.5, 300.8)
Month 48 [¶]	-	-	2474	326.2 (311.8, 341.3)	394	211.8 (189.5, 236.8)	628	192.8 (176.5, 210.6)
Anti-HPV 18								
Month 07	922	1042.6 (967.6, 1123.3)	3566	475.2 (458.8, 492.1)	501	385.8 (347.6, 428.1)	722	324.6 (297.6, 354.0)
Month 24	214	137.7 (114.8, 165.1)	3002	50.8 (48.2, 53.5)	478	31.8 (28.1, 36.0)	705	26.0 (23.5, 28.8)
Month 36 [§]	357	87.0 (74.8, 101.2)	-	-	453	32.1 (28.5, 36.3)	689	27.0 (24.5, 29.8)
Month 48 [¶]	-	-	2710	33.2 (31.5, 35.0)	444	25.2 (22.3, 28.5)	688	21.2 (19.2, 23.4)

*N = Number of individuals randomized in the respective group who received at least 1 injection.

[†]n = Number of individuals in the indicated immunogenicity population.

[‡]mMU = milli-Merck Units

[§]Month 37 for 9- to 15-year-old girls. No serology samples were collected at this time point for 16- to 26-year-old girls and women.

[¶]Month 48/End-of-study visits for 16- to 26-year-old girls and women were generally scheduled earlier than Month 48. Mean visit timing was Month 44. The studies in 9- to 15-year-old girls were planned to end prior to 48 months and therefore no serology samples were collected.

cLIA = Competitive Luminex Immunoassay

CI = Confidence Interval

GMT = Geometric Mean Titers

Table 21: Persistence of Anti-HPV cLIA Geometric Mean Titers in 9- Through 26-Year-Old Boys and Men

Assay (cLIA)/ Time Point	9- to 15-Year-Old Boys (N* = 1072)		16- to 26-Year-Old Boys and Men (N* = 2026)	
	n†	GMT (95% CI) mMU‡/mL	n†	GMT (95% CI) mMU‡/mL
Anti-HPV 6				
Month 07	884	1037.5 (963.5, 1117.3)	1094	447.2 (418.4, 477.9)
Month 24	323	134.1 (119.5, 150.5)	907	80.3 (74.9, 86.0)
Month 36 [§]	342	126.6 (111.9, 143.2)	654	72.4 (68.0, 77.2)
Month 48 [¶]	-	-	-	-
Anti-HPV 11				
Month 07	885	1386.8 (1298.5, 1481.0)	1094	624.5 (588.6, 662.5)
Month 24	324	188.5 (168.4, 211.1)	907	94.6 (88.4, 101.2)
Month 36 [§]	342	148.8 (131.1, 169.0)	654	80.3 (75.7, 85.2)
Month 48 [¶]	-	-	-	-
Anti-HPV 16				
Month 07	882	6056.5 (5601.4, 6548.6)	1137	2401.5 (2241.8, 2572.6)
Month 24	322	938.2 (825.0, 1067.0)	938	347.7 (322.5, 374.9)
Month 36 [§]	341	708.8 (613.9, 818.3)	672	306.7 (287.5, 327.1)
Month 48 [¶]	-	-	-	-
Anti-HPV 18				
Month 07	887	1357.4 (1249.4, 1474.7)	1176	402.6 (374.6, 432.6)
Month 24	324	131.9 (112.1, 155.3)	967	38.7 (35.2, 42.5)
Month 36 [§]	343	113.0 (94.7, 135.0)	690	33.4 (30.9, 36.1)
Month 48 [¶]	-	-	-	-

*N = Number of individuals randomized in the respective group who received at least 1 injection.

†n = Number of individuals in the indicated immunogenicity population.

‡mMU = milli-Merck Units

§Month 36 time point for 16- to 26-year-old boys and men; Month 37 for 9- to 15-year-old boys.

¶The studies in 9- to 15-year-old boys and girls and 16- to 26-year-old boys and men were planned to end prior to 48 months and therefore no serology samples were collected.

cLIA = Competitive Luminex Immunoassay

CI = Confidence Interval

GMT = Geometric Mean Titers

Tables 18 and 19 display the Month 7 immunogenicity data for girls and women and boys and men. Anti-HPV responses 1 month postdose 3 among 9- through 15-year-old adolescent girls were non-inferior to anti-HPV responses in 16- through 26-year-old girls and women in the combined database of immunogenicity studies for GARDASIL. Anti-HPV responses 1 month postdose 3 among 9- through 15-year-old adolescent boys were non-inferior to anti-HPV responses in 16- through 26-year-old boys and men in Study 5.

On the basis of this immunogenicity bridging, the efficacy of GARDASIL in 9- through 15-year-old adolescent girls and boys is inferred.

GMT Response to Variation in Dosing Regimen in 18- Through 26-Year-Old Women

Girls and women evaluated in the PPE population of clinical studies received all 3 vaccinations within 1 year of enrollment. An analysis of immune response data suggests that flexibility of ± 1 month for Dose 2 (i.e., Month 1 to Month 3 in the vaccination regimen) and flexibility of ± 2 months for Dose 3 (i.e., Month 4 to Month 8 in the vaccination regimen) do not impact the immune responses to GARDASIL.

Duration of the Immune Response to GARDASIL

The duration of immunity following a complete schedule of immunization with GARDASIL has not been established. The peak anti-HPV GMTs for HPV types 6, 11, 16, and 18 occurred at Month 7. Anti-HPV GMTs for HPV types 6, 11, 16, and 18 were similar between measurements at Month 24 and Month 60 in Study 2.

14.9 Long-Term Follow-Up Studies

The protection of GARDASIL against HPV-related disease continues to be studied over time in populations including adolescents (boys and girls) and women who were enrolled in the Phase 3 studies.

Persistence of Effectiveness

An extension of Study 4 used national healthcare registries in Denmark, Iceland, Norway, and Sweden to monitor endpoint cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, cervical cancer, vulvar cancer, or vaginal cancer among 2,650 girls and women 16 through 23 years of age at enrollment who were randomized to vaccination with GARDASIL and consented to be followed in the extension study. An interim analysis of the per-protocol effectiveness population included 1,902 subjects who completed the GARDASIL vaccination series within one year, were naïve to the relevant HPV type through 1 month postdose 3, had no protocol violations, and had follow-up data available. The median follow-up from initial vaccination was 6.7 years with a range of 2.8 to 8.4 years. No cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, cervical cancer, vulvar cancer, or vaginal cancer were observed over a total of 5,765 person-years at risk.

An extension of a Phase 3 study (Study 7) in which 614 girls and 565 boys 9 through 15 years of age at enrollment were randomized to vaccination with GARDASIL actively followed subjects for endpoint cases of HPV 6-, 11-, 16-, or 18-related persistent infection, CIN (any grade), AIS, VIN, VaIN, cervical cancer, vulvar cancer, vaginal cancer, and genital lesions from the initiation of sexual activity or age 16 onwards. An interim analysis of the per-protocol effectiveness population included 246 girls and 168 boys who completed the GARDASIL vaccination series within one year, were seronegative to the relevant HPV type at initiation of the vaccination series, and had not initiated sexual activity prior to receiving the third dose of GARDASIL. The median follow-up, from the first dose of vaccine, was 7.2 years with a range of 0.5 to 8.5 years. No cases of persistent infection of at least 12 months' duration and no cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, VIN, VaIN, cervical cancer, vulvar cancer, vaginal cancer, or genital lesions were observed over a total 1,105 person-years at risk. There were 4 cases of HPV 6-, 11-, 16-, or 18-related persistent infection of at least 6 months' duration, including 3 cases related to HPV 16 and 1 case related to HPV 6, none of which persisted to 12 months' duration.

Persistence of the Immune Response

The interim reports of the two extension studies described above included analyses of type-specific anti-HPV antibody titers at 9 years postdose 1 for girls and women 16 through 23 years of age at enrollment (range of 1,178 to 1,331 subjects with evaluable data across HPV types) and at 8 years postdose 1 for boys and girls 9 through 15 years of age at enrollment (range of 436 to 440 subjects with evaluable data across HPV types). Anti-HPV 6, 11, 16, and 18 GMTs as measured by cLIA were decreased compared with corresponding values at earlier time points, but the proportions of seropositive subjects ranged from 88.4% to 94.4% for anti-HPV 6, from 89.1% to 95.5% for anti-HPV 11, from 96.8% to 99.1% for anti-HPV 16, and from 60.0% to 64.1% for anti-HPV 18.

14.10 Studies with RECOMBIVAX HB [hepatitis B vaccine (recombinant)]

The safety and immunogenicity of co-administration of GARDASIL with RECOMBIVAX HB [hepatitis B vaccine (recombinant)] (same visit, injections at separate sites) were evaluated in a randomized, double-blind, study of 1871 women aged 16 through 24 years at enrollment. The race distribution of the girls and women in the clinical trial was as follows: 61.6% White; 1.6% Hispanic (Black and White); 23.8% Other; 11.9% Black; 0.8% Asian; and 0.3% American Indian.

Subjects either received GARDASIL and RECOMBIVAX HB (n = 466), GARDASIL and RECOMBIVAX HB-matched placebo (n = 468), RECOMBIVAX HB and GARDASIL-matched placebo (n = 467) or RECOMBIVAX-matched placebo and GARDASIL-matched placebo (n = 470) at Day 1, Month 2 and Month 6. Immunogenicity was assessed for all vaccines 1 month post completion of the vaccination series.

Concomitant administration of GARDASIL with RECOMBIVAX HB [hepatitis B vaccine (recombinant)] did not interfere with the antibody response to any of the vaccine antigens when GARDASIL was given concomitantly with RECOMBIVAX HB or separately.

14.11 Studies with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)]

The safety and immunogenicity of co-administration of GARDASIL with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] (same visit, injections at separate sites) were evaluated in an open-labeled, randomized, controlled study of 1040 boys and girls 11 through 17 years of age at enrollment. The race distribution of the subjects in the clinical trial was as follows: 77.7% White; 6.8% Hispanic (Black and White); 1.4% Multi-racial; 12.3% Black; 1.2% Asian; 0.2% Indian; and 0.4% American Indian.

One group received GARDASIL in one limb and both Menactra and Adacel, as separate injections, in the opposite limb concomitantly on Day 1 (n = 517). The second group received the first dose of GARDASIL on Day 1 in one limb then Menactra and Adacel, as separate injections, at Month 1 in the opposite limb (n = 523). Subjects in both vaccination groups received the second dose of GARDASIL at Month 2 and the third dose at Month 6. Immunogenicity was assessed for all vaccines 1 month post completion of the vaccination series (1 dose for Menactra and Adacel and 3 doses for GARDASIL).

Concomitant administration of GARDASIL with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] did not interfere with the antibody response to any of the vaccine antigens when GARDASIL was given concomitantly with Menactra and Adacel or separately.

16 HOW SUPPLIED/STORAGE AND HANDLING

All presentations for GARDASIL contain a suspension of 120 mcg L1 protein from HPV types 6, 11, 16, and 18 in a 0.5-mL dose. GARDASIL is supplied in vials and syringes.

Carton of one 0.5-mL single-dose vial. **NDC 0006-4045-00.**

Carton of ten 0.5-mL single-dose vials. **NDC 0006-4045-41.**

Carton of six 0.5-mL single-dose prefilled Luer-Lok[®] syringes with tip caps. **NDC 0006-4109-09.**

Carton of ten 0.5-mL single-dose prefilled Luer-Lok[®] syringes with tip caps. **NDC 0006-4109-02.**

Store refrigerated at 2 to 8°C (36 to 46°F). Do not freeze. Protect from light.

GARDASIL should be administered as soon as possible after being removed from refrigeration.

GARDASIL can be out of refrigeration (at temperatures at or below 25°C/77°F), for a total time of not more than 72 hours.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Inform the patient, parent, or guardian:

- Vaccination does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Women who receive GARDASIL should continue to undergo cervical cancer screening per standard of care.
- Recipients of GARDASIL should not discontinue anal cancer screening if it has been recommended by a health care provider.
- GARDASIL has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a person has previously been exposed through sexual activity.
- Since syncope has been reported following vaccination sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended.
- Vaccine information is required to be given with each vaccination to the patient, parent, or guardian.
- Information regarding benefits and risks associated with vaccination.

- GARDASIL is not recommended for use in pregnant women.
 - Importance of completing the immunization series unless contraindicated.
 - Report any adverse reactions to their health care provider.
-

Manuf. and Dist. by: Merck Sharp & Dohme Corp., a subsidiary of
 **MERCK & CO., INC.**, Whitehouse Station, NJ 08889, USA

For patent information: www.merck.com/product/patent/home.html

The trademarks depicted herein are owned by their respective companies.

Copyright © 2006, 2009, 2010, 2011 Merck Sharp & Dohme Corp., a subsidiary of **Merck & Co., Inc.**
All rights reserved.

uspi-v501-i-1504r021

Printed in USA

THEME - ETHICAL AND LEGAL CHALLENGES OF VACCINES AND VACCINATION

Lessons learnt in Japan from adverse reactions to the HPV vaccine: a medical ethics perspective

HIROKUNI BEPPU, MASUMI MINAGUCHI, KIYOSHI UCHIDE, KUNIHIKO KUMAMOTO, MASATO SEKIGUCHI, YUKARI YAJU

Abstract

The human papillomavirus (HPV) vaccine has been linked to a number of serious adverse reactions. The range of symptoms is diverse and they develop in a multi-layered manner over an extended period of time. The argument for the safety and effectiveness of the HPV vaccine overlooks the following flaws: (i) no consideration is given to the genetic basis of autoimmune diseases, and arguments that do not take this into account cannot assure the safety of the vaccine; (ii) the immune evasion mechanisms of HPV, which require the HPV vaccine to maintain an extraordinarily high antibody level for a long period of time for it to be effective, are disregarded; and (iii) the limitations of effectiveness of the vaccine. We also discuss various issues that came up in the course of developing, promoting and distributing the vaccine, as well as the pitfalls encountered in monitoring adverse events and epidemiological verification.

Introduction

In this paper, we review the adverse reactions following human papilloma virus (HPV) vaccination in Japan, and the measures taken by the Ministry of Health, Labour and Welfare (MHLW) (1) to withdraw active recommendation of the vaccine. These measures triggered domestic and international controversy. We also discuss various problems that occurred while developing, promoting and distributing the vaccine; the pitfalls encountered in monitoring adverse events and epidemiological verification; and the influence of big pharma on healthcare policy and research.

I. Overview of the HPV vaccine issue in Japan

HPV vaccines were approved later in Japan than in the western countries (October 2009 for Cervarix, and July 2011 for Gardasil). The vaccination rate was initially low. However, after a campaign for the promotion of the vaccine, which led to government subsidisation of the cost of the vaccine in November 2010, the vaccination rate increased exponentially. This was followed by an unexpected increase in reports of adverse events (AEs). Importantly, these vaccines gave rise to a large number of serious AEs. Table 1 shows the number of reports of serious AEs/adverse drug reactions (ADRs), defined according to the ICH E2A guidelines (2), submitted with respect to HPV vaccines by vaccine manufacturers and medical professionals at the end of February 2016 (3). These numbers far exceed those for other vaccines, even if one allows for the probability that vigilance would be higher for a newly introduced vaccine than an older, time-tested one (4,5) (Fig. 1). As these data have been compiled from voluntary reports, the actual incidence of AEs may well be far higher (6,7).

Table 1
Reports of serious AEs/ADRs of HPV vaccines in Japan (3)

Vaccines	Total dose*	Total number of inoculated persons*	Serious AE/ADR reports	
			From MAH	From medical institutes
Cervarix	6,998,266	2,590,000	835	448
Gardasil	1,924,121	800,000	124	165

*Estimated from sales data

Note: AE: adverse event; ADR: adverse drug reaction; MAH: marketing authorisation holder

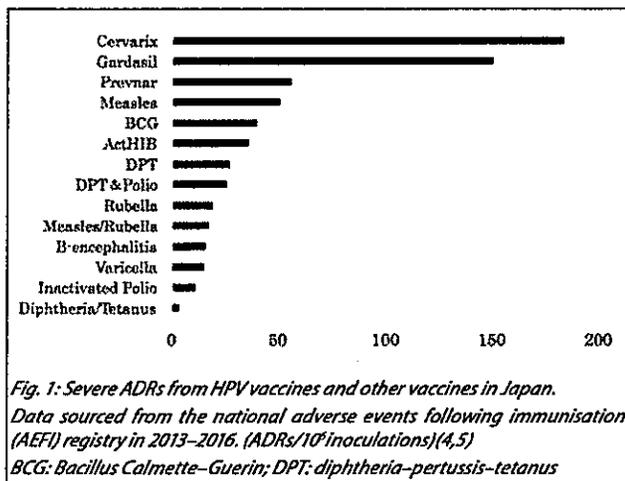
Observation period: December 2009–February 2016 (Cervarix), August 2011–February 2016 (Gardasil)

Authors: **Hirokuni Beppu** (corresponding author– hibep@nifty.com), Administrative Director of NPO DIPEX-Japan, Yokohama SOWA Clinic, Physician, Kanagawa, JAPAN; **Masumi Minaguchi** (minaguchi@san-tama.com) Attorney at law, Santama Law Firm, Secretary-General, Medwatcher Japan, Tokyo, JAPAN; **Kiyoshi Uchide** (uchide@komatsu-c.ac.jp), Special Professor, Health Information Management Stage, Komatsu College, Ishikawa, JAPAN; **Kunihiko Kumamoto** (kuma@edogawa-u.ac.jp), Professor, Department of Mass Communication, College of Media and Communication, Edogawa University, Chiba, JAPAN; **Masato Sekiguchi** (seki.kashinoki@nifty.com), Attorney at Law, Kashinoki Law Firm, Tokyo JAPAN; **Yukari Yaju** (y-yaju@slcn.ac.jp), Associate Professor, Nursing Statistics, Graduate School of Nursing Science, St. Luke's International University, Tokyo, JAPAN.

To cite: Beppu H, Minaguchi M, Uchide K, Kumamoto K, Sekiguchi M, Yaju Y. Lessons learnt in Japan from adverse reactions to the HPV vaccine: a medical ethics perspective. *Indian J Med Ethics*. 2017 Apr-Jun;2(2)NS:82-8.

©Indian Journal of Medical Ethics 2017

Other key features of the ADRs reported with HPV vaccines are the diversity of the symptoms and their development in a multi-layered manner over an extended period of time. The ADRs include complex, multi-system symptoms, such as seizures; disturbance of consciousness; systemic pain, including headache, myalgia, arthralgia, back pain and other pain; motor dysfunction, such as paralysis, muscular weakness, exhaustion and involuntary movements; numbness and sensory disturbances; autonomic symptoms, including dizziness, hypotension, tachycardia, nausea, vomiting and diarrhoea; respiratory dysfunction, including dyspnoea and



asthma; endocrine disorders, such as menstrual disorder and hypermenorrhoea; hypersensitivity to light and sound; psychological symptoms, such as anxiety, frustration, hallucinations and overeating; higher brain dysfunction and cognitive impairments, including memory impairment, disorientation and loss of concentration; and sleep disorders, including hypersomnia and sudden sleep attacks. In some cases, these symptoms impair learning and result in extreme fatigue and decreased motivation, having a negative impact on everyday life (8–11). The situation in Japan is similar to that in other countries which have also reported a specific cluster of serious and complex symptoms that develop across multiple body systems over an extended period of time (12,13).

The reason why HPV vaccines cause these characteristic adverse effects remains to be studied in the future, but one of the most plausible explanations is that these vaccines are designed to maintain an extremely high antibody titre over a long period of time. Since prolonged inflammatory reactions associated with infection are known to cause autoimmune diseases and worsening of autoimmune reactions (14), long-time antigen stimulation with HPV vaccines might also induce complex autoimmune reactions via a mechanism similar to that seen with prolonged infection.

Individuals who experienced ADRs following HPV vaccination established a voluntary liaison organisation to facilitate communication with others who also experienced ADRs in Japan. When these ADRs were reported in the mass media, HPV vaccination became a major social issue. In response to the negative press surrounding HPV vaccination, the MHLW withdrew its active recommendation in June 2013 on the grounds of “an undeniable causal relationship between persistent pain and the vaccination”(1). As a result, the inoculation rate for the vaccine decreased rapidly [from 80% at its peak to less than 1% at present (15)]. In response to this change, proponents of the HPV vaccine initiated a push-back campaign and began actively lobbying the government.

On January 20, 2014, the expert advisory committee established by the MHLW (16) presented the view that the

diverse pain and motor dysfunctions experienced by many individuals after HPV vaccination comprised psychosomatic reactions to anxiety or stimulatory pain caused by needle injection, and were not due to any components of the vaccine itself. However, doctors and researchers who examined patients with post-vaccination symptoms arrived at a completely different conclusion, highlighting both the characteristic symptoms and course, which are difficult to explain as psychosomatic reactions (9–11).

Thus, the safety of the HPV vaccine remains far from certain in Japan, justifying the public's strong distrust. Recognising the potentially negative influence of these events on public opinion in other countries, pharmaceutical companies initiated a counter-intervention strategy through public and private organisations, such as the World Health Organisation (WHO). The Global Advisory Committee on Vaccine Safety (GACVS), one of the WHO's advisory committees, claimed it had “not found any safety issue that would alter its recommendations for the use of the vaccine” and criticised the MHLW's decision to withdraw active recommendation (17).

Despite these obstacles, in July 2016, a victims' group filed a multi-plaintiff lawsuit in the district courts of Tokyo, Nagoya, Osaka and Fukuoka against the Japanese government and the two pharmaceutical companies that had produced these vaccines. Furthermore, in December of the same year, additional victims joined the multi-plaintiff lawsuit, bringing the total number of plaintiffs to 119 (18).

So far, we have reviewed the adverse reactions to HPV vaccines and the measures taken by the MHLW in Japan that provoked controversy both in Japan and abroad. In the next section, we discuss the safety and efficacy of the HPV vaccines promoted by the WHO and other organisations, and identify a flaw in the basis of their arguments in favour of the vaccines.

II. The problem with the HPV vaccine: refuting the GACVS statement (19)

a. Safety issues

Investigation by the MHLW

Regarding Japan, the GACVS statement (17) says that “review of clinical data by the national expert committee led to a conclusion that symptoms were not related to the vaccine”. However, there are major problems with the expert committee's investigation (16).

The most serious problem is that very few members of the committee actually examined patients with post-vaccination symptoms. The committee's investigation focused exclusively on pain and motor dysfunction, and ignored many other diverse symptoms that have been observed. Further, cases in which adverse events occurred more than a month after vaccination were excluded from consideration on the ground that most adverse effects of vaccines occur within one month of vaccination. However, subsequent studies have clarified that symptoms commonly appear even after a considerable period of time has elapsed since vaccination (9–11).

The methods used for determining psychosomatic reactions to be the cause of symptoms are also open to question (16). The expert advisory committee proposed four hypotheses regarding the pathophysiology of post-vaccination symptoms: (i) neurological disorder, (ii) intoxication, (iii) immunological reaction, and (iv) psychosomatic reaction. Those cases which do not conform to the committee's criteria for (i)–(iii) were regarded as having no causal relationship with the HPV vaccine. However, since the definition of the psychosomatic response is ambiguous and the diagnosis is exclusively made by the subjective judgement of the doctor, many cases are diagnosed as psychosomatic reactions.

Support for the expert advisory committee's conclusion is far from universal. Doctors and researchers who actually examined patients with post-vaccination symptoms pointed out that it is difficult to explain all symptoms as psychosomatic reactions on the basis of the results of experiments and case reports (8–11, 20–22). Prior to investigating HPV vaccine-associated neuro-immunopathy (HANS), a new disease concept proposed by Nishioka (22), Yokota et al excluded from their survey all individuals who exhibited any physical/psychological abnormality before the vaccination (9). Thus, the survey design further strengthened the conclusion that the psychosomatic response could not account for the majority of the AEs of the HPV vaccine, as claimed by the committee.

Further, as 11 of the 15 members of the expert advisory committee have conflicts of interest with vaccine manufacturers, the public is justified in requesting that a more diverse range of scientists reviews the relevant data (23). Thus, the safety of the HPV vaccine remains far from certain in Japan, justifying the public's strong concerns. Outside Japan, Jefferson et al (24) and Gøtzsche et al (25) also expressed concern about the nature and quality of regulation of the HPV vaccine by the European Medicine Agency.

Criticism of the evidence for safety mentioned in the GACVS statement

Regarding the safety of the HPV vaccine, the GACVS claimed in its statement that it had not found any safety issues warranting an alteration in its recommendations for the use of the vaccine, and criticised Japan for stopping the active promotion of HPV vaccination (17). However, the studies (26–31) cited by the GACVS as evidence for the vaccine's safety raise the following fundamental questions.

i) Genetic basis of autoimmunity

Among the pathophysiological mechanisms related to adverse reactions after vaccination, the involvement of autoimmunity is one of the most probable. The various mechanisms suggested with regard to autoimmune diseases include: molecular mimicry (32), in which a foreign antigen shares structural similarities with self-antigen; the disruption of essential mechanisms in central and peripheral immune tolerance (33); and human endogenous retroviruses genes producing functional proteins or developing antibodies against the individual's own proteins (34).

Although the aetiology has not been fully elucidated, most autoimmune diseases are complex polygenic conditions, in which the affected individual inherits multiple genetic polymorphisms that contribute to disease susceptibility, and these genes interact with environmental factors to cause the disease. It is a well-known fact that some human leucocyte antigen alleles occur at a higher frequency in patients with certain autoimmune diseases than in the general population (35).

At present, what is claimed to be the primary evidence for the safety of the HPV vaccine is that there is no statistically significant difference in the incidence of autoimmune diseases among vaccinated females and unvaccinated females or the general population. However, since the proportion of genetically susceptible people in the general population is very small and limited, simple comparisons of the incidence of autoimmune diseases between those who have been vaccinated and a control (unvaccinated) group are likely to show no significant difference. Arguments that do not take this into account cannot assure the safety of the vaccine. The baseline prevalence of many autoimmune diseases is relatively low. Thus, careful large-scale post-marketing surveillance that takes into account the immunological characteristics of individual patients is required to scientifically verify the relationship between vaccination and autoimmune diseases (36).

ii) Coding and the loss of important information

In drug regulatory agencies and the pharmaceutical industry, all AEs in a patient's medical record are coded for computer processing and thus, details contained in the raw data are "lost". As a result, the clinical significance and extent of drug risk are masked (37,38). This process results in a kind of circular reasoning, in which post-vaccination symptoms are isolated and analysed retrospectively within the framework of the existing disease concepts, instead of being viewed comprehensively.

iii) Paradigm shift

HPV is equipped with various immune evasion mechanisms, which could cause the immune system to become more tolerant to the infection, creating a microenvironment susceptible to further infection and facilitating the progression of cervical intraepithelial neoplasia (CIN). To counteract these immune evasion mechanisms, the HPV vaccine is designed to maintain an extraordinarily high level of antibodies for more than a decade (39, 40). This moves the HPV vaccine out of the paradigm of "vaccine" as it is conventionally understood. These unique characteristics of the HPV vaccine make it essential to conduct a more thorough evaluation of its safety.

b. Effectiveness

While the GACVS statement claims that "the impact of HPV vaccines on HPV-related clinical outcomes, including pre-cancerous lesions, is well established", in actuality, the effectiveness of the HPV vaccine is quite limited, as discussed below.

First, the only verified effect of the HPV vaccine is a preventive effect on pre-cancerous lesions (specifically CIN); the preventive effect on cervical cancer itself has not been established. The effects of the vaccines currently approved in Japan (Cervarix and Gardasil) on pre-cancerous lesions have been demonstrated only in the cases of HPV 16 and 18, which, according to the most reliable studies, represent only 50% of cervical cancer cases in Japan (41).

Further, 10% or fewer cases of high-risk HPV infection result in persistent infection that can cause cancer, while the large majority of any pre-cancerous lesions (CIN) that do develop resolve before becoming cancerous (42, 43). Therefore, only 0.15% of individuals infected with high-risk HPV develop (invasive) cancer (44, 45). Even if cancer develops, regular check-ups can help to detect it at an early stage and appropriate treatment (surgery, radiation and drug therapy) saves many lives. On the basis of these facts, the promotion of educational activity that emphasises the importance of screening and early detection, as well as the creation of an environment in which women feel more comfortable undergoing Pap testing, would be far more effective at preventing cervical cancer than would pressuring teenage girls to receive the existing HPV vaccination, with all its problems.

The proponents of the HPV vaccines claim that they are 98%–100% effective in preventing cervical cancer. In reality, however, the absolute risk reduction (ARR) provided by HPV vaccines is, at most, 0.1%–0.7%, on the basis of calculations using the existing data (46). Further, this indicates only the reduction in the risk of developing pre-cancerous lesions, while the risk of developing cervical cancer remains unknown.

The promotion of screening for cervical cancer is another important measure against cervical cancer. For a long time now, attention has been drawn to the low screening rate for cervical cancer in Japan compared to the western countries. In particular, young women with no experience of pregnancy are reluctant to undergo gynaecological examinations in Japan. Access to examinations by female doctors and an acceptance of self-sampling would undoubtedly increase the screening rates. In fact, the promotion of screening for cervical cancer significantly reduced the age-adjusted incidence of invasive cervical cancer in the UK (47).

III. Structural flaws: an ethics viewpoint

In the previous sections, we discussed various issues regarding the safety and effectiveness of the HPV vaccine. It is now appropriate to ask how such questionable vaccines have come into widespread use. The answer, at least with respect to Japan, can be found in a structural flaw, combined specifically with the following factors: (i) aggressive promotion by the pharmaceutical industry, (ii) trade negotiations by economic superpowers, and (iii) contemporary medicine, which is characterised by overconfidence in technology and a lack of humility with respect to listening to patients' complaints.

a. Immunisation Act and HPV vaccine promotion by manufacturers

Following the enactment of the Immunisation Act in Japan in 1948, numerous lawsuits were filed in response to vaccine-related injuries. This resulted in the establishment of a compensation system for victims and the amendment of the relevant laws and regulations. At present, vaccines are divided into three categories, as shown in Table 2(48).

According to the definitions in the Act, a vaccine for individual protection, such as the HPV vaccine, should be classified as an "optional" vaccination, which is solely the individual's choice. However, due to lobbying activities, the HPV vaccine was approved as a vaccine to be administered at public expense, and was included in the category "Routine vaccination A". Since it was recommended by the government, individuals felt obligated to receive the HPV vaccine.

The Japanese Expert Board for the Eradication of Cervical Cancer (49), one of the most powerful lobbying organisations in Japan, was founded in November 2008, around the time the HPV vaccine was being reviewed for approval. The executive members of various medical academic societies joined this group and exerted considerable influence on the legislative process, as well as on public administration and the shaping of public opinion.

Category	Responsibility of individual	Vaccination
Routine vaccination A	Duty to make effort to receive vaccination	Hib, pneumococcal, BCG, diphtheria, pertussis, tetanus, polio, measles, rubella, varicella, HPV, HB, Japanese Encephalitis
Routine vaccination B	No particular social duty	Influenza (for elderly), pneumococcal
Optional vaccination	Discretion of individual	Pneumococcal (for adults), rotavirus, etc.

According to information obtained by Medwatcher Japan(50) under the *Transparency Guideline for the Relation between Corporate Activities and Medical Institutions* (51) of the Japan Pharmaceutical Manufacturers Association, the funds received by the Expert Board from vaccine manufacturers amounted to ¥73,500,000 (¥35,000,000 in 2012 and ¥38,500,000 in 2013). In addition, the secretary of the Expert Board was found to have been working at GlaxoSmithKline Co. as the Director of Marketing for vaccines for up to eight months prior to the launch of Cervarix. These facts strongly suggest that the activity of the Expert Board was not altruistic, but was actually disguised promotion(52).

b. Pressure from outside Japan

The promotion of the HPV vaccine during Japan–US trade negotiations has also created pressure on Japan to adopt the vaccine. For many years, the promotion of vaccination has been

one of the most pressing requirements in trade negotiations with the US, Japan's most important trading partner (53, 54). The Center for Strategic and International Studies, a civilian think tank that is part of the US military-industrial complex, criticised the indecisiveness of Japan's government in reports issued in May 2014 and April 2015, reflecting the irritation of US industries (55,56).

c. Medical professionals forgetting their role

Basic defects inherent in the medical community underlie the issue of the HPV vaccine. In 2004, Sheldon Krinsky pointed out the increasing influence of commercialism in academic science and biomedical research in his book, *Science in the private interest* (57). He wrote, "...the mix of science and commerce continues to erode the ethical standards of research and diminish public confidence in its results. "In the 13 years since the publication of the book, his warning has become a reality everywhere in the world, not only in the USA. Originally, public health and pharmaco-epidemiology were the scientific fields that aimed to protect the health of individual patients and the public. However, the current reality is very far from the ideal.

Science is now misused to protect the interests of the pharmaceutical industry, and has been used to deny the causal relationship between the drug and its adverse reactions. Many researchers and experts are attempting to exclude inconvenient truths from consideration. "The taxonomy of diseases represents the nearest science has got to nature, but it remains a theoretical construct. It is the theory that should be discounted when the patient's symptoms refuse to fit, not the patient's account of the reality of their experience."(58, 59) This means that doctors must be more humble and scientifically honest. Today's diagnostics and therapeutics were created by listening to patients' voices and conducting careful examinations. It is irresponsible to dismiss a patient's complaint as a psychogenic reaction or a general phenomenon among young women without conducting a thorough examination.

IV. Considerations for solving problems

As described in section III, the introduction of HPV vaccination in Japan was promoted with an emphasis on commercial interests rather than as a public health need. This situation is not unique to Japan and has also been observed in other countries. In Australia, for example, despite the considerable doubts of the Pharmaceutical Benefits Advisory Committee about the Gardasil vaccine, the committee's decision to reject the addition of Gardasil to the national vaccination schedule was hurriedly overturned, following political interference and lobbying by other vested interests (60). In the USA, Merck & Co, Inc promoted legislation to mandate HPV vaccination for school attendance by serving as an information resource, lobbying legislators, drafting legislation, mobilising female legislators and physicians' organisations, conducting consumer marketing campaigns, and filling gaps in access to the vaccine. Legislators relied heavily on Merck for scientific information (61). The responsibility to prove the efficacy and safety of a vaccine lies with the pharmaceutical companies, and the

government is expected to monitor and guide these efforts. The current situation in which commercial interests drive government policy must be corrected from a medical ethics perspective.

At present, Japan is one of the few countries in which the active recommendation of HPV vaccination has been temporarily stopped; the regulatory authorities in other countries have not changed their policies. Although various groups of victims of vaccination have collaborated on wide-ranging activities in these countries, the regulatory authorities have not yet admitted the causal relationship between the vaccines and the victims' health injuries.

The Japanese government's decision to stop actively recommending HPV vaccination has, to an extent, encouraged regulators and patients in other countries to question the value of HPV vaccination. Japan's efforts to stop active recommendation might have been successful because of its historical background of cases of environmental pollution and drug-induced suffering (Minamata disease, thalidomide, SMON, dura mater graft-associated Creutzfeldt-Jakob disease, HIV transmitted by contaminated blood products, etc), which occurred during the post-war period of rapid economic growth. In the multi-plaintiff suits that followed the instances of environmental pollution and drug-induced suffering, the plaintiff groups sought not only compensation for damages, but also institutional reform and revisions to the law to prevent the repetition of the same mistakes (62).

This historical background has created a situation in which the mass media and regulators cannot easily ignore the victims' complaints about the side-effects of new vaccines. It is here that we may find a clue on how to solve this problem. It is necessary to enhance transparency at every step of the approval process for pharmaceutical products, from new-drug development to post-marketing surveillance. At the same time, it is crucial to strengthen the management of conflicts of interest, and develop a system by which citizens can participate directly and have a voice in the planning of public health policy(63-65).

Conflict of interest

All the authors are members of Medwatcher Japan. Masumi Minaguchi and Masato Sekiguchi are Lawyers for the plaintiffs in the HPV vaccination lawsuits.

References

1. Notification from MHLW on routine vaccination programme of HPV vaccine 2013.6.14 [Japanese][cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/stf/shingi2/0000091963.html>
2. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite guideline Clinical Safety Data Management: Definitions and Standards for Expedited Reporting E2A [cited 2017 Mar 25]. Available from: <https://www.imim.es/media/upload/arxius/MEDIA436.pdf>
3. Documents 16&17 distributed at the meeting of Council of Health Sciences, subcommittee of vaccination, ADR Working group meeting, May 23, 2016 [Japanese][cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/stf/shingi2/0000125164.html>
4. Documents distributed at the meeting of Council of Health Sciences, subcommittee of vaccination, ADR Working group meeting, April 12,

- 2016 [Japanese][cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/stf/shingi2/0000121045.html>
5. Documents distributed at the meeting of Council of Health Sciences, subcommittee of vaccination, ADR Working group meeting, May 23, 2016 [Japanese][cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/stf/shingi2/0000125164.html>
 6. Lawrence G, Gold MS, Hill R, Deeks S, Glasswell A, McIntyre PB. Annual report: Surveillance of adverse events following immunisation in Australia, 2007. *Commun Dis Intell Q Rep*. 2008 Dec;32(4):371–87.
 7. National Vaccine Information Center. An Analysis by the National Vaccine Information Center of Gardasil & Menactra Adverse Event Reports to the Vaccine Adverse Events Reporting System (VAERS), February 2009 [cited 2017 Mar 25]. Available from: <http://www.cbsnews.com/htdocs/NVICGardasilvsMenactraVAERSReportFeb2009.pdf>
 8. Kinoshita T, Abe RT, Hineno A, Tsunekawa K, Nakane S, Ikeda S. Peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine. *Intern Med*. 2014;53(19):2185–200.
 9. Yokota S, Kuroiwa Y, Nakamura I, Nakajima T, Nishioka K. General overview and discussion on HPV vaccine associated neuropathic syndrome. *Japan Medical Journal (Nihon Iji Shimpou)* 2015;4758:46–53 [Japanese].
 10. Hirai T, Kuroiwa Y, Hayashi T, Uchiyama M, Nakamura I, Yokota S, Nakajima T, Nishioka K, Iguchi Y. Adverse effects of human papilloma virus vaccination on central nervous system. *The Autonomic Nervous System*. 2016;53:49–64.
 11. Ikeda S. Neurological complications in HPV vaccination. *Brain and Nerve* 2015;67(7):835–43 [Japanese].
 12. Tomljenovic L, Shaw CA. Human papillomavirus (HPV) vaccine policy and evidence-based medicine: are they at odds? *Ann Med*. 2013 Mar;45(2):182–93. doi: 10.3109/07853890.2011.645353.
 13. Brinlh L, Theibel AC, Pors K, Mehlsen J. Suspected side effects to the quadrivalent human papilloma vaccine. *Dan Med J*. 2015;62(4):A5064.
 14. Sfriso P, Ghirardello A, Botsios C, Tonon M, Zen M, Bassi N, Bassetto F, Doria A. Infections and autoimmunity: the multifaceted relationship. *J Leukoc Biol*. 2010 Mar;87(3):385–95. doi: 10.1189/jlb.0709517. Epub 2009 Dec 16.
 15. Immunization coverage rates in Japan [cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/topics/bcg/other/5.html>
 16. Conference Minutes of Council of Health Sciences, subcommittee of vaccination, ADR Working group meeting, January 20, 2014 [Japanese] [cited 2017 Mar 25]. Available from: <http://www.mhlw.go.jp/stf/shingi2/0000091998.html>
 17. Global advisory committee on vaccine safety: statement on safety of HPV-vaccines, December 17, 2015 [cited 2017 Mar 25]. Available from: http://www.who.int/vaccine_safety/committee/GACVS_HPV_statement_17Dec2015.pdf?ua=1
 18. Plaintiffs Lawyers of HPV Vaccines Lawsuits [cited 2017 Mar 25]. Available from: <https://www.hpv-yakugai.net/>
 19. Medwatcher Japan. Submission of Refutation of GACVS (Global Advisory Committee on Vaccine Safety) statement on Safety of HPV vaccine on December 17, 2015; November 2016 [cited 2017 Mar 25]. Available from: <http://www.yakugai.gr.jp/en/topics/topic.php?id=930>
 20. Takahata K, Takashima H. A proposal for a new neurological examination for discrimination of autoimmune encephalopathy and somatoform disorders. *Neurological Therapeutics*. 2016;33(1):9–18 [Japanese].
 21. Aratani S, Fujita H, Kuroiwa Y, Usui C, Yokota S, Nakamura I, Nishioka K, Nakajima T. Murine hypothalamic destruction with vascular cell apoptosis subsequent to combined administration of human papilloma virus vaccine and pertussis toxin. *Sci Rep*. 2016 Nov 11;6:36943. doi: 10.1038/srep36943.
 22. Nishioka K, Yokota S, Matsumoto Y. Clinical features and preliminary diagnostic criteria of human papillomavirus vaccination associated with neuroimmunopathic syndrome (HANS). *Int J Rheum Dis* 2014;17(suppl 2):6–29.
 23. Medwatcher Japan: Submission of a "Request to reconsider the rules on conflict of interest (COI) for Ministry of Health, Labour and Welfare councils – In light of the COI issues with council members regarding HPV vaccines", April 2014 [cited 2017 Mar 25]. Available from: <http://www.yakugai.gr.jp/en/topics/topic.php?id=863>
 24. Jefferson T, Jørgensen L. Human papillomavirus vaccines, complex regional pain syndrome, postural orthostatic tachycardia syndrome, and autonomic dysfunction – a review of the regulatory evidence from the European Medicines Agency. *Indian J Med Ethics* 2017;2(1):30–37.
 25. Gøtzsche PC, Jørgensen KJ, MD, Jefferson T, Auken M, Brinlh L. Complaint to the European ombudsman over maladministration at the European Medicines Agency (EMA) in relation to the safety of the HPV vaccines, October 10, 2016, [cited 2017 Mar 25]. Available from: <http://nordic.cochrane.org/sites/nordic.cochrane.org/files/public/uploads/ResearchHighlights/Complaint-to-ombudsman-over-EMA.pdf>
 26. Agence nationale de sécurité du médicament et des produits de santé. Vaccins anti-HPV et risque de maladies autoimmunes: étude pharmacoépidémiologique [French]. [cited 2017 Mar 25]. Available from: http://ansm.sante.fr/content/download/80841/1023043/version/1/file/Ansm_gardasil-Hpv2_Rapport_Septembre-2015.pdf
 27. Rasmussen TA, Jørgensen MR, Bjerrum S, Jensen-Fangel S, Støvring H, Østergaard L, Søgaard OS. Use of population based background rates of disease to assess vaccine safety in childhood and mass immunisation in Denmark: nationwide population based cohort study. *BMJ*. 2012 Sep 17;345:e5823. doi: 10.1136/bmj.e5823.
 28. Arnheim-Dahlström L, Pasternak B, Svanström H, Sparén P, Hviid A. Autoimmune, neurological, and venous thromboembolic adverse events after immunization of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*. 2013 Oct 9;347:f5906. doi: 10.1136/bmj.f5906.
 29. Callréus T, Svanström H, Nielsen NM, Poulsen S, Valentiner-Branth P, Hviid A. Human papillomavirus immunization of adolescent girls and anticipated reporting of immune-mediated adverse events. *Vaccine*. 2009 May 14;27(22):2954–8. doi: 10.1016/j.vaccine.2009.02.106. Epub 2009 Mar 13.
 30. Descamps D, Hardt K, Spiessens B, Izurieta P, Verstraeten T, Breuer T, Dubin G. Safety of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine for cervical cancer prevention: a pooled analysis of 11 clinical trials. *Hum Vaccin*. 2009;5(5):332–40.
 31. Chao C, Klein NP, Velicer CM, Sy LS, Slezak JM, Takhar H, Ackerson B, Cheetham TC, Hansen J, Deosaransingh K, Emery M, Liaw KL, Jacobsen SJ. Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. *J Intern Med*. 2012;271(2):193–203. doi: 10.1111/j.1365-2796.2011.02467.x. Epub 2011 Nov 15.
 32. Cusick MF, Libbey JE, Fujinam RS. Molecular Mimicry as a Mechanism of Autoimmune Disease. *Clin Rev Allergy Immunol*. 2012;42(1):102–11.
 33. Marson A, Housley WJ, Hafler DA. Genetic basis of autoimmunity. *J Clin Invest*. 2015;125(6):2234–41.
 34. Volkman HE, Stetson DB. The enemy within: endogenous retroelements and autoimmune disease. *Nat Immunol*. 2014;15(5):415–22.
 35. Abbas AK, Lichtman AH, Pillai S. Immunologic tolerance and autoimmunity. In: Abbas AK, Lichtman AH, Pillai S (eds). *Cellular and Molecular Immunology*, 8th ed. Philadelphia: Elsevier Saunders; 2015, pp.315–337.
 36. Castiblanco J, Anaya JM. Genetics and vaccines in the era of personalized medicine. *Curr Genomics*. 2015 Feb;16(1):47–59. doi: 10.2174/1389202916666141223220551.
 37. Healy D. Doctoring the data. In: *Pharmageddon*. Berkeley and Los Angeles: Univ. of California Press; 2012, pp.96–128.
 38. Herxheimer A. Pharmacovigilance still neglects patients. *The Informed Prescriber*. 2014;29(5):75–9 [Japanese].
 39. Einstein MH, Takacs P, Chatterjee A, Sperling RS, Chakhtoura N, Blatter MM, Lalezari J, David MP, Lin L, Struyf F, Dubin G; HPV-010 Study Group. Comparison of long-term immunogenicity and safety of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine and HPV-6/11/16/18 vaccine in healthy women aged 18–45 years: end-of-study analysis of a Phase III randomized trial. *Hum Vaccin Immunother*. 2014;10(12):3435–45. doi: 10.4161/hv.36121.
 40. Naud PS, Roteli-Martins CM, De Carvalho NS, Teixeira JC, de Borja PC, Sanchez N, Zahaf T, Catteau G, Geeraerts B, Descamps D. Sustained efficacy, immunogenicity, and safety of the HPV-16/18 AS04-adjuvanted vaccine: final analysis of a long-term follow-up study up to 9.4 years post-vaccination. *Hum Vaccin Immunother*. 2014;10(8):2147–62. doi: 10.4161/hv.29532.
 41. Asato T, Maehama T, Nagai Y, Kanazawa K, Uezato H, Kariya K. A large case-control study of cervical cancer risk associated with human

- papillomavirus infection in Japan, by nucleotide sequencing-based genotyping. *J Infect Dis*. 2004 May 15;189(10):1829–32. Epub 2004 Apr 26.
42. Ho GY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med*. 1998 Feb 12;338(7):423–8.
 43. Woodman CB, Collins S, Winter H, Bailey A, Ellis J, Prior P, Yates M, Rollason TP, Young LS. Natural history of cervical human papillomavirus infection in young women: a longitudinal cohort study. *Lancet*. 2001;357(9271):1831–6.
 44. Kawana K, Yasugi T. Human papillomavirus and neoplastic disorder. *Antibiotics & Chemotherapy*. 2006;22(10):1521–8 [in Japanese].
 45. Department of vaccines and other biologicals. The current status of development of prophylactic vaccines against human papillomavirus infection. Report of a technical meeting, Geneva, February 16–18, 1999.
 46. Paavonen J, Naud P, Salmerón J, Wheeler CM, Chow SN, Apter D, Kitchener H, Castellsague X, Teixeira JC, Skinner SR, Hedrick J, Jaisamram U, Limson G, Garland S, Szarewski A, Romanowski B, Aoki FY, Schwarz TF, Poppe WA, Bosch FX, Jenkins D, Hardt K, Zahaf T, Descamps D, Struyf F, Lehtinen M, Dubin G; HPV PATRICIA Study Group. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet*. 2009;374(9686):301–14. doi: 10.1016/S0140-6736(09)61248-4. Epub 2009 Jul 6.
 47. Quinn M, Babb P, Jones J, Allen E. Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics. *BMJ*. 1999;318(7188):904–8.
 48. Immunization Act [cited 2017 Mar 25]. Available from: <http://www.japaneselawtranslation.go.jp/law/detail/?id=2778&vm=04&re=01>
 49. The Japanese Expert Board for the Eradication of Cervical Cancer [cited 2017 Mar 25]. Available from: <http://www.cczero.jp/>
 50. Medwatcher Japan. Complaint against HPV vaccine manufacturers' alleged violations of the JPMA Promotion Code for Prescription Drugs [Japanese] [cited 2017 Mar 25]. Available from: <http://www.yakugai.gr.jp/en/topics/topic.php?id=890>
 51. Transparency guideline for the relation between corporate activities and medical institutions, The Japan Pharmaceutical Manufacturers Association (JPMA) [cited 2017 Mar 25]. Available from: http://www.jpma.or.jp/english/policies_guidelines/transparency_guideline.html
 52. Complaint against HPV vaccine manufacturers' alleged violations of the JPMA Promotion Code for Prescription Drugs [cited 2017 Mar 25]. Available from: <http://www.yakugai.gr.jp/en/topics/topic.php?id=890>
 53. Annual Reform Recommendations from the Government of the United States to the Government of Japan under the U.S.-Japan Regulatory Reform and Competition Policy Initiative October 15, 2008 [cited 2017 Mar 25]. Available from: https://www.google.com/url?q=https://ustr.gov/sites/default/files/uploads/agreements/morocco/pdfs/EH1%2520USG%2520Agenda%2520Items%25202-11-11%2520FINAL.pdf&sa=U&ved=0ahUKewio496zddSAhWKH5QKHa4BDFoQFggEMAA&client=internal-uds-cse&usq=AFQjCNEf8amvE_-1ixWyJPGZcjmHAYLGAQ
 54. United States-JAPAN. Economic Harmonization Initiative, February 2011 [cited 2017 Mar 25]. Available from: <https://www.google.com/url?q=https://ustr.gov/sites/default/files/2008-2009-Regul>
 55. Wilson R, Paterson P, Larson HJ. The HPV vaccination in Japan – issues and options. CSIS, May 2014 [cited 2017 Mar 25]. Available from: https://csis-prod.s3.amazonaws.com/s3fs-public/legacy_files/files/publication/140514_Wilson_HPVVaccination_Web.pdf
 56. Wilson R, Paterson P, Chiu J, Schulz W, Larson H. HPV vaccination in Japan – the continuing debate and global impacts. CSIS, April 2015 [cited 2017 Mar 25]. Available from: https://csis-prod.s3.amazonaws.com/s3fs-public/legacy_files/files/publication/150422_Wilson_HPVVaccination2_Web.pdf
 57. Sheldon Krinsky. *Science in the private interest: has the lure of profits corrupted biomedical research?* Oxford: Rowman & Littlefield Publishers, Inc; 2003, p4.
 58. Heath I. Following the story: continuity of care in general practice. In: Greenhalgh T, Hurwitz B (eds). *Narrative based medicine*. London: BMJ Books; 1998, pp.86.
 59. Rudebeck CE. Humanism in medicine. Benevolence or realism? *Scand J Prim Health Care*. 1992 Sep;10(3):161–2.
 60. Hart E. The history of questionable fast-tracked global HPV vaccination [cited 2017 Mar 25]. Available from: <https://elizabethhart.files.wordpress.com/2013/02/the-history-of-questionable-fast-tracked-global-hpv-vaccination.pdf>
 61. Mello MM, Abiola S, Colgrove J. Pharmaceutical companies' role in state vaccination policymaking: the case of human papillomavirus vaccination. *Am J Public Health*. 2012 May;102(5):893–8. doi: 10.2105/AJPH.2011.300576. Epub 2012 Mar 15.
 62. Suzuki T, Minaguchi M, Sekiguchi M. Law and safety of drug. *Eidell Institute*; 2015, p.348 [Japanese].
 63. Chalmers I. What do I want from health research and researchers when I am a patient? *BMJ*. 1995;310(6990):1315–18.
 64. Doshi P, Dickersin K, Healy D, Vedula SS, Jefferson T. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ*. 2013 Jun 13;346:f2865. doi: 10.1136/bmj.f2865.
 65. Beppu H. Reasons why patients should take part in the planning of clinical trials. *The Informed Prescriber* 2010;25(4):45–9 [Japanese].

Identifying ethical issues in the development of vaccines and in vaccination

VEENA JOHARI

Abstract:

Vaccines are a widely accepted public health intervention. They are also a profitable tool for pharmaceutical companies manufacturing vaccines. There are many vaccines in the pipeline, for various diseases, or as combination vaccines for several diseases. However, there is also a growing concern about vaccines

and the manner in which they are developed and approved by the authorities. Approvals are fast tracked and adverse events and serious adverse events following vaccination are seldom reported once the vaccine gets its marketing approval. Thus, vaccines have been clouded with many controversies and their use as a public health tool to prevent diseases is constantly under challenge.

Public health and human rights have an intrinsic link, and any public health programme can be successful if the rights of people are respected, and upheld. A routine or compulsory vaccine programme tends to ignore rights of people that augment the legal and ethical issues relating to vaccinations. This article aims to identify the legal and ethical issues in the development of vaccines and in vaccination processes.

Author: Veena Johari (courtyardattorneys@gmail.com), Advocate, Courtyard Attorneys 47/1345, MIG Adarsh Nagar, Worli, Mumbai 400 030, Maharashtra, INDIA.

To cite: Johari V. Identifying ethical issues in the development of vaccines and in vaccination. *Indian J Med Ethics*. 2017 Apr-Jun; 2(2) NS: 88-93.

© Indian Journal of Medical Ethics 2017

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Eduardo Alvarez
Print Name

City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

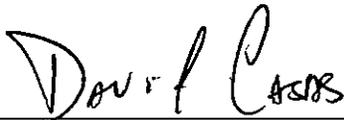
The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



Print Name

City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

DAPHNIE DIANNE DAMLIAN

Print Name



City

Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Chelsea Goncales
Print Name


City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Aida Hinosa

Print Name



City

Zip Code

My name is Cynthia Henry Keener, I am here today to represent the thousands of vaccine injured children not only in Hawaii but worldwide!

My son Makana is injured from his one yr vaccinations. Makana is now 9 yrs old.

After receiving the MMR, Varicella & Hep A vaccine at Kauai medical Clinic my son began to have jerking seizures (1YR) and still does to this day. Per the CDC website this is a severe reaction to MMR.

He has learning disabilities from brain damage all extensively documented, he has many cognitive deficits that effect his daily living. We have been tp many reputable hospitals that chose to NOT look at him being possibly vaccine damaged, only one who admitted it.

I strongly oppose the mandating of more vaccines onto the childhood vaccine schedule that's already overloaded w/ combo vaccines & single dose vaccines.

Yes the science is there to show that vaccines stop diseases, but where is the data on the adverse reactions to vaccines? I mean after all it'd be common sense right to have adverse reactions being carefully monitored right? Since there is an obvious Vaccine Injury Court.

The decision made by the US Supreme court to give drug co's total liability protection for deaths & injuries caused by government mandated vaccines is one of two admissions that vaccines can cause harm, even death & again the he obvious Vaccine Injury Court was set up for this very reason.

Does is make sense to add any more vaccines to already overloaded childhood vaccine schedule? **ABSOLUTELY NOT. DOES IT MAKE ANY SENSE WHEN CHILDREN ARE GETTING HURT & IN SOME CASES LOOSING THEIR LIVES? ABSOLUTELY NOT!!!!**

You can't trust the systemic methods of operation that many pediatricians choose to follow for God knows what reason. After all they all take an oath to try & do no harm.

There is no accountability! We got the run around and missed getting into Vaccine Injury Court by a week. Why because no one looked at my son as vaccine injured & it was right there on CDC information!

To Whom it may Concern:

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration!

Shelley Roberts

To: Department of Health Immunization Branch

Fr: Kit Uyeda, Resident of [REDACTED]

Re: Support of HAR 11-157 Proposed Rules Update

Thank you for this opportunity to provide testimony. As a community member, public health advocate, and grandparent of four children, I am writing to **strongly support the HAR 11-157 proposed rules update.**

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP). The Best Practices Guidance of the ACIP is based on scientific research and periodically updated by medical experts. Safety of the vaccines is a high priority.

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

As a grandparent and advocate for the health of all of Hawaii's children, I support the updated changes for required immunizations to attend school. This proven system to prevent illness and possible disability or death is paramount to the health and wellbeing of Hawaii's population.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

No vaccine is 100% effective for everyone and not everyone can be vaccinated. Newborns and those with compromised immune systems – such as those experiencing chemotherapy or with autoimmune conditions – cannot be immunized. If approximately 93% of the population is vaccinated, vulnerable groups will stay protected. Immunized students are protected from vaccine-preventable diseases and protect those who cannot be immunized.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



Susan Fujii
Retired Public Health Nurse



Dear Director Anderson,

My name is Miranda Gallegos, and I am writing to express my support of proposed amendments to H.A.R. Title 11, Chapter 157, Examination and Immunization. The scope of efficient immunization benefits for individuals and the State include, preventing long term healthcare costs and the potential loss of productivity. Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing in **strong support of HAR 11-157 proposed rules update.**

Specifically, the proposed amendments that address the prevention of HPV and HPV-related cancers. The HPV virus has serious repercussions such as cancer and genital warts, both of which result not only in physical ailments, but also emotional stress.

Though I did not experience my adolescent years in Hawai'i, I did experience the benefit from having these safeguards mandated in public schools in Colorado. As HPV is the most prevalent STI, statistics from the CDC state that it is so common, every person is likely to have it at least once in their life. Often presenting asymptomatic, the infected individual may not know they have it. Federally mandates for sexual education in public schools regarding the prevalence, transmittance, and protection against easily transmittable communicable infections varies by school, mission, and values. Without mandates by legislature, one of the most common infectious sexually transmitted diseases could continue to spread, threaten the health, wellbeing, and futures our youth. Mandating vaccinations and doctors visits ensures one extra measure, one more caring adult invested in the future success, health, and wellbeing of Hawai'i's youth. Parents do their best but sometimes, even the best cannot afford or know of these basic services, instead, knowingly or unknowingly risk adverse health outcomes unless a visit is urgent at that time. By then, it could already be too late. Cancer treatments, survey, hospitalizations, medications, and recovery cost far more than a doctor's visit whose fee can be waived.

The HPV vaccine is important because it is currently the most common STD virus and has no cure. About one in four—are currently infected in the United States. Every year, individuals in the US are diagnosed with cancer resulting from contracting HPV, and of those diagnosed with cancer, one-third will die from the disease.

If we can protect our youth from the potential of contracting cancer or other harmful symptoms, by adopting these regulations now, we absolutely must.

I urge you to support **HAR 11-157 proposed rules update.** Thank you for the consideration of my testimony.

Mahalo,
Miranda Gallegos





TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Bethany Agcaoili

Print Name


City


Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.

Charlene Nguyen
Print Name


City Zip Code

TESTIMONY IN SUPPORT OF HAR 11-157 RULES UPDATE

Thank you for this opportunity to provide testimony. As a community member and public health advocate, I am writing to strongly support the HAR 11-157 proposed rules update.

These proposed changes will bring Hawaii's rules into compliance with the most current recommendations of the Advisory Committee on Immunization Practices (ACIP).

The proposed rules update is especially important for students first entering 7th grade or higher to receive the HPV, MCV, and Tdap shots because of low uptake levels. This is especially true for the HPV vaccine which prevents up to six HPV-related cancers that might otherwise occur later in life.

The Centers for Disease Control and Prevention (CDC) advises that state and local vaccination requirements for daycare and school entry are important tools for maintaining high vaccination coverage rates, and in turn, lower rates of vaccine-preventable diseases.

Research demonstrates that communities with more vaccine exemptions are at greater risk for vaccine-preventable disease outbreaks. Limiting exemptions to those that are medically indicated improves protection for our entire community, including those who are particularly vulnerable, the very young and our elders.

I respectfully request that the proposed changes to HAR 11-157 be supported and passed for the health of all of our communities.

Thank you for your consideration.



Print Name



City

Zip Code

Anything put into a person's body should be a matter of personal choice. Vaccinations should not be regulated by any government agency in any way -ever!

Immune systems are weakened by dealing with so many substances unrecognized by the body. I am aware that most people/children are unaffected by these vaccines, but as their bodies are developing, some have difficulties with the body accepting them.

As the mother of five children who were vaccinated I have some sad experiences. Three had no detected reactions but their little bodies still had to figure out where to store these foreign substances. Even then I started their vaccinations at an older age than recommended.

One child developed seizures which lasted four years. Another child would run fevers and extreme swelling and redness with every vaccine.

I also have a grandson whose body seized up and was hospitalized. Long term- he had learning disabilities which he had not experienced prior to his school age vaccines.

I also feel it is dangerous to administer multiple vaccines in one injection. I would prefer that vaccines not even begin until two years of age, allowing tiny bodies to develop their neurological and immune systems and then cut down on the number of vaccines given at one time.

I am in favor of requesting the children not vaccinated to stay home from school if there is an outbreak from disease they are not vaccinated for.

Homeopathics can be used effectively to protect children not vaccinated in the normal route.

Do not pass legislation commanding all children to be vaccinated!!

If government decided to require all adults who live on Kauai to be vaccinated there would suddenly be an uproar I believe. Citizens would yell loudly that the government can not require such a thing of a person.

Aloha,

I am providing my testimony on behalf of bill HAR-11-157.....in the matter of mandatory vaccinations for children to attend school and the increase of the vaccination schedule in Hawaii. As a parent, health advocate, and special education teacher, I have serious concerns about making vaccinations mandatory for all kids. I personally have only been vaccinated for 7 vaccinations as a child and today the schedule is reaching 72. I also have never been deathly ill from any of today's required vaccinations listed yet having never received them. My immune system is doing what it should do and is able to fend off the occasional flu, and illness with out major damage.

This huge difference in my child hood to my own children's scheduled vaccinations comes with no real studies showing a change or increase in any of these diseases on any alarming level. In fact the only increase recently has been a spike in whooping cough (pertussis) and the vaccine provided has proven to be significantly ineffective. I know this because my 14 year old son (at the time) who had 3 inoculations for pertussis still became infected with the illness causing him great discomfort. My self included got the illness, but neither of us feared our life, and now because we had it we will be immune to future pertussis outbreaks. When our immune system becomes infected with an actual illness such as the flue, measles, chicken pox, or pertussis, we are creating the full spectrum of antibodies to fight off a future infection there for making it stronger and more robust. The 3 in one shots are especially harmful because they do not mimic nature the way single inoculations do. There will never be a time when the human body will need to fight 3 major illness at once such as measles, mumps, and rubella. When injecting the body with these 3 inoculations the immune system doesn't react the same as a single inoculation and instead it attacks the antibodies and stimulates an attack of the immune system increasing autoimmune diseases, which is when the immune system malfunctions due to the many assaults on it.

Now I would like to also include the adjuvants that are used to "preserve" the virus, and bacterial in each shot, they include mercury, aluminum, ammonium, sodium chloride etc..... These are technically considered poisons if a child was to accidentally consume them. In fact parents are told to take their child to the ER if this occurs yet somehow they are safe if they are injected into their blood stream? The lack of studies to show safety, the one size fits all mentality, and the private court providing vaccination injury settlement payouts to those most drastically harmed and or died due to vaccinations is proof that they are not safe and they can cause irreversible damage.

There are many genetic precursors that would be determined if a child could process the adjuvants in an inoculation, one specifically which composes roughly 10% of the population is the MTHFR genetic mutation that interferes with the body's ability to methylate, AKA detox toxins such as those in the adjuvants. The result of a child with this mutation that receives a shot could result in death, seizure disorders, brain damage, autism, mood disorders such as PANDAS, eczema, learning issues, etc....longer term effects can result in autoimmune disorders, cancer, depression, anxiety disorders, OCD.....ect.

I am NOT an anti-vaxer and this issue has been unfortunately polarized. I sympathize deeply for those parents and children that have died or become deathly ill due to some of these diseases. The problem lies with the lack of safety studies and lack of insight about genetic snips that can cause potential complications. No one can dismiss that childhood chronic illness is on the rise, especially those related to brain disorders, and autoimmune disorders. We are at a critical stage of being on the edge of medical tyranny against our population, and it is our right to determine what gets put into our children's body as well as our own bodies especially if it has not been proven to be safe and effective. The government has a long way to go to prove they are willing

to conduct long term third party studies that are not conducted by pharmaceutical industry and they need to hold pharmaceuticals liable for the injuries that occur and not give them immunity so that they have some sort of repercussion's for the many who suffer from their product.

Finally, just as one death due to measles is one death to many, the same should say that one death from a vaccination is one death to many. This is when we need to band together and demand a change in the way the system treats and regulates the very tool that was originally designed to protect the population, and ensure they get back to doing that again.

To Whom it may concern,

I have 4 children ranging from 3 years old to 19 and all my children have been vaccinated. My 3 year old is my only child that had a reaction after having his 6 month checkup and receiving vaccines. Between 6 months to 9 months we started to see a difference in our son. He no longer would respond to his name and seemed disconnected to us. I googled 9 month old not responding to his name, not making eye contact and the word Autism came up. I never knew what Autism was until that day. After reading the top 10 symptoms and my son had 7 of them I went into a heavy research online, overwhelming myself with information and buying books. I decided to take my son to our trusted pediatrician to voice my concerns. Much to my surprise our favorite pediatrician told me if I didn't update my son on his vaccines on that day he could no longer see him as a patient. He agreed with me on my sons delays and behavior and handed me a brochure from Family Support Services. I trusted our pediatrician as he promised me vaccines don't cause Autism, but my gut told me otherwise and he dropped us as a patient.

When something hits home and one of your family members is effected by an illness or condition you become very educated on that illness or condition. My son has been diagnosed with Autism and went through therapy service through the state until he turned 3. Not everyone has side effects from vaccines, some have slight fever, swollen where vaccine was issued, but some have severe side effects even death therefore I believe it should be ones choice if they want to risk side effect or death vs a chance of catching a illness that could be deadly as well. It's mandated that our children attend school till they are 18, but we have a choice based on our best interest for our individual child if that be public, charter or private. The same should be for vaccines, every child is different not everyone is a candidate to receive a vaccine. Parents know our children better than anyone including a Dr. It should be a parents choice. I'm not against those who choose to vaccinate their kids and no one should be against me choosing to not further vaccinate my kids not even the state.

I oppose these new vaccine requirements as well as any vaccine requirements to attend our public schools. I have already pulled my children from public school and they attend private school due to this matter. I believe the state enrollment will go down dramatically if these requirements are passed. Please take time to look at the truth, do your research. So many families have been effected by vaccine injury's and the numbers are on the rise.

Thank you for taking the time to read my testimony.

Aloha

A concern mother

Carmen S. Villar, MSW
Chief of Staff
Office of the Director
MS D-14
Centers for Disease Control and Prevention (CDC)
1600 Clifton Road
Atlanta, Georgia 30329-4027

August 29, 2016

Dear Ms. Villar:

We are a group of scientists at CDC that are very concerned about the current state of ethics at our agency. It appears that our mission is being influenced and shaped by outside parties and rogue interests. It seems that our mission and Congressional intent for our agency is being circumvented by some of our leaders. What concerns us most, is that it is becoming the norm and not the rare exception. Some senior management officials at CDC are clearly aware and even condone these behaviors. Others see it and turn the other way. Some staff are intimidated and pressed to do things they know are not right. We have representatives from across the agency that witness this unacceptable behavior. It occurs at all levels and in all of our respective units. These questionable and unethical practices threaten to undermine our credibility and reputation as a trusted leader in public health. We would like to see high ethical standards and thoughtful, responsible management restored at CDC. We are asking that you do your part to help clean up this house!

It is puzzling to read about transgressions in national media outlets like USA Today, The Huffington Post and The Hill. It is equally puzzling that nothing has changed here at CDC as a result. It's business as usual. The litany of issues detailed over the summer are of particular concern:

Recently, the National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP) has been implicated in a "cover up" of inaccurate screening data for the Wise Woman (WW) Program. There was a coordinated effort by that Center to "bury" the fact that screening numbers for the WW program were misrepresented in documents sent to Congress; screening numbers for 2014 and 2015 did not meet expectations despite a multi-million dollar investment; and definitions were changed and data "cooked" to make the results look better than they were. Data were clearly manipulated in irregular ways. An "internal review" that involved staff across CDC occurred and its findings were essentially suppressed so media and/or Congressional staff would not become aware of the problems. Now that both the media and Congresswoman DeLauro are aware of these issues, CDC staff have gone out of their way to delay FOIAs and obstruct any inquiry. Shouldn't NCCDPHP come clean and stop playing games? Would the ethical thing be to answer the questions fully and honestly. The public should know the true results of what they paid for, shouldn't they?

Another troubling issue at the NCCDPHP are the adventures of Drs. Barbara Bowman and Michael Pratt (also detailed in national media outlets). Both seemed to have irregular (if not questionable) relationships with Coca-Cola and ILSI representatives. Neither of these relationships were necessary (or appropriate) to uphold our mission. Neither organization added any value to the good work and science already underway at CDC. In fact, these ties have now called into question and undermined CDC's work. A cloud has been cast over the ethical and excellent work of scientists due to this wanton behavior. Was cultivating these relationships worth dragging CDC through the mud? Did Drs. Bowman and Pratt have permission to pursue these relationships from their supervisor Dr. Ursula Bauer? Did they seek and receive approval of these outside activities? CDC has a process by which such things should be vetted and reported in an ethics review, tracking and approval system (EPATS). Furthermore, did they disclose these conflicts of interest on their yearly OGE 450 filing. Is there an approved HHS 520, HHS 521 or "Request for Official Duty Activities Involving an Outside Organization" approved by Dr. Bauer or her Deputy Director Ms. Dana Shelton? An August 28, 2016 item in The Hill details these issues and others related to Dr. Pratt.

It appears to us that something very strange is going on with Dr. Pratt. He is an active duty Commissioned Corps Officer in the USPHS, yet he was "assigned to" Emory University for a quite some time. How and under what authority was this done? Did Emory University pay his salary under the terms of an IPA? Did he seek and receive an outside activity approval through EPATS and work at Emory on Annual Leave? Formal supervisor endorsement and approval (from Dr. Bauer or Ms. Shelton) is required whether done as an official duty or outside activity. If deemed official, did he file a "Request for Official Duty Activities Involving an Outside Organization" in EPATS? Apparently Dr. Pratt's position at Emory University has ended and he has accepted another position at the University of California - San Diego? Again, how is this possible while he is still an active duty USPHS Officer. Did he retire and leave government service? Is UCSD paying for his time via an IPA? Does he have an outside activity approval to do this? Will this be done during duty hours? It is rumored that Dr. Pratt will occupy this position while on Annual Leave? Really? Will Dr. Pratt be spending time in Atlanta when not on Annual Leave? Will he make an appearance at NCCDPHP (where he hasn't been seen for months). Most staff do not enjoy such unique positions supported and approved by a Center Director (Dr. Bauer). Dr. Pratt has scored a sweet deal (not available to most other scientists at CDC). Concerns about these two positions and others were recently described in The Huffington Post and The Hill. His behavior and that of management surrounding this is very troubling.

Finally, most of the scientists at CDC operate with the utmost integrity and ethics. However, this "climate of disregard" puts many of us in difficult positions. We are often directed to do things we know are not right. For example, Congress has made it very clear that domestic funding for NCCDPHP (and other CIOs) should be used for domestic work and that the bulk of NCCDPHP funding should be allocated to program (not research). If this is the case, why then is NCCDPHP taking domestic staff resources away from domestic priorities to work on global health issues? Why in FY17 is NCCDPHP diverting money away from program priorities that

directly benefit the public to support an expensive research FOA that may not yield anything that benefits the public? These actions do not serve the public well. Why is nothing being done to address these problems? Why has the CDC OD turned a blind eye to these things. The lack of respect for science and scientists that support CDC's legacy is astonishing.

Please do the right thing. Please be an agent of change.

Respectfully,

CDC Spider
(CDC Scientists Preserving Integrity, Diligence and Ethics in Research)

Cc:
CDC Ethics Office



VIA FEDEX

October 12, 2017

U.S. Department of Health & Human Services
HHS Office of the Secretary
Eric D. Hargan
Acting Secretary of Health & Human Services
200 Independence Avenue, S.W.
Washington, D.C. 20201

Re: *HHS Vaccine Safety Responsibilities and Notice Pursuant to 42 U.S.C. § 300aa-31*

Dear Secretary Hargan:

Informed Consent Action Network hereby provides notice per 42 U.S.C. § 300aa-31(b).

Americans, including the over 55 organizations listed below, whose members exceed 5 million Americans, are concerned about vaccine safety. The National Childhood Vaccine Injury Act of 1986 (the **1986 Act**) made nearly every aspect of vaccine safety the exclusive responsibility of the Department of Health & Human Services (**HHS**). As the Secretary of HHS (the **Secretary**), this means you shoulder virtually all responsibility for assuring the safety of vaccines administered to America's 78 million children.

This notice respectfully requests confirmation that certain obligations regarding vaccine safety required under the 1986 Act have been fulfilled or will forthwith be fulfilled. These specific requests are numbered sequentially in this notice. We would welcome the opportunity to meet and discuss reasonable means for complying with these requests. If that is not possible, the 1986 Act authorizes "a civil action ... against the Secretary where there is alleged a failure of the Secretary to perform any act or duty" under the 1986 Act.

I. Background

The 1986 Act granted economic immunity to pharmaceutical companies for injuries caused by their vaccines. (42 U.S.C. § 300aa-11.) The 1986 Act thereby eliminated the market force which drives safety for all other products – actual and potential product liability. Recognizing the unprecedented elimination of this market force, the 1986 Act makes HHS directly responsible for virtually every aspect of vaccine safety. (42 U.S.C. §§ 300aa-2, 300aa-27.)

When the CDC recommends a pediatric vaccine for universal use, it creates for that vaccine's maker a liability free market of 78 million children typically required by law to receive the vaccine. The number of required vaccines has grown rapidly since 1986. In 1983, the CDC recommended that babies under one receive two vaccines: DTP and Polio.¹ As of 2017, the CDC recommends that babies under one receive multiple doses of ten vaccines: DTaP, Polio, Hep B, Rotavirus, Hib, Pneumococcal, Influenza, MMR, Varicella, and Hep A.² In total, the current CDC childhood vaccine schedule includes 56 injections of 73 doses of 30 different vaccines.

II. Deficiencies in the Pre-Licensure Safety Review of Pediatric Vaccines

All drugs licensed by the FDA undergo long-term double-blind pre-licensure clinical trials during which the rate of adverse reactions in the group receiving the drug under review is compared to the rate of adverse reactions in a group receiving an inert placebo, such as a sugar pill or saline injection. For example: Enbrel's pre-licensure trials followed subjects up to 80 months and controls received a saline injection.³ Lipitor's pre-licensure trials lasted a median of 4.8 years and controls received a sugar pill.⁴ Botox's pre-licensure trials lasted a median of 51 weeks and controls received a saline injection.⁵ And even with these long-term studies, drugs are still often recalled.

In contrast, vaccines are *not* required to undergo long-term double-blind inert-placebo controlled trials to assess safety. In fact, not a single one of the clinical trials for vaccines given to babies and toddlers had a control group receiving an inert placebo. Further, most pediatric vaccines currently on the market have been approved based on studies with inadequate follow-up periods of only a few days or weeks.

For example, of the two Hepatitis B vaccines licensed by the FDA for injection into one-day-old babies, Merck's was licensed after trials that solicited adverse reactions for *only five days* after vaccination and GlaxoSmithKline's was licensed after trials that solicited adverse reactions for *only four days* after vaccination.⁶ Similarly, the HiB vaccines sold by these same companies were licensed based on trials which solicited adverse reactions for three and four days, respectively, after vaccination.⁷ The only stand-alone polio vaccine was licensed after a mere 48-hour follow-up period.⁸

¹ <https://www.cdc.gov/vaccines/schedules/images/schedule1983s.jpg>

² <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>

³ https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103795s5503lbl.pdf

⁴ https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020702s056lbl.pdf

⁵ https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103000s5302lbl.pdf

⁶ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110114.pdf>;

<https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224503.pdf>

⁷ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM253652.pdf>;

<https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM179530.pdf>

⁸ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM133479.pdf>

Moreover, these trials either had no control group or a control group which received other vaccines as a “placebo.”⁹ This means each new vaccine need only be roughly as safe as one (or in some cases numerous) previously licensed vaccines. Such flawed and unscientific study designs cannot establish the actual safety profile of any vaccine. The real adverse event rate for a vaccine can only be determined by comparing subjects receiving the vaccine with those receiving an inert placebo. Yet, this basic study design, required for every drug, is not required before or after licensing a vaccine.

The 1986 Act expressly requires that you, as the Secretary, “shall make or assure improvements in ... the licensing ... and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.” (42 U.S.C. § 300aa-27(a)(2).) Given this statutory obligation:

- (1) Please explain how HHS justifies licensing any pediatric vaccine without first conducting a long-term clinical trial in which the rate of adverse reactions is compared between the subject group and a control group receiving an inert placebo?**
- (2) Please list and provide the safety data relied upon when recommending babies receive the Hepatitis B vaccine on the first day of life?**

III. Post-Licensure Surveillance of Vaccine Adverse Events

The lack of pre-licensure safety data leaves the assessment of vaccine safety to the post-licensing period when they are being administered to children in the “real world.” To capture vaccine adverse events in the real world, the 1986 Act established the Vaccine Adverse Events Reporting System (VAERS) operated by HHS. (42 U.S.C. § 300aa-25.)

In 2016, VAERS received 59,117 reports of adverse vaccine events, including 432 deaths, 1,091 permanent disabilities, 4,132 hospitalizations, and 10,284 emergency room visits.¹⁰

However, only a tiny fraction of adverse vaccine events are reported to VAERS. An HHS-funded study by Harvard Medical School tracked reporting to VAERS over a three-year period at Harvard Pilgrim Health Care involving 715,000 patients and found that “fewer than 1% of vaccine adverse events are reported.”¹¹ A U.S. House Report similarly stated: “Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events.”¹²

⁹ Ibid.

¹⁰ <https://wonder.cdc.gov/vaers.html>

¹¹ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

¹² <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

Assuming VAERS captures a full 1 percent of adverse events – which is more than is estimated – the VAERS data above from 2016 may reflect that in that year alone there were 5,911,700 adverse vaccine events, including 43,200 deaths, 109,100 permanent disabilities, 413,200 hospitalizations, and 1,028,400 emergency room visits.

Of course, these figures are merely estimates. It would be far better if adverse events reports were automatically created and submitted to VAERS to avoid the issue of underreporting. Automated reporting would provide invaluable information that could clarify which vaccines might cause which harms and to whom, potentially avoiding these injuries and deaths.

The idea of automating adverse reaction reporting to VAERS is not new or even difficult to achieve.¹³ An agency within HHS, the Agency for Healthcare Research and Quality, sought to do exactly that in 2007 when it provided an approximately \$1 million grant to automate VAERS reporting at Harvard Pilgrim Health Care.¹⁴ The result was the successful automation of adverse event reports at Harvard Pilgrim:

*Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions ... were identified.*¹⁵

These results should have been concerning to HHS since they show that over only a three-year period, there were 35,570 reportable reactions in just 376,452 vaccine recipients.

After automating adverse events reports at Harvard Pilgrim, the developers of this system asked the CDC to take the final step of linking VAERS with the Harvard Pilgrim system so that these reports could be automatically transmitted into VAERS. Instead, the CDC refused to cooperate. As the Harvard grant recipients explained:

*Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.*¹⁶

After three years and spending \$1 million of taxpayers' money, the CDC refused to even communicate with the HHS' Harvard Medical School grant recipients. Given HHS's statutory mandate to assure safer vaccines, it should have rushed forward with automating VAERS reporting -- not ignored the requests by the HHS's Harvard grant recipients.

¹³ <https://healthit.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system>

¹⁴ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

¹⁵ Ibid.

¹⁶ Ibid.

While HHS strongly supports automating public health surveillance systems, when it comes to vaccine safety, the CDC has only supported projects that would limit VAERS to passive surveillance.¹⁷ Automation would improve safety and address many of the long-standing issues and limitations raised by CDC regarding VAERS.¹⁸ Capturing “fewer than 1% of vaccine adverse events” thirty years after the passage of the 1986 Act is unacceptable -- and potentially deadly.

The 1986 Act expressly provides that you, as the Secretary, “shall make or assure improvements in ... adverse reaction reporting ... in order to reduce the risks of adverse reactions to vaccines.” (42 U.S.C. § 300aa-27(a)(2).) Given this statutory obligation:

(3) Please explain why HHS failed to cooperate with Harvard to automate VAERS reporting? And detail any steps that HHS has taken since toward automating VAERS reporting?

(4) Please explain any specific steps taken by HHS to improve adverse reaction reporting to VAERS?

IV. Identifying What Injuries Are Caused by Vaccines

The first step in assuring safer vaccines is to identify what harms they cause. This would normally be accomplished pre-licensure by long-term, inert-placebo controlled trials – but these are never performed for vaccines. As for post-licensure monitoring, HHS has refused to improve VAERS as discussed above. Hence, assessing which vaccines cause which injuries is mainly left to post-licensure studies. HHS, unfortunately, has neglected to perform these studies.

In 1991, the Institute of Medicine (IOM) examined 22 commonly reported serious injuries following the DTP vaccine.¹⁹ The IOM concluded the scientific literature supported a causal relationship between the DTP vaccine and 6 of these injuries: acute encephalopathy, chronic arthritis, acute arthritis, shock and unusual shock-like state, anaphylaxis, and protracted inconsolable crying.²⁰ The IOM, however, found the scientific literature was insufficient to conclude whether or not the DTP vaccine can cause 12 other serious injuries:

*Aseptic meningitis; Chronic neurologic damage; Learning disabilities and attention-deficit disorder; Hemolytic anemia; Juvenile diabetes; Guillain-Barre syndrome; Erythema multiforme; Autism; Peripheral mononeuropathy; Radiculoneuritis and other neuropathies; Thrombocytopenia; Thrombocytopenic purpura*²¹

¹⁷ [http://www.ajpmonline.org/article/S0749-3797\(12\)00249-8/pdf](http://www.ajpmonline.org/article/S0749-3797(12)00249-8/pdf); <https://www.ncbi.nlm.nih.gov/pubmed/26209838>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

¹⁸ Ibid.

¹⁹ <https://www.nap.edu/read/1815/chapter/2#7>

²⁰ Ibid.

²¹ Ibid.

The IOM lamented that it “encountered many gaps and limitations in knowledge bearing directly and indirectly on the safety of vaccines” and on the poor design of the few existing studies.²² It therefore cautioned that: “If research capacity and accomplishment in this field are not improved, future reviews of vaccine safety will be similarly handicapped.”²³

In 1994, the IOM issued another report which examined the scientific literature for evidence that could either prove or disprove a causal link between 54 commonly reported serious injuries and vaccination for diphtheria, tetanus, measles, mumps, polio, hepatitis B, and Hib.²⁴ The IOM located sufficient science to support a causal connection between these vaccines and 12 injuries, including death, anaphylaxis, thrombocytopenia, and Guillain-Barre syndrome.²⁵ The IOM, however, found the scientific literature was insufficient to conclude whether or not these vaccines caused 38 other commonly reported serious injuries, including:

*Demyelinating diseases of the central nervous system, Sterility, Arthritis, Neuropathy, Residual seizure disorder, Transverse myelitis, Sensorineural deafness, Optic neuritis, Aseptic meningitis, Insulin-dependent diabetes mellitus, SIDS*²⁶

As in 1991, this IOM Report again stated, “The lack of adequate data regarding many of the adverse events under study was of major concern to the committee. Presentations at public meetings indicated that many parents and physicians share this concern.”²⁷

In 2011, more than fifteen years after the IOM Reports in 1991 and 1994, HHS paid the IOM to conduct another assessment regarding vaccine safety.²⁸ This third IOM Report reviewed the available science with regard to the 158 most common vaccine injuries claimed to have occurred from vaccination for varicella, hepatitis B, tetanus, measles, mumps, and rubella.²⁹ The IOM located science which “convincingly supports a causal relationship” with 14 of these injuries, including pneumonia, meningitis, hepatitis, MIBE, febrile seizures, and anaphylaxis.³⁰ The review found sufficient evidence to support “acceptance of a causal relationship” with 4 additional serious injuries.³¹

The IOM, however, found the scientific literature was insufficient to conclude whether or not those vaccines caused 135 other serious injuries commonly reported after their administration, including:

²² <https://www.nap.edu/read/1815/chapter/2#8>

²³ <https://www.nap.edu/read/1815/chapter/9>

²⁴ <https://www.nap.edu/read/2138/chapter/2#12>

²⁵ <https://www.nap.edu/read/2138/chapter/2#12>

²⁶ Ibid.

²⁷ <https://www.nap.edu/read/2138/chapter/12>

²⁸ <https://www.nap.edu/read/13164/chapter/2#2>

²⁹ Ibid.

³⁰ <https://www.nap.edu/read/13164/chapter/2#3>

³¹ Ibid.

*Encephalitis, Encephalopathy, Infantile Spasms, Afebrile Seizures, Seizures, Cerebellar Ataxia, Acute Disseminated Encephalomyelitis, Transverse Myelitis, Optic Neuritis, Neuromyelitis Optica, Multiple Sclerosis, Guillain-Barre Syndrome, Chronic Inflammatory Demyelinating Polyneuropathy, Brachial Neuritis, Amyotrophic Lateral Sclerosis, Small Fiber Neuropathy, Chronic Urticaria, Erythema Nodosum, Systemic Lupus Erythematosus, Polyarteritis Nodosa, Psoriatic Arthritis, Reactive Arthritis, Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Arthralgia, Autoimmune Hepatitis, Stroke, Chronic Headache, Fibromyalgia, Sudden Infant Death Syndrome, Hearing Loss, Thrombocytopenia, Immune Thrombocytopenic Purpura*³²

Thus, out of the 158 most common serious injuries reported to have been caused by the vaccines under review, the evidence supported a causal relationship for 18 of them, rejected a causal relationship for 5 of them, but for the remaining 135 vaccine-injury pairs, over 86 percent of those reviewed, the IOM found that the science simply had not been performed.³³

The 1986 Act expressly provides that you, as the Secretary, “shall promote the development of childhood vaccines that result in fewer and less adverse reactions” and “shall make or assure improvements in ... the ... labeling, warning, ... and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.” (42 U.S.C. § 300aa-27(a)(2).) The first step in reducing adverse reactions is identifying what adverse reactions are caused by vaccine. Given this statutory obligation:

- (5) For each of the 38 vaccine-injury pairs reviewed in the 1994 IOM Report which the IOM found lacked studies to determine causation, please identify the studies undertaken by the HHS to determine whether each injury is caused by vaccination?**

- (6) For each of the 135 vaccine-injury pairs reviewed in the 2011 IOM Report which the IOM found lacked studies to determine causation, please identify the studies undertaken by the HHS to determine whether each injury is caused by vaccination?**

Further to your duties to identify what injuries are caused by vaccines, the 1986 Act also expressly requires you to “make or assure improvements in ... the ... recall of reactogenic lots or batches, of vaccines ... in order to reduce the risks of adverse reactions to vaccines” and thus each “health care provider who administers a vaccine ... shall record ... in such person’s permanent

³² Ibid.

³³ Ibid.

medical record ... the vaccine manufacturer and lot number.” (42 U.S.C. §§ 300aa-25(a), 300aa-27(a)(2).) Since health care providers often fail to record this information:

(7) Please explain what HHS has done to assure that health care providers record the manufacturer and lot number for each vaccine they administer?

V. Identifying Which Children are Susceptible to Vaccine Injury

The IOM has consistently acknowledged there is individual susceptibility to serious vaccine injuries. The IOM has also acknowledged that research on such susceptibility must be done on an individual basis, considering a child’s personal genome, behaviors, microbiome, intercurrent illness, and present and past environmental exposure. HHS, unfortunately, has not conducted this research.

In 1994, the IOM, building on concerns raised in its 1991 report, stated: “The committee was able to identify little information pertaining to why some individuals react adversely to vaccines when most do not.”³⁴ The IOM urged that “research should be encouraged to elucidate the factors that put certain people at risk.”³⁵

Yet, seventeen years later, in 2011, the IOM acknowledged this research had still not been done:

Both epidemiologic and mechanistic research suggest that most individuals who experience an adverse reaction to vaccines have a preexisting susceptibility. These predispositions can exist for a number of reasons—genetic variants (in human or microbiome DNA), environmental exposures, behaviors, intervening illness, or developmental stage, to name just a few—all of which can interact...

*Some of these adverse reactions are specific to the particular vaccine, while others may not be. Some of these predispositions may be detectable prior to the administration of vaccine... much work remains to be done to elucidate and to develop strategies to document the immunologic mechanisms that lead to adverse effects in individual patients.*³⁶

In 2013, HHS commissioned the IOM to review the safety of the entire vaccine schedule.³⁷ The IOM again explained that while “most children who experience an adverse reaction to immunization have preexisting susceptibility,” the IOM:

³⁴ <https://www.nap.edu/read/2138/chapter/12#307>. See also <https://www.nap.edu/read/1815/chapter/9>

³⁵ Ibid.

³⁶ <https://www.nap.edu/read/13164/chapter/5#82>

³⁷ <https://www.nap.edu/read/13563/chapter/1>

*found that evidence assessing outcomes in sub populations of children who may be potentially susceptible to adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures and outcomes.*³⁸

HHS had failed to even define the terminology for the study of susceptible subpopulations and hence IOM admonished HHS to “develop a framework that clarifies and standardizes definitions of ... populations that are potentially susceptible to adverse events.”³⁹

The IOM correctly points out in 2011 that given the “widespread use of vaccines” and “state mandates requiring vaccination of children ... it is essential that safety concerns receive assiduous attention.”⁴⁰ This is the same call for diligent attention that the IOM made in 1991 and 1994. Unfortunately, all of these calls for action have gone unheeded. The critical scientific inquiry to identify individuals susceptible to serious vaccine injury has never been conducted.

The 1986 Act expressly provides that you, as the Secretary, “shall promote the development of childhood vaccines that result in fewer and less adverse reactions” and “shall make or assure improvements in ... the ... labeling, warning, ... and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.” (42 U.S.C. § 300aa-27(a)(2).) Given this statutory obligation:

(8) Please advise when HHS intends to begin conducting research to identify which children are susceptible to serious vaccine injury? If HHS believes it has commenced this research, please detail its activities regarding same?

VI. Removing Claim “Vaccines Do Not Cause Autism” from the CDC Website

HHS, unfortunately, has treated vaccine safety as a public relations issue rather than a public health imperative. For example, the CDC claims on its website that “Vaccines Do Not Cause Autism” even though this broad claim is plainly not supported by the scientific literature.⁴¹

Indeed, as part of the IOM’s 2011 review of vaccine safety, it was asked by HHS whether there is a causal relationship between autism and the DTaP vaccine administered to children at two, four, six, and fifteen months of age.⁴² The IOM could not locate a single study supporting

³⁸ <https://www.nap.edu/read/13563/chapter/9#130>

³⁹ Ibid.

⁴⁰ <https://www.nap.edu/read/13164/chapter/3#28>

⁴¹ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁴² <https://www.nap.edu/read/13164/chapter/2#2>

that DTaP does not cause autism.⁴³ The IOM therefore concluded: “The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid–, tetanus toxoid–, or acellular pertussis–containing vaccine and autism.”⁴⁴ The IOM’s full explanation in its 2011 Report for this finding is attached as Appendix B. In fact, the only study the IOM could locate regarding whether DTaP causes autism, (Geier and Geier, 2004), concluded there *was* an association between DTaP and autism.⁴⁵ No research has been published since 2011 that could change the IOM’s conclusion. Based on the foregoing, the CDC cannot validly make the blanket assertion that there is no causal relationship between vaccines and autism. The CDC nonetheless claims on its website that “Vaccines Do Not Cause Autism.”

As with DTaP, there are also no published studies showing that autism is not caused by Hepatitis B, Rotavirus, Hib, Pneumococcal, Inactivated Poliovirus, Influenza, Varicella, or Hepatitis A vaccines – all of which HHS recommends babies receive, typically multiple times, by one year of age.⁴⁶

Instead, HHS’s claim that “Vaccines Do Not Cause Autism” relies almost entirely upon studies exclusively studying only one vaccine, MMR (which is administered no earlier than one year of age), or only one vaccine ingredient, thimerosal, with regard to autism.⁴⁷ Putting aside the controversy surrounding these studies, studies which focus on only one vaccine and one ingredient while ignoring the entire balance of the CDC’s pediatric vaccine schedule cannot support the CDC’s overarching declaration that “Vaccines Do Not Cause Autism.”

As for the MMR vaccine, the CDC’s own Senior Scientist, Dr. William Thompson⁴⁸, recently provided a statement through his attorney that the CDC “omitted statistically significant information” showing an association between the MMR vaccine and autism in the first and only MMR-autism study ever conducted by the CDC with American children.⁴⁹ Dr. Thompson, in a recorded phone call, stated the following regarding concealing this association: “Oh my God, I can’t believe we did what we did. But we did. It’s all there. It’s all there. I have handwritten notes.”⁵⁰ Dr. Thompson further stated on that call:

I have great shame now when I meet families with kids with autism because I have been part of the problem ... the CDC is so paralyzed right now by anything related to autism. They’re not doing what they should be doing because they’re afraid to look for things that might be associated. So anyway

⁴³ <https://www.nap.edu/read/13164/chapter/12#545>

⁴⁴ Ibid.

⁴⁵ Ibid. Ironically, this study was disregarded “because it provided data from a passive surveillance system [VAERS] and lacked an unvaccinated comparison population,” which would be true of any study using VAERS data.

⁴⁶ <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>

⁴⁷ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁴⁸ Dr. Thompson has been a scientist at CDC for nearly two generations and a senior scientist on over a dozen CDC publications at the core of many of CDC’s vaccine safety claims. <https://www.ncbi.nlm.nih.gov/pubmed>

⁴⁹ <http://www.rescuepost.com/files/william-thompson-statement-27-august-2014-3.pdf>

⁵⁰ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

*there's still a lot of shame with that. ... I am completely ashamed of what I did.*⁵¹

Hence, as for the only vaccine, MMR, actually studied by the CDC with regard to autism, it appears the CDC may have concealed an association between that vaccine and autism.⁵²

When the former Director of the National Institute of Health, Dr. Bernadine Healy, was asked about whether public health authorities are correct to claim that vaccines do not cause autism, she answered: "You *can't* say that."⁵³ When asked again, Dr. Healy explained: "The more you delve into it – if you look at the basic science – if you look at the research that's been done, in animals – if you also look at some of these individual cases – *and*, if you look at the evidence that there *is* no link - what I come away with is: *The question has not been answered.*"⁵⁴

Former NIH Director Dr. Healy goes on to explain:

This is the time when we do have the opportunity to understand whether or not there are susceptible children, perhaps genetically, perhaps they have a metabolic issue, mitochondrial disorder, immunological issue, that makes them more susceptible to vaccines plural, or to one particular vaccine, or to a component of vaccine... I haven't seen major studies that focus on - three hundred kids, who got autistic symptoms within a period of a few weeks of a vaccine. I think that the public health officials have been too quick to dismiss the hypothesis as irrational, without sufficient studies of causation. ...

*The reason why they didn't want to look for those susceptibility groups was because they're afraid if they found them—however big or small they were—that that would scare the public away. First of all, I think the public's smarter than that; the public values vaccines. But, more importantly, I don't think you should ever turn your back on any scientific hypothesis because you're afraid of what it might show!*⁵⁵

The CDC has also failed to address the science supporting a link between vaccines and autism.⁵⁶ For example, the CDC has not addressed a study which found a 300% increased rate of autism among newborns receiving the hepatitis B vaccine at birth compared to those that did not.⁵⁷ Nor a recent and first ever vaccinated vs. unvaccinated pilot study which found vaccinated

⁵¹ Ibid.

⁵² Studies of MMR and autism are also erroneous because of healthy user bias, which has been emphasized as a serious source of error in epidemiological vaccine safety studies by CDC scientists. <https://doi.org/10.1093/oxfordjournals.aje.a116479>

⁵³ <http://www.cbsnews.com/news/the-open-question-on-vaccines-and-autism/>

⁵⁴ Ibid.

⁵⁵ Ibid.

⁵⁶ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁵⁷ http://hisunim.org.il/images/documents/scientific_literature/Gallagher_Goodman_HepB_2010.pdf

children had a 420% increased rate of autism and that vaccinated preterm babies had an even higher rate of autism.⁵⁸ There is also a persuasive body of science supporting a clear connection between aluminum adjuvants in vaccines and autism which the CDC, despite numerous requests, has failed to directly or substantively address.⁵⁹ Letters from three aluminum adjuvant experts on this point are attached as Appendix C.

The critical need for HHS to properly engage in vaccine safety science regarding autism is made even more vital by the fact that vaccine makers are immune from liability for vaccine injury and vaccines are not safety-tested prior to licensure to assess whether they cause autism. Without proper long-term trials comparing those receiving the vaccine to an inert-placebo group, it is impossible to know prior to licensure whether these products cause autism. There are also no follow-up studies which compare vaccinated with unvaccinated individuals and hence no supportable basis to claim that vaccines do not cause any cases of autism. For the CDC to make this claim, it must demonstrate that a child receiving the entire vaccine schedule is at no greater risk of becoming autistic than a child that is unvaccinated. No such study has ever been done. The IOM Report referenced above has confirmed that the CDC cannot make this claim even for children receiving only the DTaP vaccine, let alone the entire vaccine schedule.

The 1986 Act expressly provides that you, as the Secretary, are to “develop and disseminate vaccine information materials for distribution by health care providers to the legal representatives of any child or to any other individual receiving a vaccine set forth in the Vaccine Injury Table.” (42 U.S.C. § 300aa-26(a).) This section further provides that:

The information in such materials shall be based on available data and information ... and shall include ... (1) a concise description of the benefits of the vaccine, (2) a concise description of the risks associated with the vaccine, (3) a statement of the availability of the National Vaccine Injury Compensation Program, and (4) such other relevant information as may be determined by the Secretary.

(42 U.S.C. § 300aa-26(c).) The VIS produced for every vaccine, including for DTaP, provides that other relevant information regarding the vaccine is available at the CDC website, www.cdc.gov.⁶⁰ The CDC website in turn claims that “Vaccines Do Not Cause Autism.”⁶¹ Since HHS has chosen to incorporate the CDC’s website into the VIS as a resource, the information on that website regarding the relevant vaccine must be “based on available data and information.” *Id.* But, based on available data and information, as highlighted by the IOM, HHS cannot validly claim that “Vaccines Do Not Cause Autism.” Hence:

⁵⁸ <http://www.oatext.com/pdf/ITS-3-186.pdf>; <http://www.oatext.com/pdf/ITS-3-187.pdf>

⁵⁹ <http://vaccine-safety.s3.amazonaws.com/WhitePaper-AlumAdjuvantAutism.pdf>

⁶⁰ <https://www.cdc.gov/vaccines/hcp/vis/current-vis.html>

⁶¹ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

- (9) Please confirm that HHS shall forthwith remove the claim that “Vaccines Do Not Cause Autism” from the CDC website, or alternatively, please identify the specific studies on which HHS bases its blanket claim that no vaccines cause autism?

VII. Refusal to Conduct Vaccinated Versus Unvaccinated Study

The only scientifically valid way to answer a large portion of the questions raised regarding vaccine safety would be a long-term, properly powered and controlled study comparing the rate of all adverse events between vaccinated children and completely unvaccinated children. This is the same type of study required by HHS for every drug pre-licensure. HHS has nonetheless refused to conduct any such study, even retrospectively.

The need for this study is highlighted by the results of a few recent limited vaccinated vs. unvaccinated studies.

Dr. Peter Aaby is renowned for studying and promoting vaccines in Africa with over 300 published studies.⁶² In 2017, he published a study finding children vaccinated with DTP were 10 times more likely to die in the first 6 months of life than the unvaccinated.⁶³ Dr. Aaby’s study therefore concluded that: “All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis.”⁶⁴ More disturbing is that children vaccinated with DTP were dying from causes never associated with this vaccine, such as respiratory infections, diarrhea, and malaria.⁶⁵ This indicated that while DTP reduced the incidence of diphtheria, tetanus, and pertussis, it increased susceptibility to other infections.⁶⁶

It is equally troubling that Dr. Aaby’s study was based on data that had been collecting dust for over 30 years⁶⁷ This begs the question: what other serious vaccine injuries are we missing because of neglect to conduct proper vaccine safety science.

A pilot study comparing 650 vaccinated and unvaccinated homeschooled children in the United States provides a glimpse of the potential scope of vaccine harm.⁶⁸ The study found that, compared to completely-unvaccinated children, fully-vaccinated children had an increased risk

⁶² <https://www.ncbi.nlm.nih.gov/pubmed/?term=PETER+AABY%5BAuthor+-+Full%5D>

⁶³ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/> Dr. Aaby’s study was more reliable than other vaccine safety studies because the subjects were accurately matched. An increasingly recognized problem in vaccine safety studies is that subjects are typically not well-matched. People with pre-existing health problems are reluctant to receive a vaccine, and are therefore unwittingly used as controls. When this happens, the control group is sicker than the vaccine-exposed group at the outset of the study. Studies with this problem give wrong results, and make the vaccine look much safer than it really is. Dr. Aaby’s study was one of the few specifically designed to avoid this error.

⁶⁴ Ibid.

⁶⁵ Ibid.

⁶⁶ Ibid.

⁶⁷ Ibid.

⁶⁸ <http://www.oatext.com/pdf/IJS-3-186.pdf>

of 390% for allergies, 420% for ADHD, 420% for autism, 290% for eczema, 520% for learning disabilities, and 370% for any neuro-developmental delay.⁶⁹ Fully-vaccinated pre-term infants had an increased risk of 1,450% for a neurodevelopmental disorder, which includes a learning disability, ADHD or autism, compared to completely unvaccinated preterm infants.⁷⁰

Another recent study compared children receiving the flu shot with those receiving a saline injection in a prospective randomized double-blind study.⁷¹ Both groups had the same rate of influenza but the group receiving the flu shot had a 440% increased rate of non-influenza infection.⁷² Like the DTP study, the flu vaccine increased susceptibility to other infections.

A properly sized vaccinated versus unvaccinated study is necessary and possible. As stated by the IOM in 2013: “It is possible to make this comparison through analyses of patient information contained in large databases such as VSD.”⁷³ Senior CDC Scientist, Dr. Thompson similarly stated this type of study can and “needs to be done” but that the CDC is “not doing what they should be doing because they’re afraid to look for things that might be associated.”⁷⁴ When vaccine makers are generating over \$33 billion in vaccine revenue annually and the CDC is spending over \$5 billion annually to promote and purchase vaccines, there is no justification for not performing this study.⁷⁵

The 1986 Act expressly provides that you, as the Secretary, “shall promote the development of childhood vaccines that result in fewer and less adverse reactions” and “shall make or assure improvements in ... the ... labeling, warning, ... and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.” (42 U.S.C. § 300aa-27(a)(2).) Since comparing children receiving the vaccines recommended by the CDC with those that have not received any vaccines is the only scientifically valid way to assess the safety of the CDC’s vaccine schedule:

(10) Please advise whether HHS intends to forthwith conduct adequately powered and controlled prospective as well as retrospective studies comparing total health outcomes of

⁶⁹ Ibid.

⁷⁰ <http://www.oatext.com/pdf/ITS-3-187.pdf>

⁷¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/>

⁷² Ibid. See also http://vaccine-safety.s3.amazonaws.com/CDC_FOIA_Response_UnpublishedStudy.pdf (The CDC in 2001 apparently conducted a narrow vaccinated versus unvaccinated study comparing children receiving the Hepatitis B vaccine during the first month of life versus those who did not. The results of this study were never released by the CDC, and an abstract of the study was only recently obtained under a FOIA request. Children vaccinated with Hepatitis B vaccine in the first month of life, compared to children receiving no vaccines in the first month of life, had an increased risk of 829% for ADHD, 762% for autism, 638% for ADD, 565% for tics, 498% for sleep disorders, and 206% for speech delays. Note that while the abstract discusses comparing thimerosal exposure, since the only vaccine recommended by one month of age was Hepatitis B, and since only thimerosal containing Hepatitis B vaccine was available at the time of this study, this study appears to have primarily compared children receiving Hepatitis B with children that did not receive this vaccine.)

⁷³ <https://www.nap.edu/read/13563/chapter/2#13>

⁷⁴ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

⁷⁵ <https://www.hhs.gov/sites/default/files/fy2017-budget-in-brief.pdf>; <https://www.bccresearch.com/market-research/pharmaceuticals/vaccine-technologies-markets-report-phm014f.html>

fully/partially vaccinated children with completely unvaccinated children?

VIII. Reducing Conflicts of Interest at HHS

The 1986 Act created a system in which vaccines are licensed, recommended, encouraged, subsidized, and defended by HHS. The 1986 Act's scheme thus places HHS in charge of two competing duties. On one hand, HHS is responsible for vaccine safety. On the other hand, HHS is required to promote vaccine uptake and defend against any claim they cause any harm.

Regrettably, it appears that HHS has chosen to focus almost entirely on its vaccine promotion and defense function to such a degree that it has essentially abandoned its vaccine safety function. To restore balance, HHS must take serious steps to create an "ethics firewall" between these competing functions. HHS also must take action with regard to its vaccine committee members and employees that have conflicts with vaccine makers.

HHS Licenses & Recommends Vaccines. With regard to the FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC), which effectively decides whether to license a vaccine, in 2000 the U.S. House Committee on Government Reform (the **Committee**) "determined that conflict of interest rules employed by the FDA and the CDC have been weak, enforcement has been lax, and committee members with substantial ties to pharmaceutical companies have been given waivers to participate in committee proceedings."⁷⁶ The Committee concluded of the VRBPAC: "The overwhelming majority of members, both voting members and consultants, have substantial ties to the pharmaceutical industry."⁷⁷

With regard to the CDC's Advisory Committee on Immunization Practices (ACIP), which effectively decides whether to universally recommend a pediatric vaccine, the Committee found that ACIP members routinely fail to disclose conflicts with vaccine makers and when conflicts are disclosed "[t]he CDC grants blanket waivers to the ACIP members each year that allow them to deliberate on any subject, regardless of their conflicts."⁷⁸ The Committee drew focus on the vaccine most recently approved by the ACIP and found extensive and troubling conflicts of interest for most the ACIP members voting to recommend its universal use for children.⁷⁹ The Committee was further concerned that "ACIP liaison representatives have numerous ties to

⁷⁶ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf> (For instance, "3 out of 5 FDA advisory committee [VRBPAC] members who voted to approve the rotavirus vaccine in December 1997 [then the most recently approved vaccine by the VRBPAC] had significant financial ties to pharmaceutical companies that were developing different versions of the vaccine.")

⁷⁷ Ibid.

⁷⁸ Ibid.

⁷⁹ Ibid. (The Committee's findings were that: (1) The chairman served on Merck's Immunization Advisory Board; (2) another member, who shared the patent on a rotavirus vaccine, had a \$350,000 grant from Merck to develop the vaccine, and was a consultant for Merck; (3) another member was under contract with the Merck Vaccine Division, a principal investigator for SmithKline and received funds from various vaccine makers; (4) another member received a salary and other payments from Merck; (5) another member participated in vaccine studies with Merck, Wyeth, and SmithKline; and (6) another member received grants from Merck and SmithKline.)

vaccine manufacturers” but act like voting members of ACIP.⁸⁰ The Committee further took issue with the extensive conflicts of interests of members of ACIP’s working groups which convene behind closed doors and whose recommendations are typically rubber stamped by the ACIP.⁸¹ The Committee concluded that ACIP reflected “a system where government officials make crucial decisions affecting American children without the advice and consent of the governed.”⁸²

Despite the concerns the Committee expressed in its 2000 report, not much changed. A December 2009 report by the HHS Office of Inspector General found that the “CDC had a systemic lack of oversight of the ethics program for SGEs [a.k.a. **committee members**]”.⁸³ For example, “Most of the experts who served on advisory panels in 2007 to evaluate vaccines for flu and cervical cancer had potential conflicts that were never resolved.”⁸⁴

In fact, the Inspector General found that the “CDC certified [conflict disclosure forms] with at least one omission in 2007 for 97 percent ... of SGEs,” “58 percent ... of SGEs had at least one potential conflict of interest that CDC did not identify,” and when the CDC identified a conflict, it improperly granted broad waivers despite being castigated for this improper practice in 2000.⁸⁵ Even worse, “32 percent ... of SGEs ... had at least one potential conflict of interest that CDC identified but did not resolve” and 13 percent of SGEs were allowed to participate in committee meetings without even having a conflict disclosure form on file.⁸⁶

As the system is set up, an ACIP vote to recommend a vaccine, grants a vaccine manufacturer a liability-free market of 78 million American children, who are legally compelled to receive the vaccine, and billions of taxpayer dollars guaranteeing payment. In such a system, an ACIP vote must be completely insulated from any influence by the vaccine manufacturer. Instead, the opposite appears to be the norm.

HHS Promotes Vaccines. Moreover, while the CDC states on its website -- not less than 130 times -- that “CDC does not accept commercial support,” this is simply not true.⁸⁷ For example, the British Medical Journal reported in 2015 that: “Despite the agency’s disclaimer, the CDC does receive millions of dollars in industry gifts and funding, both directly and indirectly, and several recent CDC actions and recommendations have raised questions about the science it cites, the clinical guidelines it promotes, and the money it is taking.”⁸⁸ As another example, pharmaceutical companies and other private entities, through the “CDC Foundation,” can create and fund programs at the CDC (over half a billion dollars’ worth to-date), endow positions at the

⁸⁰ Ibid.

⁸¹ Ibid.

⁸² Ibid.

⁸³ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf>

⁸⁴ <http://www.nytimes.com/2009/12/18/health/policy/18cdc.html>

⁸⁵ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf> (Splicing down this 58% of unidentified conflicts, 40% involved employment or grants, 13% involved equity ownership, and 5% involved consulting.)

⁸⁶ Ibid.

⁸⁷ <https://search.cdc.gov/search?query=%22cdc+does+not+accept+commercial+support%22&utf8=%E2%9C%93&affiliate=cdc-main>

⁸⁸ <http://www.bmj.com/content/350/bmj.h2362>

CDC, and even place individuals to work at the CDC, paid through “private funding.” (42 U.S.C.A. § 280e-11(h)(1), (2).)

Worse, the promotion track for CDC management extends into vaccine makers. The most prominent example is former CDC Director Dr. Julie Gerberding, who headed the agency from 2002 through 2009. Dr. Gerberding oversaw several controversial studies regarding vaccines produced by Merck, which sought to silence those calling for an increase in the safety profile of those vaccines. When she left the CDC she was rewarded with the position of President of Merck Vaccines in 2010 with a reported \$2.5 million annual salary and lucrative stock options.⁸⁹

HHS Defends Vaccines. After HHS licenses, effectively mandates, and promotes a vaccine to 78 million American children with very limited safety data, this very same government agency is mandated to defend against any claim that the vaccine caused harm.

There is no other for-profit product where the very department responsible for regulating that product is statutorily required to promote its uptake and simultaneously defend against any claim it causes harm.

The Vaccine Injury Compensation Program (**VICP**) is effectively the only legal recourse in America to obtain compensation for a pediatric vaccine injury. (42 U.S.C. § 300aa-10 *et seq.*)⁹⁰ The injured must litigate against HHS and the DOJ in a quasi-judicial process filed under seal where the injured child effectively cannot obtain documents from or depose vaccine makers to prove how the vaccine caused injury. (§ 300aa-12.) DOJ and HHS have the government’s vast resources, while the injured child must secure a private attorney. (§ 300aa-15.) Moreover, the injured child’s damages are limited to \$250,000 for death and pain and suffering. (*Id.*)

Worst of all, the injured child must almost always prove “causation” – the biological mechanism by which the vaccine injured the child.⁹¹ Requiring an injured child to prove causation adds insult to injury because had HHS conducted the vaccine safety science it demands as proof in the VICP before licensing a vaccine, the child’s injury may have been avoided altogether.

This truly is the epitome of injustice: requiring a child receiving a compulsory pharmaceutical product to medically prove to HHS how the vaccine caused his or her injury, where the science to understand vaccine injuries is not being done by the government department, HHS, tasked with this job.⁹² As confirmed by the IOM, HHS has not conducted the basic science needed to even determine whether commonly claimed vaccine injuries are caused by vaccines.⁹³ It has failed to conduct even one properly sized study comparing vaccinated to

⁸⁹ <https://www.sec.gov/cgi-bin/own-disp?action=getowner&CIK=0001628884>

⁹⁰ See also *Bruesewitz v. Wyeth LLC*, 562 U.S. 223 (2011)

⁹¹ <http://www.gao.gov/assets/670/667136.pdf>

⁹² See Sections II, III, IV, V, VI, and VII above.

⁹³ See Section IV above.

unvaccinated children, despite all the resources at its disposal.⁹⁴ It is no wonder a single injured child's claim faces a high likelihood of failure in the VICP.

Many parents, doctors and scientists, as well as politicians, are legitimately concerned about the process whereby vaccines are licensed, recommended, promoted and defended by the same department. This is not because of any conspiracy, or belief an insidious intent. Rather, this system eliminates the incentive, and in fact creates a disincentive for HHS and vaccine makers, to conduct research to uncover long term chronic conditions, including the immune and neurological system disorders, which can result from the current vaccine schedule.

The 1986 Act expressly provides that you, as the Secretary, have at least equal and arguably greater responsibility for vaccine safety than for vaccine promotion. (42 U.S.C. §§ 300aa-2, 300aa-27.) In accordance with this statutory responsibility:

(11) Please advise if you will:

- a. **prohibit conflict waivers for members of HHS's vaccine committees (ACIP, VRBPAC, NVAC & ACCV)?**
- b. **prohibit HHS vaccine committee members or HHS employees with duties involving vaccines from accepting any compensation from a vaccine maker for five years?**
- c. **require that vaccine safety advocates comprise half of HHS's vaccine committees?**
- d. **allocate toward vaccine safety an amount at least equal to 50% of HHS's budget for promoting/purchasing vaccines?**
- e. **support the creation of a vaccine safety department independent of HHS?**
- f. **support the repeal of the 1986 Act to the extent it grants immunity to pharmaceutical companies for injuries caused by their vaccine products?**

IX. Conclusion

HHS can do better. With hundreds of vaccines in the pipeline it must do better. Children susceptible to vaccine injury are as deserving of protection as any other child. Avoiding injury to these children is not only a moral and ethical duty, but will in fact strengthen the vaccine program. Every parent that does not witness their child suffer a serious reaction after vaccination, such as a seizure or paralysis, is another parent that will not add their voice to the growing chorus of parents opposed to HHS's vaccine program due to safety concerns.

⁹⁴ See Section VII above.

Unless HHS performs its vital statutory obligations regarding vaccine safety, and until a frank conversation is possible regarding vaccine safety, children susceptible to vaccine injury will not be protected from such injuries. Nor will children injured by vaccines be able to access the services they need. We can do far better in protecting and serving children who are susceptible or succumb to serious injuries from vaccination. The first step in avoiding these harms and helping children already harmed is admitting there are deficiencies and working diligently to improve vaccine safety.

We respectfully request your attention to the important concerns outlined above and hope you agree that addressing these concerns is in everyone's best interest. These, in fact, reflect nothing more than what Congress already explicitly recognized when passing the 1986 Act: vaccines can and do cause serious injury and HHS needs to work diligently to identify and reduce these harms. If you would like to meet and discuss the foregoing, we would welcome that opportunity and hope to work cooperatively to address these issues.

If that is not possible, Congress, as a final resort to assure vaccine safety, authorized a "civil action ... against the Secretary where there is alleged a failure of the Secretary to perform any act or duty under" the 1986 Act. (42 U.S.C. § 300aa-31(a).) We are prepared to authorize such an action and this letter constitutes the notice required by 42 U.S.C. § 300aa-31(b). It is, however, our hope that the vaccine safety issues identified herein can be resolved cooperatively, with all interested parties working together toward the common goal of vaccine safety entrusted to HHS under the 1986 Act.

Very truly yours,

A handwritten signature in black ink, appearing to read 'Del Bigtree', written in a cursive style.

Del Bigtree

cc: See Appendix A.

Enclosures: Appendices A to C.

Appendix A

A Voice For Choice
A Voice For Choice Advocacy
Christina Hildebrand, President
530 Showers Drive, Suite 7404
Mountain View, CA 94040

Alliance For Natural Health
Gretchen DuBeau, President
3525 Piedmont Road NE B6-310
Atlanta, GA 30305

Arizona Coalition Against Mandated
Vaccines
Kelsey Davis, President
Gilbert, AZ 85212

Autism Action Network
John Gilmore, President
550 East Chester Street
Long Beach, NY 11561

Autism Giving Tree
Christina Stafford, M.Ed., BCBA, LBS,
President
660 'W' Street
King of Prussia, PA 19406

AutismOne
Ed Arranga, President
1816 West Houston Avenue
Fullerton, CA 92833

The Canary Party
Jennifer Larson, President
6533 Flying Cloud Drive, Suite 1200
Eden Prairie, MN 55344

Colorado Coalition for Vaccine Choice
Fran Sincere, President
125 S. Zephyr
Lakewood, CO 80226

DAIR Foundation
Dawn Loughborough, President
10200 US HWY 290 West
Austin, TX 78736

Elizabeth Birt Center for Autism Law and
Advocacy
Kim Mack Rosenberg, President
200 Cabrini Boulevard, Suite 66
New York, NY 10033

Enriched Parenting
Rebecca Fleischman, President
1208 Avenue M, Suite 2323
Brooklyn, NY 11230

Focus for Health Foundation
Shannon Mulvihill, R.N., Executive Director
776 Mountain Boulevard, Suite 202
Watchung, NJ 07069

Georgia Coalition for Vaccine Choice
Sandi Marcus, Founder/CEO
P.O. Box 45
Silver Creek, GA 30173

Health Choice
Mark Blaxil, President
6533 Flying Cloud Drive, Suite 1200
Eden Prairie, MN 55344

Health Choice Massachusetts
Candice Edwards, President
P.O. Box 175
Manchaug, MA 01526

Indiana for Medical Freedom
Melissa Sura, President
5424 Grapevine Drive
Indianapolis, IN 46235

Health Choice Maryland
Emily Tarsell, President
1501 Sulgrave Avenue, Suite 208
Baltimore, MD 21209

Informed Choice Washington
Jena Dalpez, President
14106 93rd Avenue NE
Kirkland, WA 98034

Health Choice Connecticut
Dr. Elissa Diamond Fields, President
P.O. Box 29
Roxbury, CT 06783

Kentucky Vaccine Rights Coalition
Jennifer Benge & Ashley Kennedy, Co-
Presidents
899 Corinth Road
Corbin, KY 40701

Health Freedom Florida
Dr. Ryan Fenn & MacKenzie Fraser, Co-
Presidents
153 Ivernia Loop
Tallahassee, FL 32312

Know The Vax
Angela Gallagher, President
4553 Aldrich Avenue North
Minneapolis, MN 55412

Health Freedom Idaho
Miste Gardner Karlfeldt, President
1045 S Ancona Ave Ste 140
Eagle, ID 83616

Learn the Risk
Brandy Vaughan, President
3463 State Street, Suite 182
Santa Barbara, CA 93105

Healthcare Freedom Hawaii
Jessica McCormick &
Natasha Sky, Co-Directors
Mililani, HI 96789

Louisiana Parents for Vaccine Rights
Melisha Dooley &
Sunny Dixon, Co-Directors
413 Toby Lane
Metairie, LA 70003

Illinois Coalition for Informed Consent
Jen Suter &
Danielle Olson, Co-Directors
Jacksonville, IL 62650

Maine Coalition for Vaccine Choice
Ginger Taylor, Director
11 High Street
Brunswick, ME 04011

March Against Monsanto
Tami Canal, President
7878 South 1960 East
South Weber, UT 84405

Moms Across America
Zen Honeycutt, President
24000 Alicia Parkway, Suite 17-236
Mission Viejo, CA 92691

Michigan for Vaccine Choice
Suzanne M. Waltman, President
22615 Francis Street
St. Clair Shores, MI 48082

Montanans For Medical Freedom
Edna Kent, Director
PO Box 1443
Florence, MT 59833

Minnesota Natural Health Coalition
Lee Beaty, President
1043 Grand Ave, Suite 317
St. Paul MN 55105

My Kids, My Choice
Rita Palma, President
2 Purdy Avenue
Baypoint, NY 11705

Minnesota Natural Health Legal Reform
Project
Leo Cashman, President
1043 Grand Ave, Suite 317
St. Paul, MN 55105

National Health Freedom Action
Jerri Johnson, President
PMB 218, 2136 Ford Parkway
St. Paul, MN 55116

Minnesota Vaccine Freedom Coalition
Angela Gallagher, President
4553 Aldrich Avenue North
Minneapolis, MN 55412

National Health Freedom Coalition
Roseanne Lindsay, President
PMB 218, 2136 Ford Parkway
St. Paul, MN 55116

Mississippi Parents for Vaccine Rights
MaryJo Perry, President
P.O. Box 141
Pelahatchie, MS 39145

New York Alliance for Vaccine Rights
Aimee Villella McBride & Maria Gavriel,
Co-Presidents
550 East Chester Street
Long Beach, NY 11561

Missouri Parents Against Vaccines
Janessa Baake & Kendal Bourne, Co-
Presidents
323 N. Fox Ridge Drive, Suite 204
Raymore, MO 64083

Ohio Advocates for Medical Freedom
Robert M. Wise, President
P.O. Box 1236
Hartville, OH 44632

Oklahomans for Vaccine and Health Choice
Liza Greve, President
P.O. Box 721356
Norman, OK 73070

Spectrum Revolution
Catharine Layton, President
357 S. Earlham Street
Orange, CA 92869

Organic Consumers Association
Ronnie Cummins, CEO
6771 South Silver Hill Dr.
Finland, MN 55603

Tennessee Coalition for Vaccine Choice
Kristen Odom-Holland, President
P.O. Box 4508
Chattanooga, TN 37405

Parents United 4 Kids
Stefanie Fetzer & Shawna Lambert, Co-
Presidents
2925 Bonanza
San Clemente, CA 92673

Vaccine Injury Awareness League
Michelle Ford, President
10866 Washington Blvd, Suite 65
Culver City, CA 90232

People Advocating Vaccine Education, Inc.
Lisa Jillani, CEO
P.O. Box 690712
Charlotte, NC 28227

Vaccine Safety Council Minnesota
Patti Carroll, President
6533 Flying Cloud Drive, Suite 1200
Eden Prairie, MN 55344

Physicians for Informed Consent
Dr. Shira Miller, Executive Director
13749 Riverside Drive
Sherman Oaks, CA 91423

Vermont Coalition for Vaccine Choice
Jennifer Stella, President
P.O. Box 74
Waitsfield, VT 05673

Rogue Recovery
Tyler Dahm, President
3221 West 96th Avenue
Westminster, CO 80031

Virginians for Health Freedom
Deborah Hommer, President
P.O. Box 2015
Spotsylvania, VA 22553

South Carolina Health Coalition
Jennifer Black & Rebekah Watson, Co-
Presidents
1754 Woodruff Road, Suite 112
Greenville, SC 29607

West Virginians for Health Freedom
Dr. Chanda Adkins, Director
108 Yorktown Court
Beckley, WV 25801

Weston A. Price Foundation
Sally Fallon Morell, President
PMB 106-380, 4200 Wisconsin Avenue NW
Washington, D.C., 20016

World Mercury Project
Robert F. Kennedy, Jr., Chairman
1227 North Peachtree Parkway, Suite 202
Peachtree City, GA 3026

Appendix B

Adverse Effects of Vaccines

Evidence and Causality

Committee to Review Adverse Effects of Vaccines
Board on Population Health and Public Health Practice
Kathleen Stratton, Andrew Ford, Erin Rusch, and Ellen Wright Clayton,
Editors

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

Weight of Epidemiologic Evidence

The epidemiologic evidence is insufficient or absent to assess an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and ataxia.

Mechanistic Evidence

The committee identified one publication reporting the development of ataxia after the administration of DTaP vaccine. Kubota and Takahashi (2008) did not provide evidence of causality beyond a temporal relationship of 2 days between vaccine administration and development of cerebellar symptoms leading to a diagnosis of acute cerebellar ataxia. The publication did not contribute to the weight of mechanistic evidence.

Weight of Mechanistic Evidence

The committee assesses the mechanistic evidence regarding an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and ataxia as lacking.

Causality Conclusion

Conclusion 10.5: The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and ataxia.

AUTISM**Epidemiologic Evidence**

The committee reviewed one study to evaluate the risk of autism after the administration of DTaP vaccine. This one study (Geier and Geier, 2004) was not considered in the weight of epidemiologic evidence because it provided data from a passive surveillance system and lacked an unvaccinated comparison population.

Weight of Epidemiologic Evidence

The epidemiologic evidence is insufficient or absent to assess an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.

Mechanistic Evidence

The committee did not identify literature reporting clinical, diagnostic, or experimental evidence of autism after the administration of vaccines containing diphtheria toxoid, tetanus toxoid, and acellular pertussis antigens alone or in combination.

Weight of Mechanistic Evidence

The committee assesses the mechanistic evidence regarding an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism as lacking.

Causality Conclusion

Conclusion 10.6: The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.

ACUTE DISSEMINATED ENCEPHALOMYELITIS

Epidemiologic Evidence

No studies were identified in the literature for the committee to evaluate the risk of acute disseminated encephalomyelitis (ADEM) after the administration of vaccines containing diphtheria toxoid, tetanus toxoid, or acellular pertussis antigens alone or in combination.

Weight of Epidemiologic Evidence

The epidemiologic evidence is insufficient or absent to assess an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccines and ADEM.

Mechanistic Evidence

The committee identified five publications of ADEM developing after the administration of vaccines containing diphtheria toxoid and tetanus toxoid antigens alone or in combination. Four publications did not provide evidence beyond temporality, one of which was deemed too short based on the possible mechanisms involved (Abdul-Ghaffar and Achar, 1994; Bolukbasi and Ozmenoglu, 1999; Hamidon and Raymond, 2003; Rogalewski et al., 2007). In addition, Rogalewski et al. (2007) reported the administration of vaccines against hepatitis B, hepatitis A, and poliovirus in

Appendix C



June 24, 2017

United States Department of Health & Human Services
National Institutes of Health
Food & Drug Administration
Centers for Disease Control & Prevention
200 Independence Avenue, S.W.
Washington, D.C. 20201

Phone 604 875 4111 Local 68375
Fax 604 875 4376
www.neuraldynamicsubc.ca

Re: *Aluminum Adjuvants*

Dear Directors:

I am writing to you in regard to aluminum adjuvants in vaccines. This subject is one my laboratory works on intensively and therefore one where I feel that I have some expertise. In particular, we have studied the impact of aluminum adjuvants in animal models of neurological disease, including autism spectrum disorder (ASD). Our relevant studies on the general topic of aluminum neurotoxicity in general and specifically in regard to adjuvants are cited below.

These studies and the broader existing literature regarding aluminum toxicity, lead almost invariably to the conclusion that aluminum in any chemical form is always neurotoxic when administered to humans. Further, I am convinced that aluminum adjuvants in vaccines may contribute to neurological disorders across the lifespan. In adults, such adjuvant may induce macrophagic myofasciitis, a disease with neuropathological aspects. In children, there is growing evidence that aluminum adjuvants may disrupt developmental processes in the central nervous system and therefore contribute to ASD in susceptible children.

Despite the foregoing, the safety of aluminum adjuvants in vaccines has not been properly studied in humans even though, pursuant to the recommended vaccine schedule published by the Centers for Disease Control (CDC), a baby may be injected with up to 3,675 micrograms of aluminum adjuvant by six months of age.

In regard to the above, it is my belief that the CDC's claim on its website that "Vaccines Do Not Cause Autism" is wholly unsupported. Given this, I remain convinced that much more research on the role of aluminum adjuvant in vaccines and neurological disorders, including ASD, is warranted and should be a research priority for the NIH and other funding bodies.

Yours sincerely,

Christopher A. Shaw, Ph.D
Professor
Dept. of Ophthalmology and Visual Sciences
University of British Columbia
828 W. 10th Ave.
Vancouver, British Columbia
Canada, V5Z1M9
Tel: 604-875-4111 (ext. 68373)
Email: cashawlab@gmail.com



Relevant Publications (Shaw Laboratory)

1. Crepeaux G, Eidi H, David MO, Baba-Amer Y, Tzavara E, giros B, authier FJ, Exley C, Shaw CA, Cadusseau J, Gherardi RK. Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective dose neurotoxicity. *Toxicology*. 375:48-57. (2016).
2. Crepeaux G, Eidi H, David M-O, Tzavara E, Giros B, Exley C, Curmi PA, Shaw CA, Gherardi RK, Cadusseau J. Highly delayed systemic translocation of aluminium-based adjuvant in CD1 mice following intramuscular injections. *J. Inorg. Biochem.* 152:199-205. (2015).
3. Shaw CA, Li D, Tomljenovic L. Are there negative CNS impacts of aluminum adjuvants in vaccines and immunotherapy? *Immunotherapy*. 6 (10):1055-1071. (2014).
4. Shaw CA, Seneff S, Kette SD, Tomljenovic L, Oller Jr JW, Davidson RM. Aluminum-induced entropy in biological systems: Implications for neurological disease. *J Toxicology*. Volume 2014, Article ID 491316. (2014).
5. Shaw CA, Kette SD, Davidson RM, Seneff S. Aluminum's role in CNS-immune system interactions leading to neurological disorders. *Immunome Res*. 9:1.
6. Shaw CA, Marler TE. Aluminum and the human diet revisited. In: *Communicative & Integrative Biology; Landes Bioscience*. 6:e26369. (2013).
7. Shaw CA, Tomljenovic L. Aluminum in the central nervous system (CNS): toxicity in humans and animals, vaccine adjuvants, and autoimmunity. *Immunol Res*. (2013).
8. Shaw CA, Li Y, Tomljenovic L. Administration of aluminum to neonatal mice in vaccine in vaccine-relevant amounts is associated with adverse long term neurological outcomes. *J Inorg Chem*. (2013).
9. Tomljenovic L, Shaw CA. Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations. *Lupus*. 21:223-230. (2012).
10. Tomljenovic L and Shaw CA. Editorial, Special Issue: The Biochemistry/Toxicity of Aluminum. *Current Inorganic Chemistry*. 2(1): 1-2. (2012).
11. Tomljenovic L and Shaw CA. Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? *J Inorg Biochem*. 105(11):1489-99. (2011).
12. Tomljenovic L and Shaw CA. Aluminum vaccine adjuvants: Are they safe? *Current Medicinal Chemistry*. 18:2630 – 2637. (2011).
13. Shaw CA and Petrik MS. Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. *J Inorganic Biochem*. 103 (11): 1555-62. (2009).
14. Petrik MS, Wong MC, Tabata RC, Garry RF, and Shaw CA. Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice. *J Neuromolecular Medicine*. 9: 83-100. (2007).

June 15, 2017

United States Department of Health & Human Services
National Institutes of Health
Food & Drug Administration
Centers for Disease Control & Prevention
200 Independence Avenue, S.W.
Washington, D.C. 20201

Re: *Aluminum Adjuvants*

Dear Directors:

I am an expert in the field of aluminum adjuvants toxicity in humans and animal models. I have been working in this field since the initial description of the Al vaccine-induced macrophagic myofasciitis in 1998. Since that time I have written 40 peer-reviewed scientific publications and one book on this subject.

I strongly support the contention that aluminum adjuvants in vaccines may have a role in the etiology of autism spectrum disorder (ASD). My view is founded on a significant and burgeoning body of peer-reviewed scientific evidence which makes the link between ASD and exposure to aluminum through vaccinations and other sources. Examples of this literature from my own group are detailed below and I urge the HHS to take them into consideration in forming any future opinion on the safety of aluminum adjuvants in vaccines.

The Center for Disease Control's claim on its website that "Vaccines Do Not Cause Autism" is unsupported with respect to aluminum adjuvants and this claim stifles the important research to determine the safety of aluminum adjuvants used in vaccines. As an expert in the field of aluminum adjuvants and aluminum toxicity I solemnly declare that more research on the role of aluminum adjuvant in vaccines and neurological disorders, including ASD, is essential and urgently required.

Yours very sincerely



Romain K. Gherardi
Professor, Neuromuscular Pathology Expert Centre
University Paris-Est, INSERM U955-E10,
Henri Mondor hospital, Créteil France
Contact at the hospital
Tel 00 (33) 1 49812746
romain.gherardi@hmn.aphp.fr

UMR U955 INSERM / UPEC

Team 10

« Biology of the neuromuscular system »

Fred Relaix, director

FrançoisJérôme Authier, co-director

Romain Gherardi, former director

Tél. +33 (0)1 49 81 27 42

Fax. +33 (0)1 49 81 27 33

romain.gherardi@inserm.fr

Selection of significant publications from our group in the field

Gherardi R. Toxic Story: deux ou trois vérités embarrassantes sur les adjuvants des vaccins. **Actes Sud** (publisher), Paris, 2016, 250 pages

Crépeaux G, Eidi H, David MO, Baba-Amer Y, Tzavara E, Giros B, Authier FJ, Exley C, Shaw CA, Cadusseau J, Gherardi RK. Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective low dose neurotoxicity. **Toxicology**. 2017 Jan 15;375:48-57.

Masson JD, Crépeaux G, Authier FJ, Exley C, Gherardi RK. [Critical analysis of reference studies on aluminium-based adjuvants toxicokinetics]. **Ann Pharm Fr**. 2017 May 30. pii: S0003-4509(17)30033-0.

Van Der Gucht A, Aoun Sebaiti M, Guedj E, Aouizerate J, Yara S, Gherardi RK, Evangelista E, Chalaye J, Cottureau AS, Verger A, Bachoud-Levi AC, Abulizi M, Itti E, Authier FJ. Brain (18)F-FDG PET Metabolic Abnormalities in Patients with Long-Lasting Macrophagic Myofasciitis. **J Nucl Med**. 2017 Mar;58(3):492-498.

Crépeaux G, Eidi H, David MO, Tzavara E, Giros B, Exley C, Curmi PA, Shaw CA, Gherardi RK, Cadusseau J. Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections. **J Inorg Biochem**. 2015 Nov;152:199-205.

Eidi H, David MO, Crépeaux G, Henry L, Joshi V, Berger MH, Sennour M, Cadusseau J, Gherardi RK, Curmi PA. Fluorescent nanodiamonds as a relevant tag for the assessment of alum adjuvant particle biodisposition. **BMC Med**. 2015 Jun 17;13:144.

Van Der Gucht A, Aoun Sebaiti M, Itti E, Aouizerate J, Evangelista E, Chalaye J, Gherardi RK, Ragunathan-Thangarajah N, Bachoud-Levi AC, Authier FJ. Neuropsychological Correlates of Brain Perfusion SPECT in Patients with Macrophagic Myofasciitis. **PLoS One**. 2015 Jun 1;10(6):e0128353.

Khan Z, Combadière C, Authier FJ, Itier V, Lux F, Exley C, Mahrouf-Yorgov M, Decroux X, Moretto P, Tillement O, Gherardi RK, Cadusseau J. Slow CCL2-dependent translocation of biopersistent particles from muscle to brain. **BMC Med**. 2013 Apr 4;11:99.

Couette M, Boisse MF, Maison P, Brugieres P, Cesaro P, Chevalier X, Gherardi RK, Bachoud-Levi AC, Authier FJ. Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction. **J Inorg Biochem**. 2009 Nov;103(11):1571-8.

Authier FJ, Sauvat S, Christov C, Chariot P, Raisbeck G, Poron MF, Yiou F, Gherardi R. Al(OH)₃-adjuvanted vaccine-induced macrophagic myofasciitis in rats is influenced by the genetic background. **Neuromuscul Disord**. 2006 May;16(5):347-52.

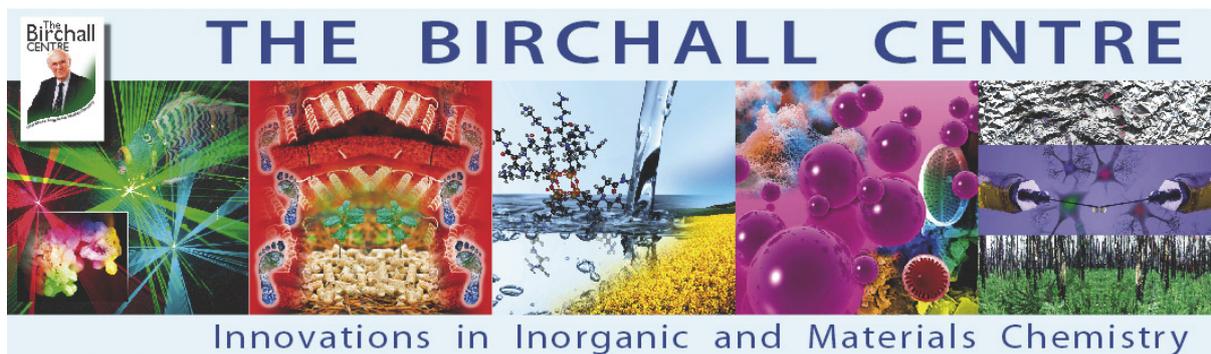
Authier FJ, Sauvat S, Champey J, Drogou I, Coquet M, Gherardi RK. Chronic fatigue syndrome in patients with macrophagic myofasciitis. **Arthritis Rheum**. 2003 Feb;48(2):569-70.

Gherardi RK. [Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome]. **Rev Neurol (Paris)**. 2003 Feb;159(2):162-4. Review. French.

Authier FJ, Cherin P, Creange A, Bonnotte B, Ferrer X, Abdelmoumni A, Ranoux D, Pelletier J, Figarella-Branger D, Granel B, Maisonobe T, Coquet M, Degos JD, Gherardi RK. Central nervous system disease in patients with macrophagic myofasciitis. **Brain**. 2001 May;124(Pt 5):974-83.

Gherardi RK, Coquet M, Cherin P, Belec L, Moretto P, Dreyfus PA, Pellissier JF, Chariot P, Authier FJ. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. **Brain**. 2001 Sep;124(Pt 9):1821-31.

Gherardi RK, Coquet M, Chérin P, Authier FJ, Laforêt P, Bélec L, Figarella-Branger D, Mussini JM, Pellissier JF, Fardeau M. Macrophagic myofasciitis: an emerging entity. **Lancet**. 1998 Aug 1;352(9125):347-52.



Tel: 01782 734080

Fax: 01782 712378

e-mail: c.exley@keele.ac.uk

<http://www.keele.ac.uk/aluminium>

June 15, 2017

United States Department of Health & Human Services
National Institutes of Health
Food & Drug Administration
Centers for Disease Control & Prevention
200 Independence Avenue, S.W.
Washington, D.C. 20201

Re: Aluminum Adjuvants

Dear Directors:

I am an expert in the field of aluminum adjuvants and aluminum toxicity. I have been working in this field for more than 30 years during which time I have written in excess of 150 peer-reviewed scientific publications on this subject.

I strongly support the contention that aluminum adjuvants in vaccines may have a role in the etiology of autism spectrum disorder (ASD). My view is founded on a significant and burgeoning body of peer-reviewed scientific evidence which makes the link between ASD and exposure to aluminum through vaccinations and other sources. Examples of this literature from my own group are detailed below and I urge the HHS to take them into consideration in forming any future opinion on the safety of aluminum adjuvants in vaccines.

The Center for Disease Control's claim on its website that "Vaccines Do Not Cause Autism" is unsupported with respect to aluminum adjuvants and this claim stifles the important research to determine the safety of aluminum adjuvants used in vaccines. As an expert in the field of aluminum adjuvants and aluminum toxicity I solemnly declare that more research on the role of aluminum adjuvant in vaccines and neurological disorders, including ASD, is essential and urgently required.

Telephone number +44 (01782) 584211

Fax +44 (01782) 712378

Yours faithfully



Christopher Exley PhD
Professor in Bioinorganic Chemistry

Honorary Professor, University of the Highlands and Islands

List of Recent, Relevant and Significant Publications From Our Group

Exley C, Siesjö P & Eriksson H (2010) The immunobiology of aluminium adjuvants: how do they really work? *Trends in Immunology* 31, 103-109.

Exley C and House E (2011) Aluminium in the human brain. *Monatshefte für Chemie - Chemical Monthly* 142, 357-363.

House E, Esiri M, Forster G, Ince PG and Exley C (2012) Aluminium, iron and copper in human brain tissues donated to the medical research council's cognitive function and ageing study. *Metallomics* 4, 56-65.

Exley C (2011) Aluminium-based adjuvants should not be used as placebos in clinical trials. *Vaccine* 29, 9289.

Exley C (2012) When an aluminium adjuvant is not an aluminium adjuvant used in human vaccination programmes. *Vaccine* 30, 2042.

Exley C (2012) The coordination chemistry of aluminium in neurodegenerative disease. *Coordination Chemistry Reviews* 256, 2142-2146.

Exley C, House E, Polwart A and Esiri MM (2012) Brain burdens of aluminium, iron and copper and their relationships with amyloid beta pathology in 60 human brains. *Journal of Alzheimer's Disease* 31, 725-730.

Davenward S, Bentham P, Wright J, Crome P, Job, D, Polwart A and Exley C (2013) Silicon-rich mineral water as a non-invasive test of the 'aluminium hypothesis' in Alzheimer's disease. *Journal of Alzheimer's Disease* 33, 423-430.

Khan Z, Combadière C, Authier FJ, Itier V, Lux F, Exley C, Mahrouf-Yorgov M, Decrouy X, Moretto P, Tillement O, Gherardi RK, and Cadusseau J (2013) Slow CCL2-dependent translocation of biopersistent particles from muscle to brain. *BMC Medicine* 11:99.

Exley C (2013) Human exposure to aluminium. *Environmental Science:Processes and Impacts* 15, 1807-1816.

Ohlsson L, Exley C, Darabi A, Sandén E, Siesjö P and Eriksson H (2013) Aluminium based adjuvants and their effects on mitochondria and lysosomes of phagocytosing cells. *Journal of Inorganic Biochemistry* 128, 229-236.

Exley C (2014) Aluminium adjuvants and adverse events in sub-cutaneous allergy immunotherapy. *Allergy, Asthma and Clinical Immunology* 10, 4.

Exley C and Vickers T (2014) Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report. *Journal of Medical Case Reports* 8,41.

Exley C (2014) What is the risk of aluminium as a neurotoxin? *Expert Review of Neurotherapeutics* 14, 589-591.

Mold M, Eriksson H, Siesjö P, Darabi A, Shardlow E and Exley C (2014) Unequivocal identification of intracellular aluminium adjuvant in a monocytic THP-1 cell line. *Scientific Reports* 4, 6287.

Telephone number +44 (01782) 584211
Fax +44 (01782) 712378

Exley C (2014) Why industry propaganda and political interference cannot disguise the inevitable role played by human exposure to aluminium in neurodegenerative diseases, including Alzheimer's disease. *Frontiers in Neurology* 5:212. doi: 10.3389/fneur.2014.00212.

Crépeaux G, Eidi H, David M-O, Tzavara E, Giros B, Exley C, Curmi PA, Shaw CA, Gherardi RK and Cadusseau J (2015) Highly delayed systemic translocation of aluminium-based adjuvant in CD1 mice following intramuscular injections. *Journal of Inorganic Biochemistry* 152, 199-205.

Exley C (2016) The toxicity of aluminium in humans. *Morphologie* 100, 51-55.

Mirza A, King A, Troakes C and Exley C (2016) The identification of aluminium in human brain tissue using lumogallion and fluorescence microscopy. *Journal of Alzheimer's Disease* 54, 1333-1338.

Mold M, Shardlow E and Exley C (2016) Insight into the cellular fate and toxicity of aluminium adjuvants used in clinically-approved human vaccinations. *Scientific Reports* 6:31578.

Mirza A, King A, Troakes C and Exley C (2017) Aluminium in brain tissue in familial Alzheimer's disease. *Journal of Trace Elements in Medicine and Biology* 40, 30-36.

Shardlow E, Mold M and Exley C (2017) From stock bottle to vaccine: Elucidating the particle size distributions of aluminium adjuvants using dynamic light scattering. *Frontiers in Chemistry* 4, 48.

Exley C (2017) Aluminium should now be considered a primary aetiological factor in Alzheimer's disease. *Journal of Alzheimer's Disease Reports* 1, 23-25.

Telephone number +44 (01782) 584211
Fax +44 (01782) 712378

Keele University, Staffordshire, ST5 5BG United Kingdom
Telephone number +44 (01782) 621111 <http://www.keele.ac.uk>

Page 1 of 3
USDC SDNY
DOCUMENT
ELECTRONICALLY FILED
DOC #:
DATE FILED: 07/09/2018

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK**

INFORMED CONSENT ACTION NETWORK,

Plaintiff,

-against-

UNITED STATES DEPARTMENT OF HEALTH
AND HUMAN SERVICES

Defendant.

STIPULATION

18-cv-03215 (JMF)

WHEREAS, 42 U.S.C. § 300aa-27, entitled "Mandate for safer childhood vaccines,"

provides as follows:

(a) General rule

In the administration of this part and other pertinent laws under the jurisdiction of the Secretary [of the Department of Health and Human Services], the Secretary shall—

(1) promote the development of childhood vaccines that result in fewer and less serious adverse reactions than those vaccines on the market on December 22, 1987, and promote the refinement of such vaccines, and

(2) make or assure improvements in, and otherwise use the authorities of the Secretary with respect to, the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, and recall of reactogenic lots or batches, of vaccines, and research on vaccines, in order to reduce the risks of adverse reactions to vaccines.

...

(c) Report

Within 2 years after December 22, 1987, and periodically thereafter, the Secretary shall prepare and transmit to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report describing the

actions taken pursuant to subsection (a) of this section during the preceding 2-year period.

WHEREAS, on August 25, 2017, Informed Consent Action Network (“ICAN”) submitted a Freedom of Information Act request (the “FOIA Request”) to the Department of Health and Human Services (“HHS” or the “Department”), which was assigned control number 2017-01119-FOIA-OS, that sought the following records:

Any and all reports transmitted to the Committee on Energy and Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate by the Secretary of HHS pursuant to 42 U.S.C. §300aa-27(c).

WHEREAS, on April 12, 2018, ICAN filed a Complaint for Declaratory and Injunctive Relief in the United States District Court, Southern District of New York against HHS seeking records, if any, responsive to the FOIA Request;

WHEREAS, the HHS Immediate Office of the Secretary (“IOS”) maintains the official correspondence file of the Secretary of HHS, including reports to Congress by the Secretary of HHS, and therefore those files were most likely to contain records responsive to the FOIA Request;

WHEREAS, on June 27, 2018, HHS sent ICAN the following response to the FOIA Request:

The [Department]’s searches for records did not locate any records responsive to your request. The Department of Health and Human Services (HHS) Immediate Office of the Secretary (IOS) conducted a thorough search of its document tracking systems. The Department also conducted a comprehensive review of all relevant indexes of HHS Secretarial Correspondence records maintained at Federal Records Centers that remain in the custody of HHS. These searches did not locate records responsive to your request, or indications that records responsive to your request and in the custody of HHS are located at Federal Records Centers.

WHEREAS, ICAN believes the foregoing response from HHS now resolves all claims asserted in this action;

IT IS HEREBY STIPULATED AND AGREED, by and between the parties by and through their respective counsel:

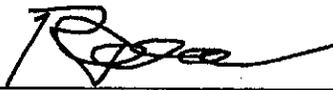
1. That the above-captioned action is voluntarily dismissed, with prejudice, pursuant to Federal Rule of Civil Procedure 41(a)(1)(A)(ii), each side to bear its own costs, attorney fees, and expenses; and

2. That this stipulation may be signed in counterparts, and that electronic (PDF) signatures may be deemed originals for all purposes.

Dated: July 6, 2018
New York, New York

KENNEDY & MODONNA LLP
Attorney for Plaintiff

By:


Robert F. Kennedy, Jr.
48 Dewitt Mills Road
Hurley, NY 12443
(845) 481-2622

Dated: July 6, 2018
New York, New York

GEOFFREY S. BERMAN
*United States Attorney
Attorney for Defendant*

By:


ANTHONY J. SUN
Assistant United States Attorney
86 Chambers Street, Third Floor
New York, New York 10007
(212) 637-2810
anthony.sun@usdoj.gov

SO ORDERED:


HON. JESSE M. FURMAN, U.S.D.J.

Dated: New York, New York
July 6, 2018

Any pending motions are moot. All conferences are vacated. The Clerk of Court is directed to close the case.



Informed Consent Action Network

For Immediate Release: July 13, 2018

US District Court Judge signs order granting Plaintiff, Informed Consent Action Network (ICAN) and counsel, Robert F. Kennedy, Jr., the relief sought in a lawsuit against the US Department of Health and Human Services (HHS)

On Monday, June 9th, the United States District Court for the Southern District of New York signed an order granting Plaintiff, the nonprofit Informed Consent Action Network (ICAN), the relief it sought against the Defendant, the United States Department of Health and Human Services, HHS. ICAN was represented by Robert F. Kennedy, Jr.

In May 2017, ICAN Founder, Del Bigtree, Robert F. Kennedy, Jr., and a handful of other individuals concerned about vaccine safety were selected by the White House to participate in a seminal meeting with the Counselor to the Secretary of HHS, the heads of the National Institute of Health, NIH, the Center for Disease Control, CDC, and Food and the Drug Administration, FDA. Del Bigtree and Robert F. Kennedy, Jr. suspected that HHS was not fulfilling its critical vaccine safety obligations as required by Congress in The National Childhood Vaccine Injury Act of 1986.

The 1986 Act granted unprecedented, economic immunity to pharmaceutical companies for injuries caused by their products and eviscerated economic incentive for them to manufacture safe vaccine products or improve the safety of existing vaccine products. Congress therefore charged the Secretary of HHS with the explicit responsibility to assure vaccine safety.

Hence, since 1986, HHS has had the primary and virtually sole responsibility to make and assure improvements in the licensing, manufacturing, adverse reaction reporting, research, safety and efficacy testing of vaccines in order to reduce the risk of adverse vaccine reactions. In order to assure HHS meets its vaccine safety obligations, Congress required as part of the 1986 Act that the Secretary of HHS submit a biennial reports to Congress detailing the improvements in vaccine safety made by HHS in the preceding two years.

ICAN therefore filed a Freedom of Information Act, FOIA, request on August 25th, 2017 to HHS seeking copies of the biennial reports that HHS was supposed to submit to Congress, starting in 1988, detailing the improvements it made every two years to vaccine safety. HHS stonewalled ICAN for eight months refusing to provide any substantive response to this request.



ICAN was therefore forced to file a lawsuit to force HHS to either provide copies of its biennial vaccine safety reports to Congress or admit it never filed these reports. The result of the lawsuit is that HHS had to finally and shockingly admit that it never, not even once, submitted a single biennial report to Congress detailing the improvements in vaccine safety. This speaks volumes to the seriousness by which vaccine safety is treated at HHS and heightens the concern that HHS doesn't have a clue as to the actual safety profile of the now 29 doses, and growing, of vaccines given by one year of age.

In contrast, HHS takes the other portions of the 1986 Act, which require promoting vaccine uptake, very seriously, spending billions annually and generating a steady stream of reports on how to improve vaccine uptake. Regrettably, HHS has chosen to focus on its obligation to increase vaccine uptake and defend against any claim vaccines cause harm in the National Injury Vaccine Compensation Program (aka, the Vaccine Court) to such a degree that it has abandoned its vaccine safety responsibilities. If HHS is not, as confirmed in Court this week, even fulfilling the simple task of filing a biennial report on vaccine safety improvements, there is little hope that HHS is actually tackling the much harder job of actually improving vaccine safety.

For additional information or interviews please contact:
Catharine Layton, COO, ICAN



IMPORTANT NOTICE TO PARENTS

School Health Requirements



State of Hawai'i Department of Health
Immunization Branch

What does Hawai'i State Law require for school attendance?

Hawai'i State Law requires all students to meet physical examination, immunization, and tuberculosis clearance requirements before they may attend any public or private school in the State.

School means any:

- Group child care home
- Day nursery
- Day care center
- Child care center
- Head Start program
- Preschool
- Kindergarten
- Elementary school
- Middle school
- Secondary school

Are exemptions allowed?

Children may be exempt from immunization requirements for medical or religious reasons, if the appropriate documentation is presented to the school. Religious exemption forms may be completed at the school that your child will attend. Medical exemptions must be obtained from your child's doctor. No other exemptions are allowed by the State.

What are the health requirements?

Physical Examination:

- Must be completed within one year before first entrance into school in Hawai'i (preschool or kindergarten through 12th grade)
- Must be performed by a U.S. licensed MD, DO, ND, APRN or PA.

Immunizations:

Immunizations required for school attendance:

- **DTaP/DTP/Td** (diphtheria/tetanus/pertussis)
- **Polio**
- **MMR** (measles, mumps, rubella)
- **Hepatitis B**
- **Hib** (*Haemophilus influenzae* type b) (for preschool attendance)
- **Varicella** (chickenpox)

All immunizations must meet minimum age and interval requirements between vaccine doses.

Tuberculosis (TB) Clearance:

For information regarding TB clearance requirements for school attendance, call (808) 832-5731 or visit health.hawaii.gov/tb.

What is required by the first day of school?

By the first day of school, all students entering school in Hawai'i for the first time must have:

1. A completed health record form to prove that a physical examination was performed within one year before school entrance, and that all immunization requirements have been met.

OR

A signed statement or appointment slip from your doctor to prove that your child has a physical examination scheduled and/or has begun the vaccination series and is waiting for the next dose in the series.

AND

2. A completed TB clearance form.

Students who have not completed the above requirements by the first day of school will not be allowed to attend school until these requirements are met.



Where do I get the “Student’s Health Record” form?

You can get a copy of the “Student’s Health Record” (Form 14) from the school where your child will be enrolled or from your child’s doctor.

What if my child is transferring from another state or territory of the U.S.?

You will need to show proof that the health requirements have been met prior to school entry. The school will accept out-of-state records that meet the State of Hawai‘i requirements for physical examination, immunizations, and tuberculosis clearance.

Which immunizations are required and how many doses does my child need?

Immunizations are required for all students entering preschool, kindergarten, and seventh grade, and for those students entering school in Hawai‘i for the first time, regardless of age.

See the table below for the specific vaccines and number of doses required.

Number of Vaccine Doses Required by Grade/Age							
Grade/Age		DTaPa ^a	Polio ^b	Hib ^c	MMR ^d	Hep B ^e	Varicella ^f
Preschool	3 months	1	1	1		1	
	5 months	2	2	1		2	
	7 months	3	2	1		2	
	16 months	3	2	1	1	2	
	19 months	4	3	1	1	3	1
K-12		5	4		2	3	1 or 2 ^g
7 ^h					2	3	1 or 2 ^g

- ^a DTaP=Diphtheria-Tetanus-Acellular Pertussis. DTP may be used in place of DTaP.
- ^b Polio=IPV (Inactivated poliovirus vaccine) or OPV (Oral poliovirus vaccine).
- ^c Hib=*Haemophilus influenzae* type b. More than one dose of Hib is recommended for children less than 15 months of age to be fully protected against *Haemophilus influenzae* type b. For preschool entry, children must have received at least one dose of Hib on or after 12 months of age.
- ^d MMR=Measles-Mumps-Rubella. The first dose of MMR vaccine must have been received on or after 12 months of age. For grades kindergarten through 12, two doses of measles vaccine are required, with at least one of the two doses being MMR vaccine.
- ^e Hep B=Hepatitis B vaccine. Required for all students born after December 31, 1992 and for 7th grade attendance.
- ^f Effective July 1, 2002. A documented history of varicella (chickenpox), signed by a U.S. licensed MD, DO, ND, APRN or PA, may be substituted for the varicella vaccine requirement. The first dose of varicella vaccine must have been received on or after 12 months of age.
- ^g Two (2) doses of varicella vaccine are required if the first dose is administered on or after the 13th birthday.
- ^h In addition to meeting the kindergarten through grade 12 immunization requirements upon first school attendance listed in the table above, all students must show evidence of having received these immunizations prior to 7th grade attendance. Students who received these vaccines in infancy or childhood do not need to receive them again, as long as all doses meet the minimum age and interval requirements.

Questions?

Hawai‘i Department of Health Immunization Branch at (808) 586-8332 or at 1(800) 933-4832.

Hawai‘i Department of Health Tuberculosis Control Branch at (808) 832-5731.

Public Health Nursing (Neighbor Islands)

Hawai‘i (808) 974-6025

Maui (808) 984-8260

Kaua‘i (808) 241-3387

Moloka‘i (808) 553-7880

Lana‘i (808) 565-7114



Nondiscrimination in Services. We provide access to our activities without regard to race, color, national origin (including language), age, sex, religion, or disability. Write or call the Hawai‘i Department of Health Immunization Branch or our departmental Affirmative Action Officer at P.O. Box 3378, Honolulu, Hawai‘i 96801-3378 or at (808) 586-4616 (voice/tty) within 180 days of a problem.



Contents lists available at SciVerse ScienceDirect

Journal of Inorganic Biochemistry

journal homepage: www.elsevier.com/locate/jinorgbio

Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?

Lucija Tomljenovic^{a,*}, Christopher A. Shaw^{a,b}^a *Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia, 828 W. 10th Ave, Vancouver, BC, Canada V5Z 1L8*^b *Departments of Ophthalmology and Visual Sciences and Experimental Medicine and the Graduate Program in Neuroscience, University of British Columbia, Vancouver, British Columbia, 828 W. 10th Ave, Vancouver, BC, Canada V5Z 1L8*

ARTICLE INFO

Article history:

Received 22 April 2011

Received in revised form 13 August 2011

Accepted 14 August 2011

Available online xxx

Keywords:

Aluminum

Adjuvants

Autism

Vaccines

Brain inflammation

Autoimmunity

ABSTRACT

Autism spectrum disorders (ASD) are serious multisystem developmental disorders and an urgent global public health concern. Dysfunctional immunity and impaired brain function are core deficits in ASD. Aluminum (Al), the most commonly used vaccine adjuvant, is a demonstrated neurotoxin and a strong immune stimulator. Hence, adjuvant Al has the potential to induce neuroimmune disorders. When assessing adjuvant toxicity in children, two key points ought to be considered: (i) children should not be viewed as “small adults” as their unique physiology makes them much more vulnerable to toxic insults; and (ii) if exposure to Al from only few vaccines can lead to cognitive impairment and autoimmunity in adults, is it unreasonable to question whether the current pediatric schedules, often containing 18 Al adjuvanted vaccines, are safe for children? By applying Hill's criteria for establishing causality between exposure and outcome we investigated whether exposure to Al from vaccines could be contributing to the rise in ASD prevalence in the Western world. Our results show that: (i) children from countries with the highest ASD prevalence appear to have the highest exposure to Al from vaccines; (ii) the increase in exposure to Al adjuvants significantly correlates with the increase in ASD prevalence in the United States observed over the last two decades (Pearson $r = 0.92$, $p < 0.0001$); and (iii) a significant correlation exists between the amounts of Al administered to preschool children and the current prevalence of ASD in seven Western countries, particularly at 3–4 months of age (Pearson $r = 0.89$ – 0.94 , $p = 0.0018$ – 0.0248). The application of the Hill's criteria to these data indicates that the correlation between Al in vaccines and ASD may be causal. Because children represent a fraction of the population most at risk for complications following exposure to Al, a more rigorous evaluation of Al adjuvant safety seems warranted.

© 2011 Published by Elsevier Inc.

1. Introduction

During prenatal and early postnatal development the brain is extremely vulnerable to neurotoxic insults [1,2]. Not only are these highly sensitive periods of rapid brain development in general [3] but also, the blood brain barrier (BBB) is incomplete and thus more permeable to toxic substances during this time [2,4,5]. Further, immune challenges during early development, including those induced by vaccines, can lead to permanent detrimental alterations of nervous and immune system function [6–9]. Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants, or repeated stimulation of the immune system by the same antigen, can overcome genetic resistance to autoimmunity in animals [10,11]. Moreover, in adult humans, a variety of conditions encompassed by the ‘Autoimmune/inflammatory syndrome induced by adjuvants’ (‘ASIA’) have been linked to exposure to aluminum (Al) vaccine adjuvants (Table 1).

In many Western countries, by the time children are 4–6 years old they will have received a total of 23–32 vaccines [12,13], many with Al adjuvants, through routine pediatric vaccine schedules [2,14]. According to the United States Food and Drug Administration (US FDA), safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic [15]. However, if a few vaccines administered to adults can result in adverse outcomes, such as the ‘ASIA’ syndrome, should we *assume* without experimental evidence that the current pediatric schedules are safe for children?

Analysis of the relevant data shows that the number of vaccinations recommended prior to school entry increased from 10 in the late 1970s to 32 in 2010 (18 of which contain Al adjuvants) [16]. During this same period, the prevalence of autism spectrum disorders (ASD) in the US also increased by as much as 2000% [16]. While such observations have been of interest, the potential role of vaccines in the development of ASD remains controversial. ASD are characterized by marked impairments in social skills, verbal communication, behavior and cognitive dysfunction [17–19]. Although the etiology of 90% of ASD is still largely unknown [20,21], a growing body of scientific literature shows that neuroimmune abnormalities (i.e., abnormal cytokine profiles, neuroinflammation and presence of autoantibodies

* Corresponding author. Tel.: +1 604 875 4111 68375; fax: +1 604 875 4376.

E-mail address: lucijat77@gmail.com (L. Tomljenovic).

Table 1
Shared aspects between autoimmune/inflammatory diseases (including ASD) and immunostimulatory properties of Al vaccine adjuvants.

Condition	Al adjuvant			
Disease	Th shift	Inflammatory profile	Inflammatory profile	General immunostimulatory effects
Arthritis ^{*,†}	Excessive Th1 [129,155]	Increased IL-1, IL-6, IL-12, TNF- α , IFN- γ , MIP-1 α and oxidative stress [129,134,155]	Increases cytokines (IL-1 α , IL-1 β , IL-4, IL-5, IL-6, IL-18, TNF- α), chemokines (IL-8, MCP-1, MIP-1 α , MIP-1 β), ROS, and nitric oxide (NO) [34,40,138,155,170,171]	Stimulates recruitment of monocytes, macrophages and granulocytes to the injection site Induces differentiation of monocytes to antigen presenting cells (APCs) Activates APCs
Autoimmune thyroid disease Inflammatory bowel disease (IBD)/Crohn's disease (CD) Type 1 diabetes mellitus [*]		Increased NLRP3 inflammasome complex signaling and NLRP3-dependent over-production of IL-1 β , IL-6, IL-18, TNF- α and reactive oxygen species (ROS) in MS, EAE, Type 1 diabetes mellitus [164–166] and animal models of IBD [167]	Activates the NLRP3 inflammasome complex and NLRP3-dependent cytokines [33,34,172]	Promotes antigen uptake and processing by APCs and enhances antigen-specific T-cell responses Increases the expression of MHC class I and II and associated co-stimulatory molecules on peripheral blood monocytes
Multiple sclerosis (MS) ^{*,†} and experimental autoimmune encephalomyelitis (EAE)				Activates the complement cascade
Systemic lupus erythematosus (SLE) [*]	Excessive Th2 [129,156]	Increased IL-10, IL-18, IL-6, IFN- γ , TNF- α [129,156,168,169]		
Macrophagic myofasciitis (MMF) and chronic fatigue syndrome (CFS) ^{*,†}	Excessive Th2 [53,157,158]	Increased IL-4, IL-6, B-cell hyperlymphocytosis, infiltration of large periodic acid-schiff (PAS)-positive macrophages, and CD8+ T lymphocytes in the absence of conspicuous muscle fibre damage [53,95,158]		Generally stimulates Th2 responses but can also induce a Th1 shift and activate cytotoxic T lymphocytes (CTLs) in the presence of other Th1 stimulators (i.e., lipopolysaccharide (LPS), CpG, recombinant influenza protein antigen [138,173–175]) Activates astrocytes and microglia [29,97,139]
Gulf War Syndrome (GWS) ^{*,†}	Mixed Th1/Th2 [159]	Increased IFN- γ , IL-5, IL-6 [159]		
Autism spectrum disorders (ASD) [*]	Both Th1 and Th2 shifts have been reported [17,160–163]	Increased IL-1 β , IL-4, IL-5, IL-6, TNF- α , IL-8, MCP-1, MIP-1 β , MHC class II Increased astrocyte and microglia reactivity [17,20]		

* Linked to Al-adjuvanted vaccines [32,101,102,176,177].

† Specifically recognized as 'Autoimmune/inflammatory syndrome induced by adjuvants' ('ASIA') [32].

against brain proteins) occur in ASD patients and may contribute to the diversity of ASD phenotypes [17,20,22–26].

Al is an experimentally demonstrated neurotoxin whose ability to impact the human nervous system has been known for decades [16,27–29]. For example, exposure to as little as 20 $\mu\text{g}/\text{kg}$ bw of Al for period >10 days is sufficient to cause neurodevelopmental delays in preterm infants [28]. In addition, Al is a potent stimulator of the immune system, indeed this is the very reason why it is used as an adjuvant [14,30–34]. Given this, it remains surprising that in spite of over 80 years of use, the safety of Al adjuvants appears to rest largely on assumptions rather than experimental evidence. For example, nothing is known about the toxicology and pharmacokinetics of Al compounds in infants and children [35]. In addition, the mechanisms by which Al adjuvants interact with the immune system remain far from clear [34,35]. In this regard it is notable that many vaccine trials usually use an Al adjuvant containing "placebo" or another vaccine as the "control" group [36–38], rather than a saline control. This study design has not allowed a direct comparison of the efficacy and safety of the antigen alone versus the Al adjuvant. In spite of these gaps in our knowledge about Al adjuvants, the use of Al in vaccines is widely regarded as safe and effective [35,39,40].

Should it be of concern that so little is known about the potential deleterious impacts of Al adjuvants on the developing central nervous system (CNS) given that worldwide, preschool children are regularly exposed to significant amounts of Al from vaccines [2,14]? To address this question, we investigated pediatric vaccine schedules from various Western countries in order to gain a better understanding of potential Al exposure from vaccines in children. Our results, supported by the Hill's criteria for establishing causality between exposure and outcome [41], suggest that a causal relationship may exist between

the amount of Al administered to preschool children at various ages through vaccination and the rising prevalence of ASD.

2. Methods

2.1. Collection of ASD prevalence data

We analyzed the currently available data from the US Department of Education Annual Reports to Congress for ASD prevalence for the period from 1991 to 2008 [42–52] in the 6–21 year-old age cohort and correlated it with the estimated total Al exposure from pediatric vaccines (given to preschool children before the age of 6 years), sourced from the US Centers for Disease Control and Prevention (CDC [12]). In addition, we obtained the most recent available data for ASD prevalence and vaccination schedules from several other countries including the United Kingdom (UK), Australia, Canada, Sweden, Finland and Iceland (see below for source references). Using the latter data, we carried out a correlation analysis to investigate the potential association between ASD prevalence and estimated vaccine-derived Al exposures in preschool children at various ages. We also correlated ASD prevalence with the number of Al-adjuvanted vaccines given to preschool children according to the relevant vaccination schedules from each country.

2.2. Calculations of Al exposure from vaccines

For the purpose of correlating ASD prevalence to Al exposure, for each country studied, we calculated the cumulative amount of Al administered from all vaccines that children receive during the specified age period (i.e., the cumulative exposure to Al at 4 months of age

includes Al from vaccines given at 2, 3 and 4 months). This rationale for using cumulative amounts of adjuvant Al in our analysis is also supported by the following observation: Al has been shown to persist at the site of injection from several months up to 8–10 years following vaccination in patients suffering from macrophagic myofasciitis, an autoimmune disease linked to Al vaccine adjuvants [53]. The number and types of pediatric vaccines were sourced from the US CDC [12], UK Department of Health [13], Public Health Agency of Canada [54], Australian Government Department of Health and Aging [55], Swedish Institute for Infectious Disease Control [56], KTL (Finish) National Public Health Institute [57] and Iceland's A Surveillance Community Network for Vaccine Preventable Infectious Diseases [58]. The Al content used was derived from an article by Offit and Jew [39] and manufacturer's product monographs (Table 2 [59–62]). Because the Al content varies between different brands of certain vaccines (Table 2), for each vaccination appointment, three possible exposures were calculated: (i) maximum, assuming exposure to vaccines with the highest Al content (i.e., 625 µg Al for DTaP from Infanrix and 225 µg Al for Hib from PedVax), (ii) mean, using the calculated mean Al-content values of different brands of DTaP and Hib (i.e., 375 µg for DTaP = (625 + 330 + 170)/3) and 112.5 µg for Hib = (0 + 225)/2); and (iii) minimum, assuming exposure to vaccines with the lowest Al content (i.e., 170 µg Al for DTaP from Tripedia and 0 µg Al for Hib from Hiberix). All three of these exposures were then correlated with the relevant ASD prevalence data. With regard to vaccine uptake in the US, we acknowledge that there are likely to be variations between individual states due to differences in adopting CDC's recommendations. However, since the ASD prevalence data pertain to the US population as a whole, rather than individual states, we felt that our overall evaluation with regard to US vaccine uptake was the most appropriate measure to use.

2.3. Exclusion/inclusion criteria

Certain vaccines were excluded from our calculations since the addition of these to childhood vaccination schedules occurred after the relevant ASD prevalence study periods. For example, in Australia, pneumococcal vaccine (PCV) was introduced in 2003 [63] and the ASD prevalence study conducted in 2005 provided data for 6–12 year-old children (1993–1999 birth cohort [64]); in Canada PCV and meningococcal serogroup C (MenC) were introduced in 2005 [65] and 2001 [66] respectively, and the ASD prevalence report was for 1987–1998 birth cohort [67]; in Sweden PCV was introduced in 2009 [68], ASD prevalence report was for 1977–1994 birth cohort [69]; in Finland, rotavirus vaccine was introduced in 2009 [70] and the ASD prevalence report was for 1979–1994 birth cohort [71]; in Iceland, meningococcal serogroup C (MenC) was introduced in 2002 [58] with ASD prevalence report for the 1984–1993 birth cohort [72]. ASD prevalence data for the US and UK were from Kogan et al. [73] and Baron-Cohen et al. [74], respectively. We included hepatitis B (HB) vaccine in our calculations for the UK vaccination schedule (at 0, 1 and 2 months [75]) since there was no rationale for excluding high risk groups from our analysis (as these groups have not been

specifically excluded from the UK ASD prevalence data [74]). We excluded HB vaccine from our calculations for Sweden and Finland since in these countries HB vaccination for high risk groups was introduced in the mid 1990s [76,77], after the relevant ASD prevalence study periods.

2.4. Statistical methods

The correlation analysis was carried out using GraphPad Prism statistical software to derive Pearson correlation coefficients (Pearson r ; due to normal data distribution) between vaccine-derived Al exposures, Al-containing vaccine number and ASD prevalence. To control for type I errors due to multiple tests, we used permutation resampling-based multiplicity adjustment for p-values according to Westfall and Young [78] to determine whether the correlation between ASD prevalence in seven Western countries and Al exposure at various ages was statistically significant. Unlike the more popular Bonferroni-Holm method, Westfall and Young accounts for correlations between variables (e.g., age of exposure) and was hence a more appropriate choice. The Westfall and Young p-value adjustment was carried out in R software. The correlation was considered statistically significant at $p < 0.05$. In all of the data provided for Al vaccine exposure, Al is expressed either as total, or per kg of body weight. The latter was calculated by dividing total Al exposure with age-specific weight, sourced from Haddad and Krishnan [79].

2.5. Hill's criteria

The Hill's criteria for causation include: (1) the strength of the association (as measured by appropriate statistical tests), (2) the consistency of the observed association (i.e., the association has been repeatedly observed by different persons and/or in different places, circumstances and times), (3) the specificity of the association (established when a single putative cause produces a specific effect), (4) the temporal relationship of the association (exposure precedes the outcomes), (5) the biological gradient or dose–response curve (an increasing amount of exposure increases the risk), (6) biological plausibility (causation is biologically plausible and agrees with a currently accepted understanding of pathological processes of the disease in question), (7) the coherence with the current knowledge (data should be congruent with generally known facts of the natural history and biology of the disease), (8) experimental or semi-experimental evidence and (9) analogy with similar evidence (i.e., different toxins may result in similar disease outcomes because they adversely affect the same underlying processes linked to a specific disease) [41]. In neuropsychiatry, four of Hill's nine criteria are considered critical to assess causality: the strength of the association (criterion 1), the consistency of the observed association (criterion 2), the biologic rationale (criterion 6) and the temporal relationship of the association (criterion 4) [80]. Obviously, if evidence exists for the remaining criteria, conclusions about causality would be further strengthened. Note also that the specificity criterion (3) is not considered necessary in neuropsychiatry [80] given that many neuropsychiatric disorders have multiple causal factors. ASD for example, are partly determined by genetic susceptibility factors and hence fit this category [17,18,20,21].

3. Results

3.1. Al exposure from vaccines in adults and children based on body weight

Table 3 shows the estimated amounts of Al administered through vaccination to preschool children in the US. At 2 months of age, US infants receive the highest amount of Al per body weight from vaccines (172.5 µg/kg bw, mean exposure) compared to other ages. Table 4 shows Al exposure from vaccines per kg of body weight in children from seven Western countries: the UK, US, Canada, Australia, Sweden, Finland and Iceland. Note that children from countries with the highest ASD prevalence (i.e., UK, US, Australia and Canada) appear to have a higher exposure to Al from vaccines than do children from Scandinavian

Table 2

Al-adjuvant content in licensed vaccines.

Al adjuvant	Vaccine	Trade name	Manufacturer	Amount (µg) per dose
Al hydroxide	DTaP	Infanrix	GlaxoSmithKline	625 [39]
	DTaP	Daptacel	Aventis Pasteur	330 [39]
	DTaP	Tripedia	Aventis Pasteur	170 [39]
	HA	Havrix	GlaxoSmithKline	250 [39]
	HB*	EngerixB	GlaxoSmithKline	250 [178]
	Hib	PedVax	Merck and Co	225 [39]
	Hib	Hiberix	GlaxoSmithKline	0 [62]
Al phosphate	Anthrax	Biothrax	Bioport Corp	600 [60]
	PCV	Prevnar	Wyeth	125 [39]
	MenC	Meningitec	Wyeth	125 [59]
Al sulfate	HB*	Recombivax	Merck and Co	250 [61]

* Pediatric dose = 250 µg, adult dose = 500 µg.

Table 3
Al administered from pediatric vaccines to children at different ages under the current US vaccination schedule [12] assuming mean exposure. Ages are expressed in months (mo).

Vaccine	Birth	2 mo	4 mo	6 mo	15 mo	24 mo	72 mo
HB	250	250		250			
DTaP*		375	375	375	375		375
Hib†		112.5	112.5	112.5	112.5		
PCV		125	125	125	125		
HA					250	250	
Total Al (µg)	250	862.5	612.5	862.5	862.5	250	375
Total Al (µg/kg bw)	73.5	172.5	107.5	113.5	78.4	19.8	19.3

* Mean value from three different brands of DTaP (Infanrix, Daptacel, Tripedia, see Table 2).

† Mean value from two different brands of Hib (PedVax and Hiberix, see Table 2).

countries where autism prevalence is lower. Table 5 shows a comparison between vaccine-derived Al exposures in adults and children. Due to their lower body weight, children attain a much higher Al exposure per kg of body weight than adults (73.5–172.5 µg/kg bw versus 7.1 µg/kg bw).

3.2. Correlation between ASD prevalence and vaccine-derived Al exposures in the US

Al exposure from vaccines in the US vaccination schedule from 1991 to 2008 shows a highly significant positive linear correlation with ASD prevalence at all three levels of exposure (Pearson $r = 0.92$, $p < 0.0001$), with 95% CI = 0.79–0.97 (Fig. 1; Table 6). In addition, we show in Table 7 that the number of Al-adjuvanted vaccines in the yearly vaccination schedules from 1991 to 2008 also yields a highly significant positive correlation with ASD prevalence (Pearson $r = 0.90$, $p < 0.0001$) with 95% CI = 0.76–0.96.

3.3. Correlation between ASD prevalence in the US, UK, Canada, Australia, Sweden, Finland and Iceland and Al exposure from pediatric vaccines

In Table 8 we show that the estimated cumulative vaccine-derived Al exposure yields a significant positive correlation with the current prevalence of ASD in seven Western countries at all three levels of exposure at 3–4 months of age. (Pearson $r = 0.89–0.94$, $p = 0.0018–0.0248$). ASD prevalence in these countries also significantly correlates with the number of Al-adjuvanted vaccines given at 3–18 months of age (Pearson $r = 0.89–0.94$, $p = 0.0018–0.0368$; Table 8).

Table 4
Estimated total Al exposure from vaccines (µg/kg bw) per vaccination schedule in various Western countries at different ages. Minimum to maximum range of exposure is given where applicable (where DTaP and Hib are scheduled). Age is expressed in months (mo).

	ASD prevalence/10,000	Birth	1 mo	2 mo	3 mo	4 mo	5 mo	6 mo
UK	157 [74]	73.5	62.5	109–245	55.7–184	73.7–193	0	0
US	110 [73]	73.5	0	109–245	0	51.8–171.1	0	71.7–161.2
Canada	65 [67]	73.5	0	84–220	0	73.7–193	0	22.4–111.8
Australia	62.5 [64]	73.5	0	84–220	0	73.7–193	0	55.3–144.7
Sweden	53.4 [69]	0	0	0	32.1–160.4	0	25.4–126.9	0
Iceland	12.4 [72]	0	0	0	32.1–160.4	0	25.4–126.9	0
Finland	12.2 [71]	0	0	0	32.1–160.4	0	25.4–126.9	0

Table 5
Comparison of Al exposure from vaccines in children and adults. An infant's vaccine-derived Al exposure of 73.5 µg Al/kg bw is equivalent to that from 10 HB vaccines given in a single day to a 70 kg adult ((73.5 µg Al/kg bw x 70 kg)/(HB dose (500 µg Al)) = 5147/500 = 10.3). The vaccine-derived Al exposure in a 2 month old receiving 172.5 µg Al/kg bw is equivalent to that from 24 HB vaccines given in a single day to a 70 kg adult ((172.5 µg Al/kg bw x 70 kg)/(HB vaccine dose (500 µg Al)) = 12075/500 = 24.2).

	An adult receiving a single HB vaccine (adult dose)	An infant receiving a single HB vaccine at birth (pediatric dose)	A 2 month old receiving the recommended set of injections (mean exposure)
Al (µg)	500	250	862.5
Bw (kg)	70	3.4	5
Total Al µg/kg bw	7.1	73.5	172.5

4. Discussion

4.1. Summary and implications of main findings

To the best of our knowledge, these results are the first to show that Al, a highly neurotoxic metal and the most commonly used vaccine adjuvant, may be a significant contributing factor to the rising prevalence of ASD in the Western world. In particular, we show here that the correlation between ASD prevalence and Al adjuvant exposure appears to be the highest at 3–4 months of age (Pearson $r = 0.89–0.94$, $p = 0.0018–0.0248$; Table 8). We also show that children from countries with the highest ASD prevalence appear to have a much higher exposure to Al from vaccines, particularly at 2 months of age (Table 4). In this respect, we note that several prominent milestones of brain development in humans coincide with these periods. These include the onset of synaptogenesis (birth), maximal growth velocity of the hippocampus (2–3 postnatal months) [3] and the onset of amygdala maturation (8 weeks postnatal age) [81]. In addition, the period between 2 and 4 months is also one of major developmental transition in many biobehavioural systems, including sleep, temperature regulation, respiration and brain wave patterns [82,83], all of which are regulated by the neuroendocrine network [84,85]. Many of these aspects of brain function are known to be impaired in autism (i.e., sleeping and brain wave patterns [86–88]).

According to the FDA, vaccines represent a special category of drugs as they are generally given to healthy individuals [15]. Further according to the FDA, “this places significant emphasis on their [vaccine] safety” [15]. While the FDA does set an upper limit for Al in vaccines at no more than 850 µg/dose [89], it is important to note that this amount was selected empirically from data showing that Al in such amounts enhanced the antigenicity of the vaccine, rather than from existing safety

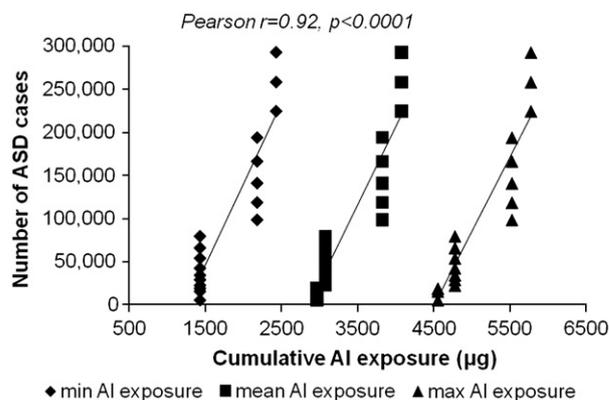


Fig. 1. Correlation between the number of children with ASD (6–21 years of age) and the estimated cumulative Al exposure (µg) from pediatric vaccines in the period from 1991 to 2008 (US data).

Table 6

Statistical analysis summary. Correlation between the number of children with ASD (6–21 years of age) and the estimated Al exposure (μg) from pediatric vaccines in the period from 1991 to 2008 (US data). Significant change is indicated by the asterisk (*).

	ASD prevalence and estimated yearly cumulative vaccine-derived Al exposures		
	Minimum	Mean	Maximum
Pearson r	0.92	0.92	0.92
95% CI	0.79–0.97	0.80–0.97	0.80 to 0.97
P value (two-tailed)	<0.0001	<0.0001	<0.0001
P value summary	*	*	*
Is the corr. significant? (p<0.05)	Yes	Yes	Yes
R ²	0.84	0.85	0.85

data or from the basis of toxicological considerations [89]. However, in preventative vaccination where a vaccine is administered to healthy individuals, a compromise in efficacy for additional margins of safety should not necessarily be viewed as an unreasonable expectation [30]. It is also of note that the FDA requires limits on Al in parenteral feeding solutions and requires warning labels about potential Al hazards, while setting no safety limits or issuing warnings for Al in vaccines [90].

The lack of an established safety margin for Al in vaccines may be concerning for numerous reasons: (i) Al is highly neurotoxic and can impair prenatal and postnatal brain development in humans and experimental animals [28,91]; (ii) a pilot study showed higher than normal Al levels in the hair, blood and/or urine of autistic children (according to the authors, the correlation between the severity of signs and symptoms and the behavioral pattern found in many patients appeared to be compatible with metabolism disturbances provoked by Al overload [92]); (iii) children are regularly exposed to much higher levels of Al adjuvants than adults (Table 5 [14]); (iv) practically nothing is known about the pharmacokinetics and toxicodynamics of Al adjuvants in children [35] and paradoxically, evaluation of pharmaco- and toxicokinetics is not required for vaccine licensing purposes [93]; (v) in adult humans, Al vaccine adjuvants have been linked to serious neurological impairments, chronic fatigue and autoimmunity (Table 1) [31,32,94–96]; (vi) injection of Al adjuvants at levels comparable to those that are administered to humans have been shown to cause motor neuron death, impairments in motor function and decrements in spatial memory capacity in young mice [29,97]; and (vii) intraperitoneal injection of Al adsorbed vaccines in 4-week old mice was followed by a transient peak in brain Al levels on the second and third days after injection [98]. The latter experiment demonstrated that even a fully developed BBB does not impede Al access to the brain tissue. Altogether, the above observations raise plausible concerns about the overall safety of the use of Al adjuvants in childhood vaccines.

An additional, concern is that for certain Al-adjuvanted vaccines the risks/benefit ratio appears to preclude widespread use. The HB vaccine, the only vaccine recommended to newborn babies, is one such example, since: (i) the HB virus is primarily transmitted through sexual contact with an infected person or by injections with contaminated material and, hence, poses no risk to infants unless the mother is a carrier [99];

Table 7

Statistical analysis summary. Correlation between the number of children with ASD (6–21 years of age) and the number of Al-adjuvanted vaccines in the yearly vaccination schedule in the period from 1991 to 2008 (US data). Significant change is indicated by the asterisk (*).

	ASD prevalence and yearly number of Al-adjuvanted vaccines
Pearson r	0.90
95% CI	0.76–0.96
P value (two-tailed)	<0.0001
P value summary	*
Is the corr. significant? (p<0.05)	Yes
R ²	0.82

Table 8

Pearson correlation summary according to age of vaccine exposure for ASD prevalence data in seven Western countries. Ages are expressed in months (mo). The adjusted p-values were derived using the resampling-based multiplicity adjustment according to Westfall and Young [78]. Note that for each country studied, the Al exposure is from all vaccines that children receive during the specified age period (i.e., the cumulative exposure to Al at 4 months of age includes Al from vaccines given at 2, 3 and 4 months). Significant change is indicated by the asterisk (*).

Age	ASD prevalence in the US, UK, Canada, Australia, Sweden, Finland and Iceland in correlation with			
	Minimum Al exposure	Mean Al exposure	Maximum Al exposure	# Al-adjuvanted vaccines
2 months				
Pearson r	0.89	0.86	0.83	0.86
95% CI	0.40–0.98	0.29–0.98	0.21–0.97	0.30–0.98
p (unadjusted)	0.0077*	0.014*	0.0199*	0.0131*
p (adjusted)	0.0346*	0.0682	0.1283	0.0594
R ²	0.79	0.73	0.69	0.74
3 months				
Pearson r	0.94	0.94	0.92	0.94
95% CI	0.63–0.99	0.62–0.99	0.55–0.99	0.50–0.99
p (unadjusted)	0.0017*	0.0019*	0.0032*	0.0014*
p (adjusted)	0.0018*	0.0018*	0.0038*	0.0018*
R ²	0.88	0.88	0.85	0.89
4 months				
Pearson r	0.89	0.90	0.90	0.93
95% CI	0.43–0.98	0.45–0.99	0.46–0.99	0.60–0.99
p (unadjusted)	0.0067*	0.0059*	0.0055*	0.0022*
p (adjusted)	0.0248*	0.020*	0.0168*	0.0038*
R ²	0.80	0.81	0.81	0.87
6 months				
Pearson r	0.85	0.83	0.82	0.90
95% CI	0.26–0.98	0.21–0.97	0.17–0.9	0.44–0.98
p (unadjusted)	0.0160*	0.0206*	0.0248*	0.0064*
p (adjusted)	0.0895	0.1333	0.157	0.0248*
R ²	0.72	0.69	0.67	0.80
18 months				
Pearson r	0.82	0.80	0.77	0.89
95% CI	0.18–0.97	0.13–0.97	0.05–0.96	0.40–0.98
p (unadjusted)	0.0227*	0.0297*	0.0408*	0.0079*
p (adjusted)	0.1467	0.1871	0.3133	0.0368*
R ²	0.68	0.64	0.60	0.79
72 months				
Pearson r	0.78	0.76	0.74	0.86
95% CI	0.055–0.97	0.03–0.96	–0.02–0.96	0.29–0.98
p (unadjusted)	0.0402*	0.0456*	0.0550	0.0138*
p (adjusted)	0.3087	0.353	0.4128	0.0682
R ²	0.60	0.58	0.55	0.73

(ii) the incidence of the HB infection in Western countries is extremely low (0.9–2.7 per 100,000) and some of these countries indeed only vaccinate high-risk groups [100]; (iii) a striking decline in the incidence of HB virus infections in these countries occurred during the second half of the 1980s, but only a minor part of this decline was due to HB vaccination since rather limited vaccination programs have been introduced in most Western countries at that time [99]; and (iv) epidemiological studies implicate HB vaccination as a risk factor for ASD. For example, in the US, males aged 0–9 years who received a complete triple series of HB vaccine were found to be significantly more susceptible to developmental disabilities [101], while those aged 3–17 years who received HB vaccination during the first month of life had a 3-fold greater risk of ASD than unvaccinated males [102]. Finally, in newborn primates, a single dose of the HB vaccine is sufficient to cause neurodevelopmental delays in acquisition of neonatal reflexes essential for survival [7]. Although the HB vaccines are adjuvanted with Al (Table 2), both the primate and the epidemiological studies mentioned above only draw attention to thimerosal (ethyl mercury vaccine preservative). This point was also noted by Dorea and Marques in their analysis of infant exposure to Al from vaccines and breast milk during the first 6 months of life [2]. These authors also noted that in general, mercury toxicity is well recognized and has been more studied and better understood than Al toxicity

[2]. Altogether, these observations suggest that, in spite of its well documented neurotoxic effects, Al is not perceived as a potential hazard in vaccines.

4.2. Dietary versus injectable Al: what is the difference?

Given the bioavailability of Al through food sources, a common assertion in relation to Al in vaccines is that children obtain much more Al from diet. From this perspective, Al from vaccination does not represent a toxicological risk factor [39,103]. However, this notion contradicts basic toxicological principles. For instance, it should be obvious that the route of exposure which bypasses the protective barriers of the gastrointestinal tract and/or the skin will likely require a lower dose to produce a toxic outcome [14,16]. In the case of Al, only ~0.25% of dietary Al is absorbed into systemic circulation [104]. In contrast, Al hydroxide (the most common adjuvant form) injected intramuscularly may be absorbed at nearly 100% efficiency over time [105]. In addition, although the half-life of enterally or parenterally absorbed Al from the body is short (approximately 24 h), the same cannot be assumed for adjuvant-Al because the sizes of most antigen-Al complexes (24 to 83 kDa [60,106,107]) are higher than the molecular weight cut-off of the glomerulus of the kidney (~18 kDa [108]) which would preclude efficient excretion of Al adjuvants. In fact, a longer elimination period is one of the major properties of effective vaccine adjuvants, including those using Al salts [2,14]. Additionally, the tightness of bonding between the Al adjuvant and the antigen is considered a desired feature that can be used to predict the immunogenicity of vaccines [109]. Experiments in adult rabbits demonstrate that even in an antigen-free form, Al-hydroxide, the most commonly used Al adjuvant (Table 2) is poorly excreted. The cumulative amount of Al-hydroxide in the urine of adult rabbits as long as 28 days post intramuscular injection was less than 6% as measured by accelerator mass spectrometry [110]. Al-phosphate was more efficiently excreted (22%) [110]. Finally, it is important to recognize that neonates have anatomical and functional differences crucial for toxicokinetics and toxicodynamics of neurotoxic metals (e.g., an immature renal system and an incomplete BBB), which would further compromise their ability to eliminate Al adjuvants [2,4,5].

4.3. Study results in relation to Hill's criteria: is there a causal relationship between Al vaccine adjuvants and the prevalence of ASD?

The positive correlation between Al exposure from vaccines and prevalence of ASD does not necessarily imply causation. However, if the correlation is strong (criterion 1), consistent (criterion 2) and if there is a biologically plausible mechanism by which it can be explained (criterion 6), as well as an appropriate temporal relationship between the proposed cause and the outcome (criterion 4), then the satisfaction of these criteria supports the notion that the two events may indeed be causally related. Our results satisfy not only all four of these criteria applicable for establishing causation in neuropsychiatry [80], but also four others. These additional criteria are: (5) biological gradient, (7) coherence with the current knowledge, (8) experimental or semi-experimental evidence and (9) the analogy with similar evidence (Table 9). These are discussed below as they are extremely relevant for the ways in which Al might induce ASD.

Thus, in total, the results of our study satisfy eight out of nine of Hill's criteria for causation [41]. The only criterion that our current study fails to satisfy is the "specificity" criterion which is actually not applicable to ASD given that the latter is recognized as a multifactorial disease [20,21,111]. Overall, an analysis of our results indicates that the adjuvant effect of Al in vaccines may be a significant etiological factor in the increasing prevalence of ASD in some Western countries.

4.4. Al-adjuvants and the immature brain and immune system

There is a growing body of data that supports a significant role for immune system-related molecules in the etiology of a variety of neurological disorders, including autism [25,111–115]. In addition, some 15 years ago, Cohen and Shoenfeld made the important observation that, "It seems that vaccines have a predilection to affect the nervous system" [116]. With regard to this statement, as well as the ensuing discussion, four key observations ought to be considered. First, there are critical periods in brain development during which even subtle immune challenges (including those induced by vaccinations) can lead to permanent detrimental alterations of brain and immune function [7,9,117,118]. Second, preschool children in developed countries are regularly exposed to significant amounts of Al adjuvants through vaccination programs (250–862.5 µg; Table 3). Such high exposures to adjuvant-Al which are repeated over relatively short intervals during these critical periods of brain development (i.e., first 2 years post-natal) constitute a significant neurotoxicological as well as an immunological challenge to neonates and young children [2,14]. Third, despite a prevalent view that peripheral immune responses do not affect brain function, overwhelming research suggests that neuro-immune cross-talk may be the norm rather than the exception [25,84,119–128]. Indeed, it is now clearly established that this bidirectional neuro-immune cross-talk plays crucial roles in immunoregulation and brain function [84,128–135]. In turn, perturbations of the neuro-immune axis have been demonstrated in many diseases encompassed in the 'ASIA' syndrome (Table 1) and are thought to be driven by a hyperactive/unrestrained immune response [130,135]. Fourth, the very same components of the neuro-immune regulatory system that are known to play key roles in proper brain development and immune function (i.e., interleukin (IL)-1, IL-6, major histocompatibility complex (MHC) class I, complement cascade [25,84,119–129,133,135]), are heavily targeted by Al adjuvants (Table 1). The latter experimental evidence suggests that Al adjuvants have all the necessary biochemical properties needed to induce neurological and immune disorders. In this regard, it is interesting to note that autism is a multisystem disorder characterized by dysfunctional immunity and impaired CNS function [17,20,22].

Although vaccines are credited for decreasing the risk of neurodevelopmental complications arising from natural infections in early childhood, the problem is that in many ways the immune challenge from vaccinations may be much greater in magnitude than that arising from a natural infection. The main reason for this is that early-life immune responses (before 6 months of age) are weaker and of shorter duration than those that are elicited in immunologically mature hosts [136,137]. Hence, in order to provoke and sustain an adequate B-cell immune response in a neonate, strong immune adjuvants and repeated closely spaced booster doses are needed [137]. Furthermore, in the absence of Al, most antigenic compounds fail to launch an adequate immune response [31,40,138], suggesting that a large part of the immunostimulatory effects of vaccines may be driven by the Al-adjuvant itself. While it is generally accepted that potency and toxicity of immune adjuvants must be adequately balanced so that the necessary immune stimulation is achieved with minimal side effects, in practical terms, such a balance is very difficult to achieve. This is because the same adjuvanted-mediated mechanisms which drive the immunostimulatory effects of vaccines have the capacity to provoke a variety of adverse reactions (Table 1). The potential hazards of vaccination with Al adjuvants thus not only arise from the possibility that a single vaccine may change the pre-programmed immune milieu in a neonate and thus compromise neural development, but also that multiple Al-adjuvanted vaccinations are administered simultaneously. Multiple exposure magnifies the inflammatory response and while this is essential for linking the innate and adaptive immune responses, it may also be responsible for the immunotoxic effects of Al adjuvants (Table 1).

Table 9

Study results in relation to Hill's criteria applicable for establishing causality between exposure and outcome.

Hill's criterion	Does the current study satisfy the criterion?	Comment
Strength (1)	Yes	The association is highly statistically significant (Tables 6–8).
Consistency (2)	Yes	The positive and statistically significant correlation between vaccine-derived Al exposures (as well as the overall uptake of Al-adjuvanted vaccines), and ASD prevalence is consistently observed in different populations (Table 8). While ours is, to the best of our knowledge, the first study to investigate the possible association between Al vaccine adjuvants and ASD, at least three more studies have found a positive association between the prevalence of autism (and developmental disabilities) and vaccination uptake in early childhood, a result consistent with our findings [101,102,179]. In addition, a recent study showed that autistic children have higher than normal levels of Al in the body (hair, blood and/or urine) [92]. In contrast, neither copper, lead nor mercury were elevated beyond normal levels in these children [92].
Specificity (3)	No	Not applicable to diseases such as ASD with possible multifactorial etiologies [79].
Biological rationale (4)	Yes	Al is a neurotoxin and a strong immune stimulator, hence, Al has the necessary biochemical properties to induce neuroimmune disorders such as ASD. The immunostimulatory properties of Al adjuvants are numerous and affect both innate and adaptive immune responses (see Table 1). Chronic hyperactivation of immune responses by repeated short-interval administration of Al-adjuvants could: (i) disrupt the delicate balance of immune mediators which is crucial for proper brain development and function (i.e., members of the MHC, complement, pro-inflammatory cytokines TNF- α , IL-1 β and IL-6 [25,119–127,141,142]); (ii) promote activation of neuroglia and brain inflammation [29,97,139]; and (iii) promote aberrant immune responses [31,32,157], all of which are known pathophysiological features of ASD [17,20,23,111,147].
Temporal relationship (5)	Yes	Up until and during the early 1980s, the prevalence of ASD was relatively low (<5 in 10,000 children [180,181]). Currently, 1 in 91 children in the US is diagnosed with ASD (110 per 10,000 [73]). In the United Kingdom, current reported ASD prevalence is 1 in 64 children (157 per 10,000 [74]). The increase in the number of vaccines given to children precedes the "autism epidemic" (i.e., from 10 in the late 70s to 32 in 2010 (18 of which contain Al adjuvants) [16]. Note also that the dramatic increase in the prevalence of ASD observed over the last three decades in the US and the UK (2000–3000%) cannot be convincingly explained by genetic factors alone nor by changes in diagnostic criteria. Concerning the latter, in many ways such criteria have become more restrictive [182]. Moreover, in a recent analysis comparing the prevalence of autism with that of other disabilities among successive birth cohorts of US school-aged children, Newschaffer et al. [180] clearly show that autism prevalence has been increasing with time, as evidenced by higher prevalences among younger birth cohorts.
Biological gradient (6)	Yes	The higher the Al exposure from vaccines, the higher the prevalence of ASD (Fig. 1; Table 4).
Coherence (7)	Yes	The same pro-inflammatory mediators that are induced by Al adjuvants were shown to be elevated in the blood, cerebrospinal fluid (CSF) and post-mortem brain tissue of ASD patients (see Table 1). Increase in pro-inflammatory mediators in autistic brains was also found concurrent with widespread activation of astro- and microglia and increased immunoreactivity to MHC class II [17], all of which can also be activated by Al-adjuvants (Table 1).
Experimental/semi-experimental evidence (8)	Yes	Al can impair prenatal and postnatal brain development in humans and experimental animals [28,91]. Other well-documented symptoms of Al intoxication in humans that are relevant to ASD include loss of speech skills, cognitive and behavioral impairments, increased incidence of seizures, increased inflammation and microglia in the brain, impairment of synaptic plasticity, synaptic loss and myelin sheath damage [16,29,91,94,183–186].
Analogy (9)	Yes	Peripheral stimulation of the immune system during critical periods of brain development can lead to ASD-related outcomes [9,118,187–189].

4.5. Al adjuvants and brain inflammation

Repeated injections of 1 mg/kg of Al nanoparticles to adult Sprague–Dawley rats is sufficient to produce significant inflammatory effects in the rat brain [139]. Comparable amounts of Al are administered to 2, 6 and 15 month old infants according to the US vaccination schedule (Table 3). Moreover, as we have demonstrated previously, only two subcutaneous injections of Al adjuvants (relevant to adult human exposure) in young male mice, spaced two weeks apart, were sufficient to cause dramatic activation of microglia and astrocytes that persisted up to 6 months post-injection. This outcome was accompanied by motor neuron death, impairments in motor function and decrements in spatial memory capacity [29,97]. What then might be the effects of repeated, closely spaced administration of Al adjuvanted vaccines (i.e., every 2–4 months from birth up until 12 months of age) in immature human infants? One possibility is that such treatment would increase the risk of chronic brain inflammation. In this regard, it is worth noting that neuroinflammatory mechanisms appear to play an important role in the pathophysiology of autism [17,20].

It is well established that peripheral immune insults can directly stimulate the synthesis of pro-inflammatory cytokines (i.e., IL-1 β , IL-6 and tumor necrosis factor (TNF)- α) within the brain [84,140], acting to promote inflammation even in the absence of a direct CNS infection. Moreover, the same pro-inflammatory mediators that are normally induced by Al adjuvants have been shown to be elevated in the blood, cerebrospinal fluid (CSF) and brain tissues of ASD patients (Table 1). The aberrant neuroinflammatory cytokine profile in autistic

brains was found concurrently with widespread microglial and astrocyte activation. In particular, microgliosis in autism coincided with increased immunoreactivity to MHC class II markers [17]. Microglia, astrocytes, as well as members of the MHC and the complement cascade are crucial regulators of synaptic connectivity, function and plasticity and play key roles in establishing and modulating neuronal circuitry in the developing CNS [25,112,119–126,141,142]. Notably, abnormal brain connectivity is well recognized as one of the hallmarks of autism [143,144]. Cerebellar Purkinje cells, which are significantly reduced in autism, are a site of prominent MHC class I expression. One hypothesis currently under investigation is that specifically timed changes in neuronal MHC class I expression could contribute to autism [143].

Given that Al adjuvants activate both MHC class I and II, components of the complement cascade, increase pro-inflammatory cytokines IL-1 β , IL-6 and TNF- α , as well as activate microglia and astrocytes in the brain (Table 1), it is possible that they may also interfere with synaptic pruning and developmental activity-dependent synaptic remodeling/plasticity. At present, there is experimental evidence that Al can impair synaptic plasticity *in vivo* [91,145,146], which can be reversed by vasopressin treatment of Al-exposed rats [146].

4.6. Al adjuvants as promoters of autoimmune/inflammatory reactions in the brain

Experimental evidence clearly shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity in animals [10]. While currently there is no

direct evidence that Al can induce autoimmunity, it is important to recognize that it certainly has a biochemical potential to do so.

Autoimmune manifestations, particularly those affecting the CNS, are prevalent in autistic individuals and do not appear to be limited to only a few nervous system antigens. For example, Vojdani et al. [147] demonstrated elevated levels of immunoglobulins (Ig)G, IgM and IgA against nine different neuron-specific antigens in ASD children. Such widespread manifestation of autoimmunity may have arisen from an alteration in the BBB which would then have enabled access of immunocompetent cells to many different central nervous system antigens [147].

Al is known to disrupt the BBB and can increase its permeability by increasing the rate of trans-membrane diffusion and by selectively altering saturable transport systems [5,148,149]. Even in an adjuvant form, Al can enter the brain [98]. Furthermore, much like mercury, Al may induce autoimmunity through the so-called “bystander” effect [150]. Finally, Al's ability to upregulate chemo-attractants such as monocyte chemoattractant protein (MCP)-1, monocyte inflammatory protein (MIP)-1 α and MIP-1 β [40], could promote the active recruitment of immunocompetent cells into the brain, leading to inflammation and/or autoimmunity. Consistent with this interpretation, post-mortem analysis of six children aged 4–17 months who died within 48 h of exposure to Al-adjuncted hexavalent vaccines revealed abnormal pathologic findings in the nervous system, including a defective BBB, infiltration of the leptomeninges by macrophages and lymphocytes, perivascular lymphocytic infiltration, diffuse infiltration of the pons, mesencephalon and cortex by T-lymphocytes and increased microglia in the hippocampus and pons [151]. The neuropathological observations made by Zinka et al. [151] are consistent with the well established immunostimulatory and neurotoxicological properties of Al vaccine adjuvants.

5. Conclusions and future directions

By satisfying eight of the Hill's criteria for establishing causality applicable to our study (Table 9), we show that Al-adjuncted vaccines may be a significant etiological factor in the rising prevalence of ASD in the Western world. We also show that children from countries with the highest ASD prevalence appear to have a much higher exposure to Al from vaccines, particularly at 2 months of age. In addition, the correlation between ASD prevalence and Al adjuvant exposure appears to be the highest at 3–4 months of age. Of note, these periods (i.e., first 4 post-natal months) coincide with several critical stages of human brain development and biobehavioural transitions that are known to be impaired in autism (i.e., onset of synaptogenesis, maximal growth velocity of the hippocampus [3], onset of amygdala maturation [81] and development of brain-wave and sleeping patterns [82,83]).

Clearly, we cannot draw definite conclusions regarding the link between Al adjuvants and autism based on an ecological study such as the present one and hence the validity of our results remains to be confirmed. A case control study with detailed examination of vaccination records and Al body burden measurements (i.e., hair, urine, blood) in autistic and a control group of children would be one step toward this goal. Nonetheless, given that the scientific evidence appears to indicate that vaccine safety is not as firmly established as often believed, it would seem ill advised to exclude pediatric vaccinations as a possible cause of adverse long-term neurodevelopmental outcomes, including those associated with autism.

We have thus provided a hypothesis which we hope will encourage future research into this area in order to resolve the issue of whether or not vaccines might be responsible in some part for the growing prevalence of autism in the developed world. Such future research should consider the following: (i) the postnatal period represents a very sensitive phase in development during which the physiology of the nervous as well as the immune system can be influenced and sometimes permanently changed [8,9,118,119,152–154]; (ii) Al is a

neurotoxin and a strong immune adjuvant (Table 1), hence Al has all the necessary biochemical properties to induce neurological and immune disorders; and (iii) autism is a multisystem disorder characterized by dysfunctional immunity and impaired brain function [17,20,22]. Because the current safety data for Al exposure in infants and children is unsatisfactory and because this demographic represents those who may be most at risk for complications following vaccination, a more rigorous evaluation of Al adjuvant safety than what has been provided to date seems warranted.

6. Competing interests

CAS is a founder and shareholder of Neurodyn Corporation, Inc. The company investigates early state adult neurological disease mechanisms and biomarkers. This work and any views expressed within it are solely those of the authors and not of any affiliated bodies or organizations. CAS and LT are in favor of a more rigorous evidence based medicine approach to vaccine safety.

Abbreviations

ASD	autism spectrum disorders
Al	aluminum
APC	antigen presenting cells
BBB	blood brain barrier
CDC	Centers for Disease Control and Prevention
CNS	central nervous system
CFS	chronic fatigue syndrome
CTL	cytotoxic T cell
DTaP	Diphtheria, Tetanus, acellular Pertussis
EAE	experimental autoimmune encephalomyelitis
FDA	Food and Drug Administration
GFAP	glial fibrillary acidic protein
GWS	Gulf War syndrome
HA	Hepatitis A
HB	Hepatitis B
Hib	Haemophilus influenza type b
IDEA	The Individuals with Disabilities Education Act
Ig	Immunoglobulin
IL	interleukin
LPS	lipopolysaccharide
MCP	monocyte chemoattractant protein
MenC	Meningococcal serogroup C
MHC	major histocompatibility complex
MIP	monocyte inflammatory protein
MMF	Macrophagic myofasciitis
MS	multiple sclerosis
NLRP3	nucleotide-binding domain, leucine-rich, repeat containing family, Pyrin-domain containing 3
NO	nitric oxide
PCV	Pneumococcal
ROS	reactive oxygen species
TNF- α	tumor necrosis factor

Acknowledgments

The authors would like to thank Dr. James Garrett for his invaluable help with statistical analysis. This work was supported by the Katlyn Fox and the Dwooskin Family Foundations.

References

- [1] M.V. Johnston, Brain & Development 17 (1995) 301–306.
- [2] J.G. Dorea, R.C. Marques, Journal of Exposure Science & Environmental Epidemiology 20 (2010) 598–601.
- [3] S. Avishai-Eliner, K.L. Brunson, C.A. Sandman, T.Z. Baram, Trends in Neurosciences 25 (2002) 518–524.

- [4] Agency for toxic substances, disease registry (ATSDR), Toxicological profile for aluminum. Atlanta, GA, <http://www.atsdr.cdc.gov/toxprofiles/tp22.html>.
- [5] W. Zheng, Journal of Toxicology, Clinical Toxicology 39 (2001) 711–719.
- [6] L. Hewitson, B.J. Lopresti, C. Stott, N.S. Mason, J. Tomko, Acta Neurobiologiae Experimentalis 70 (2010) 147–164 (Wars).
- [7] L. Hewitson, L.A. Houser, C. Stott, G. Sackett, J.L. Tomko, D. Atwood, L. Blue, E.R. White, Journal of Toxicology and Environmental Health. Part A 73 (2010) 1298–1313.
- [8] M.A. Galic, S.J. Spencer, A. Mouihate, Q.J. Pittman, Integrative and Comparative Biology 49 (2009) 237–245.
- [9] M.A. Galic, K. Riazi, J.G. Heida, A. Mouihate, N.M. Fournier, S.J. Spencer, L.E. Kalynchuk, G.C. Teskey, Q.J. Pittman, The Journal of Neuroscience 28 (2008) 6904–6913.
- [10] N.R. Rose, Lupus 19 (2010) 354–358.
- [11] K. Tsumiyama, Y. Miyazaki, S. Shiozawa, PLoS One 4 (2009) e8382.
- [12] Centers for Disease Control and Prevention (CDC), Child & Adolescent Immunization Schedules for persons aged 0–6 years, 7–18 years, and “catch-up schedule” and Past Childhood Immunization Schedules, <http://www.cdc.gov/vaccines/recs/schedules/child-schedule.htm#chgs>.
- [13] A surveillance community Network for Vaccine Preventable Infectious Diseases (EUVA.NET), The United Kingdom Childhood Vaccination Schedule, as on 19th April 20, <http://www.euvac.net/graphics/euvac/vaccination/unitedkingdom.html>.
- [14] L. Tomljenovic, C.A. Shaw, Current Medicinal Chemistry 18 (2011) 2630–2637.
- [15] Food, Drug Administration (FDA), Workshop on Non-clinical Safety Evaluation of Preventative Vaccines: Recent Advances and Regulatory Considerations (2002), <http://www.fda.gov/downloads/biologicsbloodvaccines/newsevents/workshopsmeetingsconferences/transcriptsminutes/ucm054459.pdf>.
- [16] L. Tomljenovic, Journal of Alzheimer's Disease 23 (2011) 567–598.
- [17] D.L. Vargas, C. Nascimbene, C. Krishnan, A.W. Zimmerman, C.A. Pardo, Annals of Neurology 57 (2005) 67–81.
- [18] R.J. Kelleher III, M.F. Bear, Cell 135 (2008) 401–406.
- [19] I. Rapin, R. Katzman, Annals of Neurology 43 (1998) 7–14.
- [20] C.A. Pardo, D.L. Vargas, A.W. Zimmerman, International Review of Psychiatry 17 (2005) 485–495.
- [21] K.S. Reddy, BMC Medical Genetics 6 (2005) 3.
- [22] P. Ashwood, A. Enstrom, P. Krakowiak, I. Hertz-Picciotto, R.L. Hansen, L.A. Croen, S. Ozonoff, I.N. Pessah, J. Van de Water, Journal of Neuroimmunology 204 (2008) 149–153.
- [23] R.L. Blaylock, A. Strunecka, Current Medicinal Chemistry 16 (2009) 157–170.
- [24] H.H. Coily, A. Panja, International Review of Neurobiology 71 (2005) 317–341.
- [25] P.A. Garay, A.K. McAllister, Front Synaptic Neuroscience 2 (2010) 136.
- [26] V.K. Singh, R.P. Warren, J.D. Odell, W.L. Warren, P. Cole, Brain, Behavior, and Immunity 7 (1993) 97–103.
- [27] J.R. Walton, Neurotoxicology 30 (2009) 182–193.
- [28] N.J. Bishop, R. Morley, J.P. Day, A. Lucas, The New England Journal of Medicine 336 (1997) 1557–1561.
- [29] C.A. Shaw, M.S. Petrik, Journal of Inorganic Biochemistry 103 (2009) 1555–1562.
- [30] A. Batista-Duharte, E.B. Lindblad, E. Oviedo-Orta, Toxicology Letters 203 (2011) 97–105.
- [31] E. Israeli, N. Agmon-Levin, M. Blank, Y. Shoenfeld, Lupus 18 (2009) 1217–1225.
- [32] Y. Shoenfeld, N. Agmon-Levin, Journal of Autoimmunity 36 (2011) 4–8.
- [33] S.C. Eisenbarth, O.R. Colegio, W. O'Connor, F.S. Sutterwala, R.A. Flavell, Nature 453 (2008) 1122–1126.
- [34] C. Exley, P. Siesjo, H. Eriksson, Trends in Immunology 31 (2010) 103–109.
- [35] T.C. Eickhoff, M. Myers, Vaccine 20 (Suppl. 3) (2002) S1–S4.
- [36] E. Miller, N. Andrews, P. Waight, H. Findlow, L. Ashton, A. England, E. Stanford, M. Matheson, J. Southern, E. Sheasby, D. Goldblatt, R. Borrow, Clinical and Vaccine Immunology 18 (2011) 367–372.
- [37] T. Verstraeten, D. Descamps, M.P. David, T. Zahaf, K. Hardt, P. Izurieta, G. Dubin, T. Breuer, Vaccine 26 (2008) 6630–6638.
- [38] S.M. Garland, M. Hernandez-Avila, C.M. Wheeler, G. Perez, D.M. Harper, S. Leodolter, G.W. Tang, D.G. Ferris, M. Steben, J. Bryan, F.J. Taddeo, R. Raikar, M.T. Esser, H.L. Sings, M. Nelson, J. Boslego, C. Sattler, E. Barr, L.A. Koutsky, The New England Journal of Medicine 356 (2007) 1928–1943.
- [39] P.A. Offit, R.K. Jew, Pediatrics 112 (2003) 1394–1397.
- [40] A. Seubert, E. Monaci, M. Pizza, D.T. O'Hagan, A. Wack, Journal of Immunology 180 (2008) 5402–5412.
- [41] A.B. Hill, Proceedings of the Royal Society of Medicine 58 (1965) 295–300.
- [42] U.S. Department of Education, 24th Annual Report to Congress on the Implementation of the Individuals with Disabilities Education Act, Appendix A, Data Tables, Table 1–9, Age Group 6–21, <http://www2.ed.gov/about/reports/annual/osep/2002/index.html>.
- [43] U.S. Department of Education, 26th Annual Report to Congress on the Implementation of the Individuals with Disabilities Education Act, Table 1–9, Age Group 6–21, <http://www2.ed.gov/about/reports/annual/osep/2004/index.html>.
- [44] U.S. Department of Education, 28th Annual Report to Congress on the Implementation of the Individuals with Disabilities Education Act, Table 1–9, Age Groups 3–5 and 6–21, <http://www2.ed.gov/about/reports/annual/osep/2006/parts-b-c/index.html>.
- [45] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count (2005), Table 1–3, Students ages 6 through 21 served under IDEA, Part B, by disability category and state, https://www.ideadata.org/arc_toc7.asp#partbCC.
- [46] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–7, Children and Students Served under IDEA, Part B, in the U.S. and Outlying Areas, by Age and Disability Category, 2005 https://www.ideadata.org/arc_toc7.asp#partbCC.
- [47] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–3, Students Ages 6 through 21 Served under IDEA, Part B, by Disability Category and State, 2006 https://www.ideadata.org/arc_toc8.asp#partbCC.
- [48] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–7, Children and Students Served under IDEA, Part B, in the U.S. and Outlying Areas, by Age and Disability Category, 2006 https://www.ideadata.org/arc_toc8.asp#partbCC.
- [49] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–3, Students ages 6 through 21 served under IDEA, Part B, by disability category and state, 2007 https://www.ideadata.org/arc_toc9.asp#partbCC.
- [50] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–7, Children and students served under IDEA, Part B, in the U.S. and outlying areas, by age and disability category, 2007 https://www.ideadata.org/arc_toc9.asp#partbCC.
- [51] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–3, Students ages 6 through 21 served under IDEA, Part B, by disability category and state, 2008 https://www.ideadata.org/arc_toc10.asp#partbCC.
- [52] The Individuals with Disabilities Education Act (IDEA) Data Accountability Center, Data Tables for OSEP State Reported Data, Part B Child Count, Table 1–7, Children and Students Served under IDEA, Part B, in the U.S. and Outlying Areas, by Age and Disability Category, 2008 https://www.ideadata.org/arc_toc10.asp#partbCC.
- [53] R.K. Gherardi, M. Coquet, P. Cherin, L. Belec, P. Moretto, P.A. Dreyfus, J.F. Pellissier, P. Chariot, F.J. Authier, Brain 124 (2001) 1821–1831.
- [54] Public Health Agency of Canada, Immunization Schedules for Infants and Children, source: Canadian Immunization Guide, Seventh Edition, 2006 <http://www.phac-aspc.gc.ca/im/is-cv/>.
- [55] Australian Government Department of Health and Aging, National Immunisation Program (NIP) Schedule last modified 28th April, 2010 <http://immunise.health.gov.au/internet/immunise/publishing.nsf/Content/nips2>.
- [56] Swedish Institute for Infectious Disease Control (SMITTSKYDDSIINSTITUTET), Barnvaccinationer ges enligt nedanstående tabell, <http://www.smittskyddsinstutet.se/upload/amnesomraden/vaccin/vaccinationsschema.pdf>.
- [57] KTL National Public Health Institute, Finnish National Vaccination Programme, http://www.ktl.fi/attachments/suomi/osastot/roko/roto/finnish_vaccination_programme.pdf.
- [58] A surveillance community Network for Vaccine Preventable Infectious Diseases (EUVA.NET), The Icelandic childhood vaccination schedule as on October 19th 2007 <http://www.euvac.net/graphics/euvac/vaccination/iceland.html>.
- [59] Wyeth Canada, Meningitec product monograph Date of last approval, http://www.wyeth.ca/en/products/Product%20Monographs%20PDFs/Meningitec_PM.pdf.
- [60] Bioprot Corp. Anthrax Vaccine Adsorbed (Biothrax™), Revised January 31, 2002 <http://www.fda.gov/OHRMS/DOCKETS/98fr/05n-0040-bkg0001.pdf>.
- [61] Merck&Co Inc, Recombivax HB product monograph Approved March 23, 2009 http://www.merck.ca/assets/en/pdf/products/RECOMBIVAX_HB-09_03-a_126922_E.pdf.
- [62] GlaxoSmithKline, Hiberix product information Date of last amendment 9 April, 2009 http://www.gsk.com.au/resources.aspx/vaccineproductschilddataproinfo/232/FileName/D8AE2CF1E6ED5097F04CDB946BC28E69/PL_Hiberix.pdf.
- [63] Centre for Infectious Diseases and Microbiology, What's new in pneumococcal disease-surveillance using conventional and molecular methods, <http://www.cidmpublichealth.org/resources/pdf/bsp/bsp13-june-09.pdf>.
- [64] Australian Advisory Board on Autism Spectrum Disorders, The prevalence of autism in Australia. Can it be established from existing data? Overview and Report, 2006 <http://autismaus.com.au/uploads/pdfs/PrevalenceReport.pdf>.
- [65] A. Morrow, P. De Wals, G. Petit, M. Guay, L.J. Erickson, The Canadian Journal of Infectious Diseases Medical Microbiology 18 (2007) 121–127.
- [66] P. De Wals, The Pediatric Infectious Disease Journal 23 (2004) S280–S284.
- [67] E. Fombonne, R. Zakarian, A. Bennett, L. Meng, D. McLean-Heywood, Pediatrics 118 (2006) e139–e150.
- [68] A surveillance community Network for Vaccine Preventable Infectious Diseases (EUVA.NET), The Swedish Childhood Vaccination Schedule as of 20th April, 2010 <http://www.euvac.net/graphics/euvac/vaccination/sweden.html>.
- [69] C. Gillberg, M. Cederlund, K. Lamberg, L. Zeijlon, Journal of Autism and Developmental Disorders 36 (2006) 429–435.
- [70] A surveillance community Network for Vaccine Preventable Infectious Diseases (EUVA.NET), The Finnish Childhood Vaccination Schedule as on 6 January 2011, <http://www.euvac.net/graphics/euvac/vaccination/finland.html>.
- [71] M. Kielinen, S.L. Linna, I. Moilanen, European Child & Adolescent Psychiatry 9 (2000) 162–167.
- [72] P. Magnusson, E. Saemundsen, Journal of Autism and Developmental Disorders 31 (2001) 153–163.
- [73] M.D. Kogan, S.J. Blumberg, L.A. Schieve, C.A. Boyle, J.M. Perrin, R.M. Ghandour, G.K. Singh, B.B. Strickland, E. Trevathan, P.C. van Dyck, Pediatrics 124 (2009) 1395–1403.
- [74] S. Baron-Cohen, F.J. Scott, C. Allison, J. Williams, P. Bolton, F.E. Matthews, C. Brayne, The British Journal of Psychiatry 194 (2009) 500–509.
- [75] U.K. Department of Health, Immunisation against infectious disease – “The Green Book” (2007), Part 1 Principles, practices and procedures, Chapter 11: Immunisation schedule, http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_079917.
- [76] Swedish Institute for Infectious Disease Control (SMITTSKYDDSIINSTITUTET), The present and previous Swedish general vaccination program, <http://www.smittskyddsinstutet.se/in-english/activities/the-swedish-vaccination-program/the-present-and-previous-swedish-general-vaccination-program/>.

- [77] S. Iwarson, Vaccine 16 (Suppl.) (1998) S63–S64.
- [78] P.H. Westfall, S.S. Young, Resampling-Based Multiple Testing, John Wiley & Sons, Inc., New York, 1993.
- [79] S. Haddad, C. Restieri, K. Krishnan, Journal of Toxicology and Environmental Health. Part A 64 (2001) 453–464.
- [80] R. van Reekum, D.L. Streiner, D.K. Conn, The Journal of Neuropsychiatry and Clinical Neurosciences 13 (2001) 318–325.
- [81] J. Rhawn, Neuropsychiatry, Neuropsychology, and Clinical Neuroscience, third ed Lippincott Williams & Wilkins, 1996 <http://brainmind.com/EmotionalBrainDevelopment4.html>.
- [82] M.R. Gunnar, L. Brodersen, K. Krueger, J. Rigatuso, Child Development 67 (1996) 877–889.
- [83] R.J. Ellingson, J.F. Peters, Electroencephalography and Clinical Neurophysiology 49 (1980) 112–124.
- [84] H.O. Besedovsky, A. Rey, Handbook of Neurochemistry and Molecular Neurobiology, in: A. Lajtha, H.O. Besedovsky, A. Galoyan (Eds.), Springer, 2008, p. 495.
- [85] S.W. Porges, The Neurobiology of Autism, in: M.L. Bauman, T.L. Kemper (Eds.), The Johns Hopkins University Press, Baltimore, Maryland, 2005, pp. 65–78.
- [86] M.A. Polimeni, A.L. Richdale, A.J. Francis, Journal of Intellectual Disability Research 49 (2005) 260–268.
- [87] R. Tuchman, I. Rapin, Lancet Neurology 1 (2002) 352–358.
- [88] K. Ballaban-Gil, R. Tuchman, Mental Retardation and Developmental Disabilities Research Reviews 6 (2000) 300–308.
- [89] N.W. Baylor, W. Egan, P. Richman, Vaccine 20 (Suppl. 3) (2002) S18–S23.
- [90] Food and Drug Administration (FDA) Department of Health and Human Services, Aluminum in large and small volume parenterals used in total parenteral nutrition amendment, http://edocket.access.gpo.gov/cfr_2005/aprqt/pdf/21cfr201.323.pdf.
- [91] M. Wang, J.T. Chen, D.Y. Ruan, Y.Z. Xu, Neuroscience 113 (2002) 411–419.
- [92] M.M. Lopes, L.Q.A. Caldas, Toxicology Letters 205S (2011) S60–S179.
- [93] Sanofi Pasteur MSD Limited, Revaxis, summary of Product Characteristics last updated, May 2008 <http://www.medicines.org.uk/emc/document.aspx?documentid=15259>.
- [94] M. Couette, M.F. Boisse, P. Maison, P. Brugieres, P. Cesaro, X. Chevalier, R.K. Gherardi, A.C. Bachoud-Levi, F.J. Authier, Journal of Inorganic Biochemistry 103 (2009) 1571–1578.
- [95] C. Exley, L. Swarbrick, R.K. Gherardi, F.J. Authier, Medical Hypotheses 72 (2009) 135–139.
- [96] F.J. Authier, P. Cherin, A. Creange, B. Bonnotte, X. Ferrer, A. Abdelmoumni, D. Ranoux, J. Pelletier, D. Figarella-Branger, B. Granel, T. Maissonobe, M. Coquet, J.D. Degos, R.K. Gherardi, Brain 124 (2001) 974–983.
- [97] M.S. Petrik, M.C. Wong, R.C. Tabata, R.F. Garry, C.A. Shaw, Neuromolecular Medicine 9 (2007) 83–100.
- [98] K. Redhead, G.J. Quinlan, R.G. Das, J.M. Gutteridge, Pharmacology & Toxicology 70 (1992) 278–280.
- [99] S. Iwarson, Vaccine 11 (Suppl. 1) (1993) S18–S20.
- [100] S.A. Cowan, Eurosurveillance 10, 2005 <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=2827>.
- [101] C.M. Gallagher, M.S. Goodman, Toxicological and Environmental Chemistry 90 (2008) 997–1008.
- [102] C.M. Gallagher, M.S. Goodman, Journal of Toxicology and Environmental Health. Part A 73 (2010) 1665–1677.
- [103] B.E. Eldred, A.J. Dean, T.M. McGuire, A.L. Nash, The Medical Journal of Australia 184 (2006) 170–175.
- [104] R.A. Yokel, C.L. Hicks, R.L. Florence, Food and Chemical Toxicology 46 (2008) 2261–2266.
- [105] R.A. Yokel, P.J. McNamara, Pharmacology & Toxicology 88 (2001) 159–167.
- [106] GlaxoSmithKline, Boostrix product monograph, combined diphtheria, tetanus, acellular pertussis (adsorbed) vaccine for booster vaccination date of approval October 21, 2009 http://www.gsk.ca/english/docs-pdf/Boostrix_PM_20091021_EN.pdf.
- [107] P.E. Makidon, A.U. Bielinska, S.S. Nigavekar, K.W. Janczak, J. Knowlton, A.J. Scott, N. Mank, Z. Cao, S. Rathinavelu, M.R. Beer, J.E. Wilkinson, L.P. Blanco, J.J. Landers, J.R. Baker Jr., PLoS One 3 (2008) e2954.
- [108] C. Exley, Aluminium and Medicine, Molecular and Supramolecular Bioinorganic Chemistry: Applications in Medical Sciences, in: A.L.R. Merce, J. Felcman, M.A.L. Recio (Eds.), Nova Science Publishers, Inc., New York, 2008, pp. 45–68.
- [109] P.M. Egan, M.T. Belfast, J.A. Gimenez, R.D. Sitrin, R.J. Mancinelli, Vaccine 27 (2009) 3175–3180.
- [110] S.L. Hem, Vaccine 20 (Suppl. 3) (2002) S40–S43.
- [111] P. Ashwood, S. Wills, J. Van de Water, Journal of Leukocyte Biology 80 (2006) 1–15.
- [112] B. Havik, S. Le Hellard, M. Rietschel, H. Lybaek, S. Djurovic, M. Mattheisen, T.W. Muhleisen, F. Degenhardt, L. Priebe, W. Maier, R. Breuer, T.G. Schulze, I. Agartz, I. Melle, T. Hansen, C.R. Bramham, M.M. Nothen, B. Stevens, T. Werge, O.A. Andreassen, S. Cichon, V.M. Steen, Biological Psychiatry 70 (2011) 35–42.
- [113] P. Ashwood, J. Van de Water, Clinical & Developmental Immunology 11 (2004) 165–174.
- [114] K.M. Lucin, T. Wyss-Coray, Neuron 64 (2009) 110–122.
- [115] S. Potvin, E. Stip, A.A. Sepehry, A. Gendron, R. Bah, E. Kouassi, Biological Psychiatry 63 (2008) 801–808.
- [116] A.D. Cohen, Y. Shoenfeld, Journal of Autoimmunity 9 (1996) 699–703.
- [117] S.D. Bilbo, J.C. Biedenkapp, A. Der-Avakian, L.R. Watkins, J.W. Rudy, S.F. Maier, The Journal of Neuroscience 25 (2005) 8000–8009.
- [118] G.W. Konat, B.E. Lally, A.A. Toth, A.K. Salm, Metabolic Brain Disease (2011), doi: 10.1007/s11011-011-9244-z.
- [119] B. Stevens, N.J. Allen, L.E. Vazquez, G.R. Howell, K.S. Christopherson, N. Nouri, K.D. Micheva, A.K. Mehalow, A.D. Huberman, B. Stafford, A. Sher, A.M. Litke, J.D. Lambris, S.J. Smith, S.W. John, B.A. Barres, Cell 131 (2007) 1164–1178.
- [120] L.M. Boulanger, Neuron Glia Biology 1 (2004) 283–289.
- [121] C.J. Shatz, Neuron 64 (2009) 40–45.
- [122] C.A. Goddard, D.A. Butts, C.J. Shatz, Proceedings of the National Academy of Sciences of the United States of America 104 (2007) 6828–6833.
- [123] G.S. Huh, L.M. Boulanger, H. Du, P.A. Riquelme, T.M. Brotz, C.J. Shatz, Science 290 (2000) 2155–2159.
- [124] R.A. Corriveau, G.S. Huh, C.J. Shatz, Neuron 21 (1998) 505–520.
- [125] D.P. Schafer, B. Stevens, Biochemical Society Transactions 38 (2010) 476–481.
- [126] L.M. Boulanger, Neuron 64 (2009) 93–109.
- [127] L. Fourgeaud, L.M. Boulanger, The European Journal of Neuroscience 32 (2010) 207–217.
- [128] H.O. Besedovsky, A. del Rey, Neurochemical Research 36 (2010) 1–6.
- [129] I.J. Elenkov, R.L. Wilder, G.P. Chrousos, E.S. Vizi, Pharmacological Reviews 52 (2000) 595–638.
- [130] F. Eskandari, J.J. Webster, E.M. Sternberg, Arthritis Research & Therapy 5 (2003) 251–265.
- [131] S. Rivest, Progress in Brain Research 181 (2010) 43–53.
- [132] N.P. Turrin, S. Rivest, (Maywood), Experimental Biology and Medicine 229 (2004) 996–1006.
- [133] A. del Rey, E. Roggero, A. Randolph, C. Mahuad, S. McCann, V. Rettori, H.O. Besedovsky, Proceedings of the National Academy of Sciences of the United States of America 103 (2006) 16039–16044.
- [134] A. del Rey, C. Wolff, J. Wildmann, A. Randolph, A. Hahnel, H.O. Besedovsky, R.H. Straub, Arthritis and Rheumatism 58 (2008) 3090–3099.
- [135] R.L. Wilder, Annual Review of Immunology 13 (1995) 307–338.
- [136] C.A. Siegrist, R. Aspinall, Nature Reviews. Immunology 9 (2009) 185–194.
- [137] C.A. Siegrist, Vaccine 19 (2001) 3331–3346.
- [138] S.B. Dillon, S.G. Demuth, M.A. Schneider, C.B. Weston, C.S. Jones, J.F. Young, M. Scott, P.K. Bhatnagar, S. LoCastro, N. Hanna, Vaccine 10 (1992) 309–318.
- [139] X. Li, H. Zheng, Z. Zhang, M. Li, Z. Huang, H.J. Schluessener, Y. Li, S. Xu, Nanomedicine: Nanotechnology, Biology and Medicine 5 (2009) 473–479.
- [140] S. Laye, P. Parnet, E. Goujon, R. Dantzer, Brain Research. Molecular Brain Research 27 (1994) 157–162.
- [141] B. Havik, H. Rokke, G. Dagyte, A.K. Stavrum, C.R. Bramham, V.M. Steen, Neuroscience 148 (2007) 925–936.
- [142] C. Eroglu, B.A. Barres, Nature 468 (2010) 223–231.
- [143] M.K. Belmonte, G. Allen, A. Beckel-Mitchener, L.M. Boulanger, R.A. Carper, S.J. Webb, The Journal of Neuroscience 24 (2004) 9228–9231.
- [144] B. Zikopoulos, H. Barbas, The Journal of Neuroscience 30 (2010) 14595–14609.
- [145] B. Platt, D.O. Carpenter, D. Busselberg, K.G. Reymann, G. Riedel, Experimental Neurology 134 (1995) 73–86.
- [146] M. Wang, J.T. Chen, D.Y. Ruan, Y.Z. Xu, Brain Research 899 (2001) 193–200.
- [147] A. Vojdani, A.W. Campbell, E. Anyanwu, A. Kashanian, K. Bock, E. Vojdani, Journal of Neuroimmunology 129 (2002) 168–177.
- [148] W.A. Banks, A.J. Kastin, Neuroscience and Biobehavioral Reviews 13 (1989) 47–53.
- [149] R.A. Yokel, Journal of Alzheimer's Disease 10 (2006) 223–253.
- [150] G.J. Fournie, M. Mas, B. Cautain, M. Savignac, J.F. Subra, L. Pelletier, A. Saoudi, D. Lagrange, M. Calise, P. Druet, Journal of Autoimmunity 16 (2001) 319–326.
- [151] B. Zinka, E. Rauch, A. Buettner, F. Rueff, R. Penning, Vaccine 24 (2006) 5779–5780.
- [152] S.D. Bilbo, L.H. Levkoff, J.H. Mahoney, L.R. Watkins, J.W. Rudy, S.F. Maier, Behavioral Neuroscience 119 (2005) 93–301.
- [153] S.D. Bilbo, N.J. Newsom, D.B. Sprunger, L.R. Watkins, J.W. Rudy, S.F. Maier, Brain, Behavior, and Immunity 21 (2007) 332–342.
- [154] H. Hagberg, C. Mallard, Current Opinion in Neurology 18 (2005) 117–123.
- [155] A. Lerner, Annals of the New York Academy of Sciences 1107 (2007) 329–345.
- [156] I.J. Elenkov, G.P. Chrousos, Trends in Endocrinology and Metabolism 10 (1999) 359–368.
- [157] R.K. Gherardi, Revista de Neurologia 159 (2003) 162–164 (Paris).
- [158] A. Skowera, A. Cleare, D. Blair, L. Bevis, S.C. Wessely, M. Peakman, Clinical and Experimental Immunology 135 (2004) 294–302.
- [159] G. Broderick, A. Kreitz, J. Fuite, M.A. Fletcher, S.D. Vernon, N. Klimas, Brain, Behavior, and Immunity 25 (2010) 302–313.
- [160] S. Gupta, S. Aggarwal, B. Rashanravan, T. Lee, Journal of Neuroimmunology 85 (1998) 106–109.
- [161] P. Ashwood, P. Krakowiak, I. Hertz-Picciotto, R. Hansen, I.N. Pessah, J. Van de Water, Brain, Behavior, and Immunity 25 (2011) 840–849.
- [162] V.K. Singh, Journal of Neuroimmunology 66 (1996) 143–145.
- [163] C.A. Molloy, A.L. Morrow, J. Meinzen-Derr, K. Schleifer, K. Dienger, P. Manning-Courtney, M. Altaye, M. Wills-Karp, Journal of Neuroimmunology 172 (2006) 198–205.
- [164] S. Jha, S.Y. Srivastava, W.J. Brickey, H. Iocca, A. Toews, J.P. Morrison, V.S. Chen, D. Gris, G.K. Matsushima, J.P. Ting, The Journal of Neuroscience 30 (2010) 15811–15820.
- [165] D. Gris, Z. Ye, H.A. Iocca, H. Wen, R.R. Craven, P. Gris, M. Huang, M. Schneider, S.D. Miller, J.P. Ting, Journal of Immunology 185 (2010) 974–981.
- [166] H. Wen, D. Gris, Y. Lei, S. Jha, L. Zhang, M.T. Huang, W.J. Brickey, J.P. Ting, Nature Immunology 12 (2011) 408–415.
- [167] C. Bauer, P. Dnuwell, C. Mayer, H.A. Lehr, K.A. Fitzgerald, M. Dauer, J. Tschopp, S. Endres, E. Latz, M. Sngurr, Gut 59 (2010) 1192–1199.
- [168] M. Aringer, J.S. Smolen, Lupus 13 (2004) 344–347.
- [169] A. Sabry, H. Sheashaa, A. El-Husseini, K. Mahmoud, K.F. Eldahshan, S.K. George, E. Abdel-Khalek, E.M. El-Shafey, H. Abo-Zenah, Cytokine 35 (2006) 148–153.
- [170] J.M. Brewer, Immunology Letters 102 (2006) 10–15.
- [171] H. HogenEsch, Vaccine 20 (Suppl. 3) (2002) S34–S39.

- [172] H. Li, S. Nookala, F. Re, *Journal of Immunology* 178 (2007) 5271–5276.
- [173] K.M. Smith, P. Garside, R.C. McNeil, J.M. Brewer, *Vaccine* 24 (2006) 3035–3043.
- [174] H.L. Davis, R. Weeratna, T.J. Waldschmidt, L. Tygrett, J. Schorr, A.M. Krieg, *Journal of Immunology* 160 (1998) 870–876.
- [175] C.L. Brazolot Millan, R. Weeratna, A.M. Krieg, C.A. Siegrist, H.L. Davis, *Proceedings of the National Academy of Sciences of the United States of America* 95 (1998) 15553–15558.
- [176] I. Sutton, R. Lahoria, I.L. Tan, P. Clouston, M.H. Barnett, *Multiple Sclerosis* 15 (2009) 116–119.
- [177] J.B. Classen, *The New Zealand Medical Journal* 109 (1996) 195.
- [178] GlaxoSmithKline, Engerix-B product monograph, July 2010 http://us.gsk.com/products/assets/us_engerixb.pdf.
- [179] G. DeLong, *Journal of Toxicology and Environmental Health. Part A* 74 (2011) 903–916.
- [180] C.J. Newschaffer, M.D. Falb, J.G. Gurney, *Pediatrics* 115 (2005) e277–e282.
- [181] J.G. Gurney, M.S. Fritz, K.K. Ness, P. Sievers, C.J. Newschaffer, E.G. Shapiro, *Archives of Pediatrics & Adolescent Medicine* 157 (2003) 622–627.
- [182] H. Yazbak, *Journal of American Physical Surgery* 8 (2003) 103–107.
- [183] J.R. Walton, *Neurotoxicology* 30 (2009) 1059–1069.
- [184] N.C. Bowdler, D.S. Beasley, E.C. Fritze, A.M. Goulette, J.D. Hatton, J. Hession, D.L. Ostman, D.J. Rugg, C.J. Schmittiel, *Pharmacology Biochemistry and Behavior* 10 (1979) 505–512.
- [185] J.A. Flendrig, H. Kruis, H.A. Das, *Proceedings of the European Dialysis and Transplant Association* 13 (1976) 355–368.
- [186] S.V. Verstraeten, M.S. Golub, C.L. Keen, P.I. Oteiza, *Archives of Biochemistry and Biophysics* 344 (1997) 289–294.
- [187] L. Shi, S.H. Fatemi, R.W. Sidwell, P.H. Patterson, *The Journal of Neuroscience* 23 (2003) 297–302.
- [188] L. Shi, S.E. Smith, N. Malkova, D. Tse, Y. Su, P.H. Patterson, *Brain, Behavior, and Immunity* 23 (2009) 116–123.
- [189] S.H. Fatemi, T.J. Reutiman, T.D. Folsom, H. Huang, K. Oishi, S. Mori, D.F. Smee, D.A. Pearce, C. Winter, R. Sohr, G. Juckel, *Schizophrenia Research* 99 (2008) 56–70.

REVIEW ARTICLE

Human papillomavirus (HPV) vaccine policy and evidence-based medicine: Are they at odds?

Lucija Tomljenovic¹ & Christopher A. Shaw^{1,2}

¹Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia, 828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada and ²Program in Experimental Medicine and the Graduate Program in Neuroscience, University of British Columbia, Vancouver, BC, Canada

All drugs are associated with some risks of adverse reactions. Because vaccines represent a special category of drugs, generally given to healthy individuals, uncertain benefits mean that only a small level of risk for adverse reactions is acceptable. Furthermore, medical ethics demand that vaccination should be carried out with the participant's full and informed consent. This necessitates an objective disclosure of the known or foreseeable vaccination benefits and risks. The way in which HPV vaccines are often promoted to women indicates that such disclosure is not always given from the basis of the best available knowledge. For example, while the world's leading medical authorities state that HPV vaccines are an important cervical cancer prevention tool, clinical trials show no evidence that HPV vaccination can protect against cervical cancer. Similarly, contrary to claims that cervical cancer is the second most common cancer in women worldwide, existing data show that this only applies to developing countries. In the Western world cervical cancer is a rare disease with mortality rates that are several times lower than the rate of reported serious adverse reactions (including deaths) from HPV vaccination. Future vaccination policies should adhere more rigorously to evidence-based medicine and ethical guidelines for informed consent.

Key words: Cervarix, cervical cancer, Gardasil, HPV vaccines, informed consent, vaccine adverse reactions

Introduction

In 2002 the US Food and Drug Administration (FDA) stated that vaccines represent a special category of drugs aimed mostly at healthy individuals and for prophylaxis against diseases to which an individual may never be exposed (1). This, according to the FDA, places significant emphasis on vaccine safety (1). In other words, contrary to conventional drug treatments aimed at management of existing, oftentimes severe and/or advanced disease conditions, in preventative vaccination a compromise in efficacy for the benefit of safety should not be seen as an unreasonable expectation. Furthermore, physicians are ethically obliged to

Key messages

- To date, the efficacy of HPV vaccines in preventing cervical cancer has not been demonstrated, while vaccine risks remain to be fully evaluated.
- Current worldwide HPV immunization practices with either of the two HPV vaccines appear to be neither justified by long-term health benefits nor economically viable, nor is there any evidence that HPV vaccination (even if proven effective against cervical cancer) would reduce the rate of cervical cancer beyond what Pap screening has already achieved.
- Cumulatively, the list of serious adverse reactions related to HPV vaccination worldwide includes deaths, convulsions, paraesthesia, paralysis, Guillain-Barré syndrome (GBS), transverse myelitis, facial palsy, chronic fatigue syndrome, anaphylaxis, autoimmune disorders, deep vein thrombosis, pulmonary embolisms, and cervical cancers.
- Because the HPV vaccination programme has global coverage, the long-term health of many women may be at risk against still unknown vaccine benefits.
- Physicians should adopt a more rigorous evidence-based medicine approach, in order to provide a balanced and objective evaluation of vaccine risks and benefits to their patients.

provide an accurate explanation of vaccine risks and benefits to their patients and, where applicable, a description of alternative courses of treatment. This in turn enables patients to make a fully informed decision with regard to vaccination. For example, the Australian guidelines for vaccination emphasize that for a consent to be legally valid, the following element *must* be satisfied: 'it [consent] can *only* be given after the relevant vaccine (s) and their potential risks and benefits have been explained to the individual' (emphasis added) (2). Likewise, the United Kingdom (UK) guidelines pertaining to vaccination practices state that subjects must be given

Correspondence: Lucija Tomljenovic, Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia, 828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada. E-mail: lucijat77@gmail.com

(Received 24 May 2011; accepted 31 October 2011)

adequate information on which to base their decision on whether to accept or refuse a vaccine (3). This includes having a clear explanation on vaccine risks and side-effects (3).

Surprisingly, in the United States (US), there are no governmental requirements for informed consent for vaccination (4). Such an omission leaves the door open to a failure to obtain informed consent. Nonetheless, there are regulatory agencies such as the US FDA which are empowered to assure that only demonstrably safe and effective vaccines reach the market. In addition, health authorities (i.e. US Centers for Disease Control and Prevention (CDC)) are expected to provide expert advice concerning the benefits and risks related to particular drugs, including vaccines. When these official bodies are not able to provide their normal regulatory oversight and/or if financial interests take precedence over public health, significant problems in true informed consent guidelines can occur.

What is known about the currently licensed human papillomavirus (HPV) vaccines? What are their benefits, and what are their risks? While medical authorities in a number of countries, including the US, strongly advocate their use, some members of the public have become increasingly sceptical for a variety of reasons. The key question posed by such sceptics is this: Is it possible that HPV vaccines have been promoted to women based on inaccurate information? The present article examines the evidence in order to answer this critical question.

Can the currently licensed HPV vaccines prevent cervical cancer?

Gardasil's manufacturer, Merck, states on their website that 'Gardasil does more than help prevent cervical cancer, it protects against other HPV diseases, too.' Merck further claims that 'Gardasil does not prevent all types of cervical cancer' (5). Similarly, the US CDC and the FDA claim that 'This [Gardasil] vaccine is an important cervical cancer prevention tool that will potentially benefit the health of millions of women' (6) and 'Based on all of the information we have today, CDC recommends HPV vaccination for the prevention of most types of cervical cancer' (7). All four of these statements are at significant variance with the available evidence as they imply that Gardasil can indeed protect against some types of cervical cancer.

At present there are no significant data showing that either Gardasil or Cervarix (GlaxoSmithKline) can prevent any type of cervical cancer since the testing period employed was too short to evaluate long-term benefits of HPV vaccination. The longest follow-up data from phase II trials for Gardasil and Cervarix are 5 and 8.4 years, respectively (8–10), while invasive cervical cancer takes up to 20–40 years to develop from the time of acquisition of HPV infection (10–13). Both vaccines, however, are highly effective in preventing HPV-16/18 persistent infections and the associated cervical intraepithelial neoplasia (CIN) 2/3 lesions in young women who had no HPV infection at the time of first vaccination (13–15). Nonetheless, although cervical cancer may be caused by persistent exposure to 15 out of 100 extant HPVs through sexual contact (11), even persistent HPV infections caused by 'high-risk' HPVs will usually not lead to immediate precursor lesions, let alone in the longer term to cervical cancer. The reason for this is that as much as 90% HPV infections resolve spontaneously within 2 years and, of those that do not resolve, only a small proportion may progress to cancer over the subsequent 20–40 years (10,11,16–18). Moreover, research data show that even higher degrees of atypia (such as CIN 2/3) can either resolve or stabilize over time (19). Thus, in the absence of long-term

follow-up data, it is impossible to know whether HPV vaccines can indeed prevent *some* cervical cancers or merely postpone them. In addition, neither of the two vaccines is able to clear existing HPV-16/18 infections, nor can they prevent their progression to CIN 2/3 lesions (20,21). According to the FDA, 'It is *believed* that prevention of cervical precancerous lesions is highly *likely* to result in the prevention of those cancers' (emphasis added) (22). It would thus appear that even the FDA acknowledges that the long-term benefits of HPV vaccination rest on assumptions rather than solid research data.

Gardasil and Cervarix: do the benefits of vaccination outweigh the risks?

Currently, governmental health agencies worldwide state that HPV vaccines are 'safe and effective' and that the benefits of HPV vaccination outweigh the risks (6,23,24). Moreover, the US CDC maintains that Gardasil is 'an important cervical cancer prevention tool' and therefore 'recommends HPV vaccination for the prevention of most types of cervical cancer' (6,7). However, the rationale behind these statements is unclear given that the primary claim that HPV vaccination prevents cervical cancer remains unproven. Furthermore, in the US, the current age-standardized death rate from cervical cancer according to World Health Organization (WHO) data (1.7/100,000) (Table I), is 2.5 times lower than the rate of serious adverse reactions (ADRs) from Gardasil reported to the Vaccine Adverse Event Reporting System (VAERS) (4.3/100,000 doses distributed) (Table II). In the Netherlands, the reported rate of serious ADRs from Cervarix per 100,000 doses administered (5.7) (Table II) is nearly 4-fold higher than the age-standardized death rate from cervical cancer (1.5/100,000) (Table I).

Although it may not be entirely appropriate to compare deaths alone from cervical cancer to serious ADRs from HPV vaccines, it should be re-emphasized that (in accordance with FDA guidelines) the margin of tolerance for serious ADRs for a vaccine with uncertain benefits needs to be very narrow, especially when such vaccine is administered to otherwise healthy individuals (1). HPV vaccination, even *if* proven effective as claimed, is targeting 9–12 year old girls to prevent approximately 70% of cervical cancers, some of which may cause death at a rate of 1.4–2.3/100,000 women in developed countries with effective Pap smear screening programmes (Table I). For a vaccine designed to prevent a disease with such a low death rate, the risk to those vaccinated should be minimal. Further, according to some estimates, HPV vaccination would do little to decrease the already low rate of cervical cancer in countries with regular Pap screening (10). Thus, any expected benefit from HPV vaccination will notably drop in the setting of routine Pap screening. Accordingly, the risk-to-benefit balance associated with HPV vaccination will then also become less favourable. On the other hand, in developing countries where cervical cancer deaths are much higher and Pap screening coverage low (Table I), the potential benefits of HPV vaccination are significantly hampered by high vaccine costs (25).

It should be noted that for any vaccine the number of doses that are eventually administered is lower than the number of doses that are distributed. Thus, calculations based on the latter tend to under-estimate the rate of vaccine-associated ADRs (Figure 1). Supporting this interpretation, we show in Table II and Figure 1 that for any of the two HPV vaccines, the reported rate of ADRs per 100,000 doses administered is very similar across different countries and approximately seven times higher than that

Table I. Key data on cervical cancer, HPV-16/18 prevalence, and cervical cancer prevention strategies in 22 countries. Data sourced from the World Health Organization (WHO)/Institut Catala d'Oncologia (ICO) Information Centre on HPV and cervical cancer (105).

Country	Incidence per 100,000 women (age-standardized)	Mortality per 100,000 women (age-standardized)	Mortality ranking among all cancers (all ages)	Pap screening coverage (%)	HPV-16/18 prevalence in women with low-/high-grade lesions/cervical cancer (%)	HPV vaccine introduced
Australia	4.9	1.4	17th	60.6 (All women aged 20–69 y screened every 2 y)	3.8/44.6/76.2	Yes
Netherlands	5.4	1.5	16th	59.0 (All women aged > 20 y screened every 5 y)	1.5/61.6/87.9	Yes
US	5.7	1.7	15th	83.3 (All women aged > 18 y screened every 3 y)	7.7/55/76.6	Yes
France	7.1	1.8	15th	74.9 (All women aged 20–69 y screened every 2 y)	7.6/63.4/75.6	Yes
Canada	6.6	1.9	14th	72.8 (All women aged 18–69 y screened every 3 y; Annual if at high risk)	11.8/56.2/74.3	Yes
Spain	6.3	1.9	15th	75.6 (All women aged 18–65 y screened every 3 y)	2.3/46.9/55.9	Yes
UK and Ireland	7.2	2	16th	80 (All women aged 25–64 y screened every 5 y)	2.4/61.9/79.1	Yes
Israel	5.6	2.1	14th	34.7 (All women aged 18–69 y screened every 3 y)	2.2/44.8/68.5	Yes
Germany	6.9	2.3	13th	55.9 (Women aged 20–49 y screened every 5 y)	1.4/54.1/76.8	Yes
China	9.6	4.2	7th	16.8 (All women aged 18–69 y screened every 3 y)	2.3/45.7/71	No
Viet Nam	11.5	5.7	4th	4.9 (All women aged 18–69 y screened every 3 y)	2.1/33.3/72.6	Yes
Russia	13.3	5.9	7th	70.4 (All women aged 18–69 y screened every 3y)	9.3/56/74	Yes
Brazil	24.5	10.9	2nd	64.8 (All women aged 18–69 y screened every 3 y)	4.3/54/70.7	Yes
Thailand	24.5	12.8	2nd	37.7 (All women aged 15–44 y ever screened)	4.1/33.3/73.8	Yes
Pakistan	19.5	12.9	2nd	1.9 (All women aged 18–69 y screened every 3 y)	6/59.3/96.7	Yes
South Africa	26.6	14.5	2nd	13.6 (All women aged 18–69 y screened every 3 y)	3.6/58.4/62.8	Yes
India	27	15.2	1st	2.6 (All women aged 18–69 y screened every 3 y)	6/56/82.5	Yes
Cambodia	27.4	16.2	1st	None	3.2/33.3/72.6	Yes
Nepal	32.4	17.6	1st	2.4 (All women aged 18–69y screened every 3 y)	6/59.3/82.3	No
Nigeria	33	22.9	2nd	None	4.7/41.3/50	Yes
Ghana	39.5	27.6	1st	2.7 (All women aged 18–69 y screened every 3 y)	4.6/41.3/50	Yes
Uganda	47.5	34.9	1st	None	6.7/37.9/74.1	Yes

calculated from the number of distributed doses. The latter calculations also show a comparable range across several countries (Figure 1). Given that government-official vaccine surveillance programmes routinely rely on passive reporting (26), the rate of ADRs from HPV and other vaccines may be further under-estimated.

According to some estimates, only 1–10% of the ADRs in the US are reported to VAERS (27).

The lack of data on serious ADRs in countries where routine HPV vaccination for young women is recommended and strongly promoted (Table II) greatly hampers our understanding about the

Table II. Summary of adverse reactions (ADRs) from HPV vaccines Gardasil and Cervarix. Note that the US FDA Code of Federal Regulation defines a serious adverse drug event as 'any adverse drug experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse drug experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect' (106).

Vaccine	Country	Total <i>n</i> ADRs(ref.)	Doses <i>n</i> (ref.)	Total <i>n</i> ADRs/100,000 doses	Total <i>n</i> serious ADRs(ref.)	Total <i>n</i> serious ADRs/100,000 doses
Gardasil	US	18,727 (7)	35,000,000 ^a (7)	54	1,498 (7)	4.3
	France	1,700 (34)	4,000,000 ^a (34)	43	na	–
	Australia	1,534 (39)	6,000,000 ^a (39)	26	91 ^c (26,28,29)	1.5 ^c
	Ireland	314 (33)	90,000 ^b (33)	349	na	–
Cervarix	Netherlands	575 (32)	192,000 ^b (32)	299	575 (32)	5.7
	UK	8,798 (23)	3,500,000 ^b (23)	251	na	–

na = not available.

^aDoses distributed.

^bDoses administered.

^cExcluding 2010 data(unavailable at the time of writing of this report).

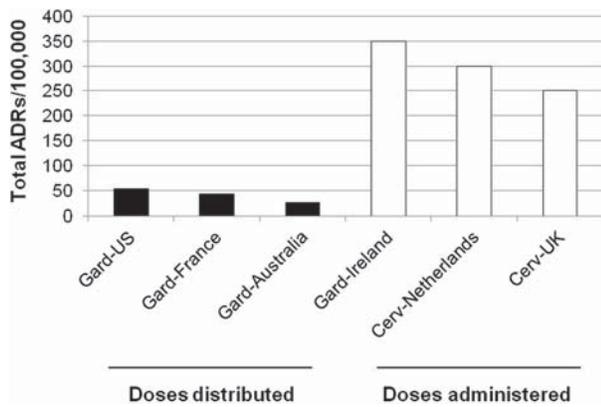


Figure 1. The rate of adverse reactions (ADRs) from Gardasil and Cervarix reported through various government-official vaccine surveillance programmes. For the data source, see Table II.

overall safety of the various HPV vaccination programmes. Nonetheless, analysis of the UK Medicines and Healthcare products Regulatory Agency (MHRA) vaccine safety data shows that there may be valid reasons for concern. For example, the total number of ADRs reported for Cervarix appears to be 24–104 times higher than that reported for any of the other vaccines in the UK immunization schedule (Figure 2).

Official reports on adverse events following immunization (AEFI) in Australia also raise concerns (26). In 2008, Australia reported an annual AEFI rate of 7.3/100,000, the highest since 2003, representing an 85% increase compared with AEFI rate from 2006 (26). This increase was almost entirely due to AEFIs reported following the commencement of the national HPV vaccination programme for females aged 12–26 years in April 2007 (705 out of a total of 1538 AEFI records). Thus, nearly 50% of all AEFIs reported during 2007 were related to the HPV vaccine. Moreover, HPV vaccine was the only suspected vaccine in 674 (96%) records, 203 (29%) had causality ratings of 'certain' or 'probable', and 43 (6%) were defined as 'serious'. The most severe AEFIs reported following HPV vaccination were anaphylaxis and convulsions. Notably, in 2007, 10 out of 13 reported anaphylaxis (77%) and 18 out of 35 convulsions (51%) occurred in women following HPV vaccination (26). During 2008, the HPV vaccine

was still the number one vaccine on the list of AEFIs in Australia, with 497 records (32% of all AEFIs), and accountable for nearly 30% of convulsions (13 out of 43) (28). During 2009, the Australian reported AEFI rate for adolescents decreased by almost 50% (from 10.4 to 5.6/100,000) (29). This decline in AEFI rates was attributed to a reduction in the numbers of HPV vaccine-related reports, following cessation of the catch-up component of the HPV programme(29). Namely, the percentage of AEFIs related to HPV vaccines was only 6.4 in 2009 (29) compared to 50 in 2007 (26). In spite of the overall significant decrease in AEFI rate, the percentage of convulsions attributable to the HPV vaccine remained comparable between 2007 and 2009 (51% (26) and 40% (29), respectively).

Cumulatively, the list of serious ADRs related to HPV vaccination in the US, UK, Australia, Netherlands, France, and Ireland includes deaths, convulsions, syncope, paraesthesia, paralysis, Guillain-Barré syndrome (GBS), transverse myelitis, facial palsy, chronic fatigue syndrome, anaphylaxis, autoimmune disorders, deep vein thrombosis, pulmonary embolisms, and pancreatitis (23,24,26,28–35).

It may be thus appropriate to ask whether it is worth risking death or a disabling lifelong neurodegenerative condition such as GBS at a preadolescent age for a vaccine that has only a theoretical potential to prevent cervical cancer, a disease that may develop 20–40 years after exposure to HPV, when, as Harper noted, the same can be prevented with regular Pap screening (36)?

It is also of note that in the post-licensure period (2006–2011), the US VAERS received 360 reports of abnormal Pap smears, 112 reports of cervical cancer dysplasia, and 11 reports of cervical cancers related to HPV vaccines (35). In a report to the FDA (37), Merck expressed two 'important concerns' regarding administration of Gardasil to girls with pre-existing HPV-16/18 infection. One was 'the potential of Gardasil to enhance cervical disease', and the other 'was the observations of CIN 2/3 or worse cases due to HPV types not contained in the vaccine'. According to Merck, 'These cases of disease due to other HPV types have the potential to counter the efficacy results of Gardasil for the HPV types contained in the vaccine.' Table 17 in Merck's report to the FDA shows that Gardasil had an observed efficacy rate of –44.6% in subjects who were already exposed to 'relevant HPV types' (37). If, as implied by Merck's own submission, Gardasil may exacerbate

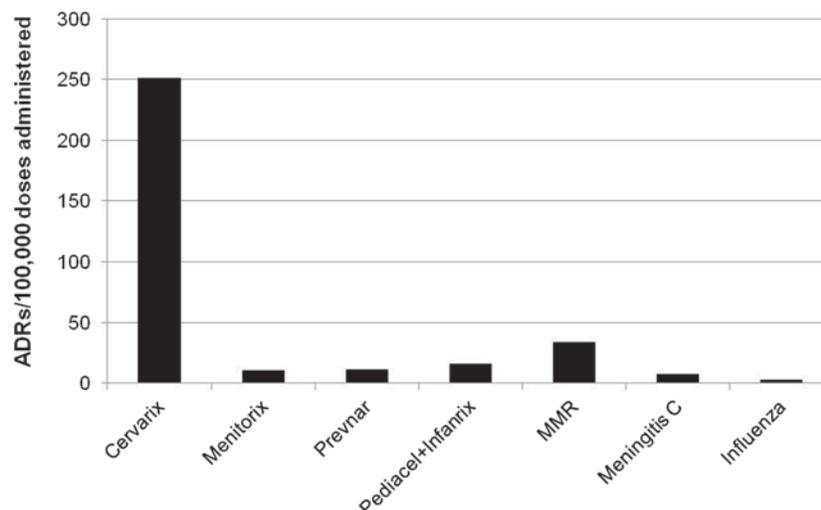


Figure 2. The rate of adverse reactions (ADRs) from Cervarix compared to that of other vaccines in the UK immunization schedule. Data sourced from the report provided by the UK Medicines and Healthcare products Regulatory Agency (MHRA) for the Joint Committee on Vaccination and Immunisation in June 2010 (23).

the very disease it is supposed to prevent, why do the US FDA and the CDC allow for preadolescent girls and young women to be vaccinated with Gardasil without prescreening them for HPV-16/18 infections?

Side-effects from HPV vaccines: are they a minor concern?

According to governmental health agencies worldwide, including the US CDC, Health Canada, the Australian Therapeutic Goods Administration (TGA), the UK MHRA, and the Irish Medicines Board (IMB), the vast majority of adverse reactions from either Gardasil or Cervarix are non-serious (6,23,24,38,39). These sources further state that most participants report brief soreness at the injection site, headache, nausea, fever, and fainting (6,23,24,38,39). Moreover, the UK MHRA and the US FDA and the CDC maintain that fainting is common with vaccines (especially among adolescents) and hence not a reason for concern (6,23). Specifically, the UK MHRA states that “Psychogenic events” including vasovagal syncope, faints and panic attacks can occur with any injection procedure’ and that ‘such events can be associated with a wide range of temporary signs and symptoms including loss of consciousness, vision disturbances, injury, limb jerking (often misinterpreted as a seizure/convulsion), limb numbness or tingling, difficulty in breathing, hyperventilation etc.’ (23).

The VAERS data show that since 2006 when it was first approved, Gardasil has been associated with 18,727 adverse reactions in the US alone, 8% of which were serious (1498) including 68 deaths (Table II). A report to any passive vaccine surveillance system does not by itself prove that the vaccine caused an ADR.

Systematic, prospective, controlled trials are needed to establish or reject causal relationships with regard to drug-related adverse reactions of any type. Nevertheless, the unusually high frequency of reports of ADRs related to HPV vaccines (Figure 2), as well as their consistent pattern (i.e. with only minor deviations, nervous system-related disorders rank the highest in frequency across different countries, followed by general/administration site conditions and gastrointestinal disorders) (Figure 3), indicates that the risks of HPV vaccination may not have been fully evaluated in clinical trials. Indeed, in their analysis of ADRs of potential autoimmune aetiology in a large integrated safety database of ASO4 adjuvanted vaccines (a novel adjuvant system composed of 3-O-desacyl-4-monophosphoryl lipid A and aluminum salts used in Cervarix), Verstraeten et al. (40) acknowledge that ‘It is important to note that none of these studies were set up primarily to study autoimmune disorders.’ If the purpose of the study was indeed to assess ADRs of ‘potential autoimmune aetiology’, as the title itself clearly states (40), then the study should have been designed to detect them. All of the eight authors of the ASO4 safety study are employees of GlaxoSmithKline (GSK), the manufacturer of Cervarix (40). These authors noted that ‘our search of the literature found no studies conducted by independent sources on this subject’ and ‘All studies included in this analysis were funded by GSK Biologicals, as was the analysis itself. GSK Biologicals was involved in the study design, data collection, interpretation and analysis, preparation of the manuscript and decision to publish’ (40).

Given that vaccines can trigger autoimmune disorders(41–44), a more rigorous safety assessment than that provided by the GSK-sponsored study would appear to have been warranted.

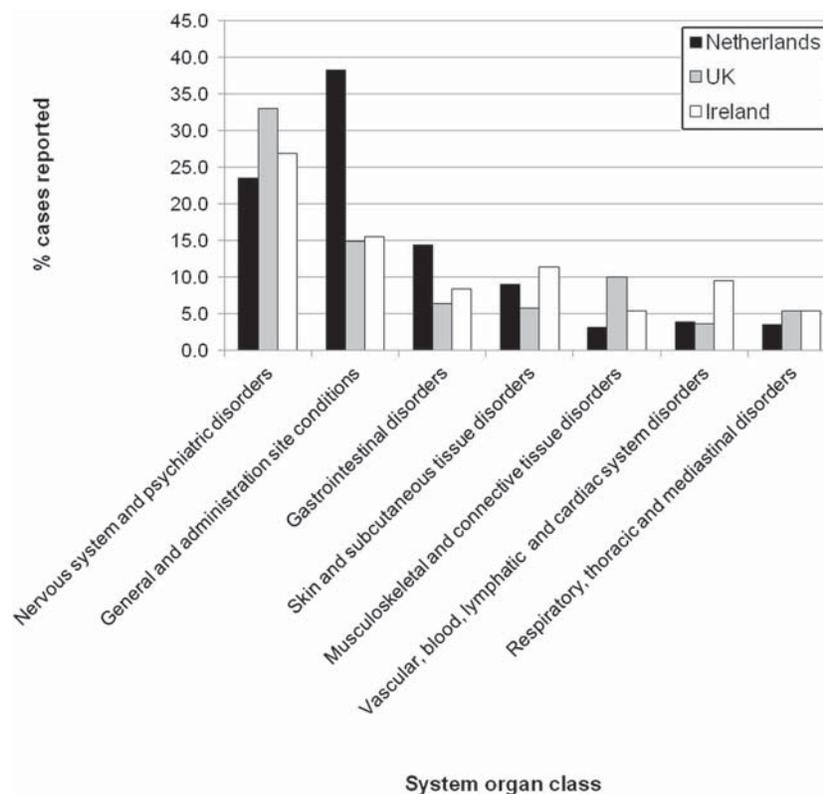


Figure 3. Percentages of reported ADRs associated with HPV vaccines for each system organ class. Data sourced from the Database of the Netherlands Pharmacovigilance Centre Lareb (32), the UK Medicines and Healthcare products Regulatory Agency (MHRA) (62), and the Irish Medicines Board (IMB) (24). The most commonly reported ADRs in the nervous system and psychiatric disorders class were headache, syncope, convulsions, dizziness, hypoaesthesia, paraesthesia, lethargy, migraine, tremors, somnolence, loss of consciousness, dysarthria, epilepsy, sensory disturbances, facial palsy, grand mal convulsion, dysstasia, dyskinesia, hallucination, and insomnia.

Meanwhile, independent scientific reports have linked HPV vaccination with serious ADRs, including death (45,46), amyotrophic lateral sclerosis (ALS) (45), acute disseminated encephalomyelitis (ADEM) (47–49), multiple sclerosis (MS) (50–52), opsoclonus-myoclonus syndrome (OMS) (which is characterized by ocular ataxia and myoclonic jerks of the extremities) (53), orthostatic hypotension (54), brachial neuritis (55), vision loss (56), pancreatitis (57), anaphylaxis (58), and postural tachycardia syndrome (POTS) (59).

ADEM and MS are serious demyelinating diseases of the central nervous system that typically follow a febrile infection or vaccination (49,50,60). Both disorders are also thought to be triggered by an autoimmune mechanism (50). Clinical symptoms include rapid onset encephalopathy, multifocal neurologic deficits, demyelinating lesions, optic neuritis, seizures, spinal conditions, and variable alterations of consciousness or mental status (47,49,60). Regarding POTS, the reported case had no other relevant factors or events preceding the symptoms onset apart from Gardasil vaccination (59). POTS is defined as the development of orthostatic intolerance (61). According to Blitshteyn, 'It is probable that some patients who develop POTS after immunization with Gardasil or other vaccines are simply undiagnosed or misdiagnosed, which leads to under-reporting and a paucity of data on the incidence of POTS after vaccination in literature' (59). Patients with POTS typically present with complaints of diminished concentration, tremulousness, dizziness and recurrent fainting, exercise intolerance, fatigue, nausea and loss of appetite (59,61). Such symptoms may be incorrectly labelled as panic disorders or chronic anxiety. Notably, symptoms of POTS appear to be among the most frequent ADRs reported after vaccination with HPV vaccines (6,23,24,39). In spite of this, health authorities worldwide do not regard these outcomes as causally related to the vaccine (6), but rather as 'psychogenic events' (23,39).

In summary, it appears that many medical authorities may have been too quick to dismiss a possible link between HPV vaccines and serious ADRs by relying heavily on data provided by the vaccine manufacturers rather than from independent research. The UK MHRA states that 'The vast majority of suspected ADRs reported to MHRA in association with Cervarix vaccine continue to be related to either the signs and symptoms of recognized side effects listed in the product information or to the injection process and not the vaccine itself (i.e. "psychogenic" in nature such as faints)' (23). It is interesting to note that the entire group of system class disorders shown in Figure 3 is regarded as unrelated to the HPV vaccine by the MHRA. According to the Agency, 'These suspected ADRs are not currently recognised as side effects of Cervarix vaccine and the available evidence does not suggest a causal link with the vaccine. These are isolated medical events which may have been coincidental with vaccination' (23,62). However, the fact that a similar pattern of system class ADRs to that in the UK has also been observed in at least two other countries argues against the MHRA conclusion and suggests the opposite, namely a causal relationship with the HPV vaccine (Figure 3).

Safety assessment of HPV vaccines in clinical trials: was it adequate?

A double-blinded, placebo-controlled trial is considered the 'gold standard' for clinical trials as it is thought to prevent potential researchers' biases from distorting the conduct of a trial and/or the interpretation of the results (63). Biases, however, may still occur due to selective publication of findings from within such trials, subject selection factors (inclusion/exclusion criteria), as well as placebo choices. With regard to the latter, according to the FDA, a placebo is 'an inactive pill, liquid, or powder that has no treatment value' (63). It is therefore surprising thus to note that no regulations govern placebo composition, given that certain placebos can influence trial outcomes (64). Specifically, placebo composition can, in principle, be manipulated to produce results that are favourable to the drug either in terms of safety or efficacy (64).

The clinical trials for Gardasil and Cervarix used an aluminum-containing placebo (15,20,40,65–69). Both HPV vaccines, like many other vaccines, are adjuvanted with aluminum in spite of well documented evidence that aluminum can be highly neurotoxic (70–72). Moreover, current research strongly implicates aluminum adjuvants in various neurological and autoimmune disorders in both humans and animals (41,73–80). It is thus becoming increasingly clear that the routine use of aluminum as a placebo in vaccine trials is not appropriate (80,81).

Notably, safety data for Gardasil presented in Merck's package insert and the FDA product approval information (82) show that compared to the saline placebo, those women receiving the aluminum-containing placebo reported approximately 2–5 times more injectionsite ADRs. On the other end, the proportion of injection site ADRs reported in the Gardasil treatment group was comparable to that of the aluminum 'control' group (Table III). Thus, Merck's own data seem to indicate that a large proportion of ADRs from the HPV vaccine were due to the effect of the aluminum adjuvant.

For the assessment of serious conditions, the manufacturer pooled the results from the study participants who received the saline placebo with those who received the aluminum-containing placebo and presented them as one 'control' group. The outcome of this procedure was that Gardasil and the aluminum 'control' group had exactly the same rate of serious conditions (2.3%) (Table IV).

In a recent meta-analysis of safety and efficacy of HPV vaccines, seven trials enrolling a total of 44,142 females were evaluated (83). Two main populations of women were defined in these trials: those who received three doses of the HPV vaccine or the aluminum-containing placebo within a year (denoted as the per-protocol population (PPP)), and those who received at least one injection of the vaccine or the placebo within the same period (intention-to-treat population (ITT)). While HPV vaccine efficacy was evaluated in both PPP and ITT cohorts, vaccine safety was primarily evaluated in the ITT cohort (83). Although ITT analysis is 'conservative' for assessment of treatment benefits (since dropouts may occur), it is 'anti-conservative' for assessment of ADRs, because ADRs will occur

Table III. Injectionsite adverse reactions (ADRs) reported in Gardasil clinical trials among 8878 female participants aged 9–26 years, 1–5 days post-vaccination(82).

ADR type	Gardasil (n = 5088)%	Aluminum (AAHS) ^a (n = 3470)%	Saline placebo (n = 320)%	Gardasil/saline	Gardasil/AAHS	AAHS/saline
Pain	83.9	75.4	48.6	1.7	1.1	1.6
Swelling	25.4	15.8	7.3	3.5	1.6	2.2
Erythema	24.7	18.4	12.1	2.0	1.3	1.5
Pruritus	3.2	2.8	0.6	3.5	1.1	4.7
Bruising	2.8	3.2	1.6	1.8	0.9	2.0

^aAAHS Control = amorphous aluminum hydroxyphosphate sulfate.

Table IV. Number of girls and women aged 9–26 years who reported a condition potentially indicative of a systemic autoimmune disorder after enrolment in Gardasil clinical trials (82).

Condition	Aluminum (AAHS)	
	Gardasil (<i>n</i> = 10,706) <i>n</i> (%)	^a (<i>n</i> = 9412) <i>n</i> (%)
Arthralgia/arthritis/arthropathy	120 (1.1)	98 (1.0)
Autoimmune thyroiditis	4 (0.0)	1 (0.0)
Coeliac disease	10 (0.1)	6 (0.1)
Insulin-dependent	2 (0.0)	4 (0.0)
Diabetes melitus insulin-dependent	2 (0.0)	2 (0.0)
Erythema nodosum	27 (0.3)	21 (0.2)
Hyperthyroidism	35 (0.3)	38 (0.4)
Hypothyroidism	7 (0.1)	10 (0.1)
Inflammatory bowel disease	2 (0.0)	4 (0.0)
Multiple sclerosis	2 (0.0)	5 (0.1)
Nephritis	2 (0.0)	0 (0.0)
Optic neuritis	4 (0.0)	3 (0.0)
Pigmentation disorder	13 (0.1)	15 (0.2)
Psoriasis	3 (0.0)	4 (0.0)
Raynaud's phenomenon	6 (0.1)	2 (0.0)
Rheumatoid arthritis	2 (0.0)	1 (0.0)
Scleroderma/morphaea	1 (0.0)	0 (0.0)
Stevens-Johnson syndrome	1 (0.0)	3 (0.0)
Sytemic lupus erythematosus	3 (0.0)	1 (0.0)
Uveitis	3 (0.0)	1 (0.0)
Total	245 (2.3)	218 (2.3)

less frequently if fewer doses of the vaccine are administered. Thus, such a selection procedure may explain why the meta-analysis found the risk-to-benefit ratio to be in favour of the HPV vaccines (83).

The seven trials included in the meta-analysis were all sponsored by the vaccine manufacturers (14,15,20,65–69). In a lengthy report of potential conflicts of interests of the FUTURE II trial study group (15), the majority of authors declared 'receiving lecture fees from Merck, Sanofi Pasteur, and Merck Sharp & Dohme'. In addition, 'Indiana University and Merck have a confidential agreement that pays the university on the basis of certain landmarks regarding the HPV vaccine.' In the 2009 *JAMA* editorial (11), Haug noted that 'When weighing evidence about risks and benefits, it is also appropriate to ask who takes the risk, and who gets the benefit. Patients and the public logically expect that only medical and scientific evidence is put on the balance. If other matters weigh in, such as profit for a company or financial or professional gains for physicians or groups of physicians, the balance is easily skewed. The balance will also tilt if the adverse events are not calculated correctly.'

Are there safe and effective alternatives to HPV vaccination?

Although approximately 275,000 women die annually from cervical cancer worldwide, almost 88% of these deaths occur in developing countries. Such disproportion of cancer deaths may be surprising given that the prevalence of HPV-16/18 in women with cervical cancer is equal in both developing and developed countries (71.0% and 70.8%, respectively) (Table V). Furthermore, HPV-16 and HPV-18 are the most oncogenic of all HPV subtypes and increasingly dominant with increasing severity of cervical cancer lesions (Table I) (84). Nonetheless, analysis of WHO data in Figure 4 shows that HPV-16/18 prevalence in women with high-grade lesions as well as cervical cancer is not a significant promoter of high cervical cancer mortality in developing countries ($P = 0.07-0.19$), but rather it is the lack of or insufficient Pap screening coverage ($P < 0.0001$). These data do not dispute that HPV-16/18 infection is a primary prerequisite for cervical cancer. However, they do point to other co-factors as necessary determinants of both disease progression and outcome (85).

The efficacy of regular Pap screening procedures in developed countries is further emphasized by the fact that such programmes helped to achieve a 70% reduction in the incidence of cervical cancer over the last five decades (10,12,86,87). Conversely, in Finland, when women stopped attending Pap screens, a 4-fold increase in cervical cancer occurred within 5 years from screening cessation (88,89).

It should be emphasized that HPV vaccination does not make Pap screening obsolete, especially since the current HPV vaccines guard only against 2 out of 15 oncogenic HPV strains. Harper noted that if HPV-vaccinated women stopped going for Pap smears, the incidence rate of cervical cancer would increase (36,86). A similar concern was also raised by French and Canadian researchers who suggested the possibility that vaccinated women might be less inclined to participate in screening programmes (87,90). Such outcomes would in turn compromise timely specialist referral of cases harbouring precancerous lesions, especially those related to HPV genotypes other than 16/18 (90).

Are HPV vaccines cost-effective?

The currently licensed HPV vaccines are among the most expensive vaccines on the market (i.e. Gardasil currently costs US \$400 for the three required doses) (87), making it unlikely that those countries with the heaviest burden of cervical cancer mortality (i.e. Uganda, Nigeria, and Ghana) would ever benefit from them. That is under the assumption that the long-term benefits from HPV vaccination (i.e. cancer prevention) were proven. For example, preadolescent HPV vaccination in Thailand is cost-effective only when assuming lifelong efficacy and a cost of 10 international dollars (I\$, a currency that provides a means of translating and comparing costs among countries) per vaccinated girl (approximately I\$2/dose) or less (91). The cost-effectiveness analysis of HPV vaccination for Eastern Africa shows a similar outcome (25). In countries where pricing is less of an issue, such as the US, HPV vaccination is only cost-effective based on the assumption of complete and lifelong vaccine efficacy and 75% coverage of the targeted preadolescent population (92,93). In the Netherlands, HPV vaccination is not cost-effective under similar assumptions (e.g. that the HPV vaccine provides lifelong protection against 70% of all cervical cancers, has no side-effects, and is administered to all women regardless of their risk of cervical cancer) (94). Note that the reason why high coverage is needed for a vaccine to be cost-effective in the developed country setting is the very low incidence of cervical cancer (due to effectiveness of Pap screening programmes). For example, to prevent a single out of 5.7/100,000 cervical cancer cases (or one out of 1.7/100,000 cervical cancer deaths) in the US, nearly every girl would need to be vaccinated for the HPV vaccine programme to be cost-effective.

The increased pressure to make the HPV vaccines mandatory for all preadolescent girls makes the cost of the HPV vaccination programme a significant issue. For example, according to a 2006 report in *The New York Times* (95), to make Gardasil mandatory would probably double the cost of the US vaccination programme: 'North Carolina, for instance, spends \$11 million annually to provide every child with seven vaccines. Gardasil alone would probably cost at least another \$10 million.' Under the assumption that the HPV vaccine offers full protection against HPV infection for 5 years, an 11-year-old girl would need 13 booster shots if she were to live to the age of 75. At a current cost of US \$120 per dose, the total cost for vaccinating one girl would thus exceed US \$1500. According to some estimates, to vaccinate every 11- and 12-year-old girl in the US would cost US \$1.5 billion and to

Table V. Key cervical cancer statistics according to the 2010 World Health Organization (WHO)/Institut Catala d'Oncologia (ICO) report on HPV and related cancers (107).

	World	Developing countries (% total)	Developed countries (% total)
Women at risk for cervical cancer (aged ≥ 15 y)	2,336,986	1,811,867 (77.5)	525,120 (22.5)
Annual number of new cases of cervical cancer	529,828	453,321 (85.6)	76,507 (14.4)
Annual number of cervical cancer deaths	275,128	241,969 (87.9)	33,159 (12.1)
Prevalence (%) of HPV-16 and/or HPV-18 among women with cervical cancer	70.9	71.0	70.8

protect only these girls for a lifetime would cost US \$7.7 billion (96). If we were to estimate just the cost of initial vaccination excluding the booster shots for 11- and 12-year-old girls, in ten years the US would spend at least 15 billion of limited health care dollars on Gardasil alone (96). Who then reaps the benefit at no risk from making the HPV vaccine mandatory? The customer or the manufacturer?

Altogether the above observations do not support the claim made by the US CDC and the FDA, that is, 'This [Gardasil] vaccine is an important cervical cancer prevention tool that will potentially benefit the health of millions of women' (6) and, instead, appear to suggest that current worldwide immunization campaigns (Table I) with either of the two HPV vaccines are neither justified by long-term health benefits nor economically viable.

How does HPV vaccine marketing and promotion line up with international ethical guidelines for informed consent?

The medical profession's ethical duty is to provide a full and accurate explanation of the benefits as well as the risks associated

with a particular drug so that a patient is able to make an informed decision regarding a treatment. If a physician fails to do so and/or if financial interests take precedence over public health, breaches of informed consent guidelines may occur. For instance, presenting information in a way which promotes fear of a disease while undervaluing potential vaccine risks is likely to encourage patients to give consent to the treatment, even when the latter has no proven significant health benefit.

Both Gardasil and Cervarix were approved by the US FDA, which in 2006 was found to be '...not positioned to meet current or emerging regulatory responsibilities', because 'its scientific base has eroded and its scientific organizational structure is weak' (97). According to the Science and Mission at Risk Report prepared by the FDA Science Board in 2006 (97), the risks of an 'under-performing' FDA are far-reaching for two main reasons. First, 'The FDA's inability to keep up with scientific advances means that American lives are at risk', and second, 'The world looks to the FDA as a leader in medicine and science. Not only can the agency not lead, it can't even keep up with the advances in science' (97).

If the FDA's decisions to approve certain drugs could by its own admission be unreliable, then the only other gate-keeper for consumer safety is the expert advice provided by other health

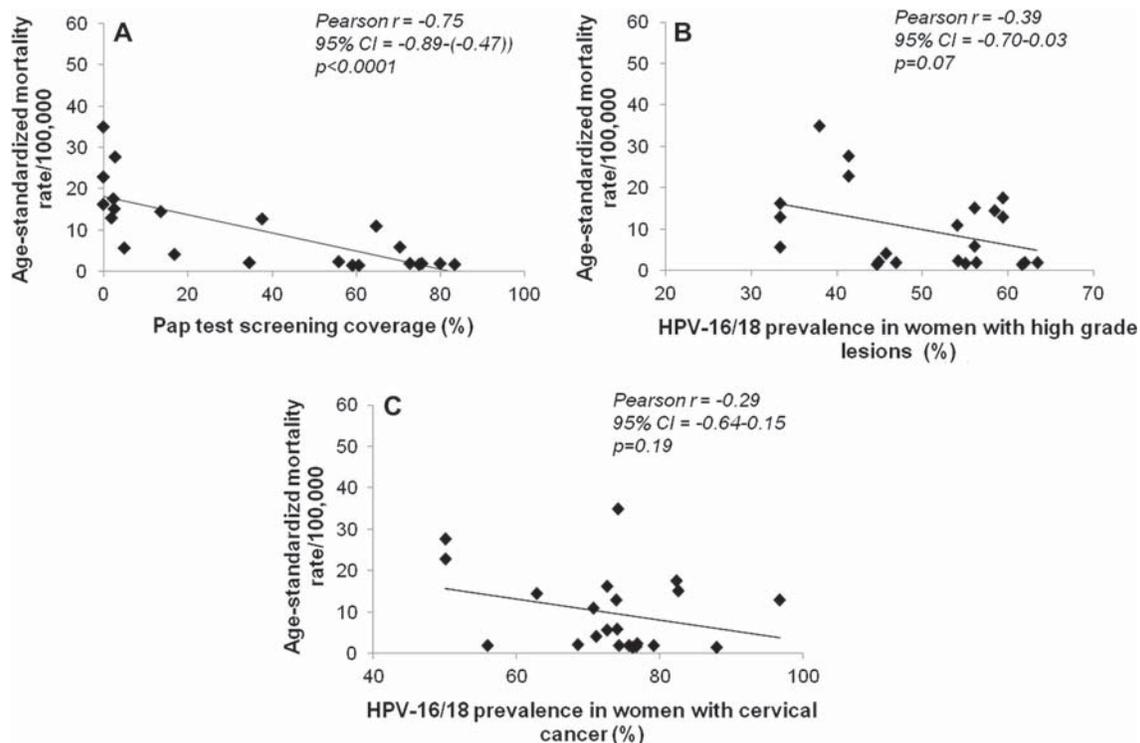


Figure 4. Correlation between cervical cancer mortality rates and A: Pap test screening coverage; B: HPV-16/18 prevalence in women with high-grade lesions (CIN 2/3, carcinoma *in situ* (CIS), and high-grade cervical squamous intraepithelial lesions (HSIL)); C: HPV-16/18 prevalence in women with cervical cancer. Data were sourced for 22 countries from World Health Organization (WHO)/Institut Catala d'Oncologia (ICO) Information Centre on HPV and cervical cancer (Table I). The correlation analysis was carried out using GraphPad Prism statistical software to derive Pearson correlation coefficients (r). The level of significance was determined using a two-tailed test. The correlation was considered statistically significant at $P < 0.05$.

authorities. The history of how HPV vaccines came to market, however, indicates that such advice was not always given from the basis of the best available evidence. A 2009 Special Communication from *JAMA* by Rothman and Rothman (98) provides compelling evidence that Gardasil manufacturer Merck funded educational programmes by professional medical associations (PMAs) as a marketing strategy to promote the use of their vaccine. The marketing campaign proceeded 'flawlessly', according to Merck's chief executive officer, and in 2006 Gardasil was named the pharmaceutical 'brand of the year' for building 'a market out of thin air' (98). The reason why the marketing campaign for Gardasil was so successful was that 'By making this vaccine's target disease cervical cancer, the sexual transmission of HPV was minimized, the threat of cervical cancer to all adolescents maximized, and the subpopulations most at risk [women in developing countries] practically ignored' (98). That these arguments were delivered by the PMAs is cause for concern, since PMAs are obligated to provide members with evidence-based data so that they in turn are able to present relevant risks and benefits to their patients (98).

India's medical authorities have also been publicly condemned after a civil society-led investigation revealed that trials for HPV vaccines in the states of Andhra Pradesh and Gujarat violated established national and international ethical guidelines on clinical research as well as children's rights (99). These events apparently occurred as a result of 'aggressive' promotional practices of the drug companies and their uncritical endorsement by India's medical associations (99). Although proclaimed as a post-licensure observational study of HPV vaccination against cervical cancer, the project was in fact a clinical trial and, as such, should have adhered to protocols mandated by the Drugs and Cosmetics Act (DCA) and the Indian Council for Medical Research (ICMR) (100). Instead, the trial was found in serious breach of both the DCA's and the ICMR's guidelines for informed consent and was terminated in April 2010, following six post-HPV vaccination deaths (99). The report in the 2011 issue of *Lancet Infectious Diseases* further reveals that both ICMR and DCA subsequently denied information on the study protocols as a 'trade secret and commercial confidence of third party' (100). According to the authors, 'It remains unclear how information from a study done in collaboration with government health organisations can be regarded as a trade secret' (100). It is worth emphasizing that the termination of HPV vaccine trials in India occurred despite an annual cervical cancer mortality rate of 15.2/100,000 women, which is over 7–10 times greater than that in the developed world (Table I). Such an outcome indicates that even situations of unmet medical needs cannot be resolved at the expense of abandoning ethical requirements for informed consent.

Questionable HPV vaccine marketing strategies were also seen in France and were eventually stopped by the action of government health authorities who found the sponsorship of several Gardasil advertisements to be in direct violation of French public health codes (101). These violations included, but were not limited to: 1) Claiming longer efficacy than was actually proven (8.5 versus 4.5 years) and 2) Making false claims (the ads in question replaced the officially approved use of Gardasil for 'the prevention of low-grade lesions' with statements indicating Gardasil should be used for 'the prevention of pre-malignant genital lesions, cancers of the cervix and external genital warts').

In the US, Merck has been heavily criticized for the fact that it spent vast sums in lobbying to make the vaccine mandatory (12,98). According to an editorial from *The American Journal of Bioethics*, even those who strongly favoured the vaccine were 'stunned at the degree to which Merck has pushed its \$400 vaccine as a mandatory measure' (102). Nonetheless, what is more

disconcerting than the aggressive marketing strategies employed by the vaccine manufacturers is the practice by which the medical profession has presented partial information to the public, namely, in a way that generates fear, thus likely promoting vaccine uptake. For example, the US CDC and the FDA state that 'Worldwide, cervical cancer is the second most common cancer in women, causing an estimated 470,000 new cases and 233,000 deaths per year' (6). The Telethon Institute for Child Health Research in Australia made a similar statement in 2006 while recruiting volunteers for a HPV vaccine study. In the opening paragraph the point was also made that cervical cancer was one of the most common causes of cancer-related deaths in women worldwide (103). A crucial fact was omitted in both instances which is that while it is certainly true that approximately a quarter of a million of women die of cervical cancer each year, 88% of these deaths occur in the developing countries and certainly not in the US nor Australia (Table V), where cervical cancer is the 15th and 17th cause of cancer-related deaths, respectively, and where mortality rates from this disease are the lowest on the planet (1.4–1.7/100,000) (Table I). Finally, contrary to the information provided by the CDC and the FDA, there is no evidence that Gardasil is 'an important cervical cancer prevention tool' (6).

It thus appears that to this date, medical and regulatory entities worldwide continue to provide inaccurate information regarding cervical cancer risk and the usefulness of HPV vaccines, thereby making informed consent regarding vaccination impossible to achieve.

Concluding remarks

Regulatory authorities are responsible for ensuring that new vaccines go through proper scientific evaluation before they are approved. An equal fiduciary responsibility rests with the medical profession to only promote vaccinations with those vaccines whose safety and efficacy have been thoroughly demonstrated. The available evidence, however, indicates that health authorities in various countries may have failed to provide an evidence-based rationale for immunization with HPV vaccines and, in doing so, may have breached international ethical guidelines for informed consent. Contrary to the information from the US CDC, Health Canada, Australian TGA, and the UK MHRA, the efficacy of Gardasil and Cervarix in preventing cervical cancer has not been demonstrated, and the long-term risks of the vaccines remain to be fully evaluated.

Current worldwide HPV immunization practices with either of the two HPV vaccines appear to be neither justified by long-term health benefits nor economically viable, nor is there any evidence that HPV vaccination would reduce the rate of cervical cancer beyond what Pap screening has already achieved. Furthermore, the frequency, the severity, as well as the consistency of the patterns of ADRs reported to various governmental vaccine surveillance programmes for both Gardasil and Cervarix (Figures 2 and 3) raise significant concerns about the overall safety of HPV vaccination programmes. Because these programmes have global coverage (Table I), the long-term health of many women may be unnecessarily at risk against still unknown vaccine benefits. Altogether these observations suggest that a reduction in the burden of cervical cancer globally might be best achieved by targeting other risk factors for this disease (i.e. smoking, use of oral contraceptives, chronic inflammation) (85) in conjunction with regular Pap test screening. The latter strategy has already been proven successful in developed nations where the incidence of cervical cancer is very low (Table I).

According to the Helsinki Declaration and the International Code of Medical Ethics (104), the well-being of the individual must be a physician's top priority, taking precedence over all other interests. Although the Declaration is addressed primarily to physicians, the World Medical Association encourages other participants in medical research involving human subjects to adopt these same principles (104). Greater efforts should thus be made to minimize the undue commercial influences on academic institutions and medical research, given that these may impede unbiased scientific inquiry into important questions about vaccine science and policy.

The almost exclusive reliance on manufacturers' sponsored studies, often of questionable quality, as a base for vaccine policy-making should be discontinued. So should be the dismissal of serious ADRs as coincidental or 'psychogenic' in spite of independent research suggesting otherwise. It can hardly be disputed in view of all the evidence (i.e. case reports and vaccineADR surveillance in various countries) that HPV vaccines do trigger serious ADRs. What does remain debatable, however, is the true frequency of these events because all systems of monitoring for vaccineADRs currently in place rely on passive reporting. Passive ADR surveillance should thus be replaced by active surveillance to better our understanding of true risks associated with particular vaccines (especially new vaccines). The presentation of partial and non-factual information regarding cervical cancer risks and the usefulness of HPV vaccines, as cited above, is, in our view, neither scientific nor ethical. None of these practices serve public health interests, nor are they likely to reduce the levels of cervical cancer. Independent evaluation of HPV vaccine safety is urgently needed and should be a priority for government-sponsored research programmes. Any future vaccination policies should adhere more rigorously to evidence-based medicine as well as strictly follow ethical guidelines for informed consent.

Declaration of interest: This work was supported by the Dwozkin, Lotus and Katlyn Fox Family Foundations. L.T. and C.A.S. conducted a histological analysis of autopsy brain samples from a Gardasil-suspected death case. C.A.S. is a founder and shareholder of Neurodyn Corporation, Inc. The company investigates early-state neurological disease mechanisms and biomarkers. This work and any views expressed within it are solely those of the authors and not of any affiliated bodies or organizations.

A portion of this information was presented at the Vaccine Safety Conference, 3–8 January 2011 (www.vaccinesafetyconference.com).

References

- Food and Drug Administration (FDA). Workshop on Non-clinical Safety Evaluation of Preventative Vaccines: Recent Advances and Regulatory Considerations. 2002 [cited 2011 May 30]. Available from: <http://www.fda.gov/downloads/biologicsbloodvaccines/newsevents/workshopsmeetingsconferences/transcriptsminutes/ucm054459.pdf>
- The Australian Immunisation Handbook, 9th edition. 1.3. Pre-vaccination Procedures. 1.3.3 Valid consent [cited 2011 September 15]. Available from: <http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook-consent>
- UK Guidance on Best Practice in Vaccine Administration. 2001 [cited 2011 September 15]. Available from: http://www.rcn.org.uk/__data/assets/pdf_file/0010/78562/001981.pdf
- Centers for Disease Control and Prevention. Vaccine Information Statements (VISs). Last modified December 6, 2010 [cited 2011 April 5]. Available from: <http://www.cdc.gov/vaccines/pubs/vis/vis-faqs.htm>
- Merck&Co. Protection with Gardasil [cited 2011 July 20]. Available from: <http://www.gardasil.com/what-is-gardasil/cervical-cancer-vaccine/index.html>
- Centers for Disease Control and Prevention. Information from FDA and CDC on Gardasil and its Safety (Archived), 2008 [cited 2011 January 25]. Available from: <http://www.cdc.gov/vaccinesafety/Vaccines/HPV/HPVArchived.html>
- Centers for Disease Control and Prevention (CDC). Reports of Health Concerns Following HPV Vaccination. Last updated: June 28, 2011 [cited 2011 July 22]. Available from: <http://www.cdc.gov/vaccine-safety/vaccines/hpv/gardasil.html>
- Villa LL, Costa RL, Petta CA, Andrade RP, Paavonen J, Iversen OE, et al. High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus-like particle vaccine through 5 years of follow-up. *Br J Cancer*. 2006;95:1459–66.
- De Carvalho N, Teixeira J, Roteli-Martins CM, Naud P, De Borja P, Zahaf T, et al. Sustained efficacy and immunogenicity of the HPV-16/18 AS04-adjuvanted vaccine up to 7.3 years in young adult women. *Vaccine*. 2010;28:6247–55.
- Harper DM, Williams KB. Prophylactic HPV vaccines: current knowledge of impact on gynecologic premalignancies. *Discov Med*. 2010;10:7–17.
- Haug C. The risks and benefits of HPV vaccination. *JAMA*. 2009;302:795–6.
- Flogging gardasil. *Nat Biotechnol*. 2007;25:261.
- Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56:1–24.
- Paavonen J, Naud P, Salmeron J, Wheeler CM, Chow SN, Apter D, et al. Efficacy of human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical infection and precancer caused by oncogenic HPV types (PATRICIA): final analysis of a double-blind, randomised study in young women. *Lancet*. 2009;374:301–14.
- The FUTURE II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med*. 2007;356:1915–27.
- Franco EL, Villa LL, Sobrinho JP, Prado JM, Rousseau MC, Désy M, et al. Epidemiology of acquisition and clearance of cervical human papillomavirus infection in women from a high-risk area for cervical cancer. *J Infect Dis*. 1999;180:1415–23.
- HoGY, Bierman R, Beardsley L, Chang CJ, Burk RD. Natural history of cervicovaginal papillomavirus infection in young women. *N Engl J Med*. 1998;338:423–8.
- Moscicki AB, Shiboski S, Broering J, Powell K, Clayton L, Jay N, et al. The natural history of human papillomavirus infection as measured by repeated DNA testing in adolescent and young women. *J Pediatr*. 1998;132:277–84.
- Ostor AG. Natural history of cervical intraepithelial neoplasia: a critical review. *Int J Gynecol Pathol*. 1993;12:186–92.
- Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, et al.; FUTURE I Investigators. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med*. 2007;356:1928–43.
- Hildesheim A, Herrero R, Wacholder S, Rodriguez AC, Solomon D, Bratti MC, et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA*. 2007;298:743–53.
- Food and Drug Administration (FDA). Gardasil (Human Papillomavirus Vaccine) Questions and Answers, June 8, 2006 [cited 2011 September 27]. Available from: <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/QuestionsaboutVaccines/ucm096052.htm>
- Medicines and Healthcare products Regulatory Agency (MHRA). Paper provided by MHRA for Joint Committee on Vaccination and Immunisation June 2010: Vaccine associated suspected adverse reactions reported via the Yellow Card scheme during 2009 [cited 2011 July 17]. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_118753.pdf
- Irish Medicines Board (IMB). Update on national monitoring experience with Gardasil. 11th November 2010 [cited 2011 July 17]. Available from: http://www.imb.ie/images/uploaded/documents/IMB_Gardasil_WebUpdate_11Nov2010.pdf
- Campos NG, Kim JJ, Castle PE, Ortendahl JD, O'Shea M, Diaz M, et al. Health and economic impact of HPV 16/18 vaccination and cervical cancer screening in Eastern Africa. *Int J Cancer*. 2011 Jun 29. [Epub ahead of print]
- Lawrence G, Gold MS, Hill R, Deeks S, Glasswell A, McIntyre PB. Annual report: Surveillance of adverse events following immunisation in Australia, 2007. *Commun Dis Intell*. 2008;32(4):371–87.
- National Vaccine Information Center. An Analysis by the National Vaccine Information Center of Gardasil & Menactra Adverse Event Reports to the Vaccine Adverse Events Reporting System (VAERS). February 2009 [cited 2011 January 25]. Available from: <http://www.nvic.org/Downloads/NVICGardasilvsMenactraVAERSReportFeb-2009u.aspx>

28. Menzies R, Mahajan D, Gold MS, Roomiani I, McIntyre P, Lawrence G. Annual report: Surveillance of adverse events following immunisation in Australia, 2008. *Commun Dis Intell*. 2009;33:365–81. Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/cdi3304>
29. Mahajan D, Roomiani I, Gold MS, Lawrence GL, McIntyre PB, Menzies RI. Annual report: Surveillance of adverse events following immunisation in Australia, 2009. *Comm Dis Intell*. 2010;34:259–76. Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/cdi3403-1>
30. Slade BA, Leidel L, Vellozzi C, Woo EJ, Hua W, Sutherland A, et al. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. *JAMA*. 2009;302:750–7.
31. Medicines and Healthcare products Regulatory Agency (MHRA). Paper provided by MHRA for Joint Committee on Vaccination and Immunisation June 2009: Vaccine associated suspected adverse reactions reported via the Yellow Card scheme during 2008 [cited 2011 July 17]. Available from: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@ab/documents/digitalasset/dh_110017.pdf
32. Database of the Netherlands Pharmacovigilance Centre Lareb. Overview adverse events following immunization in association with Cervarix. February 3, 2010 [cited 2011 July 24]. Available from: http://www.lareb.nl/documents/kwb_2010_2_cerva.pdf
33. Irish Medicines Board (IMB). Update on national monitoring experience with Gardasil. 9th February 2011 [cited 2011 July 17]. Available from: http://www.imb.ie/images/uploaded/documents/IMB_Gardasil_WebUpdate_09Feb2011.pdf
34. Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS). Vaccins contre les infections dues à certains papillomavirus humains (HPV). Gardasil®: Troisième bilan du plan de gestion des risques européen national (12/07/2011) [cited 2011 July 24]. Available from: <http://www.afssaps.fr/Dossiers-thematiques/Vaccins/Vaccins-contre-les-infections-dues-a-certains-papillomavirus-humains-HPV/%28offset%29/2>
35. CDC WONDER VAERS Request [cited 2011 September 15]. Available from: <http://wonder.cdc.gov/vaers.html>
36. Chustecka Z. HPV Vaccine: Debate Over Benefits, Marketing, and New Adverse Event Data. *Medscape Med News*. 2009 [cited 2011 January 25]. Available from: <http://www.medscape.com/viewarticle/707634>
37. Food and Drug Administration Vaccines and Related Biological Products Advisory Committee (VRBPAC) Background Document: Gardasil™ HPV Quadrivalent Vaccine. May 18, 2006 VRBPAC Meeting [cited 2011 September 15]. Available from: <http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4222B3.pdf>
38. Health Canada. Human Papillomavirus (HPV). Updated August 2010 [cited 2011 April 4]. Available from: <http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/diseases-maladies/hpv-vph-eng.php>
39. Australian Government, Department of Health and Ageing, Therapeutic Goods Administration. Human papillomavirus vaccine (GARDASIL), Advice from the Therapeutic Goods Administration. Updated 24 June 2010 [cited 2011 July 24]. Available from: <http://www.tga.gov.au/safety/alerts-medicine-gardasil-070624.htm>
40. Verstraeten T, Descamps D, David MP, Zahaf T, Hardt K, Izurieta P, et al. Analysis of adverse events of potential autoimmune aetiology in a large integrated safety database of AS04 adjuvanted vaccines. *Vaccine*. 2008;26:6630–8.
41. Shoenfeld Y, Agmon-Levin N. 'ASIA'—Autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun*. 2011;36:4–8.
42. Israeli E, Agmon-Levin N, Blank M, Shoenfeld Y. Adjuvants and autoimmunity. *Lupus*. 2009;18:1217–25.
43. Cohen AD, Shoenfeld Y. Vaccine-induced autoimmunity. *J Autoimmun*. 1996;9:699–703.
44. Agmon-Levin N, Paz Z, Israeli E, Shoenfeld Y. Vaccines and autoimmunity. *Nat Rev Rheumatol*. 2009;5:648–52.
45. Gandey A. Report of Motor Neuron Disease After HPV Vaccine. *Medscape Med News*. 2009 [cited 2011 January 25]. Available from: <http://www.medscape.com/viewarticle/711461>
46. Löwer J. Can we still recommend HPV vaccination? *MMWFortschr Med*. 2008;150:6.
47. Mendoza Plasencia Z, Gonzalez Lopez M, Fernandez Sanfeli ML, Muniz Montes JR. [Acute disseminated encephalomyelitis with tumefactive lesions after vaccination against human papillomavirus]. *Neurologia*. 2010;25:58–9.
48. Wildemann B, Jarius S, Hartmann M, Regula JU, Hametner C. Acute disseminated encephalomyelitis following vaccination against human papillomavirus. *Neurology*. 2009;72:2132–3.
49. Schaffer V, Wimmer S, Rotaru I, Topalkan R, Haring HP, Aichner FT. HPV vaccine: a cornerstone of female health a possible cause of ADEM? *J Neurol*. 2008;255:1818–20.
50. Sutton I, Latoria R, Tan IL, Clouston P, Barnett MH. CNS demyelination and quadrivalent HPV vaccination. *Mult Scler*. 2009;15:116–9.
51. Chang J, Campagnolo D, Vollmer TL, Bomprezzi R. Demyelinating disease and polyvalent human papilloma virus vaccination. *J Neurol-Neurosurg Psychiatry*. 2010;1–3.
52. Alvarez-Soria MJ, Hernandez-Gonzalez A, Carrasco-Garcia de Leon S, Del Real-Francia MA, Gallardo-Alcaniz MJ, Lopez-Gomez JL. [Demyelinating disease and vaccination of the human papillomavirus]. *Rev Neurol*. 2011;52:472–6.
53. McCarthy JE, Filiano J. Opsoclonus Myoclonus after human papilloma virus vaccine in a pediatric patient. *Parkinsonism Relat Disord*. 2009;15:792–4.
54. Mosnaim AD, Abiola R, Wolf ME, Perlmutter LC. Etiology and risk factors for developing orthostatic hypotension. *Am J Ther*. 2009;17:86–91.
55. Debeer P, De Munter P, Bruyninckx F, Devlieger R. Brachial plexus neuritis following HPV vaccination. *Vaccine*. 2008;26:4417–9.
56. Cohen SM. Multiple evanescent white dot syndrome after vaccination for human papilloma virus and meningococcus. *J Pediatr Ophthalmol Strabismus*. 2009;1–3.
57. Das A, Chang D, Biankin AV, Merrett ND. Pancreatitis following human papillomavirus vaccination. *Med J Aust*. 2008;189:178.
58. Brotherton JM, Gold MS, Kemp AS, McIntyre PB, Burgess MA, Campbell-Lloyd S. Anaphylaxis following quadrivalent human papillomavirus vaccination. *CMAJ*. 2008;179:525–33.
59. Blitshteyn S. Postural tachycardia syndrome after vaccination with Gardasil [letter to the editor]. *Eur J Neurol*. 2010;17:e52.
60. Dale RC, Brilof F, Banwell B. Pediatric central nervous system inflammatory demyelination: acute disseminated encephalomyelitis, clinically isolated syndromes, neuromyelitis optica, and multiple sclerosis. *Curr Opin Neurol*. 2009;22:233–40.
61. Low PA, Sandroni P, Joyner M, Shen WK. Postural tachycardia syndrome (POTS). *J Cardiovasc Electrophysiol*. 2009;20:352–8.
62. Medicines and Healthcare products Regulatory Agency (MHRA). Suspected adverse reactions received by the MHRA. Cervarix Human papillomavirus (HPV) vaccine (as of 29 July 2010) [cited 2011 July 24]. Available from: <http://www.mhra.gov.uk/PrintPreview/DefaultSplashPP/CON023340?ResultCount=10&DynamicListQuery=&DynamicListSortBy=xCreationDate&DynamicListSortOrder=Desc&DynamicListTitle=&PageNumber=1&Title=Human%20papillomavirus%20%28HPV%29%20vaccine>
63. Food and Drug Administration. Inside Clinical Trials: Testing Medical Products in People. Last updated May 2009 [cited 2011 April 4]. Available from: <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143531.htm>
64. Golomb BA, Erickson LC, Koperski S, Sack D, Enkin M, Howick J. What's in placebos: who knows? Analysis of randomized, controlled trials. *Ann Intern Med*. 2010;153:532–5.
65. Harper DM, Franco EL, Wheeler C, Ferris DG, Jenkins D, Schuid A, et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial. *Lancet*. 2004;364:1757–65.
66. Harper DM, Franco EL, Wheeler CM, Moscicki AB, Romanowski B, Roteli-Martins CM, et al. Sustained efficacy up to 4.5 years of a bivalent L1 virus-like particle vaccine against human papillomavirus types 16 and 18: follow-up from a randomised control trial. *Lancet*. 2006;367:1247–55.
67. Villa LL, Costa RL, Petta CA, Andrade RP, Ault KA, Giuliano AR, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. *Lancet Oncol*. 2005;6:271–8.
68. Mao C, Koutsky LA, Ault KA, Wheeler CM, Brown DR, Wiley DJ, Alvarez et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: a randomized controlled trial. *Obstet Gynecol*. 2006;107:18–27.
69. Munoz N, Manalastas R Jr, Pitisuttithum P, Tresukosol D, Monsonego J, Ault K, et al. Safety, immunogenicity, and efficacy of quadrivalent human papillomavirus (types 6, 11, 16, 18) recombinant vaccine in women aged 24–45 years: a randomised, double-blind trial. *Lancet*. 2009;373:1949–57.
70. Bishop NJ, Morley R, Day JP, Lucas A. Aluminum neurotoxicity in preterm infants receiving intravenous-feeding solutions. *N Engl J Med*. 1997;336:1557–61.
71. Walton JR. Functional impairment in aged rats chronically exposed to human range dietary aluminum equivalents. *Neurotoxicology*. 2009;30:182–93.
72. Tomljenovic L. Aluminum and Alzheimer's disease: after a century of controversy, is there a plausible link? *J Alzheimers Dis*. 2011;23:567–98.

73. Couette M, Boisse MF, Maison P, Brugieres P, Cesaro P, Chevalier X, et al. Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction. *J Inorg Biochem.* 2009;103:1571–8.
74. Authier FJ, Cherin P, Creange A, Bonnotte B, Ferrer X, Abdelmoumni A, et al. Central nervous system disease in patients with macrophagicmyofasciitis. *Brain.* 2001;124(Pt 5):974–83.
75. Exley C, Swarbrick L, Gherardi RK, Authier FJ. A role for the body burden of aluminium in vaccine-associated macrophagicmyofasciitis and chronic fatigue syndrome. *Med Hypotheses.* 2009;72:135–9.
76. Gherardi RK, Coquet M, Cherin P, Belec L, Moretto P, Dreyfus PA, Pellissier et al. Macrophagicmyofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. *Brain.* 2001;124(Pt 9):1821–31.
77. Shaw CA, Petrik MS. Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. *J Inorg Biochem.* 2009;103:1555–62.
78. Petrik MS, Wong MC, Tabata RC, Garry RF, Shaw CA. Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice. *Neuromolecular Med.* 2007;9:83–100.
79. Tomljenovic L, Shaw CA. Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? *J Inorg Biochem.* 2011;105:1489–99.
80. Tomljenovic L, Shaw CA. Aluminum vaccine adjuvants: are they safe? *Curr Med Chem.* 2011;18:2630–7.
81. Exley C. Aluminium-based adjuvants should not be used as placebos in clinical trials. *Vaccine.* 2011;29:9289.
82. Merck&Co. Gardasil product sheet. Date of Approval 2006, p. 1–26 [cited 2011 July 25]. Available from: <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf>
83. Lu B, Kumar A, Castellsague X, Giuliano AR. Efficacy and safety of prophylactic vaccines against cervical HPV infection and diseases among women: a systematic review & meta-analysis. *BMC Infect Dis.* 2011;11:13.
84. Clifford GM, Smith JS, Plummer M, Munoz N, Franceschi S. Human papillomavirus types in invasive cervical cancer worldwide: a meta-analysis. *Br J Cancer.* 2003;88:63–73.
85. Castle PE. Beyond human papillomavirus: the cervix, exogenous secondary factors, and the development of cervical precancer and cancer. *J Low Genit Tract Dis.* 2004;8:224–30.
86. Harper DM, Nieminen P, Paavonen J, Lehtinen M. Cervical cancer incidence can increase despite HPV vaccination. *Lancet Infect Dis.* 2010;10:594–5; author reply 595.
87. Lippman A, Melnychuk R, Shimmin C, Boscoe M. Human papillomavirus, vaccines and women's health: questions and cautions. *CMAJ.* 2007;177:484–7.
88. Engeland A, Haldorsen T, Tretli S, Hakulinen T, Hörte LG, Luostarinen T, et al. Prediction of cancer mortality in the Nordic countries up to the years 2000 and 2010, on the basis of relative survival analysis. A collaborative study of the five Nordic Cancer Registries. *APMIS Suppl.* 1995;49:1–161.
89. Laukkanen P, Koskela P, Pukkala E, Dillner J, Läärä E, Knekt P, et al. Time trends in incidence and prevalence of human papillomavirus type 6, 11 and 16 infections in Finland. *J Gen Virol.* 2003;84(Pt 8): 2105–9.
90. Fagot JP, Boutrelle A, Ricordeau P, Weill A, Allemand H. HPV vaccination in France: uptake, costs and issues for the National Health Insurance. *Vaccine.* 2011;29:3610–6.
91. Sharma M, Ortendahl J, van der Ham E, Sy S, Kim J. Cost-effectiveness of human papillomavirus vaccination and cervical cancer screening in Thailand. *BJOG.* 2011 Apr 12. [Epub ahead of print]
92. Kim JJ, Goldie SJ. Health and economic implications of HPV vaccination in the United States. *N Engl J Med.* 2008;359:821–32.
93. Kim JJ, Goldie SJ. Cost effectiveness analysis of including boys in a human papillomavirus vaccination programme in the United States. *BMJ.* 2009;339:b3884.
94. deKok IM, van Ballegooijen M, Habbema JD. Cost-effectiveness analysis of human papillomavirus vaccination in the Netherlands. *J Natl Cancer Inst.* 2009;101:1083–92.
95. The New York Times. U.S. Approves Use of Vaccine for Cervical Cancer. June 9, 2006 [cited 2011 September 14]. Available from: <http://www.nytimes.com/2006/06/09/health/09vaccine.html?fta=y>
96. Judicial Watch Special Report. Examining the FDA's HPV Vaccine Records Detailing the Approval Process, Side-Effects, Safety Concerns and Marketing Practices of a Large-Scale Public Health Experiment. June 30, 2008 [cited 2011 September 14]. Available from: <http://www.judicial-watch.org/documents/2008/JWReportFDAhpvVaccineRecords.pdf>
97. Food and Drug Administration (FDA). FDA Science and Mission at Risk, Report of the Subcommittee on Science and Technology 2007 [cited 2010 December 12]. Available from: http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf
98. Rothman SM, Rothman DJ. Marketing HPV vaccine: implications for adolescent health and medical professionalism. *JAMA.* 2009;302:781–6.
99. Sarojini NB, Srinivasan S, Madhavi Y, Srinivasan S, Sheno A. The HPV vaccine: science, ethics and regulation. *Econom Polit Weekly.* 2010;45:27–34.
100. Sengupta A, Sheno A, Sarojini NB, Madhavi Y. Human papillomavirus vaccine trials in India. *Lancet Infect Dis.* 2011;377:719.
101. Legifrancegouv. Le Service Public De La Diffusion Du Droit. Décision du 31 août 2010 interdisant une publicité pour un médicament mentionnée à l'article L. 5122-1, premier alinéa, du code de la santé publique destinée aux personnes habilitées à prescrire ou délivrer ces médicaments ou à les utiliser dans l'exercice de leur art [cited 2011 January 26]. Available from: <http://www.legifrance.gouv.fr/affichTexte.do?sessionId=?cidTexte=JORFTEXT000022839429&dateTexte&oldAction=rechJO&categorieLien=id>
102. McGee G, Johnson S. Has the spread of HPV vaccine marketing conveyed immunity to common sense? *Am J Bioeth.* 2007;7:1–2.
103. Telethon Institute for Child Health Research. Perth women needed for international cervical cancer study, 12 April, 2006 [cited 2011 July 26]. Available from: <http://www.ichr.uwa.edu.au/media/478>
104. World Medical Association (WMA) Declaration of Helsinki. Ethical Principles for Medical Research Involving Human Subjects [cited 2011 April 6]. Available from: <http://www.wma.net/en/30publications/10policies/b3/>
105. WHO/ICO Information Centre on Human Papilloma Virus and Cervical Cancer [cited 2011 July 20]. Available from: <http://apps.who.int/hpvcentre/statistics/dynamic/ico/SummaryReportsSelect.cfm>
106. Food and Drug Administration (FDA). CFR—Code of Federal Regulations Title 21 [cited 2011 September 19]. Available from: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.80>
107. WHO/ICO HPV Information Centre. Human papillomavirus and related cancers. Summary report update. November 15, 2010 [cited 2011 July 21]. Available from: http://apps.who.int/hpvcentre/statistics/dynamic/ico/country_pdf/XWX.pdf?CFID=5169709&CFTOKEN=39667351

157 Research Papers Supporting Vaccine/Autism Causation Ginger Taylor, MS

Mainstream research has found that vaccines and their ingredients can cause the underlying medical conditions that committed physicians and researchers are commonly finding in children who have been given an autism diagnosis. These conditions include gastrointestinal damage, immune system impairment, chronic infections, mitochondrial disorders, autoimmune conditions, neurological regression, glial cell activation, interleukin-6 secretion dysregulation, brain inflammation, damage to the blood–brain barrier, seizures, synaptic dysfunction, dendritic cell dysfunction, mercury poisoning, aluminum toxicity, gene activation and alteration, glutathione depletion, impaired methylation, oxidative stress, impaired thioredoxin regulation, mineral deficiencies, impairment of the opioid system, endocrine dysfunction, cellular apoptosis, and other disorders.

PDF available [here](#).

1. [Increased risk of developmental neurologic impairment after high exposure to thimerosal-containing vaccine in first month of life.](#)

Division of Epidemiology and Surveillance, Vaccine Safety and Development Branch, National Immunization Program, Centers for Disease Control and Prevention. 1999.

Thomas M. Verstraeten, Robert Davis, David Gu, Frank DeStefano

Background: Concern has risen on the presence of the ethylmercury containing preservative thimerosal in vaccines. We assessed the risk for neurologic and renal impairment associated with past exposure to thimerosal-containing vaccine using automated data from the Vaccine Safety Data link (VSD). VSD is a large linked database from four health maintenance organizations in Washington, Oregon and California, containing immunization, medical visit and demographic data on over 400,000 infants born between '91 and '97.

Methods: We categorized the cumulative ethylmercury exposure from Thimerosal containing vaccines after one month of life and assessed the subsequent risk of degenerative and developmental neurologic disorders and renal disorders before the age of six. We applied proportional hazard models adjusting for HMO, year of birth, and gender, excluding premature babies.

Results: We identified 286 children with degenerative and 3702 with developmental neurologic disorders, and 310 with renal disorders. The relative risk (RR) of developing a neurologic development disorder was 1.8 (95% confidence intervals [CI] =1.1-2.8) when comparing the highest exposure group at 1 month of age (cumulative dose > 25 ug) to the unexposed group. **Within this group we also found an elevated risk for the following disorders: autism (RR 7.6, 95% CI = 1.8-31.5), non organic sleep disorders (RR 5.0, 95% CI = 1.6-15.9), and speech disorders (RR 2.1, 95% (1=1.1-4.0).** For the neurologic degenerative and renal disorders group we found no significantly increased risk or a decreased risk.

Conclusion: **This analysis suggests that high exposure to ethyl mercury from thimerosal-containing vaccines in the first month of life increases the risk of subsequent development of neurologic development impairment,** but not of neurologic degenerative or renal impairment. Further confirmatory studies are needed.

2. [Pilot comparative study on the health of vaccinated and unvaccinated 6- to 12-year old U.S. children](#)

J Transl Sci 3: DOI: 10.15761/JTS.1000186, April 24, 2017

Anthony R Mawson, Azad R Bhuiyan, Brian D Ray, Binu Jacob
Department of Epidemiology and Biostatistics, School of Public Health, Jackson State University, Jackson, MS 39213, USA
National Home Education Research Institute, PO Box 13939, Salem, OR 97309, USA

Abstract

Vaccinations have prevented millions of infectious illnesses, hospitalizations and deaths among U.S. children, yet the long-term health outcomes of the vaccination schedule remain uncertain. Studies have been recommended by the U.S. Institute of Medicine to address this question. This study aimed 1) to compare vaccinated and unvaccinated children on a broad range of health outcomes, and 2) to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors. A cross-sectional study of mothers of children educated at home was carried out in collaboration with homeschool organizations in four U.S. states: Florida, Louisiana, Mississippi and Oregon. Mothers were asked to complete an anonymous online questionnaire on their 6- to 12-year-old biological children with respect to pregnancy-related factors, birth history, vaccinations, physician-diagnosed illnesses, medications used, and health services. NDD, a derived diagnostic measure, was defined as having one or more of the following three closely-related diagnoses: a learning disability, Attention Deficient Hyperactivity Disorder, and Autism Spectrum Disorder. A convenience sample of 666 children was obtained, of which 261 (39%) were unvaccinated. The vaccinated were less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but more likely to have been diagnosed with pneumonia, otitis media, allergies and NDD. After adjustment, vaccination, male gender, and preterm birth remained significantly associated with NDD. However, in a final adjusted model with interaction, vaccination but not preterm birth remained associated with NDD, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% CI: 2.8, 15.5). **In conclusion, vaccinated homeschool children were found to have a higher rate of allergies and NDD than unvaccinated homeschool children.** While vaccination remained significantly associated with NDD after controlling for other factors, preterm birth coupled with vaccination was associated with an apparent synergistic increase in the odds of NDD. Further research involving larger, independent samples and

stronger research designs is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health.

Exerpts

"NDD, a derived diagnostic measure, was defined as having one or more of the following three closely-related diagnoses: a learning disability, Attention Deficient Hyperactivity Disorder, and Autism Spectrum Disorder."

"Chronic illness

Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following: allergic rhinitis (10.4% vs. 0.4%, $p < 0.001$; OR 30.1, 95% CI: 4.1, 219.3), other allergies (22.2% vs. 6.9%, $p < 0.001$; OR 3.9, 95% CI: 2.3, 6.6), eczema/atopic dermatitis (9.5% vs. 3.6%, $p = 0.035$; OR 2.9, 95% CI: 1.4, 6.1), a learning disability (5.7% vs. 1.2%, $p = 0.003$; OR 5.2, 95% CI: 1.6, 17.4), ADHD (4.7% vs. 1.0%, $p = 0.013$; OR 4.2, 95% CI: 1.2, 14.5), **ASD (4.7% vs. 1.0%, $p = 0.013$; OR 4.2, 95% CI: 1.2, 14.5)**, any neurodevelopmental disorder (i.e., learning disability, ADHD or ASD) (10.5% vs. 3.1%, $p < 0.001$; OR 3.7, 95% CI: 1.7, 7.9) and any chronic illness (44.0% vs. 25.0%, $p < 0.001$; OR 2.4, 95% CI: 1.7, 3.3)."

3. [Hepatitis B vaccination of male neonates and autism diagnosis, NHIS 1997-2002.](#)

Gallagher CM, Goodman MS.

J Toxicol Environ Health A. 2010;73(24):1665-77. doi:
10.1080/15287394.2010.519317.

Abstract

Universal hepatitis B vaccination was recommended for U.S. newborns in 1991; however, safety findings are mixed. The association between hepatitis B vaccination of male neonates and parental report of autism diagnosis was determined. This cross-sectional study used weighted probability samples obtained from National Health Interview Survey 1997-2002 data sets. Vaccination status was determined from the vaccination record. Logistic regression was used to estimate the odds for autism diagnosis associated with neonatal hepatitis B vaccination among boys age 3-17 years, born before 1999, adjusted for race, maternal education, and two-parent household. **Boys vaccinated as neonates had threefold greater odds for autism diagnosis compared to boys never vaccinated or vaccinated after the first month of life.** Non-Hispanic white boys were 64% less likely to have autism diagnosis relative to nonwhite boys. Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period. Nonwhite boys bore a greater risk.

4. [Associations of prenatal and early childhood mercury exposure with autistic behaviors at 5 years of age: The Mothers and Children's Environmental Health \(MOCEH\) study](#)

Science of The Total Environment
Volumes 605–606, 15 December 2017, Pages 251-257

JiaRyua. , Eun-HeeHaa, Boong-NyunKimb, MinaHac, YanghoKimd,
HyesookParke, Yun-ChulHongf, Kyoung-NamKim

Department of Occupational and Environmental Medicine, School of Medicine,
Ewha Womans University, Seoul, Republic of Korea

Division of Child & Adolescent Psychiatry, Department of Psychiatry and Institute
of Human Behavioral Medicine, College of Medicine, Seoul National University,
Seoul, Republic of Korea

Department of Preventive Medicine, College of Medicine, Dankook University,
Cheonan, Republic of Korea

Department of Occupational and Environmental Medicine, Ulsan University
Hospital, University of Ulsan College of Medicine, Ulsan, Republic of Korea

Department of Preventive Medicine, School of Medicine, Ewha Womans
University, Seoul, Republic of Korea

Department of Preventive Medicine, Seoul National University College of
Medicine, Seoul, Republic of Korea

Institute of Public Health and Medical Service, Seoul National University Hospital,
Seoul, Republic of Korea

Received 26 April 2017, Revised 24 June 2017, Accepted 26 June 2017,
Available online 28 June 2017.

Abstract

Background

Although mercury is an established neurotoxin, only few longitudinal studies have investigated the association between prenatal and early childhood mercury exposure and autistic behaviors.

Methods

We conducted a longitudinal cohort study using an ongoing prospective birth cohort initiated in 2006, wherein blood mercury levels were measured at early and late pregnancy; in cord blood; and at 2 and 3 years of age. We analyzed 458 mother-child pairs. Autistic behaviors were assessed using the Social Responsiveness Scale (SRS) at 5 years of age. Both continuous SRS T-scores and T-scores dichotomized by a score of ≥ 60 or < 60 were used as outcomes.

Results

The geometric mean of mercury concentrations in cord blood was 5.52 µg/L. In adjusted models, a doubling of blood mercury levels at late pregnancy ($\beta = 1.84$, 95% confidence interval [CI]: 0.39, 3.29), in cord blood ($\beta = 2.24$, 95% CI: 0.22, 4.27), and at 2 years ($\beta = 2.12$, 95% CI: 0.54, 3.70) and 3 years ($\beta = 2.80$, 95% CI: 0.89, 4.72) of age was positively associated with the SRS T-scores. When the SRS T-scores were dichotomized, we observed positive associations with mercury levels at late pregnancy (relative risk [RR] = 1.31, 95% CI: 1.08, 1.60) and in cord blood (RR = 1.28, 95% CI: 1.01, 1.63).

Conclusion

We found that blood mercury levels at late pregnancy and early childhood were associated with more autistic behaviors in children at 5 years of age. Further study on the long-term effects of mercury exposure is recommended.

5. [The association between mercury levels and autism spectrum disorders: A systematic review and meta-analysis](#)

Journal of Trace Elements in Medicine and Biology
Volume 44, December 2017, Pages 289-297

Tina Jafari, Noushin Rostampour, Aziz A.Fallah, Afshin Hesamia

Clinical Biochemistry Research Center, Shahrekord University of Medical Sciences, Sharhekord, Iran
Department of Biochemistry and Nutrition, Faculty of Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
Department of Internal Medicine, Shahrekord University of Medical Sciences, Shahrekord, Iran
Department of Food Hygiene and Quality Control, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord 34141, Iran

Abstract

Background & aims

The relationship between mercury and autism spectrum disorders (ASD) has always been a topic of controversy among researchers. This study aimed to assess the relationship between ASD and mercury levels in hair, urine, blood, red blood cells (RBC), and brain through a meta-analysis.

Methods

A systematic search was performed in several databases including PubMed, ISI Web of Science, Cochrane register of controlled trials, Google Scholar, Scopus, and MagIran until June 2017. Case-control studies evaluating concentration of total mercury in different tissues of ASD patients and comparing them to the healthy subjects (control group) were identified. Necessary data were extracted and random effects model was used to calculate overall effect and its 95% corresponding confidence interval (CI) from the effect sizes.

Results

A total of 44 studies were identified that met the necessary criteria for meta-analysis. The mercury level in whole blood (Hedges = 0.43, 95% CI: 0.12, 0.74, P = 0.007), RBC (Hedges = 1.61, 95% CI: 0.83, 2.38, P < 0.001), and brain (0.61 ng/g, 95% CI, 0.02, 1.19, P = 0.043) was significantly higher in ASD patients than healthy subjects, whereas mercury level in hair (-0.14 mg/g, 95% CI: -0.28, -0.01, P = 0.039) was significantly lower in ASD patients than healthy subjects. The mercury level in urine was not significantly different between ASD patients and healthy subjects (0.51 mg/g creatinine, 95% CI: -0.14, 1.16, P = 0.121).

Conclusions

Results of the current meta-analysis revealed that mercury is an important causal factor in the etiology of ASD. It seems that the detoxification and excretory mechanisms are impaired in ASD patients which lead to accumulation of mercury in the body. Future additional studies on mercury levels in different tissues of ASD patients should be undertaken.

6. [The Putative Role of Environmental Mercury in the Pathogenesis and Pathophysiology of Autism Spectrum Disorders and Subtypes](#)

Molecular Neurobiology, First Online: 22 July 2017

G. Morris, K. Puri, R. E. Frye, M. Maes

1. Tir Na Nog Llanelli UK

2. Department of Medicine, Hammersmith Hospital Imperial College London, London UK

3. Division of Child and Adolescent Neurology and Children's Learning Institute, Department of Pediatrics University of Texas, Austin USA

4. Department of Psychiatry Chulalongkorn University Bangkok, Thailand

Abstract

Exposure to organic forms of mercury has the theoretical capacity to generate a range of immune abnormalities coupled with chronic nitro-oxidative stress seen in children with autism spectrum disorder (ASD). The paper discusses possible mechanisms explaining the neurotoxic effects of mercury and possible associations between mercury exposure and ASD subtypes. **Environmental mercury is neurotoxic at doses well below the current reference levels considered to be safe, with evidence of neurotoxicity in children exposed to environmental sources including fish consumption and ethylmercury-containing vaccines. Possible neurotoxic mechanisms of mercury include direct effects on sulfhydryl groups, pericytes and cerebral endothelial cells, accumulation within astrocytes, microglial activation, induction of chronic oxidative stress, activation of immune-inflammatory pathways and impairment of mitochondrial functioning. (Epi-)genetic factors which may increase susceptibility to the toxic effects of mercury in ASD include the following: a greater propensity of males to the long-term neurotoxic effects of postnatal exposure and genetic polymorphisms in glutathione**

transferases and other glutathione-related genes and in selenoproteins. Furthermore, immune and inflammatory responses to immunisations with mercury-containing adjuvants are strongly influenced by polymorphisms in the human leukocyte antigen (HLA) region and by genes encoding effector proteins such as cytokines and pattern recognition receptors. Some epidemiological studies investigating a possible relationship between high environmental exposure to methylmercury and impaired neurodevelopment have reported a positive dose-dependent effect. Retrospective studies, on the other hand, reported no relationship between a range of ethylmercury-containing vaccines and chronic neuropathology or ASD. On the basis of these results, we would argue that more clinically relevant research is required to examine whether environmental mercury is associated with ASD or subtypes. Specific recommendations for future research are discussed.

7. [Blood Mercury, Arsenic, Cadmium, and Lead in Children with Autism Spectrum Disorder.](#)

Biol Trace Elem Res. 2017 May 8. doi: 10.1007/s12011-017-1002-6.

Li H, Li H, Li Y, Liu Y, Zhao Z

Children's Hospital of Zhejiang University School of Medicine, Hangzhou, People's Republic of China.

Laboratory of Neuroinflammation, StVincent's Centre for Applied Medical Research and University of New South Wales, Sydney, NSW, Australia.

Children's Hospital of Zhejiang University School of Medicine, Hangzhou, People's Republic of China. zhaozy@zju.edu.cn.

Department of Pediatric Health Care, Children's Hospital of Zhejiang University School of Medicine, 57 Zhuganxiang Road, Hangzhou, People's Republic of China

Abstract

Environmental factors have been implicated in the etiology of autism spectrum disorder (ASD); however, the role of heavy metals has not been fully defined. This study investigated whether blood levels of mercury, arsenic, cadmium, and lead of children with ASD significantly differ from those of age- and sex-matched controls. One hundred eighty unrelated children with ASD and 184 healthy controls were recruited. **Data showed that the children with ASD had significantly ($p < 0.001$) higher levels of mercury and arsenic and a lower level of cadmium.** The levels of lead did not differ significantly between the groups. **The results of this study are consistent with numerous previous studies, supporting an important role for heavy metal exposure, particularly mercury, in the etiology of ASD.** It is desirable to continue future research into the relationship between ASD and heavy metal exposure.

8. [Protective role of alpha-lipoic acid in impairments of social and stereotyped behaviors induced by early postnatal administration of thimerosal in male rat.](#)

Neurotoxicol Teratol. 2018 Feb 23. pii: S0892-0362(17)30086-7. doi: 10.1016/j.ntt.2018.02.002.

Namvarpour Z, Nasehi M, Amini A, Zarrindast MR.

Institute for Cognitive Science Studies (ICSS), Tehran, Iran.

Institute for Cognitive Science Studies (ICSS), Tehran, Iran; Cognitive and Neuroscience Research Center (CNRC), Tehran Medical Sciences Branch, Islamic Azad University, Tehran, Iran.

Department of Biology and Anatomy, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Institute for Cognitive Science Studies (ICSS), Tehran, Iran; Department of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Abstract

Aim Thimerosal, a mercury-containing preservative has been widely used in a number of biological and drug products, including many vaccines, and has been studied as a possible etiological factor for some neurodevelopmental disabilities. Here, the protective effects of Alpha Lipoic Acid (ALA), an organosulfur compound derived from Octanoic Acid, on Thimerosal-induced behavioral abnormalities in rat were examined.

METHODS:

108 male Wistar rats were divided into three cohorts and treated as follows: 1) Thimerosal at different doses (30, 300, or 3000 $\mu\text{g Hg/kg}$) in four i.m. injections on 7, 9, 11, 15 postnatal days. 2) ALA (at doses of 5, 10 and 20 mg/kg), following the same order; 3) single dose of Thimerosal (3000 $\mu\text{g Hg/kg}$) plus ALA at different doses (5, 10 or 20 mg/kg), by the previously described method. A saline treated control group and a ALA vehicle control (0.1% NaOH) were also included. At 5 and 8 weeks after birth, rats were evaluated with behavioral tests, to assess locomotor activity, social interactions and stereotyped behaviors, respectively.

RESULTS:

The data showed that Thimerosal at all doses (30, 300 and 3000 $\mu\text{g Hg/kg}$) significantly impacted locomotor activity. Thimerosal at doses of 300 and 3000 but not 30 $\mu\text{g Hg/kg}$ impaired social and stereotyped behaviors. In contrast, ALA (at doses of 5, 10 and 20 mg/kg) did not alter behaviors by itself, at doses of 20 mg/kg, it reduced social interaction deficits induced by the highest dose of Thimerosal (3000 $\mu\text{g Hg/kg}$). Moreover, ALA, at all doses prevented the adverse effects of Thimerosal on stereotyped behaviors.

CONCLUSIONS:

the results of this preclinical study, consistent with previous studies on mice and rats, reveals that **neonatal dose-dependent exposure to Thimerosal mimicking the childhood vaccine schedule can induce abnormal social interactions and stereotyped behaviors similar to those observed in neurodevelopmental disorders such as autism**, and, for the first time, revealed that these abnormalities may be ameliorated by ALA. This indicates that ALA may protect against mercurial-induced abnormal behaviors.

9. [Gender-selective toxicity of thimerosal.](#)

Exp Toxicol Pathol. 2009 Mar;61(2):133-6. doi: 10.1016/j.etp.2008.07.002. Epub 2008 Sep 3.

Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, Ontario, Canada. don.branch@utoronto.ca

Abstract

A recent report shows a correlation of the historical use of thimerosal in therapeutic immunizations with the subsequent development of autism; however, this association remains controversial. Autism occurs approximately four times more frequently in males compared to females; thus, studies of thimerosal toxicity should take into consideration gender-selective effects. The present study was originally undertaken to determine the maximum tolerated dose (MTD) of thimerosal in male and female CD1 mice. However, during the limited MTD studies, it became apparent that thimerosal has a differential MTD that depends on whether the mouse is male or female. **At doses of 38.4-76.8mg/kg using 10% DMSO as diluent, seven of seven male mice compared to zero of seven female mice tested succumbed to thimerosal.** Although the thimerosal levels used were very high, as we were originally only trying to determine MTD, it was completely unexpected to observe a difference of the MTD between male and female mice. Thus, our studies, although not directly addressing the controversy surrounding thimerosal and autism, and still preliminary due to small numbers of mice examined, provide, nevertheless, the first report of gender-selective toxicity of thimerosal and indicate that any future studies of thimerosal toxicity should take into consideration gender-specific differences.

10. [Mercury toxicokinetics--dependency on strain and gender.](#)

Toxicol Appl Pharmacol. 2010 Mar 15;243(3):283-91. doi: 10.1016/j.taap.2009.08.026. Epub 2009 Sep 2.

Ekstrand J1, Nielsen JB, Havarinasab S, Zalups RK, Söderkvist P, Hultman P.

Molecular and Immunological Pathology, Department of Clinical and Experimental Medicine, Linköping University, Sweden.

Abstract

Mercury (Hg) exposure from dental amalgam fillings and thimerosal in vaccines is not a major health hazard, but adverse health effects cannot be ruled out in a small and more susceptible part of the exposed population. Individual differences in toxicokinetics may explain susceptibility to mercury. Inbred, H-2-congenic A.SW and B10.S mice and their F1- and F2-hybrids were given HgCl₂ with 2.0 mg Hg/L drinking water and traces of (203)Hg. Whole-body retention (WBR) was monitored until steady state after 5 weeks, when the organ Hg content was assessed. Despite similar Hg intake, **A.SW males attained a 20-30% significantly higher WBR and 2- to 5-fold higher total renal Hg retention/concentration than A.SW females and B10.S mice. A selective renal Hg accumulation but of lower magnitude was seen also in B10.S males compared with females.** Differences in WBR and organ Hg accumulation are therefore regulated by non-H-2 genes and gender. Lymph nodes lacked the strain- and gender-dependent Hg accumulation profile of kidney, liver and spleen. After 15 days without Hg A.SW mice showed a 4-fold higher WBR and liver Hg concentration, but 11-fold higher renal Hg concentration, showing the key role for the kidneys in explaining the slower Hg elimination in A.SW mice. The trait causing higher mercury accumulation was not dominantly inherited in the F1 hybrids. F2 mice showed a large inter-individual variation in Hg accumulation, showing that multiple genetic factors influence the Hg toxicokinetics in the mouse. The genetically heterogeneous human population may therefore show a large variation in mercury toxicokinetics.

11. [A Review of the Differences in Developmental, Psychiatric, and Medical Endophenotypes Between Males and Females with Autism Spectrum Disorder](#)

J Dev Phys Disabil. 2015 Feb; 27(1): 119–139.

Eric Rubenstein, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Lisa D. Wiggins, and Li-Ching Lee

Abstract

Autism spectrum disorder (ASD) is over four times more prevalent in males compared to females. Increased understanding of sex differences in ASD endophenotypes could add insight into possible etiologies and the assessment and management of the disorder. Consequently, the purpose of this review is to describe current literature regarding sex differences in the developmental, psychiatric, and medical endophenotypes of ASD in order to illustrate current knowledge and areas in need of further research. Our review found that repetitive behaviors and restricted interests are more common in males than females with ASD. Intellectual disability is more common in females than males with ASD. Attention to detail may be more common in males than females with ASD and epilepsy may be more common in females than males with ASD, although limited research in these areas prevent definitive conclusions from being drawn. There does not appear to be a sex difference in other developmental, psychiatric, and

medical symptoms associated with ASD, or the research was contradictory or too sparse to establish a sex difference. Our review is unique in that it offers detailed discussion of sex differences in three major endophenotypes of ASD. Further research is needed to better understand why sex differences exist in certain ASD traits and to evaluate whether phenotypic sex differences are related to different pathways of development, assessment, and treatment of the disorder.

12. [Mercury toxicity: Genetic susceptibility and synergistic effects](#)

Medical Veritas 2 (2005) 535–542

Boyd E. Haley, PhD. Professor and Chair, Department of Chemistry, University of Kentucky

Abstract

Mercury toxicity and intoxication (poisoning) are realities that every American needs to face. Both the Environmental Protection Agency and National Academy of Science state that between 8 to 10% of American women have mercury levels that would render any child they gave birth to neurological disorders. One of six children in the USA have a neurodevelopmental disorder according to the Centers for Disease Control and Prevention. Yet our dentistry and medicine continue to expose all patients to mercury. This article discusses the obvious sources of mercury exposures that can be easily prevented. It also points out that genetic susceptibility and exposures to other materials that synergistically enhance mercury and ethylmercury toxicity need to be evaluated, and that by their existence prevent the actual determination of a “safe level” of mercury exposure for all. The mercury sources we consider are from dentistry and from drugs, mainly vaccines, that, in today’s world are not only unnecessary sources, but also sources that are being increasingly recognized as being significantly deleterious to the health of many.

Excerpt

"4. Hormonal effects: Testosterone and Estrogen

Testosterone and estrogen-like compounds give vastly different results. Using female hormones we found them not toxic to the neurons alone and to be consistently protective against thimerosal toxicity. In fact, at high levels they could afford total protection for 24 hours against neuronal death in this test system (data not plotted). **However, testosterone which appeared protective at very low levels (0.01 to 0.1 micromolar), dramatically increased neuron death at higher levels (0.5 to 1.0 micromolar). In fact, 1.0 micromolar levels of testosterone that by itself did not significantly increase neuron death (red flattened oval), within 3 hours when added with 50 nanomolar thimerosal (solid circles) caused 100% neuron death.** Fifty nanomolar thimerosal at this time point did not significantly cause any cell death.

These testosterone results, while not conclusive because of the in vitro neuron culture type of testing, clearly demonstrated that male versus female hormones may play a major role in autism risk and may explain the

high ratio of boys to girls in autism (4 to 1) and autism related disorders."

13. [Autism: a form of lead and mercury toxicity](#)

Environ Toxicol Pharmacol. 2014 Nov;38(3):1016-24. doi: 10.1016/j.etap.2014.10.005. Epub 2014 Nov 6.

Yassa HA

Abstract

AIM: Autism is a developmental disability characterized by severe deficits in social interaction and communication. The definite cause of autism is still unknown. The aim of this study is to find out the relation between exposure to Lead and/or mercury as heavy metals and autistic symptoms, dealing with the heavy metals with chelating agents can improve the autistic symptoms.

METHOD: Blood and hair samples were obtained from 45 children from Upper Egypt with autism between the ages of 2 and 10 years and 45 children served as controls in the same age range, after taken an informed consent and fill a questionnaire to assess the risk factors. The samples were analyzed blindly for lead and mercury by using atomic absorption and ICP-MS. Data from the two groups were compared, then follow up of the autistic children after treatment with chelating agents were done.

RESULTS: The results obtained showed significant difference among the two groups, there was high level of mercury and lead among those kids with autism. Significant decline in the blood level of lead and mercury with the use of DMSA as a chelating agent. In addition, there was decline in the autistic symptoms with the decrease in the lead and mercury level in blood.

CONCLUSION: Lead and mercury considered as one of the main causes of autism. Environmental exposure as well as defect in heavy metal metabolism is responsible for the high level of heavy metals. Detoxification by chelating agents had great role in improvement of those kids.

14. Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?

J Inorg Biochem. 2011 Nov;105(11):1489-99. Epub 2011 Aug 23.
Tomljenovic L, Shaw CA.

Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia, 828 W. 10th Ave, Vancouver, BC, Canada V5Z 1L8.

Abstract

Autism spectrum disorders (ASD) are serious multisystem developmental disorders and an urgent global public health concern. Dysfunctional immunity and impaired brain function are core deficits in ASD. Aluminum (Al), the most commonly used vaccine adjuvant, is a demonstrated neurotoxin and a strong immune stimulator. Hence, adjuvant Al has the potential to induce neuroimmune disorders. When assessing adjuvant toxicity in children, two key points ought to be considered: (i) children should not be viewed as "small adults" as their unique physiology makes them much more vulnerable to toxic insults; and (ii) if exposure to Al from only few vaccines can lead to cognitive impairment and autoimmunity in adults, is it unreasonable to question whether the current pediatric schedules, often containing 18 Al adjuvanted vaccines, are safe for children? By applying Hill's criteria for establishing causality between exposure and outcome we investigated whether exposure to Al from vaccines could be contributing to the rise in ASD prevalence in the Western world. Our results show that: (i) children from countries with the highest ASD prevalence appear to have the highest exposure to Al from vaccines; (ii) the increase in exposure to Al adjuvants significantly correlates with the increase in ASD prevalence in the United States observed over the last two decades (Pearson $r=0.92$, $p<0.0001$); and (iii) a significant correlation exists between the amounts of Al administered to preschool children and the current prevalence of ASD in seven Western countries, particularly at 3-4months of age (Pearson $r=0.89-0.94$, $p=0.0018-0.0248$). **The application of the Hill's criteria to these data indicates that the correlation between Al in vaccines and ASD may be causal.** Because children represent a fraction of the population most at risk for complications following exposure to Al, a more rigorous evaluation of Al adjuvant safety seems warranted.

15. [The putative role of environmental aluminium in the development of chronic neuropathology in adults and children. How strong is the evidence and what could be the mechanisms involved?](#)

Metabolic Brain Disease, October 2017, Volume 32, Issue 5, pp 1335–1355

Gerwyn Morris, Basant K. Puri, Richard E. Frye
Tir Na Nog, Llanelli, UK, Department of MedicineImperial College London, Hammersmith Hospital, London UK, College of Medicine, Department of PediatricsUniversity of Arkansas for Medical Sciences, Arkansas Children's Hospital Research Institute, Little Rock

Abstract

The conceptualisation of autistic spectrum disorder and Alzheimer's disease has undergone something of a paradigm shift in recent years and rather than being viewed as single illnesses with a unitary pathogenesis and pathophysiology they are increasingly considered to be heterogeneous syndromes with a complex multifactorial aetiopathogenesis, involving a highly complex and diverse combination of genetic, epigenetic and environmental factors. **One such environmental factor implicated as a potential cause in**

both syndromes is aluminium, as an element or as part of a salt, received, for example, in oral form or as an adjuvant. Such administration has the potential to induce pathology via several routes such as provoking dysfunction and/or activation of glial cells which play an indispensable role in the regulation of central nervous system homeostasis and neurodevelopment. Other routes include the generation of oxidative stress, depletion of reduced glutathione, direct and indirect reductions in mitochondrial performance and integrity, and increasing the production of proinflammatory cytokines in both the brain and peripherally. The mechanisms whereby environmental aluminium could contribute to the development of the highly specific pattern of neuropathology seen in transsulfuration in Alzheimer's disease are described. Also detailed are several mechanisms whereby significant quantities of aluminium introduced via immunisation could produce chronic neuropathology in genetically susceptible children. **Accordingly, it is recommended that the use of aluminium salts in immunisations should be discontinued and that adults should take steps to minimise their exposure to environmental aluminium.**

16. [Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes.](#)

J Inorg Biochem. 2013 Nov;128:237-44. doi: 10.1016/j.jinorgbio.2013.07.022. Epub 2013 Jul 19.

Shaw CA, Li Y, Tomljenovic L.

Dept. of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, British Columbia, Canada; Program in Experimental Medicine, University of British Columbia, Vancouver, British Columbia, Canada; Program in Neuroscience, University of British Columbia, Vancouver, British Columbia, Canada. Electronic address: cashawlab@gmail.com.

Abstract

Our previous ecological studies of autism spectrum disorder (ASD) has demonstrated a correlation between increasing ASD rates and aluminium (Al) adjuvants in common use in paediatric vaccines in several Western countries. The correlation between ASD rate and Al adjuvant amounts appears to be dose-dependent and satisfies 8 of 9 Hill criteria for causality. We have now sought to provide an animal model to explore potential behavioural phenotypes and central nervous system (CNS) alterations using s.c. injections of Al hydroxide in early postnatal CD-1 mice of both sexes. Injections of a "high" and "low" Al adjuvant levels were designed to correlate to either the U.S. or Scandinavian paediatric vaccine schedules vs. control saline-injected mice. Both male and female mice in the "high Al" group showed significant weight gains following treatment up to sacrifice at 6 months of age. **Male mice in the "high Al" group showed significant changes in light-dark box tests and in various measures of behaviour in an open field. Female mice showed significant changes in the light-dark box at both doses, but no significant changes in open field behaviours. These current data implicate Al injected in early postnatal life in some CNS alterations that may be relevant for a better understanding of the aetiology of ASD.**

Repetitive administration of aluminium to neonatal mice in amounts comparable to those to children receive via routine vaccinations significantly increases anxiety and reduces exploratory behaviour and locomotor activities. The neurodisruptive effects of aluminium are long-lasting and persist for 6 months following injection.

17. [Aluminum-Induced Entropy in Biological Systems: Implications for Neurological Disease](#)

Journal of Toxicology, Volume 2014 (2014), Article ID 491316, 27 pages

Christopher A. Shaw,^{1,2,3} Stephanie Seneff,⁴ Stephen D. Kette,⁵ Lucija Tomljenovic,¹ John W. Oller Jr.,⁶ and Robert M. Davidson⁷

¹Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, 828 W. 10th Avenue, Vancouver, British Columbia, Canada V5Z 1L8

²Program Experimental Medicine, University of British Columbia, Vancouver, Canada V5Z 1L8

³Program in Neurosciences, University of British Columbia, Vancouver, Canada V5Z 1L8

⁴MIT Computer Science and Artificial Intelligence Laboratory, 32 Vassar Street, Cambridge, MA 02139, USA

⁵Hudson, FL 34667, USA

⁶Department of Communicative Disorders, University of Louisiana, Lafayette, LA 70504-3170, USA

⁷Internal Medicine Group Practice, PhyNet Inc., 4002 Technology Center, Longview, TX 75605, USA

Over the last 200 years, mining, smelting, and refining of aluminum (Al) in various forms have increasingly exposed living species to this naturally abundant metal. Because of its prevalence in the earth's crust, prior to its recent uses it was regarded as inert and therefore harmless. However, Al is invariably toxic to living systems and has no known beneficial role in any biological systems. Humans are increasingly exposed to Al from food, water, medicinals, vaccines, and cosmetics, as well as from industrial occupational exposure. Al disrupts biological self-ordering, energy transduction, and signaling systems, thus increasing biosemiotic entropy. Beginning with the biophysics of water, disruption progresses through the macromolecules that are crucial to living processes (DNAs, RNAs, proteoglycans, and proteins). It injures cells, circuits, and subsystems and can cause catastrophic failures ending in death. Al forms toxic complexes with other elements, such as fluorine, and interacts negatively with mercury, lead, and glyphosate. Al negatively impacts the central nervous system in all species that have been studied, including humans. Because of the global impacts of Al on water dynamics and biosemiotic systems, CNS disorders in

humans are sensitive indicators of the AI toxicants to which we are being exposed.

Exerpts: **"Animal models of neurological disease plainly suggest that the ubiquitous presence of AI in human beings implicates AI toxicants as causally involved in Lou Gehrig's disease (ALS), Alzheimer's disease and autism spectrum disorders."**

"All these findings plausibly implicate AI adjuvants in pediatric vaccines as causal factors contributing to increased rates of autism spectrum disorders in countries where multiple doses are almost universally administered."

18. [Clinical clues for autoimmunity and neuroinflammation in patients with autistic regression.](#)

Dev Med Child Neurol. 2017 Apr 6. doi: 10.1111/dmcn.13432.

Scott O, Shi D, Andriashek D, Clark B, Goetz HR.

Department of Paediatrics, The Hospital for Sick Children, Toronto, ON, Canada.
Faculty of Medicine and Dentistry, University of Alberta, Edmonton, AB, Canada.
Department of Pediatrics, Glenrose Rehabilitation Hospital, Edmonton, AB, Canada.

Division of Pediatric Neurology, University of Alberta, Edmonton, AB, Canada

Abstract

AIM:

Autistic regression is a unique variant within the autism spectrum disorders (ASDs), with recent reports raising the possibility of immune aetiology. This study explores clinical clues for an association between autistic regression and autoimmunity.

METHOD:

Single-centre charts of children diagnosed with ASD in 2014 were reviewed. We compared the rates of: (1) familial autoimmunity in first-degree and second-degree relatives; (2) febrile illness preceding initial parental concern, as a potential precipitant of immune activation; and (3) possible non-immune precipitants such as pregnancy and postnatal complications.

RESULTS:

The charts of 206 children with ASD and 33 diagnosed with autistic regression variant were reviewed. The incidence of febrile illness in the 6 months prior to initial parental concern was significantly higher in the children with autistic regression compared with those with ASD (30% vs 0%; $p < 0.001$). The overall prevalence of familial autoimmunity was also higher in children with autistic regression compared with those with ASD (33% vs 12%; $p < 0.001$). Type 1 diabetes and autoimmune thyroiditis were both more common in families with children with autistic regression. Other non-immune risk factors did not differ between the two groups.

INTERPRETATION:

Our findings suggest that predisposition to autoimmunity, and immune/inflammatory activation, may be associated with autistic regression.

19. [Biological plausibility of the gut-brain axis in autism.](#)

Ann N Y Acad Sci. 2017 Nov;1408(1):5-6. doi: 10.1111/nyas.13516. Epub 2017 Nov 1.

Vasquez A

Abstract

Organic abnormalities with neuroinflammatory and psychiatric consequences involving abnormal kynurenine and purine metabolism, neurotransmitter and cytokine imbalances, and altered levels of nutrients and metabolites are noted in autism, and many of these abnormalities—specifically including increased intestinal permeability, microbial metabolites, and heightened serum levels of endotoxin—originate from the gut.

20. [A comparison of temporal trends in United States autism prevalence to trends in suspected environmental factors](#)

Environ Health. 2014; 13: 73.

Cynthia D Nevison

Institute for Arctic and Alpine Research, University of Colorado, Boulder, Boulder, CO 80309-0450 USA

The prevalence of diagnosed autism has increased rapidly over the last several decades among U.S. children. Environmental factors are thought to be driving this increase and a list of the top ten suspected environmental toxins was published recently.

Methods

Temporal trends in autism for birth years 1970–2005 were derived from a combination of data from the California Department of Developmental Services (CDDS) and the United States Individuals with Disabilities Education Act (IDEA). Temporal trends in suspected toxins were derived from data compiled during an extensive literature survey. Toxin and autism trends were compared by visual inspection and computed correlation coefficients. Using IDEA data, autism prevalence vs. birth year trends were calculated independently from snapshots of data from the most recent annual report, and by tracking prevalence at a

constant age over many years of reports. The ratio of the snapshot:tracking trend slopes was used to estimate the "real" fraction of the increase in autism.

Results

The CDDS and IDEA data sets are qualitatively consistent in suggesting a strong increase in autism prevalence over recent decades. The quantitative comparison of IDEA snapshot and constant-age tracking trend slopes suggests that ~75-80% of the tracked increase in autism since 1988 is due to an actual increase in the disorder rather than to changing diagnostic criteria. Most of the suspected environmental toxins examined have flat or decreasing temporal trends that correlate poorly to the rise in autism. Some, including lead, organochlorine pesticides and vehicular emissions, have strongly decreasing trends. **Among the suspected toxins surveyed, polybrominated diphenyl ethers, aluminum adjuvants, and the herbicide glyphosate have increasing trends that correlate positively to the rise in autism.**

Conclusions

Diagnosed autism prevalence has risen dramatically in the U.S over the last several decades and continued to trend upward as of birth year 2005. The increase is mainly real and has occurred mostly since the late 1980s. In contrast, children's exposure to most of the top ten toxic compounds has remained flat or decreased over this same time frame. Environmental factors with increasing temporal trends can help suggest hypotheses for drivers of autism that merit further investigation.

21. [Toxic Metals and Essential Elements in Hair and Severity of Symptoms among Children with Autism](#)

Maedica (Buchar). 2012 Jan; 7(1): 38–48.

Eleonor BLAUROCK-BUSCH,^a Omnia R. AMIN,^b Hani H. DESSOKI,^c and Thanaa RABAH ^d

^aLecturer and Advisor, International Board of Clinical Metal Toxicology & German Medical Association of Clinical Metal Toxicology, Hersbruck, Germany

^bAssociate Professor of Psychiatry, Cairo University, Egypt

^cAssociate Professor of Psychiatry, Beni-Suef University, Egypt - Beni-Suef University

^dResearcher of Public Health and Biostatistics, National Research Center, Egypt

Address for correspondence: Eleonor Blaurock-Busch, Laboratory for Clinical and Environmental Analyses, Robenstr 20, D-912217, Hersbruck, Germania.

Phone: +0049 91514332 ; Email: ed.ecartorcim@bbew

ABSTRACT

Objective: The objective of this study was to assess the levels of ten toxic metals and essential elements in hair samples of children with autism, and to correlate the level of these elements with the severity of autism.

Method: The participants were 44 children, age 3 to 9 years, with Autistic Spectrum Disorder (ASD) according to Diagnostic and Statistical Manual of Mental Disorders 4th Edition, (DSM-IV). The severity of autistic symptomatology was measured by the Childhood Autism Rating Scale (CARS). Hair analysis was performed to evaluate the long term metal exposure and mineral level.

Results: By comparing hair concentration of autistic vs nonautistic children, elevated hair concentrations were noted for aluminum, arsenic, cadmium, mercury, antimony, nickel, lead, and vanadium. Hair levels of calcium, iron, iodine, magnesium, manganese, molybdenum, zinc, and selenium were considered deficient. There was a significant positive correlation between lead & verbal communication ($p = 0.020$) and general impression ($p = 0.008$). In addition, there was a significant negative correlation between zinc & fear and nervousness ($p = 0.022$).

Conclusion: **Our data supports the historic evidence that heavy metals play a role in the development of ASD. In combination with an inadequate nutritional status the toxic effect of metals increase along with the severity of symptoms.**

22. [Autism is an Acquired Cellular Detoxification Deficiency Syndrome with Heterogeneous Genetic Predisposition](#)

Volume 8 • Issue 1 • 1000224

Autism Open Access, an open access journal, ISSN: 2165-7890

DOI: 10.4172/2165-7890.1000224

James Lyons-Weiler*

Institute for Pure and Applied Knowledge, USA

Abstract

Neurodevelopmental disorders, including autism spectrum disorders, have a complex biological and medical basis involving diverse genetic risk and myriad environmental exposures. Teasing apart the role of specific stressors is made challenging due to the large number of apparently contributing associations, gene x environment interactions and phenomimicry. Historically, these conditions have been rare, making causality assessment at the population level infeasible. Only a few vaccines have been tested for association with autism, and it has been shown that improved diagnosis only explains a percentage of the increase in diagnosis. Now the rates are so high in some countries that public school programs cannot handle to large numbers of special needs students, and professionals are quitting their jobs due to security concerns. Here, I present a

mechanistic biomedical process model (theory) of the pathophysiology of autism that reconciles the apparent paradox between the high degree of causal heterogeneity in environmental toxins, the absence of common "autism genes" and the high degree of genetic concordance (heritability) of ASD and ASD-like traits. In brief, the environmental toxin sampling liability for ASD varies among families involving different local exposures following injury to normal cellular endoplasmic detoxification and mitochondrial processes from toxic metals. The literature strongly supports that autism is most accurately seen as an acquired cellular detoxification deficiency syndrome with heterogeneous genetic predisposition that manifests pathophysiologic consequences of accumulated, run-away cellular toxicity. At a more general level, it is a form of a toxicant-induced loss of tolerance of toxins, and of chronic and sustained ER overload ("ER hyperstress"), contributing to neuronal and glial apoptosis via the unfolded protein response (UPR). Inherited risk of impaired cellular detoxification and circulating metal re-toxification in neurons and glial cells accompanied by chronic UPR is key. This model explains the aberrant protein disorder observed in ASD; the great diversity of genes that are found to have low, but real contributions to ASD risk and the sensitivity of individuals with ASD to environmental toxins. The hindrance of detoxification and loss of cellular energetics leads to apoptosis, release of cytokines and chronic neuroinflammation and microglial activation, all observed hallmarks of ASD. Interference with the development of normal complex (redundant) synapses leads to a pathological variation in neuronal differentiation, axon and dendrite outgrowth, and synaptic protein expression. The most general outcomes are overall simplification of gross synaptic anatomy and, neurofunctionally, a loss of inhibitory feedback and aberrations in long-term connections between distant regions of the brain. Failed resolution of the ER stress response leads to re-distribution of neurotoxic metals, and the impaired neurocellular processes lead to subsequent accumulation of a variety of additional types of toxins with secondary, sometime life-threatening comorbidities such as seizures, with overlapping (not mutually exclusive) causality. Reduction of exposure to toxins known to cause mitopathy (mercury) and endoplasmic reticulum dysfunction (mercury and aluminum) during pregnancy and during the early years of development will reduce the risk of ER overload and ER hyperstress, and of ASD diagnosis. This knowledge has immediate clinical translational relevance: Post-vaccination symptoms should be heeded as a sign of susceptibility to toxin; Vitamin D can be increased to drive the healthy early phases of the unfolded protein response (UPR), and mutations in ASD genes encoding proteins with high intrinsic disorder may contraindicate the use of aluminum and mercury for carriers of risk alleles. Clinicians should be alert to a patient's Vitamin D receptor (VDR) mutational status prior to recommending increased doses. Approaches to improving overall brain health in autistics must be de-stigmatized and given high priority. Reduction of lifetime exposures of industrial and agricultural toxins will improve brain health for the entire human population. Purely genetic studies of ASD, and studies that do not include vaccination as an environmental exposure with potential liability and interactions with genes, are unethical. To qualify as science, studies must test plausible hypotheses, and the absence of association from poorly designed, unethically executed, and underpowered and unsound whole-population association studies have been harmful distractions in the quest for understanding. Skilled pediatricians and ob/gyns will seek evidence of genetic predisposition to environmental susceptibility in the form of non-synonymous substitutions in brain

proteins that require ER-folding, and they will provide informed cautions on exposures (from all sources) to environmental toxins to patients and parents of patients with signs of metal and chemical sensitivity. To aid in this, a list of ASD environmental susceptibility protein-encoded genes is presented. A clinical exome sequence test, followed by loss-of-function prediction analysis, would point to individuals most susceptible to vaccine metal-induced ER hyper stress.

23. [Assessment of infantile mineral imbalances in autism spectrum disorders \(ASDs\).](#)

Int J Environ Res Public Health. 2013 Nov 11;10(11):6027-43. doi: 10.3390/ijerph10116027.

Yasuda H1, Tsutsui T.

La Belle Vie Research Laboratory, 8-4 Nihonbashi-Tomizawacho, Chuo-ku, Tokyo 103-0006, Japan. yasuda@lbv.co.jp

Abstract

The interactions between genes and the environment are now regarded as the most probable explanation for autism. In this review, we summarize the results of a metallomics study in which scalp hair concentrations of 26 trace elements were examined for 1,967 autistic children (1,553 males and 414 females aged 0-15 years-old), and discuss recent advances in our understanding of epigenetic roles of infantile mineral imbalances in the pathogenesis of autism. In the 1,967 subjects, 584 (29.7%) and 347 (17.6%) were found deficient in zinc and magnesium, respectively, and the incidence rate of zinc deficiency was estimated at 43.5% in male and 52.5% in female infantile subjects aged 0-3 years-old. In contrast, 339 (17.2%), 168 (8.5%) and 94 (4.8%) individuals were found to suffer from high burdens of aluminum, cadmium and lead, respectively, and 2.8% or less from mercury and arsenic. High toxic metal burdens were more frequently observed in the infants aged 0-3 years-old, whose incidence rates were 20.6%, 12.1%, 7.5%, 3.2% and 2.3% for aluminum, cadmium, lead, arsenic and mercury, respectively. **These findings suggest that infantile zinc- and magnesium-deficiency and/or toxic metal burdens may be critical and induce epigenetic alterations in the genes and genetic regulation mechanisms of neurodevelopment in the autistic children, and demonstrate that a time factor "infantile window" is also critical for neurodevelopment and probably for therapy. Thus, early metallomics analysis may lead to early screening/estimation and treatment/prevention for the autistic neurodevelopment disorders.**

24. [Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism.](#)

J Biomed Sci. 2002 Jul-Aug;9(4):359-64.

Singh VK, Lin SX, Newell E, Nelson C., Department of Biology and Biotechnology Center, Utah State University, Logan, Utah 84322, USA. singhvk@cc.usu.edu

Abstract

Autoimmunity to the central nervous system (CNS), especially to myelin basic protein (MBP), may play a causal role in autism, a neurodevelopmental disorder. Because many autistic children harbor elevated levels of measles antibodies, we conducted a serological study of measles-mumps-rubella (MMR) and MBP autoantibodies. Using serum samples of 125 autistic children and 92 control children, antibodies were assayed by ELISA or immunoblotting methods. ELISA analysis showed a significant increase in the level of MMR antibodies in autistic children. Immunoblotting analysis revealed the presence of an unusual MMR antibody in 75 of 125 (60%) autistic sera but not in control sera. This antibody specifically detected a protein of 73-75 kD of MMR. This protein band, as analyzed with monoclonal antibodies, was immunopositive for measles hemagglutinin (HA) protein but not for measles nucleoprotein and rubella or mumps viral proteins. Thus the MMR antibody in autistic sera detected measles HA protein, which is unique to the measles subunit of the vaccine. Furthermore, over 90% of MMR antibody-positive autistic sera were also positive for MBP autoantibodies, suggesting a strong association between MMR and CNS autoimmunity in autism. Stemming from this evidence, we suggest that **an inappropriate antibody response to MMR, specifically the measles component thereof, might be related to pathogenesis of autism.**

25. [Infection, vaccines and other environmental triggers of autoimmunity.](#)

Autoimmunity. 2005 May;38(3):235-45.

Molina V, Shoenfeld Y., Department of Medicine B and The Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel.

Abstract

The etiology of autoimmune diseases is still not clear but genetic, immunological, hormonal and environmental factors are considered to be important triggers. Most often autoimmunity is not followed by clinical symptoms unless an additional event such as an environmental factor favors an overt expression. Many environmental factors are known to affect the immune system and may play a role as triggers of the autoimmune mosaic. Infections: bacterial, viral and parasitic infections are known to induce and exacerbate autoimmune diseases, mainly by the mechanism of molecular mimicry. This was studied for some syndromes as for the association between SLE and EBV infection, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection and more. **Vaccines, in several reports were found to be temporally followed by a new onset of autoimmune diseases. The same mechanisms that act in infectious invasion of the host, apply equally to the host response to vaccination.** It has been accepted for diphtheria and tetanus toxoid, polio and

measles vaccines and GBS. Also this theory has been accepted for MMR vaccination and development of autoimmune thrombocytopenia, MS has been associated with HBV vaccination. Occupational and other chemical exposures are considered as triggers for autoimmunity. A debate still exists about the role of silicone implants in induction of scleroderma like disease. Not only foreign chemicals and agents have been associated with induction of autoimmunity, but also an intrinsic hormonal exposure, such as estrogens. This might explain the sexual dimorphism in autoimmunity. Better understanding of these environmental risk factors will likely lead to explanation of the mechanisms of onset and progression of autoimmune diseases and may lead to effective preventive involvement in specific high-risk groups. So by diagnosing a new patient with autoimmune disease a wide anamnesis work should be done.

26. [Impact of environmental factors on the prevalence of autistic disorder after 1979](#)

Journal of Public Health and Epidemiology, Vol.6(9), pp. 271-284, September 2014

Theresa A. Deisher, Ngoc V. Doan, Angelica Omaiye, Kumiko Koyama, Sarah Bwabye

Abstract

The aim of this study was to investigate a previously overlooked, universally introduced environmental factor, fetal and retroviral contaminants in childhood vaccines, absent prior to change points (CPs) in autistic disorder (AD) prevalence with subsequent dose-effect evidence and known pathologic mechanisms of action. Worldwide population based cohort study was used for the design of this study. The United States, Western Australia, United Kingdom and Denmark settings were used. All live born infants who later developed autistic disorder delivered after 1 January 1970, whose redacted vaccination and autistic disorder diagnosis information is publicly available in databases maintained by the US Federal Government, Western Australia, UK, and Denmark. The live births, grouped by father's age, were from the US and Australia. The children vaccinated with MMRII, Varicella and Hepatitis A vaccines varied from 19 to 35 months of age at the time of vaccination. Autistic disorder birth year change points were identified as 1980.9, 1988.4 and 1996 for the US, 1987 for UK, 1990.4 for Western Australia, and 1987.5 for Denmark. Change points in these countries corresponded to introduction of or increased doses of human fetal cell line-manufactured vaccines, while no relationship was found between paternal age or Diagnostic and Statistical Manual (DSM) revisions and autistic disorder diagnosis. Further, linear regression revealed that Varicella and Hepatitis A immunization coverage was significantly correlated to autistic disorder cases. R software was used to calculate change points. **Autistic disorder change points years are coincident with introduction of vaccines manufactured using human fetal cell lines, containing fetal and retroviral contaminants, into childhood vaccine regimens. This pattern was repeated in the US, UK, Western Australia and Denmark. Thus, rising autistic disorder prevalence is directly related to vaccines manufactured utilizing human fetal cells. Increased paternal age and DSM revisions were not**

related to rising autistic disorder prevalence.

27. A Positive Association found between Autism Prevalence and Childhood Vaccination uptake across the U.S. Population

Journal of Toxicology and Environmental Health, Part A: Current Issues
Volume 74, Issue 14, 2011, Pages 903 - 916
Author: Gayle DeLonga

Abstract

The reason for the rapid rise of autism in the United States that began in the 1990s is a mystery. Although individuals probably have a genetic predisposition to develop autism, researchers suspect that one or more environmental triggers are also needed. One of those triggers might be the battery of vaccinations that young children receive. Using regression analysis and controlling for family income and ethnicity, the relationship between the proportion of children who received the recommended vaccines by age 2 years and the prevalence of autism (AUT) or speech or language impairment (SLI) in each U.S. state from 2001 and 2007 was determined. A positive and statistically significant relationship was found: The higher the proportion of children receiving recommended vaccinations, the higher was the prevalence of AUT or SLI. A 1% increase in vaccination was associated with an additional 680 children having AUT or SLI. Neither parental behavior nor access to care affected the results, since vaccination proportions were not significantly related (statistically) to any other disability or to the number of pediatricians in a U.S. state. **The results suggest that although mercury has been removed from many vaccines, other culprits may link vaccines to autism.** Further study into the relationship between vaccines and autism is warranted.

28. Neonatal administration of a vaccine preservative, thimerosal, produces lasting impairment of nociception and apparent activation of opioid system in rats.

Brain Res. 2009 Dec 8;1301:143-51. Epub 2009 Sep 9.

Olczak M, Duszczyk M, Mierzejewski P, Majewska MD. Department of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, Warsaw, Poland.

Abstract

Thimerosal (THIM), an organomercury preservative added to many child vaccines is a suspected factor in pathogenesis of neurodevelopmental disorders. We examined the pharmacokinetics of Hg in the brain, liver and kidneys after i.m. THIM injection in suckling rats and we tested THIM effect on nociception. THIM solutions were injected to Wistar and Lewis rats in a vaccination-like mode on PN days 7, 9, 11 and 15 in four equal doses. For Wistar rats these were: 12, 48, 240, 720, 1440, 2160, 3000 microg Hg/kg and for Lewis: 54, 216, 540 and 1080

microg Hg/kg. Pharmacokinetic analysis revealed that Hg from THIM injections accumulates in the rat brain in significant amounts and remains there longer than 30 days after the injection. At the 6th week of age animals were examined for pain sensitivity using the hot plate test. THIM treated rats of both strains and sexes manifested statistically significantly elevated pain threshold (latency for paw licking, jumping) on a hot plate (56 degrees C). Wistar rats were more sensitive to this effect than Lewis rats. Protracted THIM-induced hypoalgesia was reversed by naloxone (5 mg/kg, i.p.) injected before the hot plate test, indicative of involvement of endogenous opioids. This was confirmed by augmented catalepsy after morphine (2.5 mg/kg, s.c.) injection. Acute THIM injection to 6-week-old rats also produced hypoalgesia, but this effect was transient and was gone within 14 days. **Present findings show that THIM administration to suckling or adult rats impairs sensitivity to pain, apparently due to activation the endogenous opioid system.**

29. [Effect of thimerosal on the neurodevelopment of premature rats.](#)

World J Pediatr. 2013 Nov;9(4):356-60. doi: 10.1007/s12519-013-0443-z. Epub 2013 Nov 14.

Chen YN¹, Wang J, Zhang J, Li SJ, He L, Shao DD, Du HY.

The Key Laboratory of Biomedical Information Engineering of Ministry of Education, and Institute of Biomedical Engineering, School of Life Science and Technology, Xi'an Jiaotong University, Xi'an, 710049, China.

Abstract

BACKGROUND:

This study was undertaken to determine the effect of thimerosal on the neurodevelopment of premature rats.

METHODS:

Thimerosal was injected into premature SD rats at a dose of 32.8, 65.6, 98.4 or 131.2 µg/kg on postnatal day 1. Expression of dopamine D4 receptor (DRD4) and serotonin 2A receptor (5-HT_{2A}R), apoptosis in the prefrontal cortex on post-injection day 49, and learning and memory function were studied and compared with those in a control group injected with saline.

RESULTS:

Expression of DRD4 and 5-HT_{2A}R and learning function decreased, and apoptosis increased significantly in the 131.2 µg/kg group (P<0.001). Memory function was significantly impaired by 65.6 (P<0.05), 98.4 and 131.2 µg/kg (P<0.001).

CONCLUSIONS:

The negative adverse consequences on neurodevelopment observed in the present study are consistent with previous studies; this study raised serious concerns about adverse neurodevelopmental disorder such as autism in humans following the ongoing worldwide routine administration of thimerosal containing vaccines to infants.

30. [Transcriptomic analyses of neurotoxic effects in mouse brain after intermittent neonatal administration of thimerosal.](#)

Toxicol Sci. 2014 Jun;139(2):452-65. doi: 10.1093/toxsci/kfu049. Epub 2014 Mar 27.

State Key Laboratory of Biomembrane and Membrane Biotechnology, Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China. Li X1, Qu F, Xie W, Wang F, Liu H, Song S, Chen T, Zhang Y, Zhu S, Wang Y, Guo C, Tang TS.

Abstract

Thimerosal is a vaccine antimicrobial preservative which has long been suspected an iatrogenic factor possibly contributing to neurodevelopmental disorders including autism. The association between infant vaccine thimerosal exposure and autism remains an open question. Although thimerosal has been removed from mandatory childhood vaccines in the United States, thimerosal-preserved vaccines are still widely used outside of the United States especially in developing countries. Notably, thimerosal-containing vaccines are being given to the newborns within the first 12-24 h after birth in some countries. To examine the possible neurotoxic effects of early neonatal exposure to a higher level of thimerosal, FVB mice were subcutaneously injected with thimerosal-mercury at a dose which is 20× higher than that used for regular Chinese infant immunization during the first 4 months of life. Thimerosal-treated mice exhibited neural development delay, social interaction deficiency, and inclination of depression. Apparent neuropathological changes were also observed in adult mice neonatally treated with thimerosal. High-throughput RNA sequencing of autistic-behaved mice brains revealed the alternation of a number of canonical pathways involving neuronal development, neuronal synaptic function, and the dysregulation of endocrine system. Intriguingly, the elevation of anterior pituitary secreting hormones occurred exclusively in male but not in female thimerosal-treated mice, demonstrating for the first time the gender bias of thimerosal-mercury toxicity with regard to endocrine system. **Our results indicate that higher dose of neonatal thimerosal-mercury (20× higher than that used in human) is capable of inducing long-lasting substantial dysregulation of neurodevelopment, synaptic function, and endocrine system, which could be the causal involvements of autistic-like behavior in mice.**

31. Lasting neuropathological changes in rat brain after intermittent neonatal administration of thimerosal.

Folia Neuropathol. 2010;48(4):258-69. Olczak M, Duszczyk M, Mierzejewski P, Wierzbą-Bobrowicz T, Majewska MD.

Department of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, ul. Sobieskiego 9, Warsaw, Poland.

Abstract

Thimerosal, an organomercurial added as a preservative to some vaccines, is a suspected iatrogenic factor, possibly contributing to paediatric neurodevelopmental disorders including autism. We examined the effects of early postnatal administration of thimerosal (four i.m. injections, 12 or 240 µg THIM-Hg/kg, on postnatal days 7, 9, 11 and 15) on brain pathology in Wistar rats. Numerous neuropathological changes were observed in young adult rats which were treated postnatally with thimerosal. They included: ischaemic degeneration of neurons and "dark" neurons in the prefrontal and temporal cortex, the hippocampus and the cerebellum, pathological changes of the blood vessels in the temporal cortex, diminished synaptophysin reaction in the hippocampus, atrophy of astroglia in the hippocampus and cerebellum, and positive caspase-3 reaction in Bergmann astroglia. **These findings document neurotoxic effects of thimerosal, at doses equivalent to those used in infant vaccines or higher, in developing rat brain, suggesting likely involvement of this mercurial in neurodevelopmental disorders.**

32. Persistent behavioral impairments and alterations of brain dopamine system after early postnatal administration of thimerosal in rats.

Behav Brain Res. 2011 Sep 30;223(1):107-18. doi: 10.1016/j.bbr.2011.04.026. Epub 2011 Apr 28.

Olczak M, Duszczyk M, Mierzejewski P, Meyza K, Majewska MD. Department of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, 02-957 Warsaw, Poland.

Abstract

The neurotoxic organomercurial thimerosal (THIM), used for decades as vaccine preservative, is a suspected factor in the pathogenesis of some neurodevelopmental disorders. Previously we showed that neonatal administration of THIM at doses equivalent to those used in infant vaccines or higher, causes lasting alterations in the brain opioid system in rats. Here we investigated neonatal treatment with THIM (at doses 12, 240, 1440 and 3000 µg Hg/kg) on behaviors, which are characteristically altered in autism, such as locomotor activity, anxiety, social interactions, spatial learning, and on the brain dopaminergic system in Wistar rats of both sexes. Adult male and female rats, which were exposed to the entire range of THIM doses during the early postnatal life, manifested impairments of locomotor activity and increased anxiety/neophobia in the open field test. In animals of both sexes treated with the highest THIM dose, the frequency of prosocial interactions was reduced, while

the frequency of asocial/antisocial interactions was increased in males, but decreased in females. Neonatal THIM treatment did not significantly affect spatial learning and memory. THIM-exposed rats also manifested reduced haloperidol-induced catalepsy, accompanied by a marked decline in the density of striatal D₂ receptors, measured by immunohistochemical staining, suggesting alterations to the brain dopaminergic system. Males were more sensitive than females to some neurodisruptive/neurotoxic actions of THIM. **These data document that early postnatal THIM administration causes lasting neurobehavioral impairments and neurochemical alterations in the brain, dependent on dose and sex. If similar changes occur in THIM/mercurial-exposed children, they could contribute do neurodevelopmental disorders.**

33. [B-Lymphocytes from a Population of Children with Autism Spectrum Disorder and Their Unaffected Siblings Exhibit Hypersensitivity to Thimerosal](#)

J Toxicol. 2013;2013:801517. Epub 2013 Jun 9.

Sharpe MA, Gist TL, Baskin DS.

Department of Neurosurgery, The Methodist Neurological Institute, Houston, TX.

Abstract

The role of thimerosal containing vaccines in the development of autism spectrum disorder (ASD) has been an area of intense debate, as has the presence of mercury dental amalgams and fish ingestion by pregnant mothers. We studied the effects of thimerosal on cell proliferation and mitochondrial function from B-lymphocytes taken from individuals with autism, their nonautistic twins, and their nontwin siblings. Eleven families were examined and compared to matched controls. B-cells were grown with increasing levels of thimerosal, and various assays (LDH, XTT, DCFH, etc.) were performed to examine the effects on cellular proliferation and mitochondrial function. A subpopulation of eight individuals (4 ASD, 2 twins, and 2 siblings) from four of the families showed thimerosal hypersensitivity, whereas none of the control individuals displayed this response. The thimerosal concentration required to inhibit cell proliferation in these individuals was only 40% of controls. Cells hypersensitive to thimerosal also had higher levels of oxidative stress markers, protein carbonyls, and oxidant generation. **This suggests certain individuals with a mild mitochondrial defect may be highly susceptible to mitochondrial specific toxins like the vaccine preservative thimerosal.**

34. [Thimerosal-Derived Ethylmercury Is a Mitochondrial Toxin in Human Astrocytes: Possible Role of Fenton Chemistry in the Oxidation and Breakage of mtDNA](#)

J Toxicol. 2012; 2012: 373678. Published online Jun 28, 2012. doi: 10.1155/2012/373678

Martyn A. Sharpe, * Andrew D. Livingston, and David S. Baskin

Abstract

Thimerosal generates ethylmercury in aqueous solution and is widely used as preservative. We have investigated the toxicology of Thimerosal in normal human astrocytes, paying particular attention to mitochondrial function and the generation of specific oxidants. **We find that ethylmercury not only inhibits mitochondrial respiration leading to a drop in the steady state membrane potential, but also concurrent with these phenomena increases the formation of superoxide, hydrogen peroxide, and Fenton/Haber-Weiss generated hydroxyl radical. These oxidants increase the levels of cellular aldehyde/ketones. Additionally, we find a five-fold increase in the levels of oxidant damaged mitochondrial DNA bases and increases in the levels of mtDNA nicks and blunt-ended breaks. Highly damaged mitochondria are characterized by having very low membrane potentials, increased superoxide/hydrogen peroxide production, and extensively damaged mtDNA and proteins. These mitochondria appear to have undergone a permeability transition, an observation supported by the five-fold increase in Caspase-3 activity observed after Thimerosal treatment.**

35. [Thioredoxin: A novel, independent diagnosis marker in children with autism.](#)

Int J Dev Neurosci. 2014 Nov 26. pii: S0736-5748(14)00191-9. doi: 10.1016/j.ijdevneu.2014.11.007.

Zhang QB1, Gao SJ1, Zhao HX2.

Abstract

BACKGROUND:

Oxidative stress increases serum thioredoxin (TRX), a redox-regulating protein with antioxidant activity recognized as an oxidative-stress marker. The aim of this study was to assess the clinical significance of serum TRX levels in Autism spectrum disorders (ASD).

METHODS:

Eighty patients diagnosed with ASD and 100 sex and age matched typically developing children were assessed for serum TRX content at admission. TRX were assayed with solid-phase sandwich ELISA, and severity of ASD was evaluated with the Childhood Autism Rating Scale (CARS) Score.

RESULTS:

The results indicated that the median serum TRX levels were significantly ($P < 0.0001$) higher in children with ASD as compared to typically developing children [17.9(IQR: 10.7-25.8)ng/ml and 5.5(3.6-9.2)ng/ml, respectively]. Levels of TRX increased with increasing severity of ASD as defined by the CARS score. After adjusting for all other possible covariates, TRX still was an independent diagnosis marker of ASD with an adjusted OR of 1.454 (95% CI, 1.232-1.892; $P < 0.0001$). Based on the receiver operating characteristic (ROC) curve, the optimal cut-off value of serum TRX levels as an indicator for auxiliary diagnosis of autism was projected to be 10.6ng/ml. Further, we found that an increased

diagnosis of ASD was associated with TRX levels ≥ 10.6 ng/ml (adjusted OR 15.31, 95% CI: 7.36-31.85) after adjusting for possible confounders.

CONCLUSIONS:

Our study demonstrated that serum TRX levels were associated with ASD, and elevated levels could be considered as a novel, independent diagnosis indicator of ASD.

36. Inhibition of the human thioredoxin system. A molecular mechanism of mercury toxicity.

J Biol Chem. 2008 May 2;283(18):11913-23. doi: 10.1074/jbc.M710133200. Epub 2008 Mar 4.

Carvalho CM1, Chew EH, Hashemy SI, Lu J, Holmgren A.

Abstract

Mercury toxicity mediated by different forms of mercury is a major health problem; however, the molecular mechanisms underlying toxicity remain elusive. We analyzed the effects of mercuric chloride (HgCl₂) and monomethylmercury (MeHg) on the proteins of the mammalian thioredoxin system, thioredoxin reductase (TrxR) and thioredoxin (Trx), and of the glutaredoxin system, glutathione reductase (GR) and glutaredoxin (Grx). HgCl₂ and MeHg inhibited recombinant rat TrxR with IC₅₀ values of 7.2 and 19.7 nM, respectively. Fully reduced human Trx1 bound mercury and lost all five free thiols and activity after incubation with HgCl₂ or MeHg, but only HgCl₂ generated dimers. Mass spectra analysis demonstrated binding of 2.5 mol of Hg(2+) and 5 mol of MeHg(+)/mol of Trx1 with the very strong Hg(2+) complexes involving active site and structural disulfides. Inhibition of both TrxR and Trx activity was observed in HeLa and HEK 293 cells treated with HgCl₂ or MeHg. GR was inhibited by HgCl₂ and MeHg in vitro, but no decrease in GR activity was detected in cell extracts treated with mercurials. Human Grx1 showed similar reactivity as Trx1 with both mercurial compounds, with the loss of all free thiols and Grx dimerization in the presence of HgCl₂, but no inhibition of Grx activity was observed in lysates of HeLa cells exposed to mercury. Overall, mercury inhibition was selective toward the thioredoxin system. In particular, the remarkable potency of the mercury compounds to bind to the selenol-thiol in the active site of TrxR should be a major molecular mechanism of mercury toxicity.

37. Effects of selenite and chelating agents on mammalian thioredoxin reductase inhibited by mercury: implications for treatment of mercury poisoning.

FASEB J. 2011 Jan;25(1):370-81. doi: 10.1096/fj.10-157594. Epub 2010 Sep 1.

Carvalho CM1, Lu J, Zhang X, Arnér ES, Holmgren A.

Abstract

Mercury toxicity is a highly interesting topic in biomedicine due to the severe endpoints and treatment limitations. Selenite serves as an antagonist of mercury toxicity, but the molecular mechanism of detoxification is not clear. Inhibition of the selenoenzyme thioredoxin reductase (TrxR) is a suggested mechanism of toxicity. Here, we demonstrated enhanced inhibition of activity by inorganic and organic mercury compounds in NADPH-reduced TrxR, consistent with binding of mercury also to the active site selenolthiol. On treatment with 5 μ M selenite and NADPH, TrxR inactivated by HgCl₂ displayed almost full recovery of activity. Structural analysis indicated that mercury was complexed with TrxR, but enzyme-generated selenide removed mercury as mercury selenide, regenerating the active site selenocysteine and cysteine residues required for activity. The antagonistic effects on TrxR inhibition were extended to endogenous antioxidants, such as GSH, and clinically used exogenous chelating agents BAL, DMPS, DMSA, and α -lipoic acid. Consistent with the in vitro results, recovery of TrxR activity and cell viability by selenite was observed in HgCl₂-treated HEK 293 cells. These results stress the role of TrxR as a target of mercurials and provide the mechanism of selenite as a detoxification agent for mercury poisoning.

38. Serological association of measles virus and human herpesvirus-6 with brain autoantibodies in autism.

Clin Immunol Immunopathol. 1998 Oct;89(1):105-8.

Singh VK, Lin SX, Yang VC. College of Pharmacy, University of Michigan, Ann Arbor, Michigan, 48109-1065, USA.

Abstract

Considering an autoimmunity and autism connection, brain autoantibodies to myelin basic protein (anti-MBP) and neuron-axon filament protein (anti-NAFP) have been found in autistic children. In this current study, we examined associations between virus serology and autoantibody by simultaneous analysis of measles virus antibody (measles-IgG), human herpesvirus-6 antibody (HHV-6-IgG), anti-MBP, and anti-NAFP. We found that measles-IgG and HHV-6-IgG titers were moderately higher in autistic children but they did not significantly differ from normal controls. Moreover, we found that a vast majority of virus serology-positive autistic sera was also positive for brain autoantibody: (i) 90% of measles-IgG-positive autistic sera was also positive for anti-MBP; (ii) 73% of measles-IgG-positive autistic sera was also positive for anti-NAFP; (iii) 84% of HHV-6-IgG-positive autistic sera was also positive for anti-MBP; and (iv) 72% of HHV-6-IgG-positive autistic sera was also positive for anti-NAFP. **This study is the first to report an association between virus serology and brain autoantibody in autism; it supports the hypothesis that a virus-induced autoimmune response may play a causal role in autism.**

39. Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism

American Journal of Clinical Nutrition, Vol. 80, No. 6, 1611-1617, December 2004

Department of Pediatrics, University of Arkansas for Medical Sciences, and the Arkansas Children's Hospital Research Institute

Abstract

Background: Autism is a complex neurodevelopmental disorder that usually presents in early childhood and that is thought to be influenced by genetic and environmental factors. Although abnormal metabolism of methionine and homocysteine has been associated with other neurologic diseases, these pathways have not been evaluated in persons with autism.

Objective: The purpose of this study was to evaluate plasma concentrations of metabolites in the methionine transmethylation and transsulfuration pathways in children diagnosed with autism.

Design: Plasma concentrations of methionine, S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), adenosine, homocysteine, cystathionine, cysteine, and oxidized and reduced glutathione were measured in 20 children with autism and in 33 control children. On the basis of the abnormal metabolic profile, a targeted nutritional intervention trial with folinic acid, betaine, and methylcobalamin was initiated in a subset of the autistic children.

Results: Relative to the control children, the children with autism had significantly lower baseline plasma concentrations of methionine, SAM, homocysteine, cystathionine, cysteine, and total glutathione and significantly higher concentrations of SAH, adenosine, and oxidized glutathione. This metabolic profile is consistent with impaired capacity for methylation (significantly lower ratio of SAM to SAH) and increased oxidative stress (significantly lower redox ratio of reduced glutathione to oxidized glutathione) in children with autism. The intervention trial was effective in normalizing the metabolic imbalance in the autistic children.

Conclusions: **An increased vulnerability to oxidative stress and a decreased capacity for methylation may contribute to the development and clinical manifestation of autism.**

40. [Classification and adaptive behavior prediction of children with autism spectrum disorder based upon multivariate data analysis of markers of oxidative stress and DNA methylation](#)

Daniel P. Howsmon, Uwe Kruger, Stepan Melnyk, S. Jill James, Juergen Hahn

Published: March 16, 2017, <https://doi.org/10.1371/journal.pcbi.1005385>

Daniel P. Howsmon

Affiliations Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute, Troy, New York, United States of America, Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute, Troy, New York, United States of America

ORCID logo <http://orcid.org/0000-0002-7177-1342>

Uwe Kruger

Affiliation Department of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, New York, United States of America

ORCID logo <http://orcid.org/0000-0001-5664-9499>

Stepan Melnyk

Affiliation Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States of America

S. Jill James

Affiliation Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, Arkansas, United States of America

Juergen Hahn

E-mail: hahnj@rpi.edu

Affiliations Department of Chemical and Biological Engineering, Rensselaer Polytechnic Institute, Troy, New York, United States of America, Center for Biotechnology and Interdisciplinary Studies, Rensselaer Polytechnic Institute, Troy, New York, United States of America, Department of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, New York, United States of America

Abstract

The number of diagnosed cases of Autism Spectrum Disorders (ASD) has increased dramatically over the last four decades; however, there is still considerable debate regarding the underlying pathophysiology of ASD. This lack of biological knowledge restricts diagnoses to be made based on behavioral observations and psychometric tools. However, physiological measurements should support these behavioral diagnoses in the future in order to enable earlier and more accurate diagnoses. **Stepping towards this goal of incorporating biochemical data into ASD diagnosis, this paper analyzes measurements of metabolite concentrations of the folate-dependent one-carbon metabolism and transsulfuration pathways taken from blood samples of 83 participants with ASD and 76 age-matched neurotypical peers.** Fisher Discriminant Analysis enables multivariate classification of the participants as on the spectrum or neurotypical which **results in 96.1% of all neurotypical participants being correctly identified as such while still correctly identifying 97.6% of the ASD cohort.** Furthermore, kernel partial least squares is used to predict adaptive behavior, as measured by the Vineland Adaptive Behavior Composite score,

where measurement of five metabolites of the pathways was sufficient to predict the Vineland score with an R2 of 0.45 after cross-validation. This level of accuracy for classification as well as severity prediction far exceeds any other approach in this field and is a strong indicator that the metabolites under consideration are strongly correlated with an ASD diagnosis but also that the statistical analysis used here offers tremendous potential for extracting important information from complex biochemical data sets.

41. [Newborn screening for autism: in search of candidate biomarkers.](#)

Biomark Med. 2013 Apr;7(2):247-60. doi: 10.2217/bmm.12.108.

Mizejewski GJ1, Lindau-Shepard B, Pass KA.

Division of Translational Medicine, Wadsworth Center, NYS Department of Health, PO Box 509, Albany, NY 12201 0509, USA.

Abstract

BACKGROUND:

Autism spectrum disorder (ASD) represents a wide range of neurodevelopmental disorders characterized by impairments in social interaction, language, communication and range of interests. Autism is usually diagnosed in children 3-5 years of age using behavioral characteristics; thus, diagnosis shortly after birth would be beneficial for early initiation of treatment.

AIM:

This retrospective study sought to identify newborns at risk for ASD utilizing bloodspot specimens in an immunoassay.

MATERIALS & METHODS:

The present study utilized stored frozen specimens from ASD children already diagnosed at 15-36 months of age. The newborn specimens and controls were analyzed by immunoassay in a multiplex system that included 90 serum biomarkers and subjected to statistical analysis.

RESULTS:

Three sets of five biomarkers associated with ASD were found that differed from control groups. The 15 candidate biomarkers were then discussed regarding their association with ASD.

CONCLUSION:

This study determined that a statistically selected panel of 15 biomarkers successfully discriminated presumptive newborns at risk for ASD from those of nonaffected controls.

Exerpt:

"GST [Glutathione S-transferase] is a metabolic biomarker directly associated with ASD. The human gene product for GST constitutes a candidate susceptibility protein due to its tissue distribution and role in oxidative stress and methionine metabolism, which results in neuronal injury and death."

"Results of a recent study further demonstrated that glutathione, total glutathione and activity levels of GST were significantly lower in autistic patients as compared with control subjects; however, homocysteine, thioredoxin reductase and peroxidoxin levels were remarkably higher."

"Autistic children with metabolic disturbances are known to display reduced metabolic activities of GST, cysteine, glutathione and methionine, which are associated with methionine transmethylation and trans-sulfation."

42. [Altered urinary porphyrins and mercury exposure as biomarkers for autism severity in Egyptian children with autism spectrum disorder](#)

Metabolic Brain Disease

Eman M. Khaled Nagwa A. Meguid Geir Bjørklund Email author Amr Gouda Mohamed H. Bahary Adel Hashish Nermin M. Sallam Salvatore Chirumbolo Mona A. El-Bana

Abstract

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder that affects social, communication, and behavioral development. Recent evidence supported but also questioned the hypothetical role of compounds containing mercury (Hg) as contributors to the development of ASD. Specific alterations in the urinary excretion of porphyrin-containing ring catabolites have been associated with exposure to Hg in ASD patients. In the present study, the level of urinary porphyrins, as biomarkers of Hg toxicity in children with ASD, was evaluated, and its correlation with severity of the autistic behavior further explored. A total of 100 children was enrolled in the present study. They were classified into three groups: children with ASD (40), healthy controls (40), and healthy siblings of the ASD children (20). Children with ASD were diagnosed using DSM-IV-TR, ADI-R, and CARS tests. Urinary porphyrins were evaluated within the three groups using high-performance liquid chromatography (HPLC), after plasma evaluation of mercury (Hg) and lead (Pb) in the same groups.

Results showed that children with ASD had significantly higher levels of Hg, Pb, and the porphyrins pentacarboxyporphyrin, coproporphyrin, precoproporphyrin, uroporphyrins, and hexacarboxyporphyrin compared to healthy controls and healthy siblings of the ASD children. However, there was no significant statistical difference in the level of heptacarboxyporphyrin among the three groups, while a significant positive correlation between the levels of coproporphyrin and precoproporphyrin and autism severity was observed. Mothers of ASD children showed a higher percentage of dental amalgam

restorations compared to the mothers of healthy controls suggesting that high Hg levels in children with ASD may relate to the increased exposure to Hg from maternal dental amalgam during pregnancy and lactation. The results showed that the ASD children in the present study had increased blood Hg and Pb levels compared with healthy control children indicating that disordered porphyrin metabolism might interfere with the pathology associated with the autistic neurologic phenotype. **The present study indicates that coproporphyrin and precoproporphyrin may be utilized as possible biomarkers for heavy metal exposure and autism severity in children with ASD.**

43. Porphyrinuria in childhood autistic disorder: Implications for environmental toxicity

Toxicology and Applied Pharmacology, 2006

Robert Natafa, Corinne Skorupkab, Lorene Ametb, Alain Lama, Anthea Springbettc and Richard Lathed, aLaboratoire Philippe Auguste, Paris, France, Association ARIANE, Clichy, France, Department of Statistics, Roslin Institute, Roslin, UK, Pieta Research,

This new study from France utilizes a new and sophisticated measurement for environmental toxicity by assessing porphyrin levels in autistic children. It provides clear and unequivocal evidence that children with autism spectrum disorders are more toxic than their neurotypical peers.

Excerpt: "Coproporphyrin levels were elevated in children with autistic disorder relative to control groups...the elevation was significant. These data implicate environmental toxicity in childhood autistic disorder."

Abstract

To address a possible environmental contribution to autism, we carried out a retrospective study on urinary porphyrin levels, a biomarker of environmental toxicity, in 269 children with neurodevelopmental and related disorders referred to a Paris clinic (2002–2004), including 106 with autistic disorder. Urinary porphyrin levels determined by high-performance liquid chromatography were compared between diagnostic groups including internal and external control groups. Coproporphyrin levels were elevated in children with autistic disorder relative to control groups. Elevation was maintained on normalization for age or to a control heme pathway metabolite (uroporphyrin) in the same samples. The elevation was significant ($P < 0.001$). Porphyrin levels were unchanged in Asperger's disorder, distinguishing it from autistic disorder. The atypical molecule precoproporphyrin, a specific indicator of heavy metal toxicity, was also elevated in autistic disorder ($P < 0.001$) but not significantly in Asperger's. A subgroup with autistic disorder was treated with oral dimercaptosuccinic acid (DMSA) with a view to heavy metal removal. Following DMSA there was a significant ($P = 0.002$) drop in urinary porphyrin excretion. **These data implicate environmental toxicity in childhood autistic disorder.**

44. [An investigation of porphyrinuria in Australian children with autism.](#)

J Toxicol Environ Health A. 2008;71(20):1349-51. doi:
10.1080/15287390802271723.

Austin DW, Shandley K.

Swinburne Autism Bio-Research Initiative (SABRI), Faculty of Life and Social Sciences, Swinburne University of Technology, Melbourne, Australia.
daustin@swin.edu.au

Abstract

Two recent studies, from France (Nataf et al., 2006) and the United States (Geier & Geier, 2007), identified atypical urinary porphyrin profiles in children with an autism spectrum disorder (ASD). These profiles serve as an indirect measure of environmental toxicity generally, and mercury (Hg) toxicity specifically, with the latter being a variable proposed as a causal mechanism of ASD (Bernard et al., 2001; Mutter et al., 2005). To examine whether this phenomenon occurred in a sample of Australian children with ASD, an analysis of urinary porphyrin profiles was conducted. A consistent trend in abnormal porphyrin levels was evidenced when data was compared with those previously reported in the literature. The results are suggestive of environmental toxic exposure impairing heme synthesis. **Three independent studies from three continents have now demonstrated that porphyrinuria is concomitant with ASD, and that Hg may be a likely xenobiotic to produce porphyrin profiles of this nature.**

45. [Porphyrinuria in Korean children with autism: correlation with oxidative stress.](#)

J Toxicol Environ Health A. 2010;73(10):701-10. doi:
10.1080/15287391003614000.

Youn SI, Jin SH, Kim SH, Lim S.

Department of Basic Eastern Medical Science, Graduate School, KyungHee University, Seoul, Republic of Korea.

Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder believed to be associated with heavy metal exposure, especially mercury (Hg), and is characterized by disturbances in metal elimination. Various studies correlated elevated heavy metal body burden with ASD diagnoses as evidenced by increased urinary porphyrin levels in patients. Urinary porphyrins were also determined in Korean patients diagnosed with ASD (n = 65) who visited AK

Eastern Medicinal Clinic in Kangnam-gu, Seoul, from June 2007 to September 2008, compared to controls (n = 9) residing in the same area, by means of Metamatrix (CLIA-approved) laboratory testing. Further, urinary organic acids as indicators of hepatic detoxification/oxidative stress were also analyzed among patients diagnosed with ASD. Significant increases were found in patients diagnosed with ASD for proporphyrins, pentacarboxyporphyrin, precoproporphyrin, coproporphyrins, and total porphyrins. Significant correlations were observed between hepatic detoxification/oxidative stress markers and urinary porphyrins. **In agreement with published data, the present results demonstrated that measurement of porphyrins serves as a reliable tool for diagnosis of heavy metal involvement in ASD.**

46. Uncoupling of ATP-mediated Calcium Signaling and Dysregulated IL-6 Secretion in Dendritic Cells by Nanomolar Thimerosal

Environmental Health Perspectives, July 2006.

Samuel R. Goth, Ruth A. Chu Jeffrey P. Gregg

1 National Institute of Environmental Health Sciences Center for Children's Environmental Health

2 Department of Veterinary Molecular Biosciences and

3 Department of Medical Pathology, University of California–Davis, Davis, California, USA

4 MIND (Medical Investigation of Neurodevelopmental Disorders) Institute, University of California–Davis, Sacramento, California, USA

Address correspondence to I.N. Pessah, Department of Veterinary Medicine, Molecular Biosciences, 1311 Haring Hall, One Shields Ave., University of California, Davis, CA

Abstract

Dendritic cells (DCs), a rare cell type widely distributed in the soma, are potent antigen-presenting cells that initiate primary immune responses. DCs rely on intracellular redox state and calcium (Ca²⁺) signals for proper development and function, but the relationship between these two signaling systems is unclear. Thimerosal (THI) is a mercurial used to preserve vaccines and consumer products, and is used experimentally to induce Ca²⁺ release from microsomal stores. We tested adenosine triphosphate (ATP)-mediated Ca²⁺ responses of DCs transiently exposed to nanomolar THI. Transcriptional and immunocytochemical analyses show that murine myeloid immature DCs (IDCs) and mature DCs (MDCs) express inositol 1,4,5-trisphosphate receptor (IP3R) and ryanodine receptor (RyR) Ca²⁺ channels, known targets of THI. IDCs express the RyR1 isoform in a punctate distribution that is densest near plasma membranes and within dendritic processes, whereas IP3Rs are more generally distributed. RyR1 positively and negatively regulates purinergic signaling because ryanodine (Ry) blockade a) recruited 80% more ATP responders, b) shortened ATP-mediated Ca²⁺ transients > 2-fold, and c) produced a delayed

and persistent rise (≥ 2 -fold) in baseline Ca^{2+} . THI (100 nM, 5 min) recruited more ATP responders, shortened the ATP-mediated Ca^{2+} transient (≥ 1.4 -fold), and produced a delayed rise (≥ 3 -fold) in the Ca^{2+} baseline, mimicking Ry. THI and Ry, in combination, produced additive effects leading to uncoupling of IP3R and RyR1 signals. THI altered ATP-mediated interleukin-6 secretion, initially enhancing the rate of cytokine secretion but suppressing cytokine secretion overall in Dcs. **Dendritic cells are exquisitely sensitive to Thimerosal, with one mechanism involving the uncoupling of positive and negative regulation of Ca^{2+} signals contributed by RyR1.**

Excerpt: "Our findings that DCs primarily express the RyR1 channel complex and that this complex is uncoupled by very low levels of THI with dysregulated IL-6 secretion raise intriguing questions about a molecular basis for immune dysregulation and the possible role of the RyR1 complex in genetic susceptibility of the immune system to mercury."

47. [Myeloid dendritic cells frequencies are increased in children with autism spectrum disorder and associated with amygdala volume and repetitive behaviors](#)

Brain, Behavior, and Immunity, Volume 31, July 2013, Pages 69–75, Inflammation and Mental Health

Elizabeth Breecea, b, Brian Paciottib, Christine Wu Nordahlb, c, Sally Ozonoffb, c, Judy A. Van de Waterb, d, Sally J. Rogersb, c, David Amaralb, c, Paul Ashwood

a Department of Medical Microbiology and Immunology, University of California, Davis, USA

b The M.I.N.D. Institute, University of California, Davis, USA

c Department of Psychiatry and Behavioral Sciences, University of California, Davis, USA

d Division of Rheumatology, Allergy and Clinical Immunology, University of California, Davis, USA

Abstract

The pathophysiology of autism spectrum disorder (ASD) is not yet known; however, studies suggest that dysfunction of the immune system affects many children with ASD. Increasing evidence points to dysfunction of the innate immune system including activation of microglia and perivascular macrophages, increases in inflammatory cytokines/chemokines in brain tissue and CSF, and abnormal peripheral monocyte cell function. Dendritic cells are major players in innate immunity and have important functions in the phagocytosis of pathogens or debris, antigen presentation, activation of naïve T cells, induction of tolerance and cytokine/chemokine production. In this study, we assessed circulating frequencies of myeloid dendritic cells (defined as Lin-1-BDCA1+CD11c+ and Lin-1-BDCA3+CD123-) and plasmacytoid dendritic cells (Lin-1-BDCA2+CD123+ or Lin-1-BDCA4+ CD11c-) in 57 children with ASD, and 29

typically developing controls of the same age, all of who were enrolled as part of the Autism Phenome Project (APP). The frequencies of dendritic cells and associations with behavioral assessment and MRI measurements of amygdala volume were compared in the same participants. The frequencies of myeloid dendritic cells were significantly increased in children with ASD compared to typically developing controls ($p < 0.03$). Elevated frequencies of myeloid dendritic cells were positively associated with abnormal right and left amygdala enlargement, severity of gastrointestinal symptoms and increased repetitive behaviors. The frequencies of plasmacytoid dendritic cells were also associated with amygdala volumes as well as developmental regression in children with ASD. **Dendritic cells play key roles in modulating immune responses and differences in frequencies or functions of these cells may result in immune dysfunction in children with ASD. These data further implicate innate immune cells in the complex pathophysiology of ASD.**

48. Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal

Environmental Health Perspectives, Aug 2005.

Thomas Burbacher, PhD [University of Washington].

This study demonstrates clearly and unequivocally that ethyl mercury, the kind of mercury found in vaccines, not only ends up in the brain, but leaves double the amount of inorganic mercury as methyl mercury, the kind of mercury found in fish. Methyl mercury (organic mercury) has a half-life in the brain measured in days (Rice), while thimerosal (organic mercury) once in the brain converts to inorganic mercury at much higher rates, and inorganic mercury has a half-life in the brain measured in years and decades (Rooney). This work is groundbreaking because little is known about ethyl mercury, and many health authorities have asserted that the mercury found in vaccines is the "safe kind." This study also delivers a strong rebuke of the Institute of Medicine's recommendation in 2004 to no longer pursue the mercury-autism connection.

Excerpt: "A recently published IOM review (IOM 2004) appears to have abandoned the earlier recommendation [of studying mercury and autism] as well as back away from the American Academy of Pediatrics goal [of removing mercury from vaccines]. This approach is difficult to understand, given our current limited knowledge of the toxicokinetics and developmental neurotoxicity of thimerosal, a compound that has been (and will continue to be) injected in millions of newborns and infants."

Excerpt: " The average brain-to-blood partitioning ratio of total Hg in the thimerosal group was slightly higher than that in the MeHg group (3.5 ± 0.5 vs. 2.5 ± 0.3 , t-test, $p = 0.11$). **Thus, the brain to-blood Hg concentration ratio established for MeHg will underestimate the amount of Hg in the brain after exposure to thimerosal. "**

Abstract

Thimerosal is a preservative that has been used in manufacturing vaccines since the 1930s. Reports have indicated that infants can receive ethylmercury (in the form of thimerosal) at or above the U.S. Environmental Protection Agency guidelines for methylmercury exposure, depending on the exact vaccinations, schedule, and size of the infant. In this study we compared the systemic disposition and brain distribution of total and inorganic mercury in infant monkeys after thimerosal exposure with those exposed to MeHg. Monkeys were exposed to MeHg (via oral gavage) or vaccines containing thimerosal (via intramuscular injection) at birth and 1, 2, and 3 weeks of age. Total blood Hg levels were determined 2, 4, and 7 days after each exposure. Total and inorganic brain Hg levels were assessed 2, 4, 7, or 28 days after the last exposure. The initial and terminal half-life of Hg in blood after thimerosal exposure was 2.1 and 8.6 days, respectively, which are significantly shorter than the elimination half-life of Hg after MeHg exposure at 21.5 days. Brain concentrations of total Hg were significantly lower by approximately 3-fold for the thimerosal-exposed monkeys when compared with the MeHg infants, whereas the average brain-to-blood concentration ratio was slightly higher for the thimerosal-exposed monkeys (3.5 ± 0.5 vs. 2.5 ± 0.3). **A higher percentage of the total Hg in the brain was in the form of inorganic Hg for the thimerosal-exposed monkeys (34% vs. 7%).** The results indicate that MeHg is not a suitable reference for risk assessment from exposure to thimerosal-derived Hg. Knowledge of the toxicokinetics and developmental toxicity of thimerosal is needed to afford a meaningful assessment of the developmental effects of thimerosal-containing vaccines. Key words: brain and blood distribution, elimination half-life, ethylmercury, infant nonhuman primates, methylmercury, thimerosal.

49. [The retention time of inorganic mercury in the brain--a systematic review of the evidence.](#)

Toxicol Appl Pharmacol. 2014 Feb 1;274(3):425-35. doi: 10.1016/j.taap.2013.12.011. Epub 2013 Dec 22.

Rooney JP.

Academic Unit of Neurology, Trinity Biomedical Sciences Institute, Trinity College, 152-160 Pearse Street, Dublin 2, Ireland. Electronic address: jrooney@rcsi.ie.

Abstract

Reports from human case studies indicate a half-life for inorganic mercury in the brain in the order of years--contradicting older radioisotope studies that estimated half-lives in the order of weeks to months in duration. This study systematically reviews available evidence on the retention time of inorganic mercury in humans and primates to better understand this conflicting evidence. A broad search strategy was used to capture 16,539 abstracts on the Pubmed database. Abstracts were screened to include only study types containing relevant information. 131 studies of interest were identified. Only 1 primate study made a numeric estimate for the half-life of inorganic mercury (227-540 days). Eighteen human mercury poisoning cases were followed up long term including autopsy.

Brain inorganic mercury concentrations at death were consistent with a half-life of several years or longer. 5 radionuclide studies were found, one of which estimated head half-life (21 days). This estimate has sometimes been misinterpreted to be equivalent to brain half-life-which ignores several confounding factors including limited radioactive half-life and radioactive decay from surrounding tissues including circulating blood. No autopsy cohort study estimated a half-life for inorganic mercury, although some noted bioaccumulation of brain mercury with age. Modelling studies provided some extreme estimates (69 days vs 22 years). Estimates from modelling studies appear sensitive to model assumptions, however predications based on a long half-life (27.4 years) are consistent with autopsy findings. In summary, shorter estimates of half-life are not supported by evidence from animal studies, human case studies, or modelling studies based on appropriate assumptions. **Evidence from such studies point to a half-life of inorganic mercury in human brains of several years to several decades.** This finding carries important implications for pharmacokinetic modelling of mercury and potentially for the regulatory toxicology of mercury.

50. [Alkyl Mercury-Induced Toxicity: Multiple Mechanisms of Action.](#)

Rev Environ Contam Toxicol. 2017;240:105-149.

Risher JF, Tucker P.

Division of Toxicology and Human Health Sciences, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road (MS F-58), Atlanta, GA, 30333, USA.

Abstract

There are a number of mechanisms by which alkylmercury compounds cause toxic action in the body. Collectively, published studies reveal that there are some similarities between the mechanisms of the toxic action of the mono-alkyl mercury compounds methylmercury (MeHg) and ethylmercury (EtHg). This paper represents a summary of some of the studies regarding these mechanisms of action in order to facilitate the understanding of the many varied effects of alkylmercurials in the human body. The similarities in mechanisms of toxicity for MeHg and EtHg are presented and compared. **The difference in manifested toxicity of MeHg and EtHg are likely the result of the differences in exposure, metabolism, and elimination from the body, rather than differences in mechanisms of action between the two.**

Exerpts:

Summary and Conclusions

There are many commonalities/similarities in the mechanisms of toxic action of methylmercury and ethylmercury (from thimerosal)... Evidence for the similarity of the various mechanisms of toxicity include the following:

- Both MeHg and EtHg bind to the amino acid cysteine (Clarkson 1995; Wu et al. 2008)...
- Both decrease glutathione activity, thus providing less protection from the oxidative stress caused by MeHg and EtHg (Carocci et al. 2014; Ndountse and Chan (2008); Choi et al. 1996; Franco et al. 2006; Mori et al. 2007; Muller et al. 2001; Ndountse and Chan 2008; Wu et al. 2008)...
- Both disrupt glutamate homeostasis (Farina et al. 2003a, b; Manfroi et al. 2004; Mutkus et al. 2005; Yin et al. 2007).
- Both cause oxidative stress/creation of ROS (Dreiem and Seegal 2007; Garg and Chang 2006; Myhre et al. 2003; Sharpe et al. 2012; Yin et al. 2007)...
- Both cause effects on receptor binding/neurotransmitter release involving one or more transmitters (Basu et al. 2008; Coccini et al. 2000; Cooper et al. 2003; Fonfria et al. 2001; Ida-Eto et al. 2011; Ndountse and Chan 2008; Yuan and Atchison 2003).
- Both cause DNA damage or impair DNA synthesis (Burke et al. 2006; Sharpe et al. 2012; Wu et al. 2008).

51. [Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism.](#)

Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141B(8):947-56.

James SJ1, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, Baker SM, Gaylor DW.

Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital Research Institute, Little Rock, Arkansas

Abstract

Autism is a behaviorally defined neurodevelopmental disorder usually diagnosed in early childhood that is characterized by impairment in reciprocal communication and speech, repetitive behaviors, and social withdrawal. Although both genetic and environmental factors are thought to be involved, none have been reproducibly identified. The metabolic phenotype of an individual reflects the influence of endogenous and exogenous factors on genotype. As such, it provides a window through which the interactive impact of genes and environment may be viewed and relevant susceptibility factors identified. Although abnormal methionine metabolism has been associated with other neurologic disorders, these pathways and related polymorphisms have not been evaluated in autistic children. Plasma levels of metabolites in methionine transmethylation and transsulfuration pathways were measured in 80 autistic and 73 control children. In addition, common polymorphic variants known to modulate these metabolic pathways were evaluated in 360 autistic children and 205

controls. **The metabolic results indicated that plasma methionine and the ratio of S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH), an indicator of methylation capacity, were significantly decreased in the autistic children relative to age-matched controls. In addition, plasma levels of cysteine, glutathione, and the ratio of reduced to oxidized glutathione, an indication of antioxidant capacity and redox homeostasis, were significantly decreased. Differences in allele frequency and/or significant gene-gene interactions were found for relevant genes encoding the reduced folate carrier (RFC 80G > A), transcobalamin II (TCN2 776G > C), catechol-O-methyltransferase (COMT 472G > A), methylenetetrahydrofolate reductase (MTHFR 677C > T and 1298A > C), and glutathione-S-transferase (GST M1). We propose that an increased vulnerability to oxidative stress (endogenous or environmental) may contribute to the development and clinical manifestations of autism.**

52. [Brain and tissue levels of mercury after chronic methylmercury exposure in the monkey.](#)

J Toxicol Environ Health. 1989;27(2):189-98.

Rice DC

Toxicology Research Division, Health Protection Branch, Health and Welfare, Ottawa, Ontario, Canada.

Abstract

Estimated half-lives of mercury following methylmercury exposure in humans are 52-93 d for whole body and 49-164 d for blood. In its most recent 1980 review, the World Health Organization concluded that there was no evidence to suggest that brain half-life differed from whole-body half-life. In the present study, female monkeys (*Macaca fascicularis*) were dosed for at least 1.7 yr with 10, 25, or 50 micrograms/kg.d of mercury as methylmercuric chloride. Dosing was discontinued, and blood half-life was determined to be about 14 d. Approximately 230 d after cessation of dosing, monkeys were sacrificed and organ and regional brain total mercury levels determined. One monkey that died while still being dosed had brain mercury levels three times higher than levels in blood.

Theoretical calculations were performed assuming steady-state brain: blood ratios of 3, 5, or 10. Brain mercury levels were at least three orders of magnitude higher than those predicted by assuming the half-life in brain to be the same as that in blood. Estimated half-lives in brain were between 56 (brain: blood ratio of 3) and 38 (brain: blood ratio of 10) days. In addition, there was a dose-dependent difference in half-lives for some brain regions. **These data clearly indicate that brain half-life is considerably longer than blood half-life in the monkey under conditions of chronic dosing.**

53. [Interplay of glia activation and oxidative stress formation in fluoride and aluminium exposure.](#)

Pathophysiology. 2015 Mar;22(1):39-48. doi: 10.1016/j.pathophys.2014.12.001. Epub 2014 Dec 13.

Akinrinade ID1, Memudu AE2, Ogundele OM3, Ajetunmobi OI4.

BACKGROUND:

Oxidative stress formation is pivotal in the action of environmental agents which trigger the activation of glial cells and neuroinflammation to stimulate compensatory mechanisms aimed at restoring homeostasis.

AIM:

This study sets to demonstrate the interplay of fluoride (F) and aluminium (Al) in brain metabolism. Specifically, it reveals how oxidative stress impacts the activation of astrocytes (GFAP), mediates proinflammatory responses (microglia and B-cells: CD68 and CD 20 respectively) and shows the pattern of lipid peroxidation in the brain following fluoride and (or) aluminium treatment in vivo.

METHOD:

Male adult Wistar rats were treated with low and high doses of fluoride, aluminium or combination of fluoride-aluminium for 30 days. The control group received distilled water for the duration of the treatment. Blood and brain tissue homogenates were prepared for colorimetric assay of stress biomarkers [malonaldehyde (MDA) and superoxide dismutase (SOD)]. Subsequent analysis involved immunodetection of astrocytes (anti-GFAP), microglial (anti-CD68) and B-cells (anti-CD20) in coronal sections of the prefrontal cortex using antigen retrieval immunohistochemistry.

RESULT AND CONCLUSION:

Aluminium, fluoride and a combination of aluminium-fluoride treatments caused an increase in brain lipid peroxidation products and reactive oxygen species (ROS) formation. Similarly, an increase in glial activation and inflammatory response were seen in these groups versus the control. Oxidative stress induced glial activation (GFAP) and increased the expression of B cells (CD20). This also corresponded to the extent of tissue damage and lipid peroxidation observed. Taken together, the results suggest a close link between oxidative stress neuroinflammation and degeneration in aluminium-fluoride toxicity.

54. Increases in the Number of Reactive Glia in the Visual Cortex of Macaca fascicularis Following Subclinical Long-Term Methyl Mercury Exposure

Toxicology and Applied Pharmacology, 1994

Charleston JS, Bolender RP, Mottet NK, Body RL, Vahter ME, Burbacher TM., Department of Pathology, School of Medicine, University of Washington

Abstract

The number of neurons, astrocytes, reactive glia, oligodendrocytes, endothelia,

and pericytes in the cortex of the calcarine sulcus of adult female *Macaca fascicularis* following long-term subclinical exposure to methyl mercury (MeHg) and mercuric chloride (inorganic mercury; IHg) has been estimated by use of the optical volume fractionator stereology technique. Four groups of monkeys were exposed to MeHg (50 micrograms Hg/kg body wt/day) by mouth for 6, 12, 18, and 12 months followed by 6 months without exposure (clearance group). A fifth group of monkeys was administered IHg (as HgCl₂; 200 micrograms Hg/kg body wt/day) by constant rate intravenous infusion via an indwelling catheter for 3 months. Reactive glia showed a significant increase in number for every treatment group, increasing 72% in the 6-month, 152% in the 12-month, and 120% in the 18-month MeHg exposed groups, and the number of reactive glia in the clearance group remained elevated (89%). The IHg exposed group showed a 165% increase in the number of reactive glia. The IHg exposed group and the clearance group had low levels of MeHg present within the tissue; however, the level of IHg was elevated in both groups. **These results suggest that the IHg may be responsible for the increase in reactive glia.** All other cell types, including the neurons, showed no significant change in number at the prescribed exposure level and durations. The identities of the reactive glial cells and the implications for the long-term function and survivability of the neurons due to changes in the glial population following subclinical long-term exposure to mercury are discussed.

55. [Modeling the interplay between neurons and astrocytes in autism using human induced pluripotent stem cells](#)

Biological Psychiatry, Available online 3 October 2017

Fabiele Baldino Russo, Beatriz Camille Freitas, Graciela Conceição Pignatari, Isabella Rodrigues Fernandes, Jonathan Sebat, Alysson Renato Muotri, Patricia Cristina Baleeiro Beltrão-Braga

Department of Microbiology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, SP, Brazil

Department of Surgery, School of Veterinary Medicine, University of São Paulo, São Paulo, SP, Brazil

Department of Pediatrics/Rady Children's Hospital San Diego, Department of Cellular & Molecular Medicine, Stem Cell Program, University of California San Diego School of Medicine, Sanford Consortium for Regenerative Medicine, La Jolla, CA, USA

Department of Psychiatry, Cellular and Molecular Medicine, University of California, San Diego, La Jolla, CA 92093, USA

Department of Obstetrics, School of Arts, Sciences and Humanities, University of São Paulo, São Paulo, SP, Brazil

Received 12 September 2016, Revised 14 August 2017, Accepted 17 September 2017,

Abstract Background

Autism Spectrum Disorders (ASD) are neurodevelopmental disorders with unclear etiology and imprecise genetic causes. The main goal of this work was to investigate neuronal connectivity and the interplay between neurons and astrocytes from non-syndromic ASD individuals using induced Pluripotent Stem Cells (iPSCs).

Methods

Our iPSCs were derived from a clinically well-characterized cohort of three non-syndromic ASD individuals, sharing common behaviors, and three controls, two clones each. We generated mixed neural cultures analyzing synaptogenesis and neuronal activity using a multi-electrode array (MEA) platform. Furthermore, using an enriched astrocytes population we investigated their role in neuronal maintenance.

Results

Our results revealed that ASD-derived neurons had a significant decrease in synaptic gene expression and protein levels, glutamate neurotransmitter release and, consequently, reduced spontaneous firing rate. Based on co-culture experiments, we observed that ASD-derived astrocytes interfered with proper neuronal development. In contrast, control-derived astrocytes rescued the morphological neuronal phenotype and synaptogenesis defects from ASD neuronal co-cultures. Furthermore, after identifying IL-6 secretion from astrocytes in our ASD individuals as a possible culprit for neural defects, we were able to increase synaptogenesis by blocking IL-6 levels.

Conclusions

Our findings reveal astrocytes contribution to neuronal phenotype and confirm previous studies linking IL-6 and autism, suggesting potential novel therapeutic pathways for a subtype of ASD individuals. This is the first report demonstrating that glial dysfunctions could contribute to non-syndromic autism pathophysiology using iPSCs modeling disease technology.

56. Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism

Annals of Neurology, Feb 2005.

Diana L. Vargas, MD, Johns Hopkins University.

Abstract

Autism is a neurodevelopmental disorder characterized by impaired

communication and social interaction and may be accompanied by mental retardation and epilepsy. Its cause remains unknown, despite evidence that genetic, environmental, and immunological factors may play a role in its pathogenesis. To investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism, we used immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays to study brain tissues and cerebrospinal fluid (CSF) from autistic patients and determined the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles. Brain tissues from cerebellum, midfrontal, and cingulate gyrus obtained at autopsy from 11 patients with autism were used for morphological studies. Fresh-frozen tissues available from seven patients and CSF from six living autistic patients were used for cytokine protein profiling. We demonstrate an active neuroinflammatory process in the cerebral cortex, white matter, and notably in cerebellum of autistic patients. Immunocytochemical studies showed marked activation of microglia and astroglia, and cytokine profiling indicated that macrophage chemoattractant protein (MCP)-1 and tumor growth factor-beta1, derived from neuroglia, were the most prevalent cytokines in brain tissues. CSF showed a unique proinflammatory profile of cytokines, including a marked increase in MCP-1. Our findings indicate that innate neuroimmune reactions play a pathogenic role in an undefined proportion of autistic patients, suggesting that future therapies might involve modifying neuroglial responses in the brain.

Excerpt: "**Because this neuroinflammatory process appears to be associated with an ongoing and chronic mechanism of CNS dysfunction, potential therapeutic interventions should focus on the control of its detrimental effects and thereby eventually modify the clinical course of autism.**"

57. [Aluminium in brain tissue in autism](#)

Journal of Trace Elements in Medicine and Biology

Matthew Mold, Dorcas Umar, Andrew King, Christopher Exley,

The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom

Life Sciences, Keele University, Staffordshire, ST5 5BG, United Kingdom

Department of Clinical Neuropathology, Kings College Hospital, London, SE5 9RS, United Kingdom

26 November 2017

Abstract

Autism spectrum disorder is a neurodevelopmental disorder of unknown aetiology. It is suggested to involve both genetic susceptibility and environmental factors including in the latter environmental toxins. Human exposure to the environmental toxin aluminium has been linked, if tentatively, to autism spectrum disorder. Herein we have used transversely heated graphite furnace atomic absorption spectrometry to measure, for the first time, the aluminium content of

brain tissue from donors with a diagnosis of autism. We have also used an aluminium-selective fluor to identify aluminium in brain tissue using fluorescence microscopy. The aluminium content of brain tissue in autism was consistently high. The mean (standard deviation) aluminium content across all 5 individuals for each lobe were 3.82(5.42), 2.30(2.00), 2.79(4.05) and 3.82(5.17) $\mu\text{g/g}$ dry wt. for the occipital, frontal, temporal and parietal lobes respectively. **These are some of the highest values for aluminium in human brain tissue yet recorded and one has to question why, for example, the aluminium content of the occipital lobe of a 15 year old boy would be 8.74 (11.59) $\mu\text{g/g}$ dry wt.?** Aluminium-selective fluorescence microscopy was used to identify aluminium in brain tissue in 10 donors. **While aluminium was imaged associated with neurones it appeared to be present intracellularly in microglia-like cells and other inflammatory non-neuronal cells in the meninges, vasculature, grey and white matter. The pre-eminence of intracellular aluminium associated with non-neuronal cells was a standout observation in autism brain tissue and may offer clues as to both the origin of the brain aluminium as well as a putative role in autism spectrum disorder.**

58. [Microglial activation and increased microglial density observed in the dorsolateral prefrontal cortex in autism.](#)

Biol Psychiatry. 2010 Aug 15;68(4):368-76. doi: 10.1016/j.biopsych.2010.05.024.

Morgan JT1, Chana G, Pardo CA, Achim C, Semendeferi K, Buckwalter J, Courchesne E, Everall IP.
Department of Neuroscience, School of Medicine, University of California, San Diego

BACKGROUND:

In the neurodevelopmental disorder autism, several neuroimmune abnormalities have been reported. However, it is unknown whether microglial somal volume or density are altered in the cortex and whether any alteration is associated with age or other potential covariates.

METHODS:

Microglia in sections from the dorsolateral prefrontal cortex of nonmacrencephalic male cases with autism ($n = 13$) and control cases ($n = 9$) were visualized via ionized calcium binding adapter molecule 1 immunohistochemistry. In addition to a neuropathological assessment, microglial cell density was stereologically estimated via optical fractionator and average somal volume was quantified via isotropic nucleator.

RESULTS:

Microglia appeared markedly activated in 5 of 13 cases with autism, including 2 of 3 under age 6, and marginally activated in an additional 4 of 13 cases. Morphological alterations included somal enlargement, process retraction and thickening, and extension of filopodia from processes. Average microglial somal volume was significantly increased in white matter ($p = .013$), with a trend in gray matter ($p = .098$). Microglial cell density was increased in gray matter ($p = .002$). Seizure history did not influence any activation measure.

CONCLUSIONS:

The activation profile described represents a neuropathological alteration in a sizeable fraction of cases with autism. Given its early presence, microglial activation may play a central role in the pathogenesis of autism in a substantial proportion of patients. Alternatively, activation may represent a response of the innate neuroimmune system to synaptic, neuronal, or neuronal network disturbances, or reflect genetic and/or environmental abnormalities impacting multiple cellular populations.

59. [Transcriptome analysis reveals dysregulation of innate immune response genes and neuronal activity-dependent genes in autism](#)

Nature Communications 5, Article number: 5748 doi:10.1038/ncomms6748
Received 28 September 2014 Accepted 03 November 2014 Published 10 December 2014

Department of Medicine, McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA
Simone Gupta, Shannon E. Ellis, Foram N. Ashar, Anna Moes, Joel S. Bader
Dan E. Arking

Department of Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA

Joel S. Bader & Jianan Zhan

Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama 35294, USA

Andrew B. West

Abstract

Recent studies of genomic variation associated with autism have suggested the existence of extreme heterogeneity. Large-scale transcriptomics should complement these results to identify core molecular pathways underlying autism. Here we report results from a large-scale RNA sequencing effort, utilizing region-matched autism and control brains to identify neuronal and microglial genes robustly dysregulated in autism cortical brain. **Remarkably, we note that a gene expression module corresponding to M2-activation states in microglia is negatively correlated with a differentially expressed neuronal module, implicating dysregulated microglial responses in concert with altered neuronal activity-dependent genes in autism brains.** These observations provide pathways and candidate genes that highlight the interplay between innate immunity and neuronal activity in the aetiology of autism.

60. [Nanomolar aluminum induces pro-inflammatory and pro-apoptotic gene expression in human brain cells in primary culture.](#)

J Inorg Biochem. 2005 Sep;99(9):1895-8.

Lukiw WJ1, Percy ME, Kruck TP.

Neuroscience Center of Excellence and Department of Ophthalmology, Louisiana State University Health Sciences Center, 2020 Gravier Street, Suite 8B8, New Orleans, LA 70112-2272, USA. wlukiw@lsuhsc.edu

Abstract

Aluminum, the most abundant neurotoxic metal in our biosphere, has been implicated in the etiology of several neurodegenerative disorders including Alzheimer's disease (AD). To further understand aluminum's influence on gene expression, we examined total messenger RNA levels in untransformed human neural cells exposed to 100 nanomolar aluminum sulfate using high density DNA microarrays that interrogate the expression of every human gene. Preliminary data indicate that of the most altered gene expression levels, 17/24 (70.8%) of aluminum-affected genes, and 7/8 (87.5%) of aluminum-induced genes exhibit expression patterns similar to those observed in AD. The seven genes found to be significantly up-regulated by aluminum encode pro-inflammatory or pro-apoptotic signaling elements, including NF-kappaB subunits, interleukin-1beta precursor, cytosolic phospholipase A2, cyclooxygenase-2, beta-amyloid precursor protein and DAXX, a regulatory protein known to induce apoptosis and repress transcription. **The promoters of genes up-regulated by aluminum are enriched in binding sites for the stress-inducible transcription factors HIF-1 and NF-kappaB, suggesting a role for aluminum, HIF-1 and NF-kappaB in driving atypical, pro-inflammatory and pro-apoptotic gene expression.** The effect of aluminum on specific stress-related gene expression patterns in human brain cells clearly warrant further investigation.

61. [Aberrant NF-kappaB expression in autism spectrum condition: a mechanism for neuroinflammation.](#)

Front Psychiatry. 2011 May 13;2:27. doi: 10.3389/fpsyt.2011.00027. eCollection 2011.

Young AM1, Campbell E, Lynch S, Suckling J, Powis SJ.

Bute Medical School, University of St. Andrews Fife, Scotland, UK.

Abstract

Autism spectrum condition (ASC) is recognized as having an inflammatory component. Post-mortem brain samples from patients with ASC display neuroglial activation and inflammatory markers in cerebrospinal fluid, although little is known about the underlying molecular mechanisms. Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) is a protein found in almost all cell types and mediates regulation of immune response by inducing the expression of inflammatory cytokines and chemokines, establishing a feedback mechanism that can produce chronic or excessive inflammation. This article describes immunodetection and immunofluorescence measurements of NF-kB in human post-mortem samples of orbitofrontal cortex tissue donated to two

independent centers: London Brain Bank, Kings College London, UK (ASC: n = 3, controls: n = 4) and Autism Tissue Program, Harvard Brain Bank, USA (ASC: n = 6, controls: n = 5). The hypothesis was that concentrations of NF- κ B would be elevated, especially in activated microglia in ASC, and pH would be concomitantly reduced (i.e., acidification). Neurons, astrocytes, and microglia all demonstrated increased extranuclear and nuclear translocated NF- κ B p65 expression in brain tissue from ASC donors relative to samples from matched controls. These between-groups differences were increased in astrocytes and microglia relative to neurons, but particularly pronounced for highly mature microglia. Measurement of pH in homogenized samples demonstrated a 0.98-unit difference in means and a strong ($F = 98.3$; $p = 0.00018$) linear relationship to the expression of nuclear translocated NF- κ B in mature microglia. Acridine orange staining localized pH reductions to lysosomal compartments. **In summary, NF- κ B is aberrantly expressed in orbitofrontal cortex in patients with ASC, as part of a putative molecular cascade leading to inflammation, especially of resident immune cells in brain regions associated with the behavioral and clinical symptoms of ASC.**

62. [A Study of Nuclear Transcription Factor-Kappa B in Childhood Autism](#)

PLoS One. 2011; 6(5): e19488.

Usha S. Naik,¹ Charitha Gangadharan,² Kanakalatha Abbagani,¹ Balakrishna Nagalla,³ Niranjana Dasari,¹ and Sunil K. Manna^{2,*}
Monica Uddin, Editor

Department of Psychiatry, Osmania Medical College, Hyderabad, India
Laboratory of Immunology, Centre for DNA Fingerprinting and Diagnostics,
Nampally, Hyderabad, India
National Institute of Nutrition, Hyderabad, India
University of Michigan, United States of America

Abstract

Background

Several children with autism show regression in language and social development while maintaining normal motor milestones. A clear period of normal development followed by regression and subsequent improvement with treatment, suggests a multifactorial etiology. The role of inflammation in autism is now a major area of study. Viral and bacterial infections, hypoxia, or medication could affect both foetus and infant. These stressors could upregulate transcription factors like nuclear factor kappa B (NF- κ B), a master switch for many genes including some implicated in autism like tumor necrosis factor (TNF). On this hypothesis, it was proposed to determine NF- κ B in children with autism.

Methods

Peripheral blood samples of 67 children with autism and 29 control children were evaluated for NF- κ B using electrophoretic mobility shift assay (EMSA). A

phosphor imaging technique was used to quantify values. The fold increase over the control sample was calculated and statistical analysis was carried out using SPSS 15.

Results

We have noted significant increase in NF- κ B DNA binding activity in peripheral blood samples of children with autism. When the fold increase of NF- κ B in cases (n=67) was compared with that of controls (n=29), there was a significant difference (3.14 vs. 1.40, respectively; $p < 0.02$).

Conclusion

This finding has immense value in understanding many of the known biochemical changes reported in autism. As NF- κ B is a response to stressors of several kinds and a master switch for many genes, autism may then arise at least in part from an NF- κ B pathway gone awry.

63. Autism: A Brain Disorder, or A Disorder That Affects the Brain?

Clinical Neuropsychiatry, 2005

Martha R. Herbert M.D., Ph.D., Harvard University

Autism is defined behaviorally, as a syndrome of abnormalities involving language, social reciprocity and hyperfocus or reduced behavioral flexibility. It is clearly heterogeneous, and it can be accompanied by unusual talents as well as by impairments, but its underlying biological and genetic basis is unknown. Autism has been modeled as a brain-based, strongly genetic disorder, but emerging findings and hypotheses support a broader model of the condition as a genetically influenced and systemic. These include imaging, neuropathology and psychological evidence of pervasive (and not just specific) brain and phenotypic features; postnatal evolution and chronic persistence of brain, behavior and tissue changes (e.g. inflammation) and physical illness symptomatology (e.g. gastrointestinal, immune, recurrent infection); overlap with other disorders; and reports of rate increases and improvement or recovery that support a role for modulation of the condition by environmental factors (e.g. exacerbation or triggering by toxins, infectious agents, or others stressors, or improvement by treatment). Modeling autism more broadly encompasses previous work, but also encourages the expansion of research and treatment to include intermediary domains of molecular and cellular mechanisms, as well as chronic tissue, metabolic and somatic changes previously addressed only to a limited degree. The heterogeneous biologies underlying autism may conceivably converge onto the autism profile via multiple mechanisms on the one hand and processing and connectivity abnormalities on the other may illuminate relevant final common pathways and contribute to focusing on the search for treatment targets in this biologically and etiologically heterogeneous behavioral syndrome.

64. [Multivariate techniques enable a biochemical classification of children with autism spectrum disorder versus typically-developing peers: A comparison and validation study](https://doi.org/10.1002/btm2.10095)

Daniel P. Howsmon Troy Vargason Robert A. Rubin Leanna Delhey Marie Tippet Shannon Rose Sirish C. Bennuri John C. Slattery Stepan Melnyk S. Jill James Richard E. Frye Juergen Hahn

Bioengineering & Translational Medicine, 14 May 2018

<https://doi.org/10.1002/btm2.10095>

Funding information National Institutes of Health, Grant/Award Number: 1R01AI110642

Abstract

Autism spectrum disorder (ASD) is a developmental disorder which is currently only diagnosed through behavioral testing. Impaired folate-dependent one carbon metabolism (FOCM) and transsulfuration (TS) pathways have been implicated in ASD, and recently a study involving multivariate analysis based upon Fisher Discriminant Analysis returned very promising results for predicting an ASD diagnosis. This article takes another step toward the goal of developing a biochemical diagnostic for ASD by comparing five classification algorithms on existing data of FOCM/TS metabolites, and also validating the classification results with new data from an ASD cohort. The comparison results indicate a high sensitivity and specificity for the original data set and up to a 88% correct classification of the ASD cohort at an expected 5% misclassification rate for typically-developing controls. These results form the foundation for the development of a biochemical test for ASD which promises to aid diagnosis of ASD and provide biochemical understanding of the disease, applicable to at least a subset of the ASD population.

65. Activation of Methionine Synthase by Insulin-like Growth Factor-1 and Dopamine: a Target for Neurodevelopmental Toxins and Thimerosal

Mol Psychiatry. 2004 Apr;9(4):358-70.

Waly M, Olteanu H, Banerjee R, Choi SW, Mason JB, Parker BS, Sukumar S, Shim S, Sharma A, Benzecry JM, Power-Charnitsky VA, Deth RC. Department of Pharmaceutical Sciences, Northeastern University, Boston, MA

Abstract

Methylation events play a critical role in the ability of growth factors to promote normal development. Neurodevelopmental toxins, such as ethanol and heavy metals, interrupt growth factor signaling, raising the possibility that they might exert adverse effects on methylation. We found that insulin-like growth factor-1

(IGF-1)- and dopamine-stimulated methionine synthase (MS) activity and folate-dependent methylation of phospholipids in SH-SY5Y human neuroblastoma cells, via a PI3-kinase- and MAP-kinase-dependent mechanism. The stimulation of this pathway increased DNA methylation, while its inhibition increased methylation-sensitive gene expression. Ethanol potently interfered with IGF-1 activation of MS and blocked its effect on DNA methylation, whereas it did not inhibit the effects of dopamine. Metal ions potently affected IGF-1 and dopamine-stimulated MS activity, as well as folate-dependent phospholipid methylation: Cu(2+) promoted enzyme activity and methylation, while Cu(+), Pb(2+), Hg(2+) and Al(3+) were inhibitory. The ethylmercury-containing preservative thimerosal inhibited both IGF-1- and dopamine-stimulated methylation with an IC(50) of 1 nM and eliminated MS activity. Our findings outline a novel growth factor signaling pathway that regulates MS activity and thereby modulates methylation reactions, including DNA methylation. **The potent inhibition of this pathway by ethanol, lead, mercury, aluminum and thimerosal suggests that it may be an important target of neurodevelopmental toxins.**

66. Validation of the Phenomenon of Autistic Regression Using Home Videotapes

Archives of General Psychiatry, 2005

Emily Werner, PhD; Geraldine Dawson, PhD, University of Washington

Abstract

Objective To validate parental report of autistic regression using behavioral data coded from home videotapes of children with autism spectrum disorder (ASD) vs typical development taken at 12 and 24 months of age.

Design Home videotapes of 56 children's first and second birthday parties were collected from parents of young children with ASD with and without a reported history of regression and typically developing children. Child behaviors were coded by raters blind to child diagnosis and regression history. A parent interview that elicited information about parents' recall of early symptoms from birth was also administered.

Setting Participants were recruited from a multidisciplinary study of autism conducted at a major university.

Participants Fifteen children with ASD with a history of regression, 21 children with ASD with early-onset autism, and 20 typically developing children and their parents participated.

Main Outcome Measures Observations of children's communicative, social, affective, repetitive behaviors, and toy play coded from videotapes of the toddlers' first and second birthday parties.

Results Analyses revealed that infants with ASD with regression show similar use of joint attention and more frequent use of words and babble compared with typical infants at 12 months of age. In contrast, infants with ASD with early onset

of symptoms and no regression displayed fewer joint attention and communicative behaviors at 12 months of age. By 24 months of age, both groups of toddlers with ASD displayed fewer instances of word use, vocalizations, declarative pointing, social gaze, and orienting to name as compared with typically developing 24-month-olds.

Parent interview data suggested that some children with regression displayed difficulties in regulatory behavior before the regression occurred.

Conclusion **This study validates the existence of early autistic regression.**

67. Blood Levels of Mercury Are Related to Diagnosis of Autism: A Reanalysis of an Important Data Set

Journal of Child Neurology, Vol. 22, No. 11, 1308-1311 (2007)

M. Catherine DeSoto, PhD, Robert T. Hitlan, PhD -Department of Psychology, University of Northern Iowa, Cedar Falls, Iowa

Abstract

The question of what is leading to the apparent increase in autism is of great importance. Like the link between aspirin and heart attack, even a small effect can have major health implications. If there is any link between autism and mercury, it is absolutely crucial that the first reports of the question are not falsely stating that no link occurs. **We have reanalyzed the data set originally reported by Ip et al. in 2004 and have found that the original p value was in error and that a significant relation does exist between the blood levels of mercury and diagnosis of an autism spectrum disorder. Moreover, the hair sample analysis results offer some support for the idea that persons with autism may be less efficient and more variable at eliminating mercury from the blood.**

68. Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure

Entropy, November 7, 2012

Stephanie Seneff, Robert M. Davidson and Jingjing Liu

Computer Science and Artificial Intelligence Laboratory, Massachusetts Institute of Technology, Cambridge, MA 02139, USA, Internal Medicine Group Practice, PhyNet, Inc., Longview, TX 75604, USA

Abstract

Autism is a condition characterized by impaired cognitive and social skills,

associated with compromised immune function. The incidence is alarmingly on the rise, and environmental factors are increasingly suspected to play a role. This paper investigates word frequency patterns in the U.S. CDC Vaccine Adverse Events Reporting System (VAERS) database. Our results provide strong evidence supporting a link between autism and the aluminum in vaccines. A literature review showing toxicity of aluminum in human physiology offers further support. Mentions of autism in VAERS increased steadily at the end of the last century, during a period when mercury was being phased out, while aluminum adjuvant burden was being increased. Using standard log-likelihood ratio techniques, we identify several signs and symptoms that are significantly more prevalent in vaccine reports after 2000, including cellulitis, seizure, depression, fatigue, pain and death, which are also significantly associated with aluminum-containing vaccines. **We propose that children with the autism diagnosis are especially vulnerable to toxic metals such as aluminum and mercury due to insufficient serum sulfate and glutathione. A strong correlation between autism and the MMR (Measles, Mumps, Rubella) vaccine is also observed, which may be partially explained via an increased sensitivity to acetaminophen administered to control fever.**

69. [Glutathione-related factors and oxidative stress in autism, a review.](#)

Curr Med Chem. 2012;19(23):4000-5.

Ghanizadeh A1, Akhondzadeh S, Hormozi M, Makarem A, Abotorabi-Zarchi M, Firoozabadi A.

Research Center for Psychiatry and Behavioral Sciences, Shiraz University of Medical Sciences, School of Medicine, Shiraz, Iran. ghanizad@sina.tums.ac.ir

Abstract

Autism spectrum disorders are complex neuro-developmental disorders whose neurobiology is proposed to be associated with oxidative stress which is induced by reactive oxygen species. The process of oxidative stress can be a target for therapeutic interventions. In this study, we aimed to review the role of oxidative stress, plasma glutathione (GSH), and related factors as the potential sources of damage to the brain as well as the possible related factors which reduce the oxidative stress. Methylation capacity, sulfates level, and the total glutathione level are decreased in autism. On the other hand, both oxidized glutathione and the ratio of oxidized to reduced glutathione are increased in autism. In addition, the activity of glutathione peroxidase, superoxide dismutase, and catalase, as a part of the antioxidative stress system are decreased. **The current literature suggests an imbalance of oxidative and anti-oxidative stress systems in autism. Glutathione is involved in neuro-protection against oxidative stress and neuro-inflammation in autism by improving the anti-oxidative stress system. Decreasing the oxidative stress might be a potential treatment for autism.**

70. Developmental Regression and Mitochondrial Dysfunction in a Child With Autism

J Child Neurol. 2006 Feb;21(2):170-2.

Jon S. Poling, MD, PhD, Department of Neurology and Neurosurgery
Johns Hopkins Hospital

Abstract

Autistic spectrum disorders can be associated with mitochondrial dysfunction. We present a singleton case of developmental regression and oxidative phosphorylation disorder in a 19-month-old girl. Subtle abnormalities in the serum creatine kinase level, aspartate aminotransferase, and serum bicarbonate led us to perform a muscle biopsy, which showed type I myofiber atrophy, increased lipid content, and reduced cytochrome c oxidase activity. There were marked reductions in enzymatic activities for complex I and III. Complex IV (cytochrome c oxidase) activity was near the 5% confidence level. To determine the frequency of routine laboratory abnormalities in similar patients, we performed a retrospective study including 159 patients with autism (Diagnostic and Statistical Manual of Mental Disorders-IV and Childhood Autism Rating Scale) not previously diagnosed with metabolic disorders and 94 age-matched controls with other neurologic disorders. Aspartate aminotransferase was elevated in 38% of patients with autism compared with 15% of controls ($P < .0001$). The serum creatine kinase level also was abnormally elevated in 22 (47%) of 47 patients with autism. These data suggest that further metabolic evaluation is indicated in autistic patients and that defects of oxidative phosphorylation might be prevalent.

Excerpt: "Children who have (mitochondrial-related) dysfunctional cellular energy metabolism might be more prone to undergo autistic regression between 18 and 30 months of age if they also have infections or immunizations at the same time."

71. Oxidative Stress in Autism: Elevated Cerebellar 3-nitrotyrosine Levels

American Journal of Biochemistry and Biotechnology 4 (2): 73-84, 2008

Elizabeth M. Sajdel-Sulkowska, - Dept of Psychiatry, Harvard Medical School

Shows a potential link between mercury and the autopsied brains of young people with autism. A marker for oxidative stress was 68.9% higher in autistic brain tissue than controls (a statistically significant result), while mercury levels were 68.2% higher.

Abstract

It has been suggested that oxidative stress and/or mercury compounds play an

important role in the pathophysiology of autism. This study compared for the first time the cerebellar levels of the oxidative stress marker 3-nitrotyrosine (3-NT), mercury (Hg) and the antioxidant selenium (Se) levels between control and autistic subjects. Tissue homogenates were prepared in the presence of protease inhibitors from the frozen cerebellar tissue of control (n=10; mean age, 15.5 years; mean PMI, 15.5 hours) and autistic (n=9; mean age 12.1 years; mean PMI, 19.3 hours) subjects. The concentration of cerebellar 3-NT, determined by ELISA, in controls ranged from 13.69 to 49.04 pmol g⁻¹ of tissue; the concentration of 3-NT in autistic cases ranged from 3.91 to 333.03 pmol g⁻¹ of tissue. Mean cerebellar 3-NT was elevated in autism by 68.9% and the increase was statistically significant (p=0.045). Cerebellar Hg, measured by atomic absorption spectrometry ranged from 0.9 to 35 pmol g⁻¹ tissue in controls (n=10) and from 3.2 to 80.7 pmol g⁻¹ tissue in autistic cases (n=9); the 68.2% increase in cerebellar Hg was not statistically significant. However, there was a positive correlation between cerebellar 3-NT and Hg levels (r=0.7961, p=0.0001). A small decrease in cerebellar Se levels in autism, measured by atomic absorption spectroscopy, was not statistically significant but was accompanied by a 42.9% reduction in the molar ratio of Se to Hg in the autistic cerebellum. While preliminary, the results of the present study add elevated oxidative stress markers in brain to the growing body of data reflecting greater oxidative stress in autism.

Excerpt: The preliminary data suggest a need for more extensive studies of oxidative stress, its relationship to the environmental factors and its possible attenuation by antioxidants in autism.”

72. Large Brains in Autism: The Challenge of Pervasive Abnormality

Neuroscientist. 2005 Oct;11(5):417-40.

Herbert MR., Harvard University

Pediatric Neurology, Center for Morphometric Analysis, Massachusetts General Hospital, Charleston, MA

Abstract

The most replicated finding in autism neuroanatomy—a tendency to unusually large brains—has seemed paradoxical in relation to the specificity of the abnormalities in three behavioral domains that define autism. We now know a range of things about this phenomenon, including that brains in autism have a growth spurt shortly after birth and then slow in growth a few short years afterward, that only younger but not older brains are larger in autism than in controls, that white matter contributes disproportionately to this volume increase and in a nonuniform pattern suggesting postnatal pathology, that functional connectivity among regions of autistic brains is diminished, and that neuroinflammation (including microgliosis and astrogliosis) appears to be present in autistic brain tissue from childhood through adulthood. Alongside these pervasive brain tissue and functional abnormalities, there have arisen theories of pervasive or widespread neural information processing or signal coordination

abnormalities (such as weak central coherence, impaired complex processing, and underconnectivity), which are argued to underlie the specific observable behavioral features of autism. This convergence of findings and models suggests that a systems- and chronic disease-based reformulation of function and pathophysiology in autism needs to be considered, and it opens the possibility for new treatment targets..

Excerpt: "**Oxidative stress, brain inflammation, and microgliosis have been much documented in association with toxic exposures including various heavy metals...the awareness that the brain as well as medical conditions of children with autism may be conditioned by chronic biomedical abnormalities such as inflammation opens the possibility that meaningful biomedical interventions may be possible well past the window of maximal neuroplasticity in early childhood because the basis for assuming that all deficits can be attributed to fixed early developmental alterations in neural architecture has now been undermined.**"

73. Evidence of Toxicity, Oxidative Stress, and Neuronal Insult in Autism

J Toxicol Environ Health B Crit Rev. 2006 Nov-Dec;9(6):485-99.

Kern JK, Jones AM.

Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas

Abstract

According to the Autism Society of America, autism is now considered to be an epidemic. The increase in the rate of autism revealed by epidemiological studies and government reports implicates the importance of external or environmental factors that may be changing. This article discusses the evidence for the case that some children with autism may become autistic from neuronal cell death or brain damage sometime after birth as result of insult; and addresses the hypotheses that toxicity and oxidative stress may be a cause of neuronal insult in autism. The article first describes the Purkinje cell loss found in autism, Purkinje cell physiology and vulnerability, and the evidence for postnatal cell loss. Second, the article describes the increased brain volume in autism and how it may be related to the Purkinje cell loss. Third, the evidence for toxicity and oxidative stress is covered and the possible involvement of glutathione is discussed. Finally, the article discusses what may be happening over the course of development and the multiple factors that may interplay and make these children more vulnerable to toxicity, oxidative stress, and neuronal insult.

74. Oxidative Stress in Autism

Pathophysiology. 2006 Aug;13(3):171-81. Epub 2006 Jun 12.

Chauhan A, Chauhan V.

NYS Institute for Basic Research in Developmental Disabilities, 1050 Forest Hill Road, Staten Island, NY

Abstract

Autism is a severe developmental disorder with poorly understood etiology. Oxidative stress in autism has been studied at the membrane level and also by measuring products of lipid peroxidation, detoxifying agents (such as glutathione), and antioxidants involved in the defense system against reactive oxygen species (ROS). Lipid peroxidation markers are elevated in autism, indicating that oxidative stress is increased in this disease. Levels of major antioxidant serum proteins, namely transferrin (iron-binding protein) and ceruloplasmin (copper-binding protein), are decreased in children with autism. There is a positive correlation between reduced levels of these proteins and loss of previously acquired language skills in children with autism. The alterations in ceruloplasmin and transferrin levels may lead to abnormal iron and copper metabolism in autism. The membrane phospholipids, the prime target of ROS, are also altered in autism. The levels of phosphatidylethanolamine (PE) are decreased, and phosphatidylserine (PS) levels are increased in the erythrocyte membrane of children with autism as compared to their unaffected siblings. Several studies have suggested alterations in the activities of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase in autism. Additionally, altered glutathione levels and homocysteine/methionine metabolism, increased inflammation, excitotoxicity, as well as mitochondrial and immune dysfunction have been suggested in autism. Furthermore, environmental and genetic factors may increase vulnerability to oxidative stress in autism. Taken together, these studies suggest increased oxidative stress in autism that may contribute to the development of this disease. A mechanism linking oxidative stress with membrane lipid abnormalities, inflammation, aberrant immune response, impaired energy metabolism and excitotoxicity, leading to clinical symptoms and pathogenesis of autism is proposed.

Excerpt: **"Upon completion of this article, participants should be able to: 1. Be aware of laboratory and clinical evidence of greater oxidative stress in autism. 2. Understand how gut, brain, nutritional, and toxic status in autism are consistent with greater oxidative stress. 3. Describe how anti-oxidant nutrients are used in the contemporary treatment of autism."**

75. Thimerosal Neurotoxicity is Associated with Glutathione Depletion: Protection with Glutathione Precursors

Neurotoxicology. 2005 Jan;26(1):1-8.

James SJ, Slikker W 3rd, Melnyk S, New E, Pogribna M, Jernigan S.

Department of Pediatrics, University of Arkansas for Medical Sciences and Arkansas Children's Hospital Research Institute, Little Rock, AR

Abstract

Thimerosal is an antiseptic containing 49.5% ethyl mercury that has been used for years as a preservative in many infant vaccines and in flu vaccines. Environmental methyl mercury has been shown to be highly neurotoxic, especially to the developing brain. Because mercury has a high affinity for thiol (sulfhydryl (-SH)) groups, the thiol-containing antioxidant, glutathione (GSH), provides the major intracellular defense against mercury-induced neurotoxicity. Cultured neuroblastoma cells were found to have lower levels of GSH and increased sensitivity to thimerosal toxicity compared to glioblastoma cells that have higher basal levels of intracellular GSH. **Thimerosal-induced cytotoxicity was associated with depletion of intracellular GSH in both cell lines.** Pretreatment with 100 microM glutathione ethyl ester or N-acetylcysteine (NAC), but not methionine, resulted in a significant increase in intracellular GSH in both cell types. Further, pretreatment of the cells with glutathione ethyl ester or NAC prevented cytotoxicity with exposure to 15 microM Thimerosal. Although Thimerosal has been recently removed from most children's vaccines, it is still present in flu vaccines given to pregnant women, the elderly, and to children in developing countries. The potential protective effect of GSH or NAC against mercury toxicity warrants further research as possible adjunct therapy to individuals still receiving Thimerosal-containing vaccinations.

76. [Toxic metals and oxidative stress part I: mechanisms involved in metal-induced oxidative damage.](#)

Curr Top Med Chem. 2001 Dec;1(6):529-39.

Ercal N1, Gurer-Orhan H, Aykin-Burns N.

University of Missouri-Rolla, Department of Chemistry, 65409-0010, USA.
nercal@umr.edu

Abstract

Toxic metals (lead, cadmium, mercury and arsenic) are widely found in our environment. Humans are exposed to these metals from numerous sources, including contaminated air, water, soil and food. Recent studies indicate that transition metals act as catalysts in the oxidative reactions of biological macromolecules therefore the toxicities associated with these metals might be due to oxidative tissue damage. Redox-active metals, such as iron, copper and chromium, undergo redox cycling whereas redox-inactive metals, such as lead, cadmium, mercury and others deplete cells' major antioxidants, particularly thiol-containing antioxidants and enzymes. Either redox-active or redox-inactive metals may cause an increase in production of reactive oxygen species (ROS) such as hydroxyl radical (HO.), superoxide radical (O₂⁻) or hydrogen peroxide (H₂O₂). Enhanced generation of ROS can overwhelm cells' intrinsic antioxidant defenses, and result in a condition known as "oxidative stress". Cells under oxidative stress display various dysfunctions due to lesions caused by ROS to lipids, proteins and DNA. **Consequently, it is suggested that metal-induced**

oxidative stress in cells can be partially responsible for the toxic effects of heavy metals. Several studies are underway to determine the effect of antioxidant supplementation following heavy metal exposure. Data suggest that antioxidants may play an important role in abating some hazards of heavy metals. In order to prove the importance of using antioxidants in heavy metal poisoning, pertinent biochemical mechanisms for metal-induced oxidative stress should be reviewed.

77. Aluminum adjuvant linked to gulf war illness induces motor neuron death in mice

Neuromolecular Med. 2007;9(1):83-100.

Petrik MS, Wong MC, Tabata RC, Garry RF, Shaw CA.

Department of Ophthalmology and Program in Neuroscience, University of British Columbia, Vancouver, British Columbia, Canada.

Abstract

Gulf War illness (GWI) affects a significant percentage of veterans of the 1991 conflict, but its origin remains unknown. Associated with some cases of GWI are increased incidences of amyotrophic lateral sclerosis and other neurological disorders. Whereas many environmental factors have been linked to GWI, the role of the anthrax vaccine has come under increasing scrutiny. Among the vaccine's potentially toxic components are the adjuvants aluminum hydroxide and squalene. To examine whether these compounds might contribute to neuronal deficits associated with GWI, an animal model for examining the potential neurological impact of aluminum hydroxide, squalene, or aluminum hydroxide combined with squalene was developed. Young, male colony CD-1 mice were injected with the adjuvants at doses equivalent to those given to US military service personnel. All mice were subjected to a battery of motor and cognitive-behavioral tests over a 6-mo period postinjections. Following sacrifice, central nervous system tissues were examined using immunohistochemistry for evidence of inflammation and cell death. Behavioral testing showed motor deficits in the aluminum treatment group that expressed as a progressive decrease in strength measured by the wire-mesh hang test (final deficit at 24 wk; about 50%). Significant cognitive deficits in water-maze learning were observed in the combined aluminum and squalene group (4.3 errors per trial) compared with the controls (0.2 errors per trial) after 20 wk. Apoptotic neurons were identified in aluminum-injected animals that showed significantly increased activated caspase-3 labeling in lumbar spinal cord (255%) and primary motor cortex (192%) compared with the controls. Aluminum-treated groups also showed significant motor neuron loss (35%) and increased numbers of astrocytes (350%) in the lumbar spinal cord. The findings suggest a possible role for the aluminum adjuvant in some neurological features associated with GWI and possibly an additional role for the combination of adjuvants.

78. [Enrichment of Elevated Plasma F2t-Isoprostane Levels in Individuals with Autism Who Are Stratified by Presence of Gastrointestinal Dysfunction](#)

PLoS ONE 8(7): e68444.

Gorrindo P, Lane CJ, Lee EB, McLaughlin B, Levitt P (July 3, 2013)

Funding: This work was supported in part by National Institutes of Health awards National Institute of Child Health and Human Development R21HD065289 (PL), National Institute of General Medical Sciences T32GM07347 for the Vanderbilt Medical Scientist Training Program (PG), National Center for Research Resources TL1RR024978 (PG), and National Center for Advancing Translational Sciences UL1TR000445 for the Vanderbilt Institute for Clinical and Translational Research. Additional support was provided by the Marino Autism Research Institute, the Pediatric Clinical Research Center at Vanderbilt University, The Scott Family Foundation, and the Vanderbilt Autism Treatment Network Site, a program funded by Autism Speaks.

Abstract Etiology is unknown in the majority of individuals with autism spectrum disorder (ASD). One strategy to investigate pathogenesis is to stratify this heterogeneous disorder based on a prominent phenotypic feature that enriches for homogeneity within population strata. Co-occurring gastrointestinal dysfunction (GID) characterizes a subset of children with ASD. Our current objective was to investigate a potential pathophysiological measure to test the hypothesis that children with both ASD and GID have a more severe metabolic dysfunction than children with ASD-only, given that the highly metabolically active brain and gastrointestinal system may additively contribute measurable impairment. Plasma levels of F2t-Isoprostanes (F2-IsoPs), a gold standard biomarker of oxidative stress, were measured in 87 children in four groups: ASD-GID, ASD-only, GID-only and Unaffected. F2-IsoP levels were elevated in all 3 clinical groups compared to the Unaffected group, with the ASD-GID group significantly elevated above the ASD-only group (mean, SD in pg/mg: ASD-GID 53.6, 24.4; ASD-only 36.5, 13.3; $p = 0.007$). Adjusting for age, sex, and triglyceride levels, F2-IsoP levels remained significantly different between study groups, with a moderate effect size of $\eta^2 = 0.187$ ($p = 0.001$). **Elevation in peripheral oxidative stress is consistent with, and may contribute to, the more severe functional impairments in the ASD-GID group.** With unique medical, metabolic, and behavioral features in children with ASD-GID, the present findings serve as a compelling rationale for both individualized approaches to clinical care and integrated studies of biomarker enrichment in ASD subgroups that may better address the complex etiology of ASD.

79. [Reduced levels of mercury in first baby haircuts of autistic children.](#)

Int J Toxicol. 2003 Jul-Aug;22(4):277-85.

Holmes AS, Blaxill MF, Haley BE.

Abstract

Reported rates of autism have increased sharply in the United States and the United Kingdom. One possible factor underlying these increases is increased exposure to mercury through thimerosal-containing vaccines, but vaccine exposures need to be evaluated in the context of cumulative exposures during gestation and early infancy. Differential rates of postnatal mercury elimination may explain why similar gestational and infant exposures produce variable neurological effects. First baby haircut samples were obtained from 94 children diagnosed with autism using Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM IV) criteria and 45 age- and gender-matched controls. Information on diet, dental amalgam fillings, vaccine history, Rho D immunoglobulin administration, and autism symptom severity was collected through a maternal survey questionnaire and clinical observation. Hair mercury levels in the autistic group were 0.47 ppm versus 3.63 ppm in controls, a significant difference. The mothers in the autistic group had significantly higher levels of mercury exposure through Rho D immunoglobulin injections and amalgam fillings than control mothers. Within the autistic group, hair mercury levels varied significantly across mildly, moderately, and severely autistic children, with mean group levels of 0.79, 0.46, and 0.21 ppm, respectively. Hair mercury levels among controls were significantly correlated with the number of the mothers' amalgam fillings and their fish consumption as well as exposure to mercury through childhood vaccines, correlations that were absent in the autistic group. Hair excretion patterns among autistic infants were significantly reduced relative to control. These data cast doubt on the efficacy of traditional hair analysis as a measure of total mercury exposure in a subset of the population. In light of the biological plausibility of mercury's role in neurodevelopmental disorders, the present study provides further insight into one possible mechanism by which early mercury exposures could increase the risk of autism.

80. A Case Series of Children with Apparent Mercury Toxic Encephalopathies Manifesting with Clinical Symptoms of Regressive Autistic Disorder

J Toxicol Environ Health A. 2007 May 15;70(10):837-51.

Geier DA, Geier MR.

Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA.

Abstract

Impairments in social relatedness and communication, repetitive behaviors, and stereotypic abnormal movement patterns characterize autism spectrum disorders (ASDs). It is clear that while genetic factors are important to the pathogenesis of ASDs, mercury exposure can induce immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with ASDs. The Institutional Review Board of the Institute for Chronic Illnesses (Office for Human Research Protections, U.S. Department of Health and Human Services, IRB number IRB00005375) approved the present study. A case series of nine patients

who presented to the Genetic Centers of America for a genetic/developmental evaluation are discussed. Eight of nine patients (one patient was found to have an ASD due to Rett's syndrome) (a) had regressive ASDs; (b) had elevated levels of androgens; (c) excreted significant amounts of mercury post chelation challenge; (d) had biochemical evidence of decreased function in their glutathione pathways; (e) had no known significant mercury exposure except from Thimerosal-containing vaccines/Rho(D)-immune globulin preparations; and (f) had alternate causes for their regressive ASDs ruled out. There was a significant dose-response relationship between the severity of the regressive ASDs observed and the total mercury dose children received from Thimerosal-containing vaccines/Rho (D)-immune globulin preparations. Based upon differential diagnoses, 8 of 9 patients examined were exposed to significant mercury from Thimerosal-containing biologic/vaccine preparations during their fetal/infant developmental periods, and subsequently, between 12 and 24 mo of age, **these previously normally developing children suffered mercury toxic encephalopathies that manifested with clinical symptoms consistent with regressive ASDs. Evidence for mercury intoxication should be considered in the differential diagnosis as contributing to some regressive ASDs.**

81. [The Changing Prevalence of Autism In California](#)

Journal of Autism and Developmental Disorders, April 2003
Mark Blaxill, MBA

This study helps to refute the supposition made by some researchers that autism's epidemic may only be due to "diagnostic substitution".

Excerpt: **"They have suggested that 'diagnostic substitution' accounts for an apparent increase in the incidence of autism in California that is not real. This hypothesized substitution is not supported by proper and detailed analyses of the California data."**

82. [California Autism Prevalence Trends from 1931 to 2014 and Comparison to National ASD Data from IDEA and ADDM.](#)

J Autism Dev Disord. 2018 Jul 5.

Nevison C, Blaxill M, Zahorodny W.

Abstract

Time trends in U.S. autism prevalence from three ongoing datasets [Individuals with Disabilities Education Act, Autism and Developmental Disabilities Monitoring Network, and California Department of Developmental Services (CDDS)] are calculated using two different methods: (1) constant-age tracking of 8 year-olds and (2) age-resolved snapshots. The data are consistent across methods in showing a strong upward trend over time. The prevalence of autism in the CDDS

dataset, the longest of the three data records, increased from 0.001% in the cohort born in 1931 to 1.2% among 5 year-olds born in 2012. **This increase began around ~ 1940 at a rate that has gradually accelerated over time, including notable change points around birth years 1980, 1990 and, most recently, 2007.**

83. [Diagnostic Substitution for Intellectual Disability: A Flawed Explanation for the Rise in Autism](#)

Journal of Autism and Developmental Disorders First Online: 06 June 2017, DOI: 10.1007/s10803-017-3187-0

Cynthia D. Nevison, Mark Blaxill

Abstract

Time trends in autism spectrum disorder (ASD) and intellectual disability (ID) prevalence from the United States Individuals with Disabilities Education Act data were computed from 2000 to 2011 for each state and each age from 6 to 17.

These trends did not support the hypothesis that diagnostic substitution for ID can explain the ASD rise over recent decades, although the hypothesis appeared more plausible when the data were aggregated across all states and ages. Nationwide ID prevalence declined steeply over the last two decades, but the decline was driven mainly by ~15 states accounting for only one-fourth of the U.S. school population. **More commonly, including in the most populous states, ID prevalence stayed relatively constant while ASD prevalence rose sharply.**

84. Mitochondrial Energy-Deficient Endophenotype in Autism

American Journal of Biochemistry and Biotechnology 4 (2): 198-207, 2008

J. Jay Gargus and Faiqa Imtiaz

Department of Physiology and Biophysics and Department of Pediatrics, Section of Human Genetics, School of Medicine, University of California, Irvine, Arabian Diagnostics Laboratory, King Faisal Specialist Hospital and Research Centre

Abstract: While evidence points to a multigenic etiology of most autism, the pathophysiology of the disorder has yet to be defined and the underlying genes and biochemical pathways they subserve remain unknown. Autism is considered to be influenced by a combination of various genetic, environmental and immunological factors; more recently, evidence has suggested that increased vulnerability to oxidative stress may be involved in the etiology of this multifactorial disorder.

Furthermore, recent studies have pointed to a subset of autism associated with the biochemical endophenotype of mitochondrial energy deficiency, identified as

a subtle impairment in fat and carbohydrate oxidation. This phenotype is similar, but more subtle than those seen in classic mitochondrial defects. In some cases the beginnings of the genetic underpinnings of these mitochondrial defects are emerging, such as mild mitochondrial dysfunction and secondary carnitine deficiency observed in the subset of autistic patients with an inverted duplication of chromosome 15q11-q13. In addition, rare cases of familial autism associated with sudden infant death syndrome (SIDS) or associated with abnormalities in cellular calcium homeostasis, such as malignant hyperthermia or cardiac arrhythmia, are beginning to emerge. **Such special cases suggest that the pathophysiology of autism may comprise pathways that are directly or indirectly involved in mitochondrial energy production** and to further probe this connection three new avenues seem worthy of exploration: 1) metabolomic clinical studies provoking controlled aerobic exercise stress to expand the biochemical phenotype, 2) high-throughput expression arrays to directly survey activity of the genes underlying these biochemical pathways and 3) model systems, either based upon neuronal stem cells or model genetic organisms, to discover novel genetic and environmental inputs into these pathways.

85. Pathways to Defective Brain Function and Plasticity

American Journal of Biochemistry and Biotechnology 4 (2): 167-176, 2008

Matthew P. Anderson, Brian S. Hooker and Martha R. Herbert
Departments of Neurology and Pathology, Harvard Medical School/Beth Israel Deaconess Medical Center, Harvard Institutes of Medicine, High Throughput Biology Team, Fundamental Science Directorate, Pacific Northwest National Laboratory, Pediatric Neurology/Center for Morphometric Analysis, Massachusetts General Hospital/Harvard Medical School, and Center for Child and Adolescent Development, Cambridge Health Alliance/Harvard Medical School

Abstract: We review evidence to support a model where the disease process underlying autism may begin when an in utero or early postnatal environmental, infectious, seizure, or autoimmune insult triggers an immune response that increases reactive oxygen species (ROS) production in the brain that leads to DNA damage (nuclear and mitochondrial) and metabolic enzyme blockade and that these inflammatory and oxidative stressors persist beyond early development (with potential further exacerbations), producing ongoing functional consequences. In organs with a high metabolic demand such as the central nervous system, the continued use of mitochondria with damaged DNA and impaired metabolic enzyme function may generate additional ROS which will cause persistent activation of the innate immune system leading to more ROS production. Such a mechanism would self-sustain and possibly progressively worsen. The mitochondrial dysfunction and altered redox signal transduction pathways found in autism would conspire to activate both astroglia and microglia. These activated cells can then initiate a broad-spectrum proinflammatory gene response. Beyond the direct effects of ROS on neuronal function, receptors on

neurons that bind the inflammatory mediators may serve to inhibit neuronal signaling to protect them from excitotoxic damage during various pathologic insults (e.g., infection). **In autism, over-zealous neuroinflammatory responses could not only influence neural developmental processes, but may more significantly impair neural signaling involved in cognition in an ongoing fashion.** This model makes specific predictions in patients and experimental animal models and suggests a number of targets sites of intervention. Our model of potentially reversible pathophysiological mechanisms in autism motivates our hope that effective therapies may soon appear on the horizon.

86. Heavy-Metal Toxicity—With Emphasis on Mercury

John Neustadt, ND, and Steve Pieczenik, MD, PhD

Research Review

Conclusion: Metals are ubiquitous in our environment, and exposure to them is inevitable. However, not all people accumulate toxic levels of metals or exhibit symptoms of metal toxicity, suggesting that genetics play a role in their potential to damage health. **Metal toxicity creates multisystem dysfunction, which appears to be mediated primarily through mitochondrial damage from glutathione depletion.**

Accurate screening can increase the likelihood that patients with potential metal toxicity are identified. The most accurate screening method for assessing chronic-metals exposure and metals load in the body is a provoked urine test.

87. Evidence of Mitochondrial Dysfunction in Autism and Implications for Treatment

American Journal of Biochemistry and Biotechnology 4 (2): 208-217, 2008

Daniel A. Rossignol, J. Jeffrey Bradstreet, International Child Development Resource Center,

Abstract

Classical mitochondrial diseases occur in a subset of individuals with autism and are usually caused by genetic anomalies or mitochondrial respiratory pathway deficits. However, in many cases of autism, there is evidence of mitochondrial dysfunction (MtD) without the classic features associated with mitochondrial disease. MtD appears to be more common in autism and presents with less severe signs and symptoms. It is not associated with discernable mitochondrial pathology in muscle biopsy specimens despite objective evidence of lowered mitochondrial functioning. **Exposure to environmental toxins is the likely etiology for MtD in autism. This dysfunction then contributes to a number of diagnostic symptoms and comorbidities observed in autism including: cognitive impairment, language deficits, abnormal energy metabolism,**

chronic gastrointestinal problems, abnormalities in fatty acid oxidation, and increased oxidative stress. MtD and oxidative stress may also explain the high male to female ratio found in autism due to increased male vulnerability to these dysfunctions.

Biomarkers for mitochondrial dysfunction have been identified, but seem widely under-utilized despite available therapeutic interventions. Nutritional supplementation to decrease oxidative stress along with factors to improve reduced glutathione, as well as hyperbaric oxygen therapy (HBOT) represent supported and rationale approaches. The underlying pathophysiology and autistic symptoms of affected individuals would be expected to either improve or cease worsening once effective treatment for MtD is implemented.

88. [Evidence of Mitochondrial Dysfunction in Autism: Biochemical Links, Genetic-Based Associations, and Non-Energy-Related Mechanisms](#)

Oxid Med Cell Longev. 2017 May 29.

Keren K. Griffiths and Richard J. Levy

Department of Anesthesiology, Columbia University Medical Center, New York, NY, USA

Abstract

Autism spectrum disorder (ASD), the fastest growing developmental disability in the United States, represents a group of neurodevelopmental disorders characterized by impaired social interaction and communication as well as restricted and repetitive behavior. The underlying cause of autism is unknown and therapy is currently limited to targeting behavioral abnormalities. Emerging studies suggest a link between mitochondrial dysfunction and ASD. Here, we review the evidence demonstrating this potential connection. We focus specifically on biochemical links, genetic-based associations, non-energy related mechanisms, and novel therapeutic strategies.

Conclusion

The literature reviewed here suggests a link between abnormalities in mitochondrial homeostasis and ASD and provides biochemical and genetic evidence to support a role for mitochondrial dysfunction in the pathogenesis of the autism phenotype. Mechanistically, the connection may involve defects in bioenergetic capacity as well as non-energy related pathways. However, it is not clear if mitochondrial impairments cause ASD or if they are merely associated with the disease process. Positive patient behavioral responses to conventional mitochondrial disease therapies are promising, however, further investigation is necessary. Future work should focus on determining how mitochondrial dysfunction causes the autistic phenotype as well as how defects in mitochondrial homeostasis predispose individuals to ASD via interaction with environmental toxins, dietary factors, and epigenetic modifications during critical periods of development. Establishing a causative

relationship between mitochondrial dysfunction and ASD and elucidating the exact mechanisms will permit the development of more precisely targeted therapies in the future. Ultimately, with improved knowledge and innovation, we may one day be able to prevent or cure autism.

89. Proximity to point sources of environmental mercury release as a predictor of autism prevalence

Health & Place, 2008

Raymond F. Palmer, Stephen Blanchard, Robert Wood
University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, Our Lady of the Lake University, San Antonio Texas, Chair, Department of Sociology

This study should be viewed as hypothesis-generating - a first step in examining the potential role of environmental mercury and childhood developmental disorders. Nothing is known about specific exposure routes, dosage, timing, and individual susceptibility. **We suspect that persistent low-dose exposures to various environmental toxicants, including mercury, that occur during critical windows of neural development among genetically susceptible children (with a diminished capacity for metabolizing accumulated toxicants) may increase the risk for developmental disorders such as autism.** Successfully identifying the specific combination of environmental exposures and genetic susceptibilities can inform the development of targeted prevention intervention strategies.

90. Epidemiology of autism spectrum disorder in Portugal: prevalence, clinical characterization, and medical conditions

Developmental Medicine & Child Neurology, 2007

Guiomar Oliveira MD PhD, Centro de Desenvolvimento da Criança, Hospital Pediátrico de Coimbra; Assunção Ataíde BSc, Direcção Regional de Educação do Centro Coimbra;
Carla Marques MSc, Centro de Desenvolvimento da Criança, Hospital Pediátrico de Coimbra; Teresa S Miguel BSc, Direcção Regional de Educação do Centro, Coimbra;
Ana Margarida Coutinho BSc, Instituto Gulbenkian de Ciência, Oeiras; Luísa Mota-Vieira PhD, Unidade de Genética e Patologia moleculares, Hospital do Divino Espírito Santo, Ponta Delgada, Açores; Esmeralda Gonçalves PhD; Nazaré Mendes Lopes PhD, Faculdade de Ciências e Tecnologia, Universidade de Coimbra; Vítor Rodrigues MD PhD; Henrique Carmona da Mota MD PhD, Faculdade de Medicina, Universidade de Coimbra, Coimbra; Astrid Moura

Vicente PhD, Instituto Gulbenkian de Ciência, Oeiras, Portugal.

*Correspondence to first author at Hospital Pediátrico de Coimbra, Av Bissaya Barreto, 3000-076 Coimbra, Portugal. E-mail: guiomar@hpc.chc.min-saude.pt

Abstract: The objective of this study was to estimate the prevalence of autistic spectrum disorder (ASD) and identify its clinical characterization, and medical conditions in a paediatric population in Portugal. A school survey was conducted in elementary schools, targeting 332 808 school-aged children in the mainland and 10 910 in the Azores islands. Referred children were directly assessed using the Diagnostic and Statistical Manual of Mental Disorders (4th edn), the Autism Diagnostic Interview–Revised, and the Childhood Autism Rating Scale. Clinical history and a laboratory investigation was performed. In parallel, a systematic multi-source search of children known to have autism was carried out in a restricted region. The global prevalence of ASD per 10 000 was 9.2 in mainland, and 15.6 in the Azores, with intriguing regional differences. **A diversity of associated medical conditions was documented in 20%, with an unexpectedly high rate of mitochondrial respiratory chain disorders.**

91. Thimerosal induces neuronal cell apoptosis by causing cytochrome c and apoptosis-inducing factor release from mitochondria.

International Journal of Molecular Medicine, 2006

Yel L, Brown LE, Su K, Gollapudi S, Gupta S. Department of Medicine, University of California, Irvine, CA 92697, USA. lyel@uci.edu

There is a worldwide increasing concern over the neurological risks of thimerosal (ethylmercury thiosalicylate) which is an organic mercury compound that is commonly used as an antimicrobial preservative. In this study, we show that thimerosal, at nanomolar concentrations, induces neuronal cell death through the mitochondrial pathway. Thimerosal, in a concentration- and time-dependent manner, decreased cell viability as assessed by calcein-ethidium staining and caused apoptosis detected by Hoechst 33258 dye. Thimerosal-induced apoptosis was associated with depolarization of mitochondrial membrane, generation of reactive oxygen species, and release of cytochrome c and apoptosis-inducing factor (AIF) from mitochondria to cytosol. Although thimerosal did not affect cellular expression of Bax at the protein level, we observed translocation of Bax from cytosol to mitochondria. Finally, caspase-9 and caspase-3 were activated in the absence of caspase-8 activation. Our data suggest that thimerosal causes apoptosis in neuroblastoma cells by changing the mitochondrial microenvironment.

92. Mitochondrial mediated thimerosal-induced apoptosis in a human neuroblastoma cell line (SK-N-SH).

Neurotoxicology. 2005

Humphrey ML, Cole MP, Pendergrass JC, Kinningham KK. Department of Pharmacology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV 25704-9388, USA.

Environmental exposure to mercurials continues to be a public health issue due to their deleterious effects on immune, renal and neurological function. Recently the safety of thimerosal, an ethyl mercury-containing preservative used in vaccines, has been questioned due to exposure of infants during immunization. Mercurials have been reported to cause apoptosis in cultured neurons; however, the signaling pathways resulting in cell death have not been well characterized. Therefore, the objective of this study was to identify the mode of cell death in an in vitro model of thimerosal-induced neurotoxicity, and more specifically, to elucidate signaling pathways which might serve as pharmacological targets. Within 2 h of thimerosal exposure (5 microM) to the human neuroblastoma cell line, SK-N-SH, morphological changes, including membrane alterations and cell shrinkage, were observed. Cell viability, assessed by measurement of lactate dehydrogenase (LDH) activity in the medium, as well as the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay, showed a time- and concentration-dependent decrease in cell survival upon thimerosal exposure. In cells treated for 24 h with thimerosal, fluorescence microscopy indicated cells undergoing both apoptosis and oncosis/necrosis. To identify the apoptotic pathway associated with thimerosal-mediated cell death, we first evaluated the mitochondrial cascade, as both inorganic and organic mercurials have been reported to accumulate in the organelle. Cytochrome c was shown to leak from the mitochondria, followed by caspase 9 cleavage within 8 h of treatment. In addition, poly(ADP-ribose) polymerase (PARP) was cleaved to form a 85 kDa fragment following maximal caspase 3 activation at 24 h. Taken together these findings suggest deleterious effects on the cytoarchitecture by thimerosal and initiation of mitochondrial-mediated apoptosis.

93. Possible Immunological Disorders in Autism: Concomitant Autoimmunity and Immune Tolerance

The Egyptian Journal of Immunology, 2006

Maha I. Sh. Kawashti, Omnia R. Amin Nadia G. Roweby

Microbiology Department, Faculty of Medicine (For Girls), Al Azhar University, Cairo, Egypt, Psychiatry Department, Faculty of Medicine, Cairo University, Cairo, Egypt and Serology Lab King Fahad General Hospital, Jeddah, K.S.A.

Abstract: Autism is a pervasive developmental disorder that affect children early in their life. Immunological disorders is one of several contributing factors that have been suggested to cause autism. Thirty autistic children aged 3-6 years and

thirty non-autistic psychologically-free siblings were studied. Circulating IgA and IgG autoantibodies to casein and gluten dietary proteins were detected by enzyme-immunoassays (EIA). Circulating IgG antibodies to measles, mumps and rubella vaccine (M.M.R) and cytomeglovirus were investigated by EIA. Results revealed high seropositivity for autoantibodies to casein and gluten: 83.3% and 50% respectively in autistic children as compared to 10% and 6.7% positivity in the control group. Surprisingly, circulating anti-measles, anti-mumps and anti-rubella IgG were positive in only 50%, 73.3% and 53.3% respectively as compared to 100% positivity in the control group. Anti-CMV IgG was positive in 43.3% of the autistic children as compared to 7% in the control group. **It is concluded that, autoimmune response to dietary proteins and deficient immune response to measles, mumps and rubella vaccine antigens might be associated with autism, as a leading cause or a resulting event.** Further research is needed to confirm these findings.

94. [Pediatric Vaccines Influence Primate Behavior, and Amygdala Growth and Opioid Ligand Binding](#)

Friday, May 16, 2008: IMFAR

L. Hewitson , Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, PA B. Lopresti , Radiology, University of Pittsburgh, Pittsburgh, PA C. Stott , Thoughtful House Center for Children, Austin, TX J. Tomko , Pittsburgh Development Center, University of Pittsburgh, Pittsburgh, PA L. Houser , Pittsburgh Development Center, University of Pittsburgh, Pittsburgh, PA E. Klein , Division of Laboratory Animal Resources, University of Pittsburgh, Pittsburgh, PA C. Castro , Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, PA G. Sackett , Psychology, Washington National Primate Research Center, Seattle, WA S. Gupta , Medicine, Pathology & Laboratory Medicine, University of California - Irvine, Irvine, CA D. Atwood , Chemistry, University of Kentucky, Lexington, KY L. Blue , Chemistry, University of Kentucky, Lexington, KY E. R. White , Chemistry, University of Kentucky, Lexington, KY A. Wakefield , Thoughtful House Center for Children, Austin, TX

Abstract

Background: Macaques are commonly used in pre-clinical vaccine safety testing, but the combined childhood vaccine regimen, rather than individual vaccines, has not been studied. Childhood vaccines are a possible causal factor in autism, and abnormal behaviors and anomalous amygdala growth are potentially inter-related features of this condition.

Objectives: The objective of this study was to compare early infant cognition and behavior with amygdala size and opioid binding in rhesus macaques receiving the recommended childhood vaccines (1994-1999), the majority of which contained the bactericidal preservative ethylmercurithiosalicylic acid (thimerosal).

Methods: Macaques were administered the recommended infant vaccines,

adjusted for age and thimerosal dose (exposed; N=13), or saline (unexposed; N=3). Primate development, cognition and social behavior were assessed for both vaccinated and unvaccinated infants using standardized tests developed at the Washington National Primate Research Center. Amygdala growth and binding were measured serially by MRI and by the binding of the non-selective opioid antagonist [¹¹C]diprenorphine, measured by PET, respectively, before (T1) and after (T2) the administration of the measles-mumps-rubella vaccine (MMR).

Results: Compared with unexposed animals, significant neurodevelopmental deficits were evident for exposed animals in survival reflexes, tests of color discrimination and reversal, and learning sets. Differences in behaviors were observed between exposed and unexposed animals and within the exposed group before and after MMR vaccination. Compared with unexposed animals, exposed animals showed attenuation of amygdala growth and differences in the amygdala binding of [¹¹C]diprenorphine. Interaction models identified significant associations between specific aberrant social and non-social behaviors, isotope binding, and vaccine exposure.

Conclusions: This animal model, which examines for the first time, behavioral, functional, and neuromorphometric consequences of the childhood vaccine regimen, mimics certain neurological abnormalities of autism. The findings raise important safety issues while providing a potential model for examining aspects of causation and disease pathogenesis in acquired disorders of behavior and development.

95. Thimerosal exposure in infants and neurodevelopmental disorders: An assessment of computerized medical records in the Vaccine Safety Datalink.

Young HA, Geier DA, Geier MR.

The George Washington University School of Public Health and Health Services, Department of Epidemiology and Biostatistics, United States.

Abstract

The study evaluated possible associations between neurodevelopmental disorders (NDs) and exposure to mercury (Hg) from Thimerosal-containing vaccines (TCVs) by examining the automated Vaccine Safety Datalink (VSD). A total of 278,624 subjects were identified in birth cohorts from 1990-1996 that had received their first oral polio vaccination by 3 months of age in the VSD. The birth cohort prevalence rate of medically diagnosed International Classification of Disease, 9th revision (ICD-9) specific NDs and control outcomes were calculated. Exposures to Hg from TCVs were calculated by birth cohort for specific exposure windows from birth-7 months and birth-13 months of age. Poisson regression analysis was used to model the association between the prevalence of outcomes and Hg doses from TCVs. **Consistent significantly increased rate ratios were observed for autism, autism spectrum disorders,**

tics, attention deficit disorder, and emotional disturbances with Hg exposure from TCVs. By contrast, none of the control outcomes had significantly increased rate ratios with Hg exposure from TCVs. Routine childhood vaccination should be continued to help reduce the morbidity and mortality associated with infectious diseases, but efforts should be undertaken to remove Hg from vaccines. Additional studies should be conducted to further evaluate the relationship between Hg exposure and NDs.

96. Glutathione, oxidative stress and neurodegeneration

Schulz JB, Lindenau J, Seyfried J, Dichgans J.
Neurodegeneration Laboratory, Department of Neurology, University of Tübingen, Germany.

Eur J Biochem. 2000 Aug;267(16):4904-11.

Abstract

There is significant evidence that the pathogenesis of several neurodegenerative diseases, including Parkinson's disease, Alzheimer's disease, Friedreich's ataxia and amyotrophic lateral sclerosis, may involve the generation of reactive oxygen species and mitochondrial dysfunction. Here, we review the evidence for a disturbance of glutathione homeostasis that may either lead to or result from oxidative stress in neurodegenerative disorders. Glutathione is an important intracellular antioxidant that protects against a variety of different antioxidant species. An important role for glutathione was proposed for the pathogenesis of Parkinson's disease, because a decrease in total glutathione concentrations in the substantia nigra has been observed in preclinical stages, at a time at which other biochemical changes are not yet detectable. Because glutathione does not cross the blood-brain barrier other treatment options to increase brain concentrations of glutathione including glutathione analogs, mimetics or precursors are discussed.

97. [Hepatitis B triple series vaccine and developmental disability in US children aged 1-9 years](#)

Carolyn Gallagher a; Melody Goodman, Graduate Program in Public Health, Stony Brook University Medical Center, Health Sciences Center, New York, USA

Journal Toxicological & Environmental Chemistry, Volume 90, Issue 5 September 2008 , pages 997 - 1008

Abstract

This study investigated the association between vaccination with the Hepatitis B triple series vaccine prior to 2000 and developmental disability in children aged

1–9 years (n = 1824), proxied by parental report that their child receives early intervention or special education services (EIS). National Health and Nutrition Examination Survey 1999–2000 data were analyzed and adjusted for survey design by Taylor Linearization using SAS version 9.1 software, with SAS callable SUDAAN version 9.0.1. The odds of receiving EIS were approximately nine times as great for vaccinated boys (n = 46) as for unvaccinated boys (n = 7), after adjustment for confounders. **This study found statistically significant evidence to suggest that boys in United States who were vaccinated with the triple series Hepatitis B vaccine, during the time period in which vaccines were manufactured with thimerosal, were more susceptible to developmental disability than were unvaccinated boys.**

98. [IL-4 mediates the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination that involves the down-regulation of the IL4 receptor in the hippocampus](#)

Cytokine

Xiao Wang, Junhua Yang, Zhiwei Xing, Hongyang Zhang, Yaru Wen, Fangfang Qi, Zejie Zuo, Jie Xu, Zhibin Yao

Department of Anatomy and Neurobiology, Zhongshan School of Medicine, Sun Yat-sen University, PR China
Guangdong Province Key Laboratory of Brain Function and Disease, Zhongshan School of Medicine, Sun Yat-sen University, PR China

ABSTRACT

We have previously verified that neonatal hepatitis B vaccination induced hippocampal neuroinflammation and behavior impairments in mice. However, the exact mechanism of these effects remain unclear. In this study, we observed that neonatal hepatitis B vaccination induced an anti-inflammatory cytokine response lasting for 4–5 weeks in both the serum and the hippocampus, primarily indicated by elevated IL-4 levels. Three weeks after the vaccination schedule, however, hepatitis B vaccine (HBV)-mice showed delayed hippocampal neuroinflammation. In periphery, IL-4 is the major cytokine induced by this vaccine. Correlation analyses showed a positive relationship in the IL-4 levels between serum and hippocampus in HBV-mice. Thus, we investigated whether neonatal over-exposure to systemic IL-4 influences brain and behavior. We observed that mice injected intraperitoneally with recombinant mouse IL-4 (mIL-4) during early life had similar neuroinflammation and cognition impairment similar to those induced by neonatal hepatitis B vaccination. Next, the mechanism underlying the effects of IL-4 on brain in mice was explored using a series of experiments. In brief, these experiments showed that IL-4 mediates the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination, which involves the permeability of neonatal blood–brain barrier and the down-regulation of IL-4 receptor. **This finding suggests that clinical events concerning neonatal IL-4 over-exposure, including neonatal hepatitis B**

vaccination and allergic asthma in human infants, may have adverse implications for brain development and cognition.

99. [The risk of neurodevelopmental disorders at age 10 years associated with blood concentrations of interleukins 4 and 10 during the first postnatal month of children born extremely preterm.](#)

Cytokine. 2018 May 12;110:181-188. doi: 10.1016/j.cyto.2018.05.004.

Leviton A, Joseph RM, Allred EN, Fichorova RN, O'Shea TM, Kuban KKC, Dammann O7.

Boston Children's Hospital and Harvard Medical School, Boston, MA, USA.

Electronic address: alan.leviton@childrens.harvard.edu.

Boston University School of Medicine, Boston, MA, USA.

Boston Children's Hospital and Harvard Medical School, Boston, MA, USA.

Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA.

University of North Carolina School of Medicine, Chapel Hill, NC, USA.

Boston Medical Center and Boston University School of Medicine, Boston, MA, USA.

Tufts University School of Medicine, Boston, MA 02111, USA; Perinatal Neuroepidemiology Unit, Department of Gynecology and Obstetrics, Hannover Medical School, 30623 Hannover, Germany

Abstract

BACKGROUND:

Interleukin (IL)-4 and IL-10 are viewed mainly as anti-inflammatory cytokines. Yet, high concentrations have also been associated with inflammation-related diseases in newborns.

METHODS:

We measured the concentrations of IL-4 and IL-10, as well as IL-8 and ICAM-1 in blood specimens collected on postnatal day 21 (N = 555), day 28 (N = 521), and both days 21 and 28 (N = 449) from children born extremely preterm (EP) (<28 weeks gestation) who at age 10 years had a DAS-II IQ Z-score > -2 (which approximates a score of >70) and the following assessments, CCC-2, and CSI-4, DAS-II, NEPSY-II, OWLS-II, SCQ, and WIAT-III. Selected children also were assessed with the ADI-R and the ADOS-2. We modeled the risk of low scores or dysfunctions associated with top quartile concentrations of IL-4 and IL-10 on each day and on both days.

RESULTS:

The risks of low scores on the Animal Sorting and Arrows components of the NEPSY-II, both components of the OWLS-II, and the PseudoWord and Spelling components of the WIAT-III were heightened among children who had top quartile concentrations of IL-4 on postnatal days 21 and 28. Children who had

high concentrations of IL-10 on days 21 and 28, individually and collectively, were at increased risk of low scores on the WIAT-III Spelling component. High concentrations of IL-4 on day 28 were associated with autism spectrum disorder (ASD). High concentrations of IL-10 on day 28 were also associated with a doubling of ASD risk, but this did not achieve statistical significance. Top quartile concentrations of IL-4 and IL10 on both days were not associated with increased risk of social, language, or behavioral dysfunctions.

CONCLUSION:

Among children born EP, those who had top quartile concentrations of IL-4 and/or IL-10 on postnatal days 21 and/or 28 were more likely than their peers to have low scores on components of the NEPSY-II, OWLS-II, and WIAT-III assessments, as well as identification as having an ASD.

100. Induction of metallothionein in mouse cerebellum and cerebrum with low-dose thimerosal injection.

Minami T, Miyata E, Sakamoto Y, Yamazaki H, Ichida S., Department of Life Sciences, School of Science & Engineering, Kinki University, 3-4-1 Kowakae, Higashi-osaka, Osaka, 577-8502, Japan, minamita@life.kindai.ac.jp.

Cell Biology and Toxicology. 2009 Apr 9. [Epub ahead of print]

Abstract

Thimerosal, an ethyl mercury compound, is used worldwide as a vaccine preservative. We previously observed that the mercury concentration in mouse brains did not increase with the clinical dose of thimerosal injection, but the concentration increased in the brain after the injection of thimerosal with lipopolysaccharide, even if a low dose of thimerosal was administered. Thimerosal may penetrate the brain, but is undetectable when a clinical dose of thimerosal is injected; therefore, the induction of metallothionein (MT) messenger RNA (mRNA) and protein was observed in the cerebellum and cerebrum of mice after thimerosal injection, as MT is an inducible protein. MT-1 mRNA was expressed at 6 and 9 h in both the cerebrum and cerebellum, but MT-1 mRNA expression in the cerebellum was three times higher than that in the cerebrum after the injection of 12 microg/kg thimerosal. MT-2 mRNA was not expressed until 24 h in both organs. MT-3 mRNA was expressed in the cerebellum from 6 to 15 h after the injection, but not in the cerebrum until 24 h. MT-1 and MT-3 mRNAs were expressed in the cerebellum in a dose-dependent manner. Furthermore, MT-1 protein was detected from 6 to 72 h in the cerebellum after 12 microg/kg of thimerosal was injected and peaked at 10 h. MT-2 was detected in the cerebellum only at 10 h. In the cerebrum, little MT-1 protein was detected at 10 and 24 h, and there were no peaks of MT-2 protein in the cerebrum. In conclusion, MT-1 and MT-3 mRNAs but not MT-2 mRNA are easily expressed in the cerebellum rather than in the cerebrum by the injection of low-dose thimerosal. It is thought that the cerebellum is a sensitive organ against thimerosal. **As a result of the present findings, in combination with the brain**

pathology observed in patients diagnosed with autism, the present study helps to support the possible biological plausibility for how low-dose exposure to mercury from thimerosal-containing vaccines may be associated with autism.

101. Mercury induces inflammatory mediator release from human mast cells

Duraisamy Kempuraj, Shahrzad Asadi, Bodi Zhang, Akrivi Manola, Jennifer Hogan, Erika Peterson, Theoharis C Theoharides

Journal of Neuroinflammation 2010, 7:20 doi:10.1186/1742-2094-7-20

Abstract

Background: Mercury is known to be neurotoxic, but its effects on the immune system are less well known. Mast cells are involved in allergic reactions, but also in innate and acquired immunity, as well as in inflammation. Many patients with Autism Spectrum Disorders (ASD) have “allergic” symptoms; moreover, the prevalence of ASD in patients with mastocytosis, characterized by numerous hyperactive mast cells in most tissues, is 10-fold higher than the general population suggesting mast cell involvement. We, therefore, investigated the effect of mercuric chloride (HgCl₂) on human mast cell activation.

Methods: Human leukemic cultured LAD2 mast cells and normal human umbilical cord blood-derived cultured mast cells (hCBMCs) were stimulated by HgCl₂ (0.1-10 μM) for either 10 min for beta-hexosaminidase release or 24 hr for measuring vascular endothelial growth factor (VEGF) and IL-6 release by ELISA.

Results: HgCl₂ induced a 2-fold increase in β-hexosaminidase release, and also significant VEGF release at 0.1 and 1 μM (311±32 pg/106 cells and 443±143 pg/106 cells, respectively) from LAD2 mast cells compared to control cells (227±17 pg/106 cells, n=5, p<0.05). Addition of HgCl₂ (0.1 μM) to the proinflammatory neuropeptide substance P (SP, 0.1 μM) had synergistic action in inducing VEGF from LAD2 mast cells. HgCl₂ also stimulated significant VEGF release (360 ± 100 pg/106 cells at 1 μM, n=5, p<0.05) from hCBMCs compared to control cells (182 ±57 pg/106 cells), and IL-6 release (466±57 pg/106 cells at 0.1 μM) compared to untreated cells (13±25 pg/106 cells, n=5, p<0.05). Addition of HgCl₂ (0.1 μM) to SP (5 μM) further increased IL-6 release. Conclusions: HgCl₂ stimulates VEGF and IL-6 release from human mast cells. **This phenomenon could disrupt the blood-brain-barrier and permit brain inflammation. As a result, the findings of the present study provide a biological mechanism for how low levels of mercury may contribute to ASD pathogenesis.**

102. [Brain enlargement is associated with regression in preschool-age boys with autism spectrum disorders](#)

Neuroscience

Medical Investigation of Neurodevelopmental Disorders (M.I.N.D.) Institute and Department of Psychiatry and Behavioral Sciences, UC Davis School of Medicine, University of California, Sacramento, CA 95817; Departments of Psychiatry and Biostatistics, Harvard University Schools of Medicine and Public Health, McLean Hospital, Belmont, MA 02478; and Department of Radiology, UC Davis School of Medicine, University of California, Sacramento, CA 95817

Proc Natl Acad Sci U S A. 2011 Dec 13; 108(50): 20195–20200.
Published online 2011 Nov 28. doi: 10.1073/pnas.1107560108

Christine Wu Nordahl, Nicholas Lange, Deana D. Li, Lou Ann Barnett, Aaron Lee, Michael H. Buonocore, Tony J. Simon, Sally Rogers, Sally Ozonoff, and David G. Amarala,

ABSTRACT

Autism is a heterogeneous disorder with multiple behavioral and biological phenotypes. Accelerated brain growth during early childhood is a well-established biological feature of autism. Onset pattern, i.e., early onset or regressive, is an intensely studied behavioral phenotype of autism. There is currently little known, however, about whether, or how, onset status maps onto the abnormal brain growth. We examined the relationship between total brain volume and onset status in a large sample of 2- to 4-y-old boys and girls with autism spectrum disorder (ASD) [n = 53, no regression (nREG); n = 61, regression (REG)] and a comparison group of age-matched typically developing controls (n = 66). We also examined retrospective head circumference measurements from birth through 18 mo of age. **We found that abnormal brain enlargement was most commonly found in boys with regressive autism. Brain size in boys without regression did not differ from controls.** Retrospective head circumference measurements indicate that head circumference in boys with regressive autism is normal at birth but diverges from the other groups around 4–6 mo of age. There were no differences in brain size in girls with autism (n = 22, ASD; n = 24, controls). **These results suggest that there may be distinct neural phenotypes associated with different onsets of autism.** For boys with regressive autism, divergence in brain size occurs well before loss of skills is commonly reported. Thus, rapid head growth may be a risk factor for regressive autism.

103. [Blood–brain barrier and intestinal epithelial barrier alterations in autism spectrum disorders](#)

Maria Fiorentino, Anna Sapone, Stefania Senger, Stephanie S. Camhi, Sarah M. Kadzielski, Timothy M. Buie, Deanna L. Kelly, Nicola Cascella and Alessio Fasano

Abstract

Background

Autism spectrum disorders (ASD) are complex conditions whose pathogenesis may be attributed to gene–environment interactions. There are no definitive mechanisms explaining how environmental triggers can lead to ASD although the involvement of inflammation and immunity has been suggested. Inappropriate antigen trafficking through an impaired intestinal barrier, followed by passage of these antigens or immune-activated complexes through a permissive blood–brain barrier (BBB), can be part of the chain of events leading to these disorders. Our goal was to investigate whether an altered BBB and gut permeability is part of the pathophysiology of ASD.

Methods

Postmortem cerebral cortex and cerebellum tissues from ASD, schizophrenia (SCZ), and healthy subjects (HC) and duodenal biopsies from ASD and HC were analyzed for gene and protein expression profiles. Tight junctions and other key molecules associated with the neurovascular unit integrity and function and neuroinflammation were investigated.

Results

Claudin (CLDN)-5 and -12 were increased in the ASD cortex and cerebellum. CLDN-3, tricellulin, and MMP-9 were higher in the ASD cortex. IL-8, tPA, and IBA-1 were downregulated in SCZ cortex; IL-1b was increased in the SCZ cerebellum. Differences between SCZ and ASD were observed for most of the genes analyzed in both brain areas. CLDN-5 protein was increased in ASD cortex and cerebellum, while CLDN-12 appeared reduced in both ASD and SCZ cortices. In the intestine, 75% of the ASD samples analyzed had reduced expression of barrier-forming TJ components (CLDN-1, OCLN, TRIC), whereas 66% had increased pore-forming CLDNs (CLDN-2, -10, -15) compared to controls.

Conclusions

In the ASD brain, there is an altered expression of genes associated with BBB integrity coupled with increased neuroinflammation and possibly impaired gut barrier integrity. While these findings seem to be specific for ASD, the possibility of more distinct SCZ subgroups should be explored with additional studies.

Acta Neurobiol Exp 2010, 70: 147–164 Polish Neuroscience Society - PTBUN,
Nencki Institute of Experimental Biology

Laura Hewitson^{1,2,*}, Brian J. Lopresti³, Carol Stott⁴, N. Scott Mason³ and
Jaime Tomko¹

Department of Obstetrics and Gynecology, University of Pittsburgh School of
Medicine, Pittsburgh, PA, USA; Thoughtful House Center for Children, Austin,
TX, USA; Department of Radiology, University of Pittsburgh School of Medicine,
Pittsburgh, PA, USA; ⁴Independent Chartered Scientist, Cambridge, UK;

Abstract

This longitudinal, case-control pilot study examined amygdala growth in rhesus macaque infants receiving the complete US childhood vaccine schedule (1994-1999). Longitudinal structural and functional neuroimaging was undertaken to examine central effects of the vaccine regimen on the developing brain. Vaccine-exposed and saline-injected control infants underwent MRI and PET imaging at approximately 4 and 6 months of age, representing two specific timeframes within the vaccination schedule. Volumetric analyses showed that exposed animals did not undergo the maturational changes over time in amygdala volume that was observed in unexposed animals. After controlling for left amygdala volume, the binding of the opioid antagonist [¹¹C]diprenorphine (DPN) in exposed animals remained relatively constant over time, compared with unexposed animals, in which a significant decrease in [¹¹C]DPN binding occurred. **These results suggest that maturational changes in amygdala volume and the binding capacity of [¹¹C]DPN in the amygdala was significantly altered in infant macaques receiving the vaccine schedule. The macaque infant is a relevant animal model in which to investigate specific environmental exposures and structural/functional neuroimaging during neurodevelopment.**

105. Cultured lymphocytes from autistic children and non-autistic siblings up-regulate heat shock protein RNA in response to thimerosal challenge.

Neurotoxicology. 2006 Sep;27(5):685-92. Epub 2006 Jun 16.

Walker SJ, Segal J, Aschner M.

Department of Physiology and Pharmacology, Wake Forest University School of
Medicine, Winston-Salem, NC 27156, USA. swalker@wfubmc.edu

Abstract

Abstract

There are reports suggesting that some autistic children are unable to mount an adequate response following exposure to environmental toxins. This potential deficit, coupled with the similarity in clinical presentations of autism and some

heavy metal toxicities, has led to the suggestion that heavy metal poisoning might play a role in the etiology of autism in uniquely susceptible individuals. Thimerosal, an anti-microbial preservative previously added routinely to childhood multi-dose vaccines, is composed of 49.6% ethyl mercury. Based on the levels of this toxin that children receive through routine immunization schedules in the first years of life, it has been postulated that thimerosal may be a potential triggering mechanism contributing to autism in susceptible individuals. One potential risk factor in these individuals may be an inability to adequately up-regulate metallothionein (MT) biosynthesis in response to presentation of a heavy metal challenge. To investigate this hypothesis, cultured lymphocytes (obtained from the Autism Genetic Resource Exchange, AGRE) from autistic children and non-autistic siblings were challenged with either 10 microM ethyl mercury, 150 microM zinc, or fresh media (control). Following the challenge, total RNA was extracted and used to query "whole genome" DNA microarrays. Cultured lymphocytes challenged with zinc responded with an impressive up-regulation of MT transcripts (at least nine different MTs were over-expressed) **while cells challenged with thimerosal responded by up-regulating numerous heat shock protein transcripts, but not MTs. Although there were no apparent differences between autistic and non-autistic sibling responses in this very small sampling group, the differences in expression profiles between those cells treated with zinc versus thimerosal were dramatic.** Determining cellular response, at the level of gene expression, has important implications for the understanding and treatment of conditions that result from exposure to neurotoxic compounds.

106. Sorting out the spinning of autism: heavy metals and the question of incidence

Acta Neurobiol Exp 2010, 70: 165–176

Mary Catherine DeSoto* and Robert T. Hitlan, Department of Psychology, University of Northern Iowa, Cedar Falls, Iowa, USA

The reasons for the rise in autism prevalence are a subject of heated professional debate. Featuring a critical appraisal of some research used to question whether there is a rise in cases and if rising levels of autism are related to environmental exposure to toxins (Soden et al. 2007, Thompson et al. 2007, Barbaresi et al. 2009) we aim to evaluate the actual state of scientific knowledge. In addition, we surveyed the empirical research on the topic of autism and heavy metal toxins. Overall, the various causes that have led to the increase in autism diagnosis are likely multi-faceted, and understanding the causes is one of the most important health topics today. We argue that scientific research does not support rejecting the link between the neurodevelopmental disorder of autism and toxic exposures.

107. Urinary Porphyrin Excretion in Neurotypical and Autistic Children

Environ Health Perspect. 2010 Oct;118(10):1450-7. Epub 2010 Jun 24.

Woods JS, Armel SE, Fulton DI, Allen J, Wessels K, Simmonds PL, Granpeesheh D, Mumper E, Bradstreet JJ, Echeverria D, Heyer NJ, Rooney JP., Department of Environmental and Occupational Health Sciences, University of Washington

Abstract

BACKGROUND: Increased urinary concentrations of pentacarboxyl-, precopro- and copro-porphyrins have been associated with prolonged mercury (Hg) exposure in adults, and comparable increases have been attributed to Hg exposure in children with autism (AU).

OBJECTIVES: This study was designed to measure and compare urinary porphyrin concentrations in neurotypical (NT) children and same-age children with autism, and to examine the association between porphyrin levels and past or current Hg exposure in children with autism.

METHODS: This exploratory study enrolled 278 children 2-12 years of age. We evaluated three groups: AU, pervasive developmental disorder-not otherwise specified (PDD-NOS), and NT. Mothers/caregivers provided information at enrollment regarding medical, dental, and dietary exposures. Urine samples from all children were acquired for analyses of porphyrin, creatinine, and Hg. Differences between groups for mean porphyrin and Hg levels were evaluated. Logistic regression analysis was conducted to determine whether porphyrin levels were associated with increased risk of autism.

RESULTS: Mean urinary porphyrin concentrations are naturally high in young children and decline by as much as 2.5-fold between 2 and 12 years of age. Elevated copro- ($p < 0.009$), hexacarboxyl- ($p < 0.01$) and pentacarboxyl- ($p < 0.001$) porphyrin concentrations were significantly associated with AU but not with PDD-NOS. No differences were found between NT and AU in urinary Hg levels or in past Hg exposure as determined by fish consumption, number of dental amalgam fillings, or vaccines received. **CONCLUSIONS: These findings identify disordered porphyrin metabolism as a salient characteristic of autism.** Hg exposures were comparable between diagnostic groups, and a porphyrin pattern consistent with that seen in Hg-exposed adults was not apparent.

108. Mitochondrial dysfunction in autism spectrum disorders: a systematic review and meta-analysis

Molecular Psychiatry advance online publication 25 January 2011;doi: 10.1038/mp.2010.136

Abstract

A comprehensive literature search was performed to collate evidence of mitochondrial dysfunction in autism spectrum disorders (ASDs) with two primary objectives. First, features of mitochondrial dysfunction in the general population of children with ASD were identified. Second, characteristics of mitochondrial dysfunction in children with ASD and concomitant mitochondrial disease (MD) were compared with published literature of two general populations: ASD children without MD, and non-ASD children with MD. The prevalence of MD in the general population of ASD was 5.0% (95% confidence interval 3.2, 6.9%), much higher than found in the general population (~0.01%). The prevalence of abnormal biomarker values of mitochondrial dysfunction was high in ASD, much higher than the prevalence of MD. Variances and mean values of many mitochondrial biomarkers (lactate, pyruvate, carnitine and ubiquinone) were significantly different between ASD and controls. Some markers correlated with ASD severity. Neuroimaging, in vitro and post-mortem brain studies were consistent with an elevated prevalence of mitochondrial dysfunction in ASD. Taken together, these findings suggest children with ASD have a spectrum of mitochondrial dysfunction of differing severity. Eighteen publications representing a total of 112 children with ASD and MD (ASD/MD) were identified. The prevalence of developmental regression (52%), seizures (41%), motor delay (51%), gastrointestinal abnormalities (74%), female gender (39%), and elevated lactate (78%) and pyruvate (45%) was significantly higher in ASD/MD compared with the general ASD population. The prevalence of many of these abnormalities was similar to the general population of children with MD, suggesting that ASD/MD represents a distinct subgroup of children with MD. Most ASD/MD cases (79%) were not associated with genetic abnormalities, raising the possibility of secondary mitochondrial dysfunction. Treatment studies for ASD/MD were limited, although improvements were noted in some studies with carnitine, co-enzyme Q10 and B-vitamins. Many studies suffered from limitations, including small sample sizes, referral or publication biases, and variability in protocols for selecting children for MD workup, collecting mitochondrial biomarkers and defining MD. **Overall, this evidence supports the notion that mitochondrial dysfunction is associated with ASD.** Additional studies are needed to further define the role of mitochondrial dysfunction in ASD.

109. Sensitization effect of thimerosal is mediated in vitro via reactive oxygen species and calcium signaling.

Toxicology. 2010 July - August;274(1-3):1-9. Epub 2010 May 10.

Migdal C, Foggia L, Tailhardat M, Courtellemont P, Haftek M, Serres M.

Thimerosal, a mercury derivative composed of ethyl mercury chloride (EtHgCl) and thiosalicylic acid (TSA), is widely used as a preservative in vaccines and

cosmetic products and causes cutaneous reactions. Since dendritic cells (DCs) play an essential role in the immune response, the sensitization potency of chemicals was studied in vitro using U937, a human promyelomonocytic cell line that is used as a surrogate of monocytic differentiation and activation. Currently, this cell line is under ECVAM (European Center for the Validation of Alternative Methods) validation as an alternative method for discriminating chemicals. Thimerosal and mercury derivatives induced in U937 an overexpression of CD86 and interleukin (IL)-8 secretion similarly to 1-chloro-2,4-dinitrobenzene (DNCB), a sensitizer used as a positive control for DC activation. Non-sensitizers, dichloronitrobenzene (DCNB), TSA and sodium dodecyl sulfate (SDS), an irritant, had no effect. U937 activation was prevented by cell pretreatment with N-acetyl-L-cysteine (NAC) but not with thiol-independent antioxidants except vitamin E which affected CD86 expression by preventing lipid peroxidation of cell membranes. Thimerosal, EtHgCl and DNCB induced glutathione (GSH) depletion and reactive oxygen species (ROS) within 15min; another peak was detected after 2h for mercury compounds only. MitoSOX, a specific mitochondrial fluorescent probe, confirmed that ROS were essentially produced by mitochondria in correlation with its membrane depolarization. Changes in mitochondrial membrane permeability induced by mercury were reversed by NAC but not by thiol-independent antioxidants. Thimerosal and EtHgCl also induced a calcium (Ca²⁺) influx with a peak at 3h, suggesting that Ca²⁺ influx is a secondary event following ROS induction as Ca²⁺ influx was suppressed after pretreatment with NAC but not with thiol-independent antioxidants. Ca²⁺ influx was also suppressed when culture medium was deprived of Ca²⁺ confirming the specificity of the measure. **In conclusion, these data suggest that thimerosal induced U937 activation via oxidative stress from mitochondrial stores and mitochondrial membrane depolarization with a primordial effect of thiol groups.** A cross-talk between ROS and Ca²⁺ influx was demonstrated.

110. [What's going on? The question of time trends in autism.](#)

Public Health Rep. 2004 Nov-Dec;119(6):536-51.

Blaxill MF.

Abstract

Increases in the reported prevalence of autism and autistic spectrum disorders in recent years have fueled concern over possible environmental causes. The author reviews the available survey literature and finds evidence of large increases in prevalence in both the United States and the United Kingdom that cannot be explained by changes in diagnostic criteria or improvements in case ascertainment. Incomplete ascertainment of autism cases in young child populations is the largest source of predictable bias in prevalence surveys; however, this bias has, if anything, worked against the detection of an upward trend in recent surveys. Comparison of autism rates by year of birth for specific geographies provides the strongest basis for trend assessment. Such comparisons show large recent increases in rates of autism and autistic

spectrum disorders in both the U.S. and the U.K. Reported rates of autism in the United States increased from < 3 per 10,000 children in the 1970s to > 30 per 10,000 children in the 1990s, a 10-fold increase. In the United Kingdom, autism rates rose from < 10 per 10,000 in the 1980s to roughly 30 per 10,000 in the 1990s. Reported rates for the full spectrum of autistic disorders rose from the 5 to 10 per 10,000 range to the 50 to 80 per 10,000 range in the two countries. A precautionary approach suggests that the rising incidence of autism should be a matter of urgent public concern.

111. [Vaccines and Autism](#)

Laboratory medicine, September 2002, number 9, volume 33

Bernard Rimland, PhD, Woody McGinnis, MD

Autism Research Institute, San Diego, CA

Excerpt: "**Vaccinations may be one of the triggers for autism. Substantial data demonstrate immune abnormality in many autistic children consistent with impaired resistance to infection, activation of inflammatory response, and autoimmunity. Impaired resistance may predispose to vaccine injury in autism.**"

112. Theoretical aspects of autism: Causes—A review

Journal of Immunotoxicology, January-March 2011, Vol. 8, No. 1, Pages 68-79

Helen V. Ratajczak, PhD

Autism, a member of the pervasive developmental disorders (PDDs), has been increasing dramatically since its description by Leo Kanner in 1943. First estimated to occur in 4 to 5 per 10,000 children, the incidence of autism is now 1 per 110 in the United States, and 1 per 64 in the United Kingdom, with similar incidences throughout the world. Searching information from 1943 to the present in PubMed and Ovid Medline databases, this review summarizes results that correlate the timing of changes in incidence with environmental changes. Autism could result from more than one cause, with different manifestations in different individuals that share common symptoms. Documented causes of autism include genetic mutations and/or deletions, viral infections, and encephalitis following vaccination. **Therefore, autism is the result of genetic defects and/or inflammation of the brain. The inflammation could be caused by a defective placenta, immature blood-brain barrier, the immune response of the mother to infection while pregnant, a premature birth, encephalitis in the child after birth, or a toxic environment.**

113. [Preterm birth, vaccination and neurodevelopmental disorders: a cross-sectional study of 6- to 12-year-old vaccinated and unvaccinated children](#)

Anthony R Mawson, Azad R Bhuiyan, Brian D Ray, Binu Jacob
Department of Epidemiology and Biostatistics, School of Public Health, Jackson State University, Jackson, MS 39213, USA
National Home Education Research Institute, PO Box 13939, Salem, OR 97309, USA

J Transl Sci 3: DOI: 10.15761/JTS.1000187, April 24, 2017

Abstract

From about 8% to 27% of extremely preterm infants develop symptoms of autism spectrum disorder, but the causes are not well understood. Preterm infants receive the same doses of the recommended vaccines and on the same schedule as term infants. The possible role of vaccination in neurodevelopmental disorders (NDD) among premature infants is unknown, in part because pre-licensure clinical trials of pediatric vaccines have excluded ex-preterm infants. This paper explores the association between preterm birth, vaccination and NDD, based on a secondary analysis of data from an anonymous survey of mothers, comparing the birth history and health outcomes of vaccinated and unvaccinated homeschooled children 6 to 12 years of age. A convenience sample of 666 children was obtained, of which 261 (39%) were unvaccinated, 7.5% had an NDD (defined as a learning disability, Attention Deficit Hyperactivity Disorder and/or Autism Spectrum Disorder), and 7.7% were born preterm. **No association was found between preterm birth and NDD in the absence of vaccination, but vaccination was significantly associated with NDD in children born at term (OR 2.7, 95% CI: 1.2, 6.0). However, vaccination coupled with preterm birth was associated with increasing odds of NDD, ranging from 5.4 (95% CI: 2.5, 11.9) compared to vaccinated but non-preterm children, to 14.5 (95% CI: 5.4, 38.7) compared to children who were neither preterm nor vaccinated.** The results of this pilot study suggest clues to the epidemiology and causation of NDD but question the safety of current vaccination practices for preterm infants. Further research is needed to validate and investigate these associations in order to optimize the impact of vaccines on children's health.

114. [Iatrogenic exposure to mercury after hepatitis B vaccination in preterm infants](#)

The Journal of Pediatrics, Volume 136, Issue 5, May 2000, Pages 679–681

Gregory V. Stajich, PharmD, Gaylord P. Lopez, PharmD, ABAT, Sokei W. Harry, MBBS, MPH, William R. Sexson, MD
Mercer University, Southern School of Pharmacy, Atlanta, Georgia; Georgia Poison Center, Grady Health System, Atlanta; Georgia Poison Center, Georgia

Health System, Atlanta and Emory University, School of Medicine, Atlanta, Georgia.

Thimerosal, a derivative of mercury, is used as a preservative in hepatitis B vaccines. We measured total mercury levels before and after the administration of this vaccine in 15 preterm and 5 term infants. Comparison of pre- and post-vaccination mercury levels showed a significant increase in both preterm and term infants after vaccination. **Additionally, post-vaccination mercury levels were significantly higher in preterm infants as compared with term infants.** Because mercury is known to be a potential neurotoxin to infants, further study of its pharmacodynamics is warranted.

115. [Infants born late/moderately preterm are at increased risk for a positive autism screen at 2 years of age.](#)

J Pediatr. 2015 Feb;166(2):269-75.e3. doi: 10.1016/j.jpeds.2014.10.053. Epub 2014 Dec 2.

Guy A1, Seaton SE2, Boyle EM2, Draper ES2, Field DJ2, Manktelow BN2, Marlow N3, Smith LK2, Johnson S4.

1Department of Health Sciences, University of Leicester, Leicester, United Kingdom; School of Psychology, University of Warwick, Coventry, United Kingdom.

2Department of Health Sciences, University of Leicester, Leicester, United Kingdom.

3Department of Academic Neonatology, Institute for Women's Health, University College London, London, United Kingdom.

4Department of Health Sciences, University of Leicester, Leicester, United Kingdom. Electronic address: sjj19@le.ac.uk.

Abstract

OBJECTIVES:

To assess the prevalence of positive screens using the Modified Checklist for Autism in Toddlers (M-CHAT) questionnaire and follow-up interview in late and moderately preterm (LMPT; 32-36 weeks) infants and term-born controls.

STUDY DESIGN:

Population-based prospective cohort study of 1130 LMPT and 1255 term-born infants. Parents completed the M-CHAT questionnaire at 2-years corrected age. Parents of infants with positive questionnaire screens were followed up with a telephone interview to clarify failed items. The M-CHAT questionnaire was re-scored, and infants were classified as true or false positives. Neurosensory, cognitive, and behavioral outcomes were assessed using parent report.

RESULTS:

Parents of 634 (57%) LMPT and 761 (62%) term-born infants completed the M-CHAT questionnaire. LMPT infants had significantly higher risk of a positive questionnaire screen compared with controls (14.5% vs 9.2%; relative risk [RR]

1.58; 95% CI 1.18, 2.11). After follow-up, significantly more LMPT infants than controls had a true positive screen (2.4% vs 0.5%; RR 4.52; 1.51, 13.56). This remained significant after excluding infants with neurosensory impairments (2.0% vs 0.5%; RR 3.67; 1.19, 11.3).

CONCLUSIONS:

LMPT infants are at significantly increased risk for positive autistic screen.

An M-CHAT follow-up interview is essential as screening for autism spectrum disorders is especially confounded in preterm populations. Infants with false positive screens are at risk for cognitive and behavioral problems.

116. [Preterm birth and mortality and morbidity: a population-based quasi-experimental study.](#)

JAMA Psychiatry. 2013 Nov;70(11):1231-40. doi: 10.1001/jamapsychiatry.2013.2107.

D'Onofrio BM1, Class QA, Rickert ME, Larsson H, Långström N, Lichtenstein P.

Department of Psychological and Brain Sciences, Indiana University-Bloomington.

Abstract

IMPORTANCE:

Preterm birth is associated with increased mortality and morbidity. However, previous studies have been unable to rigorously examine whether confounding factors cause these associations rather than the harmful effects of being born preterm.

OBJECTIVE:

To estimate the extent to which the associations between early gestational age and offspring mortality and morbidity are the result of confounding factors by using a quasi-experimental design, the sibling-comparison approach, and by controlling for statistical covariates that varied within families.

DESIGN, SETTING, AND PARTICIPANTS:

A population-based cohort study, combining Swedish registries to identify all individuals born in Sweden from 1973 to 2008 (3,300,708 offspring of 1,736,735 mothers) and link them with multiple outcomes.

MAIN OUTCOMES AND MEASURES:

Offspring mortality (during infancy and throughout young adulthood) and psychiatric (psychotic or bipolar disorder, autism, attention-deficit/hyperactivity disorder, suicide attempts, substance use, and criminality), academic (failing grades and educational attainment), and social (partnering, parenthood, low income, and social welfare benefits) outcomes through 2009.

RESULTS:

In the population, there was a dose-response relationship between early gestation and the outcome measures. **For example, extreme preterm birth (23-27 weeks of gestation) was associated with infant mortality (odds ratio, 288.1; 95% CI, 271.7-305.5), autism (hazard ratio [HR], 3.2; 95% CI, 2.6-4.0), low educational attainment (HR, 1.7; 1.5-2.0), and social welfare benefits (HR,**

1.3; 1.2-1.5) compared with offspring born at term. The associations between early gestation and mortality and psychiatric morbidity generally were robust when comparing differentially exposed siblings and controlling for statistical covariates, whereas the associations with academic and some social problems were greatly or completely attenuated in the fixed-effects models.

CONCLUSIONS AND RELEVANCE:

The mechanisms responsible for the associations between preterm birth and mortality and morbidity are outcome-specific. Associations between preterm birth and mortality and psychiatric morbidity are largely independent of shared familial confounds and measured covariates, consistent with a causal inference.

However, some associations, particularly predicting suicide attempt, educational attainment, and social welfare benefits, are the result of confounding factors. The findings emphasize the importance of both reducing preterm birth and providing wraparound services to all siblings in families with an offspring born preterm.

117. Ancestry of pink disease (infantile acrodynia) identified as a risk factor for autism spectrum disorders.

goal

J Toxicol Environ Health A. 2011 Sep 15;74(18):1185-94.

Shandley K, Austin DW.

Swinburne Autism Bio-Research Initiative (SABRI), Brain and Psychological Sciences Research Centre, Swinburne University of Technology, Hawthorn, Victoria, Australia.

Abstract

Pink disease (infantile acrodynia) was especially prevalent in the first half of the 20th century. Primarily attributed to exposure to mercury (Hg) commonly found in teething powders, the condition was developed by approximately 1 in 500 exposed children. The differential risk factor was identified as an idiosyncratic sensitivity to Hg. Autism spectrum disorders (ASD) have also been postulated to be produced by Hg. Analogous to the pink disease experience, Hg exposure is widespread yet only a fraction of exposed children develop an ASD, suggesting sensitivity to Hg may also be present in children with an ASD. The objective of this study was to test the hypothesis that individuals with a known hypersensitivity to Hg (pink disease survivors) may be more likely to have descendants with an ASD. Five hundred and twenty-two participants who had previously been diagnosed with pink disease completed a survey on the health outcomes of their descendants. The prevalence rates of ASD and a variety of other clinical conditions diagnosed in childhood (attention deficit hyperactivity disorder, epilepsy, Fragile X syndrome, and Down syndrome) were compared to well-established general population prevalence rates. The results showed the prevalence rate of ASD among the grandchildren of pink disease survivors (1 in 22) to be significantly higher than the comparable general population prevalence rate (1 in 160). **The results support the hypothesis that Hg sensitivity may be a heritable/genetic risk factor for ASD.**

118. Risk Factors for Autistic Regression: Results of an Ambispective Cohort Study.

J Child Neurol. 2012 Jan 30. [Epub ahead of print]

Zhang Y, Xu Q, Liu J, Li SC, Xu X., Department of Child Health Care, Children's Hospital of Fudan University, Shanghai, China.

Abstract

A subgroup of children diagnosed with autism experience developmental regression featured by a loss of previously acquired abilities. The pathogeny of autistic regression is unknown, although many risk factors likely exist. To better characterize autistic regression and investigate the association between autistic regression and potential influencing factors in Chinese autistic children, we conducted an ambispective study with a cohort of 170 autistic subjects.

Analyses by multiple logistic regression showed significant correlations between autistic regression and febrile seizures (OR = 3.53, 95% CI = 1.17-10.65, P = .025), as well as with a family history of neuropsychiatric disorders (OR = 3.62, 95% CI = 1.35-9.71, P = .011). This study suggests that febrile seizures and family history of neuropsychiatric disorders are correlated with autistic regression.

119. [Early Seizures Prematurely Unsilence Auditory Synapses to Disrupt Thalamocortical Critical Period Plasticity.](#)

Cell Rep. 2018 May 29;23(9):2533-2540. doi: 10.1016/j.celrep.2018.04.108.

Sun H, Takesian AE, Wang TT, Lippman-Bell JJ, Hensch TK, Jensen FE.

Department of Neurology, Perelman School of Medicine, University of Pennsylvania

F.M. Kirby Neurobiology Center, Department of Neurology, Boston Children's Hospital, Harvard Medical School

Department of Neuroscience, Carleton University

Abstract

Heightened neural excitability in infancy and childhood results in increased susceptibility to seizures. Such early-life seizures are associated with language deficits and autism that can result from aberrant development of the auditory cortex. Here, we show that early-life seizures disrupt a critical period (CP) for tonotopic map plasticity in primary auditory cortex (A1). We show that this CP is characterized by a prevalence of "silent," NMDA-receptor (NMDAR)-only, glutamate receptor synapses in auditory cortex that become

"unsilenced" due to activity-dependent AMPA receptor (AMPA) insertion. Induction of seizures prior to this CP occludes tonotopic map plasticity by prematurely unsilencing NMDAR-only synapses. Further, brief treatment with the AMPAR antagonist NBQX following seizures, prior to the CP, prevents synapse unsilencing and permits subsequent A1 plasticity. These findings reveal that early-life seizures modify CP regulators and suggest that therapeutic targets for early post-seizure treatment can rescue CP plasticity.

120. [MMR vaccination and febrile seizures: evaluation of susceptible subgroups and long-term prognosis.](#)

Vestergaard M1, Hviid A, Madsen KM, Wohlfahrt J, Thorsen P, Schendel D, Melbye M, Olsen J.

JAMA. 2004 Jul 21;292(3):351-7.

Abstract

CONTEXT:

The rate of febrile seizures increases following measles, mumps, and rubella (MMR) vaccination but it is unknown whether the rate varies according to personal or family history of seizures, perinatal factors, or socioeconomic status. Furthermore, little is known about the long-term outcome of febrile seizures following vaccination.

OBJECTIVES:

To estimate incidence rate ratios (RRs) and risk differences of febrile seizures following MMR vaccination within subgroups of children and to evaluate the clinical outcome of febrile seizures following vaccination.

DESIGN, SETTING, AND PARTICIPANTS:

A population-based cohort study of all children born in Denmark between January 1, 1991, and December 31, 1998, who were alive at 3 months; 537,171 children were followed up until December 31, 1999, by using data from the Danish Civil Registration System and 4 other national registries.

MAIN OUTCOME MEASURES:

Incidence of first febrile seizure, recurrent febrile seizures, and subsequent epilepsy.

RESULTS:

A total of 439,251 children (82%) received MMR vaccination and 17,986 children developed febrile seizures at least once; 973 of these febrile seizures occurred within 2 weeks of MMR vaccination. The RR of febrile seizures increased during the 2 weeks following MMR vaccination (2.75; 95% confidence interval [CI], 2.55-2.97), and thereafter was close to the observed RR for nonvaccinated children. The RR did not vary significantly in the subgroups of children that had been defined by their family history of seizures, perinatal factors, or socioeconomic status. At 15 to 17 months, the risk difference of febrile seizures within 2 weeks following MMR vaccination was 1.56 per 1000 children overall (95% CI, 1.44-1.68), 3.97 per 1000 (95% CI, 2.90-5.40) for siblings of children with a history of febrile seizures, and 19.47 per 1000 (95% CI, 16.05-23.55) for children with a

personal history of febrile seizures. Children with febrile seizures following MMR vaccinations had a slightly increased rate of recurrent febrile seizures (RR, 1.19; 95% CI, 1.01-1.41) but no increased rate of epilepsy (RR, 0.70; 95% CI, 0.33-1.50) compared with children who were nonvaccinated at the time of their first febrile seizure.

CONCLUSIONS:

MMR vaccination was associated with a transient increased rate of febrile seizures but the risk difference was small even in high-risk children. The long-term rate of epilepsy was not increased in children who had febrile seizures following vaccination compared with children who had febrile seizures of a different etiology.

121. [Common variants associated with general and MMR vaccine-related febrile seizures](#)

Bjarke Feenstra, Björn Pasternak, Frank Geller, Lisbeth Carstensen, Tongfei Wang, Fen Huang, Jennifer L Eitson, Mads V Hollegaard, Henrik Svanström, Mogens Vestergaard, David M Hougaard, John W Schoggins, Lily Yeh Jan, Mads Melbye & Anders Hviid

Nature Genetics (2014) doi:10.1038/ng.3129

Received 20 May 2014 Accepted 03 October 2014 Published online 26 October 2014

Abstract

Febrile seizures represent a serious adverse event following measles, mumps and rubella (MMR) vaccination. We conducted a series of genome-wide association scans comparing children with MMR-related febrile seizures, children with febrile seizures unrelated to vaccination and controls with no history of febrile seizures. Two loci were distinctly associated with MMR-related febrile seizures, harboring the interferon-stimulated gene IFI44L (rs273259: $P = 5.9 \times 10^{-12}$ versus controls, $P = 1.2 \times 10^{-9}$ versus MMR-unrelated febrile seizures) and the measles virus receptor CD46 (rs1318653: $P = 9.6 \times 10^{-11}$ versus controls, $P = 1.6 \times 10^{-9}$ versus MMR-unrelated febrile seizures). Furthermore, four loci were associated with febrile seizures in general, implicating the sodium channel genes SCN1A (rs6432860: $P = 2.2 \times 10^{-16}$) and SCN2A (rs3769955: $P = 3.1 \times 10^{-10}$), a TMEM16 family gene (ANO3; rs114444506: $P = 3.7 \times 10^{-20}$) and a region associated with magnesium levels (12q21.33; rs11105468: $P = 3.4 \times 10^{-11}$). Finally, we show the functional relevance of ANO3 (TMEM16C) with electrophysiological experiments in wild-type and knockout rats.

122. [Adverse events following 12 and 18 month vaccinations: a population-based, self-controlled case series analysis.](#)

PLoS One. 2011;6(12):e27897. Epub 2011 Dec 12.

Wilson K, Hawken S, Kwong JC, Deeks S, Crowcroft NS, Van Walraven C, Potter BK, Chakraborty P, Keelan J, Pluscauskas M, Manuel D. Department of Medicine, Ottawa Hospital Research Institute, University of Ottawa, Ottawa, Canada. kwilson@ohri.ca

Abstract

BACKGROUND:

Live vaccines have distinct safety profiles, potentially causing systemic reactions one to 2 weeks after administration. In the province of Ontario, Canada, live MMR vaccine is currently recommended at age 12 months and 18 months.

METHODS:

Using the self-controlled case series design we examined 271,495 12 month vaccinations and 184,312 18 month vaccinations to examine the relative incidence of the composite endpoint of emergency room visits or hospital admissions in consecutive one day intervals following vaccination. These were compared to a control period 20 to 28 days later. In a post-hoc analysis we examined the reasons for emergency room visits and the average acuity score at presentation for children during the at-risk period following the 12 month vaccine.

RESULTS:

Four to 12 days post 12 month vaccination, children had a 1.33 (1.29-1.38) increased relative incidence of the combined endpoint compared to the control period, or at least one event during the risk interval for every 168 children vaccinated. Ten to 12 days post 18 month vaccination, the relative incidence was 1.25 (95%, 1.17-1.33) which represented at least one excess event for every 730 children vaccinated. The primary reason for increased events was statistically significant elevations in emergency room visits following all vaccinations. There were non-significant increases in hospital admissions. **There were an additional 20 febrile seizures for every 100,000 vaccinated at 12 months.**

CONCLUSIONS:

There are significantly elevated risks of primarily emergency room visits approximately one to two weeks following 12 and 18 month vaccination. Future studies should examine whether these events could be predicted or prevented.

123. [Reduced GABAergic Action in the Autistic Brain.](#)

Curr Biol. 2015 Dec 16. pii: S0960-9822(15)01413-X. doi: 10.1016/j.cub.2015.11.019.

Robertson CE1, Ratai EM2, Kanwisher N3.

1Harvard Society of Fellows, Harvard University, Cambridge, MA 02138, USA; McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, MA 02138, USA. Electronic address: carolinerobertson@fas.harvard.edu.

2Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA.

3McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, MA 02138, USA.

Abstract

An imbalance between excitatory/inhibitory neurotransmission has been posited as a central characteristic of the neurobiology of autism [1], inspired in part by the striking prevalence of seizures among individuals with the disorder [2]. Evidence supporting this hypothesis has specifically implicated the signaling pathway of the inhibitory neurotransmitter, γ -aminobutyric acid (GABA), in this putative imbalance: GABA receptor genes have been associated with autism in linkage and copy number variation studies [3-7], fewer GABA receptor subunits have been observed in the post-mortem tissue of autistic individuals [8, 9], and GABAergic signaling is disrupted across heterogeneous mouse models of autism [10]. Yet, empirical evidence supporting this hypothesis in humans is lacking, leaving a gulf between animal and human studies of the condition. Here, we present a direct link between GABA signaling and autistic perceptual symptomatology. We first demonstrate a robust, replicated autistic deficit in binocular rivalry [11], a basic visual function that is thought to rely on the balance of excitation/inhibition in visual cortex [12-15]. **Then, using magnetic resonance spectroscopy, we demonstrate a tight linkage between binocular rivalry dynamics in typical participants and both GABA and glutamate levels in the visual cortex. Finally, we show that the link between GABA and binocular rivalry dynamics is completely and specifically absent in autism.** These results suggest a disruption in inhibitory signaling in the autistic brain and forge a translational path between animal and human models of the condition.

124. [Administration of thimerosal to infant rats increases overflow of glutamate and aspartate in the prefrontal cortex: protective role of dehydroepiandrosterone sulfate.](#)

Neurochem Res. 2012 Feb;37(2):436-47. Epub 2011 Oct 21.

Duszczyk-Budhathoki M, Olczak M, Lehner M, Majewska MD. Marie Curie Chairs Program, Department of Pharmacology and Physiology of Nervous System, Institute of Psychiatry and Neurology, 02-957, Warsaw, Poland.

Abstract

Thimerosal, a mercury-containing vaccine preservative, is a suspected factor in the etiology of neurodevelopmental disorders. We previously showed that its administration to infant rats causes behavioral, neurochemical and neuropathological abnormalities similar to those present in autism. Here we examined, using microdialysis, the effect of thimerosal on extracellular levels of neuroactive amino acids in the rat prefrontal cortex (PFC). Thimerosal administration (4 injections, i.m., 240 μ g Hg/kg on postnatal days 7, 9, 11, 15) induced lasting changes in amino acid overflow: an increase of glutamate and aspartate accompanied by a decrease of glycine and alanine; measured 10-14

weeks after the injections. Four injections of thimerosal at a dose of 12.5 µg Hg/kg did not alter glutamate and aspartate concentrations at microdialysis time (but based on thimerosal pharmacokinetics, could have been effective soon after its injection). Application of thimerosal to the PFC in perfusion fluid evoked a rapid increase of glutamate overflow. Coadministration of the neurosteroid, dehydroepiandrosterone sulfate (DHEAS; 80 mg/kg; i.p.) prevented the thimerosal effect on glutamate and aspartate; the steroid alone had no influence on these amino acids. Coapplication of DHEAS with thimerosal in perfusion fluid also blocked the acute action of thimerosal on glutamate. In contrast, DHEAS alone reduced overflow of glycine and alanine, somewhat potentiating the thimerosal effect on these amino acids. **Since excessive accumulation of extracellular glutamate is linked with excitotoxicity, our data imply that neonatal exposure to thimerosal-containing vaccines might induce excitotoxic brain injuries, leading to neurodevelopmental disorders.** DHEAS may partially protect against mercurials-induced neurotoxicity.

125. Neonatal Administration of Thimerosal Causes Persistent Changes in Mu Opioid Receptors in the Rat Brain

Neurochem Res. 2010 November; 35(11): 1840–1847.

Mieszko Olczak, Michalina Duszczyk, Pawel Mierzejewski, Teresa Bobrowicz, and Maria Dorota Majewska¹, Department of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, Sobieskiego 9 str., 02-957 Warsaw, Poland, Department of Forensic Medicine, Medical University of Warsaw, Oczeni 1 str., 02-007 Warsaw, Poland, Department of Neuropathology, Institute of Psychiatry and Neurology, 02-957 Warsaw, Poland, Department of Biology and Environmental Science, University of Cardinal Stefan Wyszyński, Wóycickiego Str. 1/3, 01-815 Warsaw, Poland

Abstract

Thimerosal added to some pediatric vaccines is suspected in pathogenesis of several neurodevelopmental disorders. Our previous study showed that thimerosal administered to suckling rats causes persistent, endogenous opioid-mediated hypoalgesia. Here we examined, using immunohistochemical staining technique, the density of µ-opioid receptors (MORs) in the brains of rats, which in the second postnatal week received four i.m. injections of thimerosal at doses 12, 240, 1,440 or 3,000 µg Hg/kg. The periaqueductal gray, caudate putamen and hippocampus were examined. Thimerosal administration caused dose-dependent statistically significant increase in MOR densities in the periaqueductal gray and caudate putamen, but decrease in the dentate gyrus, where it was accompanied by the presence of degenerating neurons and loss of synaptic vesicle marker (synaptophysin). **These data document that exposure to thimerosal during early postnatal life produces lasting alterations in the densities of brain opioid receptors along with other neuropathological changes, which may disturb brain development.**

126. Unanswered Questions: A Review of Compensated Cases of Vaccine-Induced Brain Injury

Pace Environmental Law Review, vol. 28, no. 2, 2011

Mary Holland, Louis Conte, Robert Krakow and Lisa Colin

Executive Summary

In 1986, Congress created the Vaccine Injury Compensation Program (VICP) under the National Childhood Vaccine Injury Act (1986 Law). This Program has original jurisdiction for children's claims of vaccine injury. Because almost all children receive multiple vaccinations for daycare and school, it is critically important that the Program provides fundamental fairness, due process and transparency.

This empirical investigation, published in a peer-reviewed law journal, examines claims that the VICP compensated for vaccine-induced encephalopathy and seizure disorder. The VICP has compensated approximately 2,500 claims of vaccine injury since the inception of the program. This study found 83 cases of acknowledged vaccine-induced brain damage that include autism, a disorder that affects speech, social communication and behavior. In 21 published cases of the Court of Federal Claims, which administers the VICP, the Court stated that the petitioners had autism or described autism unambiguously. In 62 remaining cases, the authors identified settlement agreements where Health and Human Services (HHS) compensated children with vaccine-induced brain damage, who also have autism or an autism spectrum disorder.

Parents reported the existence of autism in telephone interviews and supplied supplemental materials including medical diagnoses, school records, and completed, standard autism screening questionnaires to verify their reports. In 39 of the 83 cases, or 47% of the cases of vaccine injury reviewed, there is confirmation of autism or autism spectrum disorder beyond parental report.

This finding of autism in compensated cases of vaccine injury is significant. U.S. government spokespeople have been asserting no vaccine-autism link for more than a decade. This finding calls into question the decisions of the Court of Federal Claims in the Omnibus Autism Proceeding in 2009 and 2010 and the statement of Health and Human Services on its website that "HHS has never concluded in any case that autism was caused by vaccination."

Using publicly available information, the investigation shows that the VICP has been compensating cases of vaccine-induced brain damage associated with autism for more than twenty years. This investigation suggests that officials at HHS, the Department of Justice and the Court of Federal Claims may have been aware of this association but failed to publicly disclose it.

The study calls on Congress to thoroughly investigate the VICP, including a medical investigation of compensated claims of vaccine injury. This investigation calls on Congress to get answers to these critically important unanswered questions.

127. [Integrating experimental \(in vitro and in vivo\) neurotoxicity studies of low-dose thimerosal relevant to vaccines.](#)

Neurochem Res. 2011 Jun;36(6):927-38. doi: 10.1007/s11064-011-0427-0. Epub 2011 Feb 25.

Dórea JG, Faculty of Health Sciences, Universidade de Brasília, CP 04322, 70919-970, Brasília, DF, Brazil. dorea@rudah.com.br

Abstract

There is a need to interpret neurotoxic studies to help deal with uncertainties surrounding pregnant mothers, newborns and young children who must receive repeated doses of Thimerosal-containing vaccines (TCVs). This review integrates information derived from emerging experimental studies (in vitro and in vivo) of low-dose Thimerosal (sodium ethyl mercury thiosalicylate). Major databases (PubMed and Web-of-science) were searched for in vitro and in vivo experimental studies that addressed the effects of low-dose Thimerosal (or ethylmercury) on neural tissues and animal behaviour. Information extracted from studies indicates that: (a) activity of low doses of Thimerosal against isolated human and animal brain cells was found in all studies and is consistent with Hg neurotoxicity; (b) the neurotoxic effect of ethylmercury has not been studied with co-occurring adjuvant-AI in TCVs; (c) animal studies have shown that exposure to Thimerosal-Hg can lead to accumulation of inorganic Hg in brain, and that (d) doses relevant to TCV exposure possess the potential to affect human neuro-development. Thimerosal at concentrations relevant for infants' exposure (in vaccines) is toxic to cultured human-brain cells and to laboratory animals. The persisting use of TCV (in developing countries) is counterintuitive to global efforts to lower Hg exposure and to ban Hg in medical products; its continued use in TCV requires evaluation of a sufficiently nontoxic level of ethylmercury compatible with repeated exposure (co-occurring with adjuvant-AI) during early life.

128. Hepatitis B vaccine induces apoptotic death in Hepa1-6 cells

Apoptosis. 2012 Jan 17. Hamza H, Cao J, Li X, Li C, Zhu M, Zhao S.

Key Lab of Agricultural Animal Genetics, Breeding, and Reproduction of Ministry of Education, College of Animal Science and Technology, Huazhong Agricultural University, Wuhan, 430070, People's Republic of China, Heyam68_hamza@yahoo.com.

Abstract

Vaccines can have adverse side-effects, and these are predominantly associated with the inclusion of chemical additives such as aluminum hydroxide adjuvant. The objective of this study was to establish an in vitro model system amenable to mechanistic investigations of cytotoxicity induced by hepatitis B vaccine, and to investigate the mechanisms of vaccine-induced cell death. The mouse liver hepatoma cell line Hepa1-6 was treated with two doses of adjuvanted (aluminium hydroxide) hepatitis B vaccine (0.5 and 1 µg protein per ml) and cell integrity was measured after 24, 48 and 72 h. Hepatitis B vaccine exposure increased cell apoptosis as detected by flow cytometry and TUNEL assay. Vaccine exposure was accompanied by significant increases in the levels of activated caspase 3, a key effector caspase in the apoptosis cascade. Early transcriptional events were detected by qRT-PCR. We report that hepatitis B vaccine exposure resulted in significant upregulation of the key genes encoding caspase 7, caspase 9, Inhibitor caspase-activated DNase (ICAD), Rho-associated coiled-coil containing protein kinase 1 (ROCK-1), and Apoptotic protease activating factor 1 (Apaf-1). Upregulation of cleaved caspase 3,7 were detected by western blot in addition to Apaf-1 and caspase 9 expressions argues that cell death takes place via the intrinsic apoptotic pathway in which release of cytochrome c from the mitochondria triggers the assembly of a caspase activation complex. **We conclude that exposure of Hepa1-6 cells to a low dose of adjuvanted hepatitis B vaccine leads to loss of mitochondrial integrity, apoptosis induction, and cell death, apoptosis effect was observed also in C2C12 mouse myoblast cell line after treated with low dose of vaccine (0.3, 0.1, 0.05 µg/ml).** In addition In vivo apoptotic effect of hepatitis B vaccine was observed in mouse liver.

129. [Thimerosal Induces Apoptosis in a Neuroblastoma Model via the cJun N-Terminal Kinase Pathway.](#)

Toxicological Sciences 92 (1). 246-253

ML Herdman, A Marcelo, Y Huang, RM Niles, Dhar S & Kinningham KK. (2006).

Department of Pharmacology, Joan C. Edwards School of Medicine, 1542 Spring Valley Drive, Marshall University, Huntington, WV USA

EXCERPT: In recent years, controversy has surrounded the use of thimerosal in vaccines as mercury is a known neurotoxin and nephrotoxin. Since the controversy began in the late 1990's, much of the thimerosal has been removed from vaccines administered to children in the United States. However, it remains in some, such as the influenza vaccine, and is added to multidose vials used in countries around the world. Studies concentrating on thimerosal-induced neurotoxicity are limited, and exposure guidelines, such as those set by the Food and Drug Administration, are based on research with methylmercury.

Interestingly, some in vitro and in vivo studies suggest that ethylmercury may react differently than methylmercury (Aschner and Aschner, 1990; Harry et al., 2004; Magos et al., 1985). Few studies with thimerosal have focused on determining specific signaling pathways involved in neurotoxicity. Establishing these pathways may be an important step in discovering methods of alleviating toxic outcomes in patients exposed to thimerosal....Our study is the first demonstration that thimerosal can induce the activation of JNK and AP-1 in the SK-N-SH neuroblastoma cell line. We showed that activation of cJun and AP-1 transcriptional activity following thimerosal treatment does not appear to be involved in the induction of apoptosis, as demonstrated with the studies using the cJun dominant negative. Furthermore, we were able to show that JNK is an essential upstream component of this pathway through the use of the JNK inhibitor SP600125. This compound was able to attenuate activation of downstream components of mitochondrial-mediated cell death and subsequently protect the cells from apoptosis. These results are significant because identifying specific signaling pathways activated in response to thimerosal exposure presents pharmacological targets for attenuating potential toxicity in patients exposed to thimerosal-containing products.

130. Maternal thimerosal exposure results in aberrant cerebellar oxidative stress, thyroid hormone metabolism, and motor behavior in rat pups; sex- and strain-dependent effects.

Cerebellum. 2012 Jun;11(2):575-86. doi: 10.1007/s12311-011-0319-5.

Sulkowski ZL, Chen T, Midha S, Zavacki AM, Sajdel-Sulkowska EM, Department of Psychiatry, Harvard Medical School and Brigham and Women's Hospital, Boston, MA, USA.

Abstract

Methylmercury (Met-Hg) and ethylmercury (Et-Hg) are powerful toxicants with a range of harmful neurological effects in humans and animals. While Met-Hg is a recognized trigger of oxidative stress and an endocrine disruptor impacting neurodevelopment, the developmental neurotoxicity of Et-Hg, a metabolite of thimerosal (TM), has not been explored. We hypothesized that TM exposure during the perinatal period impairs central nervous system development, and specifically the cerebellum, by the mechanism involving oxidative stress. To test this, spontaneously hypertensive rats (SHR) or Sprague-Dawley (SD) rat dams were exposed to TM (200 µg/kg body weight) during pregnancy (G10-G15) and lactation (P5-P10). Male and female neonates were evaluated for auditory and motor function; cerebella were analyzed for oxidative stress and thyroid metabolism. TM exposure resulted in a delayed startle response in SD neonates and decreased motor learning in SHR male (22.6%), in SD male (29.8%), and in SD female (55.0%) neonates. TM exposure also resulted in a significant increase in cerebellar levels of the oxidative stress marker 3-nitrotyrosine in SHR female (35.1%) and SD male (14.0%) neonates. The activity of cerebellar type 2 deiodinase, responsible for local intra-brain conversion of thyroxine to the active hormone, 3',3,5-triiodothyronine (T3), was significantly decreased in TM-exposed

SHR male (60.9%) pups. This coincided with an increased (47.0%) expression of a gene negatively regulated by T3, *Odf4* suggesting local intracerebellar T3 deficiency. **Our data thus demonstrate a negative neurodevelopmental impact of perinatal TM exposure which appears to be both strain- and sex-dependent.**

131. [The rise in autism and the role of age at diagnosis.](#)

Epidemiology. 2009 Jan;20(1):84-90. doi: 10.1097/EDE.0b013e3181902d15.

Hertz-Picciotto I, Delwiche L., Department of Public Health Sciences, University of California, Davis, California 95616, USA. ihp@ucdavis.edu

Abstract

BACKGROUND:

Autism prevalence in California, based on individuals eligible for state-funded services, rose throughout the 1990s. The extent to which this trend is explained by changes in age at diagnosis or inclusion of milder cases has not been previously evaluated.

METHODS:

Autism cases were identified from 1990 through 2006 in databases of the California Department of Developmental Services, which coordinates services for individuals with specific developmental disorders. The main outcomes were population incident cases younger than age 10 years for each quarter, cumulative incidence by age and birth year, age-specific incidence rates stratified by birth year, and proportions of diagnoses by age across birth years.

RESULTS:

Autism incidence in children rose throughout the period. Cumulative incidence to 5 years of age per 10,000 births rose consistently from 6.2 for 1990 births to 42.5 for 2001 births. Age-specific incidence rates increased most steeply for 2- and 3-year olds. The proportion diagnosed by age 5 years increased only slightly, from 54% for 1990 births to 61% for 1996 births. Changing age at diagnosis can explain a 12% increase, and inclusion of milder cases, a 56% increase.

CONCLUSIONS:

Autism incidence in California shows no sign yet of plateauing. Younger ages at diagnosis, differential migration, changes in diagnostic criteria, and inclusion of milder cases do not fully explain the observed increases. Other artifacts have yet to be quantified, and as a result, the extent to which the continued rise represents a true increase in the occurrence of autism remains unclear.

132. [Slow CCL2-dependent translocation of biopersistent particles from muscle to brain](#)

Zakir Khan^{1,2}, Christophe Combadière^{3,4,5}, François-Jérôme Authier^{1,2,6}, Valérie Itier^{1,11,2}, François Lux^{7,8}, Christopher Exley⁹, Meriem Mahrouf-Yorgov^{1,11,2}, Xavier Decrouy^{1,2}, Philippe Moretto¹⁰, Olivier Tillement^{7,8},

Romain K Gherardi^{1,12,2,6*†} and Josette Cadusseau^{1,11,12,2*†}

Author Affiliations

1 Inserm, U955, 8 rue du Général Sarrail, Créteil, 94010, France

2 Université Paris Est, Faculté de Médecine, 8 rue du Général Sarrail, Créteil, 94010, France

3 Inserm, UMR-S 945, 91 Boulevard de l'Hôpital, Paris, 75013, France

4 Université Pierre et Marie Curie, Faculté de Médecine, 11 Boulevard de l'Hôpital, Paris, 75013, France

5 AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Service d'Immunologie, 11 Boulevard de l'Hôpital, Paris, 75013, France

6 AP-HP, Hôpital H. Mondor - A. Chenevier, Service d'Histologie, Centre de Référence Neuromusculaire GNMH, 51 Avenue du Maréchal de Lattre de Tassigny, Créteil, 94000, France

7 CNRS UMR 5620, Laboratoire de Physico-Chimie des Matériaux Luminescents, 2 rue Victor Grignard, Villeurbanne, 69622, France

8 Université Claude Bernard Lyon 1, 2 rue Victor Grignard, Villeurbanne, 69622, France

9 The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, UK

10 CNRS UMR 5797, Centre d'Etudes Nucléaires de Bordeaux Gradignan, Allée du haut Vignaud, Gradignan, 33175, France

11 Faculté des Sciences et Technologie, UPEC, 61 Avenue du Général de Gaulle, Créteil, France

12 IMRB Team 10, Faculté de Médecine, 8 rue du Général Sarrail, Créteil, F-94010, France

BMC Medicine 2013, 11:99 doi:10.1186/1741-7015-11-99, 4 April 2013

Abstract

Background

Long-term biodistribution of nanomaterials used in medicine is largely unknown. This is the case for alum, the most widely used vaccine adjuvant, which is a nanocrystalline compound spontaneously forming micron/submicron-sized agglomerates. Although generally well tolerated, alum is occasionally detected within monocyte-lineage cells long after immunization in presumably susceptible

individuals with systemic/neurologic manifestations or autoimmune (inflammatory) syndrome induced by adjuvants (ASIA).

Methods:

On the grounds of preliminary investigations in 252 patients with alum-associated ASIA showing both a selective increase of circulating CCL2, the major monocyte chemoattractant, and a variation in the CCL2 gene, we designed mouse experiments to assess biodistribution of vaccine-derived aluminum and of alum-particle fluorescent surrogates injected in muscle. Aluminum was detected in tissues by Morin stain and particle induced X-ray emission (PIXE) Both 500 nm fluorescent latex beads and vaccine alum agglomerates-sized nanohybrids (Al-Rho) were used.

Results:

Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection. Both fluorescent materials injected into muscle translocated to draining lymph nodes (DLNs) and thereafter were detected associated with phagocytes in blood and spleen. Particles linearly accumulated in the brain up to the six-month endpoint; they were first found in perivascular CD11b+ cells and then in microglia and other neural cells. DLN ablation dramatically reduced the biodistribution. Cerebral translocation was not observed after direct intravenous injection, but significantly increased in mice with chronically altered blood-brain-barrier. Loss/gain-of-function experiments consistently implicated CCL2 in systemic diffusion of Al-Rho particles captured by monocyte-lineage cells and in their subsequent neurodelivery. Stereotactic particle injection pointed out brain retention as a factor of progressive particle accumulation.

Conclusion

Nanomaterials can be transported by monocyte-lineage cells to DLNs, blood and spleen, and, similarly to HIV, may use CCL2-dependent mechanisms to penetrate the brain. This occurs at a very low rate in normal conditions explaining good overall tolerance of alum despite its strong neurotoxic potential. **However, continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe, especially in the case of overimmunization or immature/altered blood brain barrier or high constitutive CCL-2 production.**

133. [Thimerosal and autism? A plausible hypothesis that should not be dismissed.](#)

Med Hypotheses. 2004;62(5):788-94.

Blaxill MF, Redwood L, Bernard S.

Abstract

The autism-mercury hypothesis first described by Bernard et al. has generated much interest and controversy. The Institute of Medicine (IOM) reviewed the connection between mercury-containing vaccines and neurodevelopmental

disorders, including autism. They concluded that the hypothesis was biologically plausible but that there was insufficient evidence to accept or reject a causal connection and recommended a comprehensive research program. Without citing new experimental evidence, a number of observers have offered opinions on the subject, some of which reject the IOM's conclusions. In a recent review, Nelson and Bauman argue that a link between the preservative thimerosal, the source of the mercury in childhood vaccines, is improbable. In their defense of thimerosal, these authors take a narrow view of the original hypothesis, provide no new evidence, and rely on selective citations and flawed reasoning. We provide evidence here to refute the Nelson and Bauman critique and to defend the autism-mercury hypothesis.

134. Autism Spectrum Disorders in Relation to Distribution of Hazardous Air Pollutants in the SF Bay Area

Environmental Health Perspectives – Vol. 114 No. 9, September, 2006

Gayle Windham, Div. of Environmental and Occupational Disease Control,
California Department of Health Services

284 ASD children & 657 controls, born in 1994 in Bay Area, were assigned exposure levels by birth tract for 19 chemicals. Risks for autism were elevated by 50% in tracts with the highest chlorinated solvents and heavy metals. The highest risk compounds were mercury, cadmium, nickel, trichloroethylene, and vinyl chloride, and the risk from heavy metals was almost twice as high as solvents.

Excerpt: “Our results suggest a potential association between autism and estimated metal concentrations, and possibly solvents, in ambient air around the birth residence.”

135. Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas

Health Place. 2006 Jun;12(2):203-9.

Palmer RF, Blanchard S, Stein Z, Mandell D, Miller C.

University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, 7703 Floyd Curl Drive, San Antonio, Texas

Abstract

The association between environmentally released mercury, special education and autism rates in Texas was investigated using data from the Texas Education Department and the United States Environmental Protection Agency. A Poisson regression analysis adjusted for school district population size, economic and

demographic factors was used. There was a significant increase in the rates of special education students and autism rates associated with increases in environmentally released mercury. On average, for each 1,000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism. The association between environmentally released mercury and special education rates were fully mediated by increased autism rates. This ecological study suggests the need for further research regarding the association between environmentally released mercury and developmental disorders such as autism. These results have implications for policy planning and cost analysis.

136. [Autism spectrum disorder prevalence and proximity to industrial facilities releasing arsenic, lead or mercury.](#)

Sci Total Environ. 2015 Dec 1;536:245-51. doi: 10.1016/j.scitotenv.2015.07.024. Epub 2015 Jul 25.

Dickerson AS¹, Rahbar MH², Han I³, Bakian AV⁴, Bilder DA⁵, Harrington RA⁶, Pettygrove S⁷, Durkin M⁸, Kirby RS⁹, Wingate MS¹⁰, Tian LH¹¹, Zahorodny WM¹², Pearson DA¹³, Moyé LA^{3rd}¹⁴, Baio J¹⁵.

¹Biostatistics/Epidemiology/Research Design (BERD) Core, Center for Clinical and Translational Sciences (CCTS), University of Texas Health Science Center at Houston, Houston, TX 77030, USA. Electronic address:

Aisha.S.Dickerson@uth.tmc.edu.

²Biostatistics/Epidemiology/Research Design (BERD) Core, Center for Clinical and Translational Sciences (CCTS), University of Texas Health Science Center at Houston, Houston, TX 77030, USA; Division of Epidemiology, Human Genetics, and Environmental Sciences (EHGES), University of Texas School of Public Health at Houston, University of Texas Health Science Center at Houston, Houston, TX 77030, USA. Electronic address:

Mohammad.H.Rahbar@uth.tmc.edu.

³Division of Epidemiology, Human Genetics, and Environmental Sciences (EHGES), University of Texas School of Public Health at Houston, University of Texas Health Science Center at Houston, Houston, TX 77030, USA. Electronic address: Inkyu.Han@uth.tmc.edu.

⁴Division of Child Psychiatry, Department of Psychiatry, University of Utah School of Medicine, Salt Lake City, UT 84108, USA. Electronic address:

Amanda.Bakian@hsc.utah.edu.

⁵Division of Child Psychiatry, Department of Psychiatry, University of Utah School of Medicine, Salt Lake City, UT 84108, USA. Electronic address:

Deborah.Bilder@hsc.utah.edu.

⁶Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 21205, USA. Electronic address: rharrin5@jhu.edu.

⁷Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, AZ 85721, USA. Electronic address: sydney@u.arizona.edu.

8Waisman Center, University of Wisconsin School of Medicine and Public Health, Madison, WI 53726, USA. Electronic address: mdurkin@wisc.edu.

9Department of Community and Family Health, College of Public Health, University of South Florida, Tampa, FL 33612, USA. Electronic address: rkirby@health.usf.edu.

10Department of Health Care Organization and Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL 35205, USA.. Electronic address: mslay@uab.edu.

11National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. Electronic address: bsr4@cdc.gov.

12Department of Pediatrics, Rutgers New Jersey Medical School, Newark, NJ 07103, USA. Electronic address: zahorodn@njms.rutgers.edu.

13Department of Psychiatry and Behavioral Sciences, University of Texas Medical School, Houston, TX 77054, USA. Electronic address: Deborah.A.Pearson@uth.tmc.edu.

14Division of Biostatistics, University of Texas School of Public Health at Houston, Houston, TX 77030, USA. Electronic address: Lemuel.A.Moye@uth.tmc.edu.

15National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. Electronic address: xzb1@cdc.gov.

Abstract

Prenatal and perinatal exposures to air pollutants have been shown to adversely affect birth outcomes in offspring and may contribute to prevalence of autism spectrum disorder (ASD). **For this ecologic study, we evaluated the association between ASD prevalence, at the census tract level, and proximity of tract centroids to the closest industrial facilities releasing arsenic, lead or mercury** during the 1990s. We used 2000 to 2008 surveillance data from five sites of the Autism and Developmental Disabilities Monitoring (ADDM) network and 2000 census data to estimate prevalence. Multi-level negative binomial regression models were used to test associations between ASD prevalence and proximity to industrial facilities in existence from 1991 to 1999 according to the US Environmental Protection Agency Toxics Release Inventory (USEPA-TRI). Data for 2489 census tracts showed that after adjustment for demographic and socio-economic area-based characteristics, ASD prevalence was higher in census tracts located in the closest 10th percentile compared of distance to those in the furthest 50th percentile (adjusted RR=1.27, 95% CI: (1.00, 1.61), P=0.049). **The findings observed in this study are suggestive of the association between urban residential proximity to industrial facilities emitting air pollutants and higher ASD prevalence.**

137. [Inflammatory Responses to Trivalent Influenza Virus Vaccine Among Pregnant Women](#)

Vaccine. 2011 Nov 8;29(48):8982-7. doi: 10.1016/j.vaccine.2011.09.039. Epub 2011 Sep 22.

Christian LM, Iams JD, Porter K, Glaser R.

Department of Psychiatry, The Ohio State University Medical Center, Columbus, OH

Abstract

Objective

In the U.S., seasonal trivalent influenza vaccination (TIV) is currently universally recommended for all pregnant women. However, data on the maternal inflammatory response to vaccination is lacking and would better delineate the safety and clinical utility of immunization. In addition, for research purposes, vaccination has been used as a mild immune trigger to examine in vivo inflammatory responses in nonpregnant adults. The utility of such a model in pregnancy is unknown. Given the clinical and empirical justifications, the current study examined the magnitude, time course, and variance in inflammatory responses following seasonal influenza virus vaccination among pregnant women.

Methods

Women were assessed prior to and at one day (n=15), two days (n=10), or approximately one week (n=21) following TIV. Serum interleukin (IL)-6, tumor necrosis factor (TNF)- α , C-reactive protein (CRP), and macrophage migration inhibitory factor (MIF) were determined by high sensitivity immunoassay.

Results

Significant increases in CRP were seen at one and two days post-vaccination (ps <.05). A similar effect was seen for TNF- α , for which an increase at two days post-vaccination approached statistical significance (p = .06). There was considerable variability in magnitude of response; coefficients of variation for change at two days post-vaccination ranged from 122% to 728%, with the greatest variability in IL-6 responses at this timepoint.

Conclusions

Trivalent influenza virus vaccination elicits a measurable inflammatory response among pregnant women. There is sufficient variability in response for testing associations with clinical outcomes. As adverse perinatal health outcomes including preeclampsia and preterm birth have an inflammatory component, a tendency toward greater inflammatory responding to immune triggers may predict risk of adverse outcomes, providing insight into biological mechanisms underlying risk. The inflammatory response elicited by vaccination is substantially milder and more transient than seen in infectious illness, arguing for the clinical value of vaccination. However, further research is needed to confirm that the mild inflammatory response elicited by vaccination is benign in pregnancy

138. [Elevated maternal C-reactive protein and autism in a national birth cohort.](#)

Mol Psychiatry. 2013 Jan 22. doi: 10.1038/mp.2012.197.

Brown AS, Sourander A, Hinkka-Yli-Salomäki S, McKeague IW, Sundvall J,

Surcel HM.

Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York State Psychiatric Institute, New York, NY, USA, Department of Epidemiology, Columbia University Mailman School of Public Health, New York, NY, USA.

Abstract

Autism is a complex neuropsychiatric syndrome with a largely unknown etiology. Inflammation during pregnancy may represent a common pathway by which infections and other insults increase risk for the disorder. Hence, we investigated the association between early gestational C-reactive protein (CRP), an established inflammatory biomarker, prospectively assayed in maternal sera, and childhood autism in a large national birth cohort with an extensive serum biobank. Other strengths of the cohort included nearly complete ascertainment of pregnancies in Finland (N=1.2 million) over the study period and national psychiatric registries consisting of virtually all treated autism cases in the population. Increasing maternal CRP levels, classified as a continuous variable, were significantly associated with autism in offspring. For maternal CRP levels in the highest quintile, compared with the lowest quintile, there was a significant, 43% elevated risk. This finding suggests that maternal inflammation may have a significant role in autism, with possible implications for identifying preventive strategies and pathogenic mechanisms in autism and other neurodevelopmental disorders. *Molecular Psychiatry* advance online publication, 22 January 2013; doi:10.1038/mp.2012.197.

139. [What is regressive autism and why does it occur? Is it the consequence of multi-systemic dysfunction affecting the elimination of heavy metals and the ability to regulate neural temperature?](#)

N Am J Med Sci. 2009 July; 1(2): 28–47.

Graham E. Ewing

Montague Healthcare, Nottingham United Kingdom

Abstract

There is a compelling argument that the occurrence of regressive autism is attributable to genetic and chromosomal abnormalities, arising from the overuse of vaccines, which subsequently affects the stability and function of the autonomic nervous system and physiological systems. That sense perception is linked to the autonomic nervous system and the function of the physiological systems enables us to examine the significance of autistic symptoms from a systemic perspective. Failure of the excretory system influences elimination of heavy metals and facilitates their accumulation and subsequent manifestation as neurotoxins: the long-term consequences of which would lead to neurodegeneration, cognitive and developmental problems. It may also influence regulation of neural hyperthermia. This article explores the issues and concludes

that sensory dysfunction and systemic failure, manifested as autism, is the inevitable consequence arising from subtle DNA alteration and consequently from the overuse of vaccines.

140. [Neurologic adverse events following vaccination](#)

Prog Health Sci 2012, Vol 2 , No1

Sienkiewicz D.*, Kułak W., Okurowska-Zawada B., Paszko-Patej G.

Department of Pediatric Rehabilitation of the Medical University of Białystok, Poland

Abstract

The present review summarizes data on neurological adverse events following vaccination in the relation to intensity, time of onset, taking into account the immunological and non-immunological mechanisms. The authors described the physiological development of the immune system and the possible immune system responses following vaccination. Toxic property of thimerosal - a mercury-containing preservative used in some vaccines was presented. The neurological complications after vaccination were described. The role of vaccination in the natural course of infectious diseases and the current immunizations schedule in Poland was discussed.

Discussion by Sienkiewicz et. al.:

"Among the "major" neurological complications, usually manifesting more than 48 hours after vaccination and which might be the cause of permanent damage to the central nervous system (CNS), the following are listed: seizures - especially if there is no increase in body temperature, hypotonic-hyporesponsive episodes, postvaccinal encephalitis, postvaccinal encephalopathy [6, 8-11] and autism [10, 12-14]."

141. [Immunological and autoimmune considerations of Autism Spectrum Disorders.](#)

J Autoimmun. 2013 Jul 15. pii: S0896-8411(13)00073-5. doi: 10.1016/j.jaut.2013.05.005.

Gesundheit B, Rosenzweig JP, Naor D, Lerer B, Zachor DA, Procházka V, Melamed M, Kristt DA, Steinberg A, Shulman C, Hwang P, Koren G, Walfisch A, Passweg JR, Snowden JA, Tamouza R, Leboyer M, Farge-Bancel D, Ashwood P.

Jerusalem, Israel.

Abstract

Autism Spectrum Disorders (ASD) are a group of heterogeneous

neurodevelopmental conditions presenting in early childhood with a prevalence ranging from 0.7% to 2.64%. Social interaction and communication skills are impaired and children often present with unusual repetitive behavior. The condition persists for life with major implications for the individual, the family and the entire health care system. While the etiology of ASD remains unknown, various clues suggest a possible association with altered immune responses and ASD. Inflammation in the brain and CNS has been reported by several groups with notable microglia activation and increased cytokine production in postmortem brain specimens of young and old individuals with ASD. Moreover several laboratories have isolated distinctive brain and CNS reactive antibodies from individuals with ASD. Large population based epidemiological studies have established a correlation between ASD and a family history of autoimmune diseases, associations with MHC complex haplotypes, and abnormal levels of various inflammatory cytokines and immunological markers in the blood. In addition, there is evidence that antibodies that are only present in some mothers of children with ASD bind to fetal brain proteins and may be a marker or risk factor for ASD. Studies involving the injection of these ASD specific maternal serum antibodies into pregnant mice during gestation, or gestational exposure of Rhesus monkeys to IgG subclass of these antibodies, have consistently elicited behavioral changes in offspring that have relevance to ASD. We will summarize the various types of studies associating ASD with the immune system, critically evaluate the quality of these studies, and attempt to integrate them in a way that clarifies the areas of immune and autoimmune phenomena in ASD research that will be important indicators for future research.

142. [Identification of Unique Gene Expression Profile in Children with Regressive Autism Spectrum Disorder \(ASD\) and Ileocolitis](#)

PLoS ONE 8(3): e58058. doi:10.1371/journal.pone.0058058

Walker SJ, Fortunato J, Gonzalez LG, Krigsman A

Abstract

Gastrointestinal symptoms are common in children with autism spectrum disorder (ASD) and are often associated with mucosal inflammatory infiltrates of the small and large intestine. Although distinct histologic and immunohistochemical properties of this inflammatory infiltrate have been previously described in this ASDGI group, molecular characterization of these lesions has not been reported. In this study we utilize transcriptome profiling of gastrointestinal mucosal biopsy tissue from ASDGI children and three non-ASD control groups (Crohn's disease, ulcerative colitis, and histologically normal) in an effort to determine if there is a gene expression profile unique to the ASDGI group. Comparison of differentially expressed transcripts between the groups demonstrated that non-pathologic (normal) tissue segregated almost completely from inflamed tissue in all cases. Gene expression profiles in intestinal biopsy tissue from patients with Crohn's disease, ulcerative colitis, and ASDGI, while having significant overlap with each other, also showed distinctive features for

each group. **Taken together, these results demonstrate that ASDGI children have a gastrointestinal mucosal molecular profile that overlaps significantly with known inflammatory bowel disease (IBD), yet has distinctive features that further supports the presence of an ASD-associated IBD variant, or, alternatively, a prodromal phase of typical inflammatory bowel disease.** Although we report qPCR confirmation of representative differentially expressed transcripts determined initially by microarray, these findings may be considered preliminary to the extent that they require further confirmation in a validation cohort.

143. [Early Disruption of the Microbiome Leading to Decreased Antioxidant Capacity and Epigenetic Changes: Implications for the Rise in Autism](#)

Front. Cell. Neurosci., 15 August 2018 | <https://doi.org/10.3389/fncel.2018.00256>

Rebecca S. Eshraghi, Richard C. Deth, Rahul Mittal, Mayank Aranke, Sae-In S. Kay⁴, Baharak Moshiree and Adrien A. Eshraghi

Currently, 1 out of every 59 children in the United States is diagnosed with autism. While initial research to find the possible causes for autism were mostly focused on the genome, more recent studies indicate a significant role for epigenetic regulation of gene expression and the microbiome. In this review article, **we examine the connections between early disruption of the developing microbiome and gastrointestinal tract function, with particular regard to susceptibility to autism. The biological mechanisms that accompany individuals with autism are reviewed in this manuscript including immune system dysregulation, inflammation, oxidative stress, metabolic and methylation abnormalities as well as gastrointestinal distress.** We propose that these autism-associated biological mechanisms may be caused and/or sustained by dysbiosis, an alteration to the composition of resident commensal communities relative to the community found in healthy individuals and its redox and epigenetic consequences, changes that in part can be due to early use and over-use of antibiotics across generations. Further studies are warranted to clarify the contribution of oxidative stress and gut microbiome in the pathophysiology of autism. A better understanding of the microbiome and gastrointestinal tract in relation to autism will provide promising new opportunities to develop novel treatment modalities.

144. [Methylomic analysis of monozygotic twins discordant for autism spectrum disorder and related behavioural traits](#)

Mol Psychiatry. 2014 Apr;19(4):495-503. doi: 10.1038/mp.2013.41. Epub 2013 Apr 23.

Wong CC1, Meaburn EL2, Ronald A2, Price TS3, Jeffries AR1, Schalkwyk LC1, Plomin R1, Mill J4.

1 King's College London, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, De Crespigny Park, London, UK.

2 1] King's College London, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, De Crespigny Park, London, UK [2] Department of Psychological Sciences, Birkbeck, University of London, London, UK.

3 1] King's College London, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, De Crespigny Park, London, UK [2] Institute of Translational Medicine and Therapeutics, School of Medicine, University of Pennsylvania, PA, USA.

4 1] King's College London, MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, De Crespigny Park, London, UK [2] University of Exeter Medical School, Exeter University, St Luke's Campus, Exeter, UK.

Abstract

Autism spectrum disorder (ASD) defines a group of common, complex neurodevelopmental disorders. Although the aetiology of ASD has a strong genetic component, there is considerable monozygotic (MZ) twin discordance indicating a role for non-genetic factors. Because MZ twins share an identical DNA sequence, disease-discordant MZ twin pairs provide an ideal model for examining the contribution of environmentally driven epigenetic factors in disease. We performed a genome-wide analysis of DNA methylation in a sample of 50 MZ twin pairs (100 individuals) sampled from a representative population cohort that included twins discordant and concordant for ASD, ASD-associated traits and no autistic phenotype. Within-twin and between-group analyses identified numerous differentially methylated regions associated with ASD. **In addition, we report significant correlations between DNA methylation and quantitatively measured autistic trait scores across our sample cohort. This study represents the first systematic epigenomic analyses of MZ twins discordant for ASD and implicates a role for altered DNA methylation in autism.**

"Excerpt

These findings concur with mounting data suggesting that environmentally mediated effects on the epigenome may be relatively common and important for disease."

145. [Correlations between gene expression and mercury levels in blood of boys with and without autism.](#)

Neurotox Res. 2011 Jan;19(1):31-48. doi: 10.1007/s12640-009-9137-7. Epub 2009 Nov 24.

Stamova B1, Green PG, Tian Y, Hertz-Picciotto I, Pessah IN, Hansen R, Yang X, Teng J, Gregg JP, Ashwood P, Van de Water J, Sharp FR.

Department of Neurology, University of California at Davis Medical Center, Sacramento, CA 95817, USA. boryana.stamova@ucdmc.ucdavis.edu

Abstract

Gene expression in blood was correlated with mercury levels in blood of 2- to 5-year-old boys with autism (AU) compared to age-matched typically developing (TD) control boys. This was done to address the possibility that the two groups might metabolize toxicants, such as mercury, differently. RNA was isolated from blood and gene expression assessed on whole genome Affymetrix Human U133 expression microarrays. Mercury levels were measured using an inductively coupled plasma mass spectrometer. Analysis of covariance (ANCOVA) was performed and partial correlations between gene expression and mercury levels were calculated, after correcting for age and batch effects. To reduce false positives, only genes shared by the ANCOVA models were analyzed. Of the 26 genes that correlated with mercury levels in both AU and TD boys, 11 were significantly different between the groups ($P(\text{Diagnosis} \times \text{Mercury}) \leq 0.05$). The expression of a large number of genes ($n = 316$) correlated with mercury levels in TD but not in AU boys ($P \leq 0.05$), the most represented biological functions being cell death and cell morphology. Expression of 189 genes correlated with mercury levels in AU but not in TD boys ($P \leq 0.05$), the most represented biological functions being cell morphology, amino acid metabolism, and antigen presentation. These data and those in our companion study on correlation of gene expression and lead levels show that AU and TD children display different correlations between transcript levels and low levels of mercury and lead. These findings might suggest different genetic transcriptional programs associated with mercury in AU compared to TD children.

146. [Abnormal immune response to brain tissue antigen in the syndrome of autism.](#)

Am J Psychiatry. 1982 Nov;139(11):1462-5.

Weizman A, Weizman R, Szekely GA, Wijzenbeek H, Livni E.

Abstract

Cell-mediated immune response to human myelin basic protein was studied by the macrophage migration inhibition factor test in 17 autistic patients and a control group of 11 patients suffering from other mental diseases included in the differential diagnosis of the syndrome of autism. Of the 17 autistic patients, 13 demonstrated inhibition of macrophage migration, whereas none of the nonautistic patients showed such a response. **The results indicate the existence of a cell-mediated immune response to brain tissue in the syndrome of autism.**

147. [Detection and sequencing of measles virus from peripheral mononuclear cells from patients with inflammatory bowel disease and autism.](#)

Dig Dis Sci. 2000 Apr;45(4):723-9.

Kawashima H, Mori T, Kashiwagi Y, Takekuma K, Hoshika A, Wakefield A.

Department of Paediatrics, Tokyo Medical University, Japan.

Abstract

It has been reported that measles virus may be present in the intestine of patients with Crohn's disease. Additionally, a new syndrome has been reported in children with autism who exhibited developmental regression and gastrointestinal symptoms (autistic enterocolitis), in some cases soon after MMR vaccine. It is not known whether the virus, if confirmed to be present in these patients, derives from either wild strains or vaccine strains. In order to characterize the strains that may be present, we have carried out the detection of measles genomic RNA in peripheral mononuclear cells (PBMC) in eight patients with Crohn's disease, three patients with ulcerative colitis, and nine children with autistic enterocolitis. As controls, we examined healthy children and patients with SSPE, SLE, HIV-1 (a total of eight cases). RNA was purified from PBMC by Ficoll-paque, followed by reverse transcription using AMV; cDNAs were subjected to nested PCR for detection of specific regions of the hemagglutinin (H) and fusion (F) gene regions. Positive samples were sequenced directly, in nucleotides 8393-8676 (H region) or 5325-5465 (from noncoding F to coding F region). One of eight patients with Crohn disease, one of three patients with ulcerative colitis, and three of nine children with autism, were positive. Controls were all negative. The sequences obtained from the patients with Crohn's disease shared the characteristics with wild-strain virus. **The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with being vaccine strains.** The results were concordant with the exposure history of the patients. Persistence of measles virus was confirmed in PBMC in some patients with chronic intestinal inflammation.

148. [Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations](#)

Lupus. 2012 Feb;21(2):223-30. doi: 10.1177/0961203311430221.

L Tomljenovic, CA Shaw

Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, BC, Canada

Departments of Ophthalmology and Visual Sciences and Experimental Medicine

and the Graduate Program in Neuroscience, University of British Columbia, Vancouver, BC, Canada

Lucija Tomljenovic, Post-doctoral fellow, Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences, University of British Columbia

Abstract

Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function. Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity. In some developed countries, by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of aluminum (Al) adjuvants through routine vaccinations. According to the US Food and Drug Administration, safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic. Taken together, these observations raise plausible concerns about the overall safety of current childhood vaccination programs. When assessing adjuvant toxicity in children, several key points ought to be considered: (i) infants and children should not be viewed as “small adults” with regard to toxicological risk as their unique physiology makes them much more vulnerable to toxic insults; (ii) in adult humans Al vaccine adjuvants have been linked to a variety of serious autoimmune and inflammatory conditions (i.e., “ASIA”), yet children are regularly exposed to much higher amounts of Al from vaccines than adults; (iii) it is often assumed that peripheral immune responses do not affect brain function. However, **it is now clearly established that there is a bidirectional neuro-immune cross-talk that plays crucial roles in immunoregulation as well as brain function. In turn, perturbations of the neuro-immune axis have been demonstrated in many autoimmune diseases encompassed in “ASIA” and are thought to be driven by a hyperactive immune response; and (iv) the same components of the neuro-immune axis that play key roles in brain development and immune function are heavily targeted by Al adjuvants.** In summary, research evidence shows that increasing concerns about current vaccination practices may indeed be warranted. Because children may be most at risk of vaccine-induced complications, a rigorous evaluation of the vaccine-related adverse health impacts in the pediatric population is urgently needed.

149. [Etiology of autism spectrum disorders: Genes, environment, or both?](#)

OA Autism 2014 Jun 10;2(2):11

C Shaw, S Sheth, D Li, L Tomljenovic
University of British Columbia, Vancouver, British Columbia, Canada

Introduction

Thus far, most of the research on both neurodevelopmental and neurodegenerative disorders has been focused on finding the presumed underlying genetic causes, while much less emphasis has been put on potential environmental factors. While some forms of autism are clearly genetic, the fact remains that heritability factors cannot adequately explain all reported cases nor their drastic increase over the last few decades. In particular, studies on twins have now shown that common environmental factors account for 55% of their risk for developing autism while genetic susceptibility explains only 37% of cases. Because the prenatal environment and early postnatal environment are shared between twins and because overt symptoms of autism emerge around the end of the first year of life, it is likely that at least some of the environmental factors contributing to the risk of autism exert their deleterious neurodevelopmental effect during this early period of life. Indeed, evidence has now emerged showing that autism may in part result from early-life immune insults induced by environmental xenobiotics. One of the most common xenobiotic with immunostimulating as well as neurotoxic properties to which infants under two years of age are routinely exposed worldwide is the aluminum (Al) vaccine adjuvant. In this review we discuss the mechanisms by which Al can induce adverse neurological and immunological effects and how these may provide important clues of Al's putative role in autism. Because of the tight connection between the development of the immune and the central nervous system, the possibility that immune-overstimulation in early infancy via vaccinations may play a role in neurobehavioural disorders needs to be carefully considered.

Conclusion

There is now sufficient evidence from both human and animal studies showing that cumulative exposure to aluminium adjuvants is not as benign as previously assumed. Given that vaccines are the only medical intervention that we attempt to deliver to every living human on earth and that by far the largest target population for vaccination are healthy children, a better appreciation and understanding of vaccine adjuvant risks appears warranted.

150. [Thiol-modulated mechanisms of the cytotoxicity of thimerosal and inhibition of DNA topoisomerase II alpha.](#)

Chem Res Toxicol. 2008 Feb;21(2):483-93.

Wu X, Liang H, O'Hara KA, Yalowich JC, Hasinoff BB.

Faculty of Pharmacy, University of Manitoba, 50 Sifton Road, Winnipeg, Manitoba, R3T 2N2, Canada.

Abstract

Thimerosal is an organic mercury compound that is widely used as a preservative in vaccines and other solution formulations. The use of thimerosal has caused concern about its ability to cause neurological abnormalities due to mercury accumulation during a normal schedule of childhood vaccinations. While

the chemistry and the biological effects of methylmercury have been well-studied, those of thimerosal have not. Thimerosal reacted rapidly with cysteine, GSH, human serum albumin, and single-stranded DNA to form ethylmercury adducts that were detectable by mass spectrometry. These results indicated that thimerosal would be quickly metabolized in vivo because of its reactions with protein and nonprotein thiols. **Thimerosal also potently inhibited the decatenation activity of DNA topoisomerase II alpha, likely through reaction with critical free cysteine thiol groups.** Thimerosal, however, did not act as a topoisomerase II poison and the lack of cross-resistance with a K562 cell line with a decreased level of topoisomerase II alpha (K/VP.5 cells) suggested that inhibition of topoisomerase II alpha was not a significant mechanism for the inhibition of cell growth. **Depletion of intracellular GSH with buthionine sulfoximine treatment greatly increased the K562 cell growth inhibitory effects of thimerosal, which showed that intracellular glutathione had a major role in protecting cells from thimerosal.** Pretreatment of thimerosal with glutathione did not, however, change its K562 cell growth inhibitory effects, a result consistent with the rapid exchange of the ethylmercury adduct among various thiol-containing cellular reactants. Thimerosal-induced single and double strand breaks in K562 cells were consistent with a rapid induction of apoptosis. In conclusion, these studies have elucidated some of the chemistry and biological activities of the interaction of thimerosal with topoisomerase II alpha and protein and nonprotein thiols and with DNA.

151. [Topoisomerases facilitate transcription of long genes linked to autism](#)

Nature (2013) doi:10.1038/nature12504

Received 17 January 2013 Accepted 24 July 2013 Published online 28 August 2013

Ian F. King, Chandri N. Yandava, Angela M. Mabb, Jack S. Hsiao, Hsien-Sung Huang, Brandon L. Pearson, J. Mauro Calabrese, Joshua Starmer, Joel S. Parker, Terry Magnuson, Stormy J. Chamberlain, Benjamin D. Philpot & Mark J. Zylka

Abstract

Topoisomerases are expressed throughout the developing and adult brain and are mutated in some individuals with autism spectrum disorder (ASD). However, how topoisomerases are mechanistically connected to ASD is unknown. Here we find that topotecan, a topoisomerase 1 (TOP1) inhibitor, dose-dependently reduces the expression of extremely long genes in mouse and human neurons, including nearly all genes that are longer than 200 kilobases. Expression of long genes is also reduced after knockdown of Top1 or Top2b in neurons, highlighting that both enzymes are required for full expression of long genes. By mapping RNA polymerase II density genome-wide in neurons, we found that this length-dependent effect on gene expression was due to impaired transcription elongation. Interestingly, many high-confidence ASD candidate genes are exceptionally long and were reduced in expression after TOP1 inhibition. **Our findings suggest that chemicals and genetic mutations that impair**

topoisomerases could commonly contribute to ASD and other neurodevelopmental disorders.

152. [Aluminum in the central nervous system \(CNS\): toxicity in humans and animals, vaccine adjuvants, and autoimmunity.](#)

Immunol Res. 2013 Jul;56(2-3):304-16.

Shaw CA, Tomljenovic L.

Abstract

We have examined the neurotoxicity of aluminum in humans and animals under various conditions, following different routes of administration, and provide an overview of the various associated disease states. The literature demonstrates clearly negative impacts of aluminum on the nervous system across the age span. In adults, aluminum exposure can lead to apparently age-related neurological deficits resembling Alzheimer's and has been linked to this disease and to the Guamanian variant, ALS-PDC. Similar outcomes have been found in animal models. In addition, injection of aluminum adjuvants in an attempt to model Gulf War syndrome and associated neurological deficits leads to an ALS phenotype in young male mice. In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders. Many of the features of aluminum-induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome.

153. [Transcriptomic Analyses of Neurotoxic Effects in Mouse Brain After Intermittent Neonatal Administration of Thimerosal.](#)

Toxicol Sci. 2014 Apr 4.

Li X1, Qu F, Xie W, Wang F, Liu H, Song S, Chen T, Zhang Y, Zhu S, Wang Y, Guo C, Tang TS.

Abstract

Thimerosal is a vaccine antimicrobial preservative which has long been suspected an iatrogenic factor possibly contributing to neurodevelopmental disorders including autism. The association between infant vaccine thimerosal exposure and autism remains an open question. Although thimerosal has been removed from mandatory childhood vaccines in the United States, thimerosal-preserved vaccines are still widely used outside of the United States especially in developing countries. Notably, thimerosal-containing vaccines are being given to the newborns within the first 12-24 h after birth in some countries. To examine

the possible neurotoxic effects of early neonatal exposure to a higher level of thimerosal, FVB mice were subcutaneously injected with thimerosal-mercury at a dose which is 20× higher than that used for regular Chinese infant immunization during the first 4 months of life. Thimerosal-treated mice exhibited neural development delay, social interaction deficiency, and inclination of depression. Apparent neuropathological changes were also observed in adult mice neonatally treated with thimerosal. High-throughput RNA sequencing of autistic-behaved mice brains revealed the alternation of a number of canonical pathways involving neuronal development, neuronal synaptic function, and the dysregulation of endocrine system. Intriguingly, the elevation of anterior pituitary secreting hormones occurred exclusively in male but not in female thimerosal-treated mice, demonstrating for the first time the gender bias of thimerosal-mercury toxicity with regard to endocrine system. Our results indicate that higher dose of neonatal thimerosal-mercury (20× higher than that used in human) is capable of inducing long-lasting substantial dysregulation of neurodevelopment, synaptic function, and endocrine system, which could be the causal involvements of autistic-like behavior in mice.

154. [Self-organized criticality theory of autoimmunity.](#)

PLoS One. 2009 Dec 31;4(12):e8382. doi: 10.1371/journal.pone.0008382.

Tsumiyama K1, Miyazaki Y, Shiozawa S.

Department of Biophysics, Kobe University Graduate School of Health Science, Kobe, Japan.

Abstract

BACKGROUND:

The cause of autoimmunity, which is unknown, is investigated from a different angle, i.e., the defect in immune 'system', to explain the cause of autoimmunity.

METHODOLOGY/PRINCIPAL FINDINGS:

Repeated immunization with antigen causes systemic autoimmunity in mice otherwise not prone to spontaneous autoimmune diseases. Overstimulation of CD4(+) T cells led to the development of autoantibody-inducing CD4(+) T (aiCD4(+) T) cell which had undergone T cell receptor (TCR) revision and was capable of inducing autoantibodies. The aiCD4(+) T cell was induced by de novo TCR revision but not by cross-reaction, and subsequently overstimulated CD8(+) T cells, driving them to become antigen-specific cytotoxic T lymphocytes (CTL). These CTLs could be further matured by antigen cross-presentation, after which they caused autoimmune tissue injury akin to systemic lupus erythematosus (SLE).

CONCLUSIONS/SIGNIFICANCE:

Systemic autoimmunity appears to be the inevitable consequence of overstimulating the host's immune 'system' by repeated immunization with

antigen, to the levels that surpass system's self-organized criticality.

155. [Can Awareness of Medical Pathophysiology in Autism Lead to Primary Care Autism Prevention Strategies?](#)

Elizabeth Mumper, MD, FAAP

N A J Med Sci. 2013;6(3):134-144. DOI: 10.7156/najms.2013.0603134

Abstract

Emerging research suggests that the timing of environmental factors in the presence of genetic predispositions has influenced the increase in autism spectrum disorders over the past several decades. A review of the medical literature suggests that autism may be impacted by environmental toxicants, breastfeeding duration, gut flora composition, nutritional status, acetaminophen use, vaccine practices and use of antibiotics and/or frequency of infections. The author reports her retrospective clinical research in a general pediatric practice (Advocates for Children), which shows a modest trend toward lower prevalence of autism than her previous pediatric practice or recent CDC data. Out of 294 general pediatrics patients followed since 2005 there were zero new cases of autism (p value 0.014). Given the prevalence of autism for that cohort of 1 in 50 children in the United States, it is important to consider implementing strategies in primary care practice that could potentially modify environmental factors or affect the timing of environmental triggers contributing to autism.

156. [Autism: a novel form of mercury poisoning](#)

Medical Hypotheses (2001) 56(4), 462–471, 2001 Harcourt Publishers Ltd
doi: 10.1054/mehy.2000.1281,

S. Bernard, A. Enayati, L. Redwood, H. Roger, T. Binstock

ARC Research, Cranford, New Jersey, USA

Summary Autism is a syndrome characterized by impairments in social relatedness and communication, repetitive behaviors, abnormal movements, and sensory dysfunction. Recent epidemiological studies suggest that autism may affect 1 in 150 US children. Exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism, and the similarities extend to neuroanatomy, neurotransmitters, and biochemistry. Thimerosal, a preservative added to many vaccines, has become a major source of mercury in children who, within their first two years, may have received a quantity of mercury that exceeds safety guidelines. A review of medical literature and US government data suggests that: (i) many cases of idiopathic autism are induced by early mercury exposure from

thimerosal; (ii) this type of autism represents an unrecognized mercurial syndrome; and (iii) genetic and non-genetic factors establish a predisposition whereby thimerosal's adverse effects occur only in some children.

157. [Autistic disturbances of affective contact.](#)

Nervous Child 2, 217-250 (1943)

Kanner L.
Johns Hopkins University

“Case 3. Richard M. was referred to the Johns Hopkins Hospital on February 5, 1941, at 3 years, 3 months of age, with the complaint of deafness because he did not talk and did not respond to questions.”

“Following smallpox vaccination at 12 months, he had an attack of diarrhea and fever, from which he recovered in somewhat less than a week.”

“In September, 1940, the mother, in commenting on Richard's failure to talk, remarked in her notes: I can't be sure just when he stopped the imitation of words sounds. It seems that he has gone backward mentally gradually for the last two years.”

Richard M:

November 1937 – Born

November 1938 – Vaccinated with Smallpox vaccine

September 1940 – Mother reports developmental regression beginning approximately two years previously

February 1941 – Referred to Hopkins for evaluation

1943 – Becomes the third child to be described as autistic by Leo Kanner in his disorder defining paper, the first paper published on autism.

Can HPV Vaccine Cause Injury and Death?

The most commonly reported side effects of HPV vaccination include pain, swelling, and redness at the injection site, nausea, headache, fever, fatigue, and muscle or joint pain. Fainting – referred to as a syncopal episode - following HPV vaccination has been frequently reported and as a result, it is recommended that individuals receiving the vaccine remain sitting or lying down to prevent syncope and any potential injuries that may result from a fall.¹ However, more severe reactions have also been reported in HPV vaccine clinical trials and to the federal Vaccine Adverse Events Reporting System (VAERS). See Human Papillomavirus (HPV) Quick Facts for 2018 reports of HPV vaccine reactions, hospitalizations, injuries and deaths made to VAERS.

Some of the adverse events reported by the manufacturers during pre-licensing clinical trials included:

Gardasil - injection site pain, swelling, redness and bruising, fever, headache, nausea, dizziness, syncope, sometimes in conjunction with seizure-like activity, anaphylaxis, diarrhea, vomiting, cough, upper respiratory tract infection, nasal congestion, insomnia, malaise, oropharyngeal pain, nasopharyngitis, upper abdominal pain, gastroenteritis, appendicitis, pelvic inflammatory disease, urinary tract infection, pneumonia, pulmonary embolism, pyelonephritis, bronchospasm, and death.²

Cervarix - injection site pain, redness, bruising and swelling, syncope, fatigue, headache, gastrointestinal symptoms, rash, fever, arthralgia, myalgia, urticarial, urinary tract infection, back pain, dysmenorrhea, nasopharyngitis, influenza, vaginal infection, pharyngitis, chlamydia infection, arthritis, rheumatoid arthritis, Celiac disease, diabetes mellitus, erythema nodosum, inflammatory bowel disease, hyperthyroidism, hypothyroidism, multiple sclerosis, transverse myelitis, systemic lupus erythematosus, thrombocytopenia, vasculitis, optic neuritis, vitiligo, and death.³

Gardasil 9 - injection site pain, swelling, redness, and bruising, syncope, fever, headache, nausea, dizziness, fatigue, diarrhea, upper respiratory tract infection, upper abdominal pain, oropharyngeal pain, myalgia, asthmatic crisis, anaphylaxis, and death.⁴

Gardasil 9 reported post marketing adverse events include: pulmonary embolus, idiopathic thrombocytopenic purpura, lymphadenopathy, autoimmune hemolytic anemia, pancreatitis, asthenia, chills, fatigue, malaise, bronchospasm, urticarial, anaphylaxis, acute disseminated encephalomyelitis, dizziness, transverse myelitis, Guillain-Barré syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with other seizure-like activity and tonic-clonic movements) sometimes resulting in injury from falling, deep vein thrombosis, cellulitis, myalgia, arthralgia, and death.

In 2007, NVIC reviewed adverse events reported to the Vaccine Adverse Events Reporting System (VAERS), and noted a statistically significant increased risk of Guillain-Barre Syndrome (GBS) and other serious adverse events when Gardasil was administered with other vaccines, especially the meningococcal vaccine, Menactra. The analysis noted a 1,130 percent increase in GBS, a 674 percent increase in injuries from falls after loss of consciousness, a 234 percent increase in coordination and neuromuscular problems, a 118 percent increase in cardiac problems, a 114 percent increase in respiratory problems and a 30.1 percent increase in convulsions and central nervous system problems when Gardasil was administered with Menactra.⁵

During the past decade, there have been numerous studies and reports linking HPV vaccination to chronic illnesses in children and young adults. These include anaphylaxis,⁶ lupus,^{7,8} erythema multiforme,⁹ acute disseminated encephalomyelitis,^{10,11,12} transverse myelitis,¹³ amyotrophic lateral

sclerosis (ALS),¹⁴ central nervous system demyelination,^{15 16} multiple sclerosis,¹⁷ including pediatric multiple sclerosis,¹⁸ Guillain-Barre Syndrome,^{19 20} pancreatitis,^{21 22} inflammatory bowel syndrome,²³ brachial plexus neuritis,²⁴ brachial neuritis,²⁵ optic neuritis,²⁶ neuromyelitis optica,²⁷ opsoclonus myoclonus,²⁸ evanescent white dot syndrome,^{29 30} acute cerebellar ataxia,³¹ autoimmune hepatitis,³² autoimmune neuromyotonia,³³ vasculitis,³⁴ thrombocytopenic purpura,³⁵ immune thrombocytopenic purpura,³⁶ Postural Orthostatic Tachycardia Syndrome (POTS),^{37 38 39} Complex Regional Pain Syndrome (CRPS),⁴⁰ Chronic Fatigue Syndrome (CFS),⁴¹ and peripheral sympathetic nerve dysfunction.⁴² A published questionnaire⁴³ of HPV vaccination recipients focusing on a combination of chronic illness including POTS, CRPS, and fibromyalgia found that 93 percent of individuals reporting symptoms related to these conditions were still incapacitated and unable to work or attend school four years after vaccination. Additionally, several studies have linked HPV vaccination to primary ovarian failure resulting in impaired fertility^{44 45 46 47}. A 2018 study found lower pregnancy rates in women who had received HPV vaccination.⁴⁸

Adverse events following HPV vaccination have also been linked to a relatively new medical condition termed Autoimmune/inflammatory Syndrome Induced by Adjuvants (ASIA).⁴⁹ In 2011, Dr. Yehuda Shoenfeld, the founder and head of the Zabludowicz Center for Autoimmune Diseases in Israel, published a paper associating four medical conditions - Gulf War syndrome (GWS), macrophagic myofasciitis syndrome (MMF) (a syndrome previously related to the use of aluminum adjuvants), siliconosis (a condition related to silicone breast implants) and post-vaccination phenomena (chronic illness following vaccination) to a previous adjuvant exposure.

Dr. Shoenfeld noted that patients suffering from these conditions presented with very similar clinical symptoms. Since then, published studies have linked the aluminum adjuvant found in the HPV vaccine several to chronic health conditions including postural tachycardia syndrome (POTS),⁵⁰ primary ovarian failure (POF),⁵¹ chronic epipharyngitis,⁵² pseudo-neurological syndrome,⁵³ and severe somatoform and dysautonomic syndromes.⁵⁴ An epidemiological study of data collected from the federal Vaccine Adverse Events Reporting System (VAERS) estimated that 3.6 out of 100,000 doses of HPV vaccination resulted in symptoms that were consistent with a diagnosis of ASIA.⁵⁵

An animal study on the effects of HPV vaccination found that both the HPV antigens and the aluminum adjuvant appear to have the ability to trigger autoimmune reactions and neuroinflammation in female mice, leading to changes in behavior patterns.⁵⁶

Studies linking HPV vaccination to sudden death in previously healthy women have also been published. A 2012 published case study of two deaths following HPV vaccination concluded that the HPV-16L1 antigens present in HPV vaccines have the potential to cause fatal autoimmune vasculopathies.⁵⁷ Also in 2012, Sin Hang Lee, a research scientist and board certified pathologist, published a case study involving the sudden and unexplained death of a young woman six months after completing a three dose series of Gardasil. Dr. Lee found in the blood and spleen HPV-16 gene DNA that were similar to HPV-16 gene DNA fragments in Gardasil. The HPV-16 LI gene DNA was bound to the same aluminum adjuvant found in the vaccine, which protected it from degradation. It continues to be unknown whether or not these HPV DNA fragments played a role in the girl's death.

A 2017 article published in *Drug Safety* reviewed safety concerns associated with HPV vaccination.⁵⁸ Data reported to reported to adverse reaction reporting systems from several countries were analyzed and found to contain relatively high numbers of reports for headache, dizziness, fatigue, and syncope associated with prolonged hospitalization or debilitation. While some of the reports listed Postural Orthostatic Tachycardia Syndrome (POTS), Complex Regional Pain Syndrome (CRPS) or Chronic Fatigue Syndrome (CFS) as a diagnosis, the vast majority of the reports lacked any diagnosis. This study also found significantly higher number of events involving a

combination of dizziness and headache with either syncope or fatigue following HPV vaccination compared to adverse reactions of other vaccines. It was also noted that these combinations of symptoms were first reported in countries that were the earliest to approve and recommend HPV vaccination and that reported symptoms persisted globally.

Due to these findings, others have questioned whether current drug and vaccine safety monitoring tools have the ability to adequately detect and respond to signals indicating that a serious problem may exist with a product currently on the market.⁵⁹ Additionally, a 2018 study noted that only about half of the available clinical trials involving HPV vaccines had been completed before the vaccines were approved by both the Federal Drug Administration (FDA) and the European Medicines Agency (EMA).⁶⁰ The study also noted that drug manufacturers only published the results of about two-thirds of the HPV clinical trials, leaving the study's authors to question whether drug manufacturers were selectively choosing which clinical data to publish.

In December 2017, Slate Magazine published a cover story on the pre-licensure clinical trials of the Gardasil vaccine.⁶¹ This investigational report determined that Merck's pre-licensure safety studies "used a convoluted method that made objective evaluation and reporting of potential side effects impossible during all but a few weeks of its years long trial."⁶² The article noted that Merck's clinical trial investigators were permitted to use personal judgment when reporting medical problems as an adverse event, essentially allowing study investigators to decide what symptoms might possibly be related to vaccination. Study investigators were also allowed to list new health issues following vaccination as medical history, not adverse events, and limited safety follow up to 14 days following each of the three doses of Gardasil vaccination. Slate's investigation located several women involved in Gardasil's pre-licensure trials who reported chronic illness post-vaccination to study investigators, yet their symptoms were never reported by Merck.

In April 2018, the *Indian Journal of Medical Ethics* published a report suggesting that Sweden's increase in cervical cancer rates might be associated with HPV vaccination. The study's author, concerned that he may be targeted for questioning a vaccine's safety or efficacy, chose to publish under an assumed name without contacting the journal in advance. Initially, the journal chose to allow the article to be published despite the deception after determining that the author had both the necessary credentials and faced a credible threat of harm, stating "the issues raised by it are important and discussion on it is in the public interest."⁶³ However, two weeks later, after receiving "valuable advice from the journal's editorial board and others", the article was retracted.⁶⁴ The journal, however, stated that they "hope that the hypothesis of possible harm of vaccinating women previously exposed to HPV is carefully explored in future studies."⁶⁵ Data from Gardasil's pre-licensure clinical trials had previously demonstrated a higher incidence of cervical intraepithelial neoplasia (CIN) grade 2 and 3 in women previously infected with the particular strain targeted by the vaccine.⁶⁶

According to federal VAERS data, 430 deaths following the HPV vaccination have been reported following HPV vaccination.⁶⁷ However, the number of HPV vaccine related injuries and deaths reported to VAERS is assumed to underreported as explained below.

Even though the National Childhood Vaccine Injury Act of 1986 legally required pediatricians and other vaccine providers to report serious health problems following vaccination to the federal vaccine adverse event reporting system (VAERS), many doctors and other health care providers giving vaccines to children and adults fail to report vaccine-related health problem to VAERS. The evidence suggests that only one to 10 percent of serious health problems that occur after use of prescription drugs or vaccines in the U.S. are ever reported to federal health officials who are responsible for regulating the safety of drugs and vaccines and issue national vaccine policy recommendations.^{68 69 70 71 72}

As of July 1, 2018, 387 claims have been filed to the federal Vaccine Injury Compensation Program (VICP) for 14 deaths and 373 injuries that occurred after HPV vaccination. To date, the U.S. Court of Claims has compensated 128 of the 387 children and adults who filed claims for HPV vaccine injuries.⁷³

For example, an HPV vaccine injury claim was filed and awarded by the VICP for Christina Tarsell. Christina was a 21-year-old college student majoring in studio arts at Bard College when she received a series of three Gardasil shots. A talented athlete, artist and honor roll student, she died suddenly and without explanation shortly after the third shot in June 2008. Ten years later, in 2018, the government conceded the case and awarded compensation to her mother for Christina's vaccine-related death.⁷⁴

IMPORTANT NOTE: NVIC encourages you to become fully informed about HPV and the HPV vaccine by reading all sections in the Table of Contents , which contain many links and resources such as the manufacturer product information inserts, and to speak with one or more trusted health care professionals before making a vaccination decision for yourself or your child. This information is for educational purposes only and is not intended as medical advice.

[« Return to HPV Table of Contents](#)

[« Return to Vaccines & Diseases Table of Contents](#)

References

¹ CDC. Human Papillomavirus (HPV) Vaccine Safety. Jan. 30, 2018

² FDA. Gardasil – Product insert. Apr. 24, 2015.

³ FDA. Cervarix – Product insert. Apr. 25, 2016.

⁴ FDA. Gardasil 9 – Product insert. Feb. 9, 2018.

⁵ NVIC. Analysis Shows Greater Risk of GBS Reports When HPV Vaccine Is Given with Meningococcal and Other Vaccines. Aug. 15, 2007.

⁶ Brotherton JML, Gold MS. et al. Anaphylaxis following quadrivalent human papillomavirus vaccination. *CMAJ*. 2008 Sep 9; 179(6): 525–533.

⁷ Soldevilla HF, Briones SF, Navarra SV. Systemic lupus erythematosus following HPV immunization or infection? *Lupus*. 2012 Feb;21(2):158-61

⁸ Gatto M, Agmon-Levin N. et al. Human papillomavirus vaccine and systemic lupus erythematosus. *Clin Rheumatol*. (2013) 32: 1301.

⁹ Katoulis AC, Liakou A. et al. Erythema multiforme following vaccination for human papillomavirus. *Dermatology* 2010;220:60–2.

¹⁰ Sekiguchi K, Yasui N. et al. Two cases of acute disseminated encephalomyelitis following vaccination against human papilloma virus. *Intern Med*. 2016 Nov 1; 55(21): 3181–3184.

¹¹ Yoneda M. Acute Disseminated Encephalomyelitis Following Immunization with Human Papillomavirus Vaccines. *Intern Med*. 2016 Nov 1; 55(21): 3077–3078.

¹² Wildemann B, Jarius S. et al. ACUTE DISSEMINATED ENCEPHALOMYELITIS FOLLOWING VACCINATION AGAINST HUMAN PAPILLOMA VIRUS. *Neurology*. Jun.16, 2009; 72 (24).

¹³ Fernandez-Fournier M, Diaz de Teran J. et al. Early cervical myelitis after human papilloma virus vaccination. *Neurol Neuroimmunol Neuroinflamm*. 2014 Sep 11;1(3):e31

- [14](#) Laino C. 2 ALS Cases May Be Linked to Gardasil Vaccine. *WebMD*. Oct. 16, 2009
- [15](#) Chang J, Campagnolo D. et al. Demyelinating disease and polyvalent human papilloma virus vaccination. *J Neurol Neurosurg Psychiatry*. 2011 Nov;82(11):1296-8.
- [16](#) Álvarez-Soria MJ, Hernández-González A, et al. Demyelinating disease and vaccination of the human papillomavirus. *Rev Neurol*. 2011 Apr 16;52(8):472-6.
- [17](#) Sutton I, Lahoria R. et al. CNS demyelination and quadrivalent HPV vaccination. *Mult Scler*. 2009 Jan;15(1):116-9.
- [18](#) Hu Y, Tornes L, Lopez-Alberola R. Two Cases of Pediatric Multiple Sclerosis after Human Papillomavirus Vaccination (P4.353) *Neurology*. Apr. 10, 2018; 90 (15 Supplement)
- [19](#) Souayah N, Michas-Martin PA. et al. Guillain–Barré syndrome after Gardasil vaccination: Data from Vaccine Adverse Event Reporting System 2006–2009. *Vaccine*. 2011 Jan 29;29(5):886-9.
- [20](#) Miranda S, Chaignot C. et al. Human papillomavirus vaccination and risk of autoimmune diseases: A large cohort study of over 2 million young girls in France. *Vaccine*. 2017 Aug 24;35(36):4761-4768.
- [21](#) Das A, Chang D. et al. Pancreatitis following human papillomavirus vaccination. *Med J Aust*. 2008 Aug 4;189(3):178.
- [22](#) Bizjak M, Bruck O. et al. Pancreatitis after human papillomavirus vaccination: a matter of molecular mimicry. *Immunol Res*. 2017 Feb;65(1):164-167.
- [23](#) Miranda S, Chaignot C. et al. Human papillomavirus vaccination and risk of autoimmune diseases: A large cohort study of over 2 million young girls in France. *Vaccine*. 2017 Aug 24;35(36):4761-4768.
- [24](#) Debeer P, De Munter P. et al. Brachial plexus neuritis following HPV vaccination. *Vaccine*. 2008 Aug 18;26(35):4417-9.
- [25](#) Taras JS, King JJ, et al. Brachial neuritis following quadrivalent human papilloma virus (HPV) vaccination. *Hand (N Y)*. 2011 Dec; 6(4): 454–456.
- [26](#) DiMario FJ, Jr, Hajjar M. et al. A 16-year-old girl with bilateral visual loss and left hemiparesis following an immunization against human papilloma virus. *J Child Neurol*. 2010 Mar;25(3):321-7.
- [27](#) Menge T, Cree B. et al. Neuromyelitis optica following human papillomavirus vaccination. *Neurology*. 2012 Jul 17;79(3):285-7.
- [28](#) McCarthy JE, Filiano J. Opsoclonus myoclonus after human papilloma virus vaccine in a pediatric patient. *Parkinsonism Relat Disord*. 2009 Dec;15(10):792-4.
- [29](#) Ogino K, Kishi S, Yoshimura N. Multiple Evanescent White Dot Syndrome after Human Papillomavirus Vaccination. *Case Rep Ophthalmol*. 2014 Jan-Apr; 5(1): 38–43.
- [30](#) Cohen SM. Multiple Evanescent White Dot Syndrome After Vaccination for Human Papilloma Virus and Meningococcus. *J Pediatr Ophthalmol Strabismus*. 2009 Jun 25.
- [31](#) Yonee C, Toyoshima M. et al. Association of acute cerebellar ataxia and human papilloma virus vaccination: a case report. *Neuropediatrics* 2013;44:265–7.
- [32](#) Della Corte C, Carlucci A. et al. Autoimmune hepatitis type 2 following anti-papillomavirus vaccination in a 11-year-old girl. *Vaccine*. 2011 Jun 24;29(29-30):4654-6.
- [33](#) Cerami C, Corbo M. et al. Autoimmune neuromyotonia following human papilloma virus vaccination. *Muscle Nerve*. Mar 2013;47(3):466–7.
- [34](#) Melo Gomes S, Glover M. et al. Vasculitis following HPV immunization. *Rheumatology (Oxford)*. 2013 Mar;52(3):581-2.
- [35](#) Pugnet G, Ysebaert L. et al. Immune thrombocytopenic purpura following human papillomavirus vaccination. *Vaccine*. 2009 Jun 8;27(28):3690.

- [36](#) Bizjak M, Bruck O. et al. Vaccinations and secondary immune thrombocytopenia with antiphospholipid antibodies by human papillomavirus vaccine. *Semin Hematol.* 2016 Apr;53 Suppl 1:S48-50.
- [37](#) Blitshteyn S. Postural tachycardia syndrome following human papillomavirus vaccination. *Eur. J. Neurol.* 2014 21: 135-139.
- [38](#) Tomljenovic L, Colafrancesco S. et al. Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the "Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants" Case Report and Literature Review. *J Investig Med High Impact Case Rep.* 2014 Jan-Mar; 2(1): 2324709614527812.
- [39](#) Brinth LS, Pors K. et al. Orthostatic intolerance and postural tachycardia syndrome as suspected adverse effects of vaccination against human papilloma virus. *Vaccine.* 2015 May 21;33(22):2602-5.
- [40](#) Richards S, Chalkiadis G. et al. Complex regional pain syndrome following immunization. *Arch Dis Child.* 2012 Oct;97(10):913-5
- [41](#) Tomljenovic L, Colafrancesco S. et al. Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the "Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants" Case Report and Literature Review. *J Investig Med High Impact Case Rep.* 2014 Jan-Mar; 2(1): 2324709614527812.
- [42](#) Kinoshita T, Abe RT. et al. Peripheral sympathetic nerve dysfunction in adolescent Japanese girls following immunization with the human papillomavirus vaccine. *Intern Med.* 2014;53(19):2185-200.
- [43](#) Martínez-Lavín M, Martínez-Martínez LA, Reyes-Loyola P. et al. HPV vaccination syndrome. A questionnaire-based study. *Clin Rheumatol.* 2015 Nov;34(11):1981-3.
- [44](#) Little D, Ward HR. Premature ovarian failure 3 years after menarche in a 16-year-old girl following human papillomavirus vaccination. *BMJ Case Rep.* Sep. 30, 2012.
- [45](#) Colafrancesco S, Perricone C. et al. Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants. *Am J Reprod Immunol.* 2013 Oct;70(4):309-16
- [46](#) Little DT, Ward HR. Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination: A Case Series Seen in General Practice. *J Investig Med High Impact Case Rep.* 2014 Oct 28;2(4):2324709614556129.
- [47](#) Gruber N, Shoenfeld Y. A link between human papilloma virus vaccination and primary ovarian insufficiency: current analysis. *Curr Opin Obstet Gynecol.* 2015 Aug;27(4):265-70.
- [48](#) DeLong, G. A lowered probability of pregnancy in females in the USA aged 25–29 who received a human papillomavirus vaccine injection. *J Toxicol Environ Health A.* 2018;81(14):661-674.
- [49](#) Shoenfeld Y, Agmon-Levin N. 'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun.* 2011 Feb;36(1):4-8
- [50](#) Tomljenovic L, Colafrancesco S. et al. Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the "Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants" Case Report and Literature Review. *J Investig Med High Impact Case Rep.* 2014 Jan-Mar; 2(1): 2324709614527812.
- [51](#) Colafrancesco S, Perricone C. et al. Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants. *Am J Reprod Immunol.* 2013 Oct;70(4):309-16
- [52](#) Hotta O, Tanaka A. et al. Involvement of chronic epipharyngitis in autoimmune (auto-inflammatory) syndrome induced by adjuvants (ASIA). *Immunol Res.* 2017 Feb;65(1):66-71.
- [53](#) Poddighe D, Castelli L. et al. A sudden onset of a pseudo-neurological syndrome after HPV-16/18 AS04-adjuvated vaccine: might it be an autoimmune/inflammatory syndrome induced by adjuvants (ASIA) presenting as a somatoform disorder? *Immunol Res.* 2014;60(2–3):236–246.
- [54](#) Palmieri B, Poddighe D. et al. Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature. *Immunol Res.* 2017; 65(1): 106–116.
- [55](#) Pellegrino P, Perrone V. et al. The epidemiological profile of ASIA syndrome after HPV vaccination: an evaluation based on the Vaccine Adverse Event Reporting Systems. *Immunol Res.* 2015 Feb;61(1-2):90-6.

- [56](#) Inbar R, Weiss R. et al. Behavioral abnormalities in female mice following administration of aluminum adjuvants and the human papillomavirus (HPV) vaccine Gardasil. *Immunol Res.* 2017 Feb;65(1):136-149
- [57](#) Tomljenovic L, Shaw CA. Death after Quadrivalent Human Papillomavirus (HPV) Vaccination: Causal or Coincidental? *Pharmaceutical Regulatory Affairs: Open Access* 2012,S12:001
- [58](#) Chandler RE, Juhlin K. et al. Current Safety Concerns with Human Papillomavirus Vaccine: A Cluster Analysis of Reports in VigiBase®. *Drug Saf.* 2017; 40(1): 81–90.
- [59](#) Chandler RE. Safety Concerns with HPV Vaccines Continue to Linger: Are Current Vaccine Pharmacovigilance Practices Sufficient? *Drug Saf.* 2017; 40(12): 1167–1170.
- [60](#) Jørgensen L, Gøtzsche PC, Jefferson T. et al. Index of the human papillomavirus (HPV) vaccine industry clinical study programmes and non-industry funded studies: a necessary basis to address reporting bias in a systematic review. *Syst Rev.* 2018; 7: 8.
- [61](#) Joelving F. What the Gardasil Testing May Have Missed. *Slate.* Dec. 17, 2017.
- [62](#) Ibid
- [63](#) EDITORIAL NOTE Statement on Corrections. *Indian J Med Ethics.* May 9, 2018.
- [64](#) Andersson L. Comment - RETRACTED: Increased incidence of cervical cancer in Sweden: Possible link with HPV vaccination. *Indian J Med Ethics.* May 26, 2018.
- [65](#) Ibid
- [66](#) FDA Center for Biologics Evaluation and Research. Vaccines and Related Biological Products Advisory Committee Meeting. May 18, 2006.
- [67](#) MedAlerts Search Results. Apr. 30, 2018.
- [68](#) Lazarus R. Electronic Support for Public Health-Vaccine Adverse Event Reporting System (ESP:VAERS). Harvard Pilgrim Health Care, Inc.
- [69](#) Kessler DA, the Working Group, Natanblut S, et al. A New Approach to Reporting Medication and Device Adverse Effects and Product Problems. *JAMA.* 1993;269(21):2765-2768.
- [70](#) FDA.gov. Kessler DA. Introducing MEDWatch: A New Approach to Reporting Medication and Device Adverse Effects and Product Problems. Reprint from *JAMA.* June 9, 1993.
- [71](#) Braun M. Vaccine adverse event reporting system (VAERS): usefulness and limitations. Johns Hopkins Bloomberg School of Public Health
- [72](#) Rosenthal S, Chen R. The reporting sensitivities of two passive surveillance systems for vaccine adverse events. *Am J Public Health* 1995; 85: pp. 1706-9.
- [73](#) U.S. Department of Health and Human Services. National Vaccine Injury Compensation Program Data Report - updated July 1, 2018. Jul. 1, 2018.
- [74](#) Court Listener. Tarsell v. Secretary of Health and Human Services, 10-251 (Fed. Cl. 2018) United States Court of Federal Claims. Mar. 26, 2018.

Vaccingate:

Initial results on Infanrix Hexa chemical composition

When we started these analysis, from the metagenomics to the chemical ones, we had a lot of questions and we were only looking for answers... After these first results, more questions have arisen and so did the concerns!

The quali-quantitative analysis of organic compound is of great importance in the pharmacological field, as potential safety problems arise from the new production processes of biological drugs and from the complex structural and biological characteristics of these products.

In Infanrix Hexa we found

- chemical contamination from the manufacturing process or cross-contamination with other manufacturing lines;
- chemical toxins;
- bacterial peptide toxins;
- insoluble and indigestible macromolecule that reacts to the protein assay, but cannot be recognized by any protein databases.

We have not found:

- Protein antigens of diphtheria toxoids, tetanus, pertussis, hepatitis B, haemophilus influenzae B, Poliomyelitis 1-2-3;
- Formaldehyde and glutaraldehyde, phenoxyethanol, antibiotic residues indicated in the composition;

In Infanrix Hexa there are six antigens

Tetanus, diphtheria and pertussis toxoids, D antigens of Poliomyelitis 1-2-3, hepatitis B proteins obtained with genetic engineering and Haemophilus polysaccharides chemically linked to tetanus toxoid as carrier. Toxoids are created by treatments with formaldehyde and glutaraldehyde that should remove toxicity keeping intact their ability to stimulate protective antibodies against original toxins.

We were expecting to find the three toxoids and the other antigens not modified by treatment with formaldehyde and glutaraldehyde, to separate the antigens from each other and to be digestible by the enzyme specific for proteins (trypsin). **We have found instead a real polymer, insoluble and indigestible, that we supposed to be the set of antigens chemically bound together (has to be defined if this is present as an aggregate of the individual antigens or a single macromolecule), on which we can find in literature partial information regarding the single antigens.**

This macromolecule could not be recognized in any way by the protein databases, and in fact it turned out to be a solid compound of an unknown chemical structure.

Proteins solubility and their digestion (i.e. the capacity to divide them into small peptide fragments) are two typical proteins characteristics that not only makes it possible to study them through some specific analysis methods **but are also fundamental for the interaction with the immune system to create protective antibodies**, because if the protein structure is heavily altered from the original one, the new antibodies result completely different from those that are able to attack the original antibodies causing illnesses.¶

Since this polymer we have encountered, derived from the antigenic mix, is not only different for its spatial conformation but it's chemically different, so **we can state that we are not facing antigens similar to the original ones but in the form of a compound with an unknown and unpredictable toxicity and efficacy.**

Not only vaccine antigens have been not detected, there were also 65 signs of chemical contaminants of which only 35% is known, there are among these various processing residues and cross-contaminations from other manufacturing lines, and their identification will be checked during the second level of the analytical study (i.e. with standard controls).

7 chemical toxins among these signals have also been identified, probably deriving from chemical contaminants of the manufacturing process or other manufacturing lines at the vaccine manufacturing site; these toxins have a structure that could probably be partially derived from the formaldehyde, glutaraldehyde and cyanogen bromide reaction with other chemical contaminants in the vaccine. We'd like to point out that the toxicity of many of these toxins have been confirmed and published in Pubchem or Toxnet and this poses important safety problems, issues and concerns.



From the protein and peptide fraction study, various free peptides of bacterial origin have been obtained probably coming from the bacterial culture cells used for the antigen extraction. Literature reports bacterial peptides as potential allergens⁵ and also as capable of inducing autoimmune reactions⁶ and these too put a safety issue that needs to be further clarified with the regulatory bodies.

Coming back to the two basic principles that have been our topic on this analysis path, we reaffirm what we have said in the recent interview on the scientific journal Nature: we are inquiring the vaccines efficacy and safety and we can't quite understand how it is possible to claim that this vaccine is even able to generate the 6 protective antibodies - reason why it is designed for - and furthermore to understand how this cluster made of 6 neurotoxic antigens bound together can be claimed as not toxic for newborns.

Infanrix Hexa hexavalent, as for the method we have commissioned, casts major doubts on both its effectiveness and on its safety...

One thing is for sure: we will not stop to proceed.



Study on the chemical composition profile of Infanrix Hexa

Introduction and description of the need

The quali-quantitative analysis of organic compounds is of great importance in the pharmacological field¹, as potential safety problems arise from the new production processes of biological drugs and from the complex structural and biological characteristics of these products.²

The review of the registration dossiers for military vaccines that we find in the final report³ of the Parliamentary Commission of Inquiry "Depleted Uranium"⁴ revealed the presence of protein-chemical contaminants and impurities, which required further analytical study. Our association has decided to take charge of it, as far as possible.

This project is part of the above-mentioned insights. It has been therefore necessary to develop a technology capable of analyzing a wide spectrum of molecules of chemical, metabolic and protein origin in order to evaluate the quality of the obtained results.

A method has been therefore developed, based on SANIST technology to test vaccines for purity and safety (further information below).

Results and Discussion

1. Analysis of the composition declared in the vaccine leaflet

Compound	Presence	Ionic species
Amino acids	YES	[M+H] ⁺
Formaldehyde ⁵	Not detected	-
Lactose anhydrous	YES	[M+H-H ₂ O] ⁺
Vitamins	Not detectable	-
Water	YES	[M+H] ⁺
Neomycin	Weak signal	[M+2H] ²⁺
Diphtheria Toxoid ⁶	Not detected	[M+nH] ^{nt}
Tetanus Toxoid ⁷	Not detected	[M+nH] ^{nt}
Pertussis Toxoid ⁸	Not detected	[M+nH] ^{nt}
Filamentous Haemagglutinin Adhesin (FHA)	Not detected	[M+nH] ^{nt}
Pertactin (PRN)	Not detected	[M+nH] ^{nt}
Haemophilus Influenzae B polysaccharide ⁹	Not detected	[M+nH] ^{nt}
Polyribosylribitol Phosphate (PRP) ¹⁰	Not detectable	-
Polymyxin ¹⁰	Non rilevabile	-

¹ Lett Appl Microbiol. 2015 Feb;60(2):174-80. doi: 10.1111/lam.12355 - <https://www.ncbi.nlm.nih.gov/pubmed/25376111>

² Fuchs F., Biochimie. 2002 Nov;84(11):1173-9 - <https://www.ncbi.nlm.nih.gov/pubmed/12595146>

³ <http://www.camera.it/leg17/491?idL.legislatura=17&categoria=022bis&tipologiaDoc=documento&numero=023&doc=pdf>

⁴ http://www.camera.it/leg17/436?shadow_organo_parlamentare=2588

⁵ <https://pubchem.ncbi.nlm.nih.gov/compound/formaldehyde>

⁶ <https://www.who.int/biologicals/vaccines/diphtheria/en/>

⁷ <https://www.who.int/ith/vaccines/tetanus/en/>

⁸ <http://www.who.int/biologicals/vaccines/pertussis/en/>

⁹ https://www.who.int/biologicals/areas/vaccines/haemophilus/haemophilus_influenzae_tvpbe_Hib/en/

¹⁰ <https://www.sciencedirect.com/topics/neuroscience/polymyxin>



2. Protein fraction analysis

According to the manufacturer, Infanrix Hexa vaccine contains some proteins. The sample has been analyzed for the identification of these proteins. At a visual analysis, the sample appears milky.

Different analysis have been conducted on the sample:

2.1 - 1st analysis: Digestion as it is

To start with, the sample has been subjected to an enzymatic digestion process: 10 μL of a raw sample has been treated with 50 μL Trypsin, left overnight in thermoblock at 37 ° C. A 1 mg / mL hemoglobin control has been prepared and treated as the sample.

This analysis revealed the absence of any proteins in the sample.

2.2 - 2nd Analysis: Digestion of Precipitate

The sample has been then subjected to further analysis by separating, by centrifugation, the liquid part from the solid part of the milky suspension. All the supernatant has been taken. The remaining precipitate has been treated with 30 μL Trypsin and left overnight in thermoblock at 37 ° C. A 1 mg / mL hemoglobin control has been prepared and treated as the sample. After digestion, the sample and the control have been centrifuged. The supernatant has been taken and placed in vials for analysis. 20 μL osmotized H_2O have been added in order to give enough volume for injection.

This analysis revealed the absence of any proteins in the sample.

2.3 - 3rd analysis: Bradford assay

To identify the actual presence of proteins, Infanrix Hexa vaccine has been subjected to the Bradford assay. 200 μL of the raw sample has been treated with 300 μL osmotic H_2O to obtain volume. Then 500 μL of Bradford reagent have been added. After a visual analysis, we can confirm the presence of proteins or peptide sequences given by the blue color (see Figure below):



Based on the calibration line, a protein concentration of 1.099 mg/mL was detected.

2.4 - 4th analysis: Digestion as it is at 57 ° C

After Bradford's assay, 20 μL of the raw sample has been treated with 80 μL of Trypsin. A 1 mg / mL hemoglobin control has been prepared and treated as the sample. They have been left in thermoblock at 37 ° C for 4 hours and then at 57 ° C for 30 minutes. The sample and the control have



then been subjected to centrifugation and the supernatant has been taken and placed in vial for analysis.

In order to process the data thus obtained, the Mascot¹¹ database has been initially used but **nothing has been found**. Therefore, the GMP has been used but also in this case **no protein sequences have been detected**. By the DeNovo research, the following peptide sequences that do not meet the trypsin cutting criteria and therefore potentially belong to free peptides have been identified. Below is the detected sequences list:

YLSA	YLSA	SLGS	HNLPFT
QLYTCC	CHFAHD	WRASST	SYLPFT
SAGE	HLLNMT	YSDDQC	NMAWW
DEV	CHPPYL	TDTENW	GPFRVW
AEYHW	TLAPRF	ALAPWF	RWGPLH
DEV	GSAAG	MNFHR	DSYWH
VLYACPP	DEV	NSNWW	WGC
	SNGYY	VFHRF	

These sequences have been filed into the MS-BLAST¹² search engine obtaining the characterizations reported in Table 1. As can be seen, they have been potentially attributed by structural similarity to proteins of the bacterial world. **The proteins relating to the antigens present in the vaccine have not been detected**. This may be due to its extensive structural modification, introduced by formaldehyde and glutaraldehyde. In fact, the database research has been carried out Without considering the m/z variation introduced by the above-mentioned compounds

It is important to verify whether these changes have led to cross-linked macromolecular complexes shaping. In this regard, we will ask for further analysis using MALDI-TOF-MS¹³ technology widely acknowledged in clinical practice for the study of high weight macromolecules,

Table 1 - Batch #1 (A21CD072D)

Name of Protein	Organism	Total Score
▪ hypothetical protein CALCODRAFT_501505	▪ Calocera cornea HHB 12733	159
▪ erg4/erg24 family protein	▪ Dictyostelium lacteum	154
▪ 3-phenylpropionic acid transporter	▪ Rhodopseudomonas palustris	154
▪ hypothetical protein LAESUDRAFT_731137	▪ Laetiporus sulphureus 93-53	149
▪ aldehyde ferredoxin oxidoreductase ▪ aldehyde ferredoxin oxidoreductase	▪ Alkaliphilus oremlandii ▪ Alkaliphilus oremlandii OhILAs	138
▪ hypothetical protein KAFR_OH02570	▪ Kazachstania africana CBS 2517	136
▪ hypothetical protein	▪ Pseudoxanthomonas mexicana	136
▪ hypothetical protein	▪ Endozoicomonas elysicola	135
▪ Homeodomain-like DNA binding domain-containing transcription factor	▪ Phycomyces blakesleeanus NRRL 1555(-)	110
▪ transcriptional regulator ▪ DNA-binding protein	▪ Streptomyces clavuligerus ▪ Streptomyces clavuligerus ATCC 27064	109
▪ glycosyl hydrolase family 3 N-terminal domain protein	▪ Firmicutes bacterium CAG:56	108
▪ PREDICTED: zinc finger CCCH domain-containing protein 69-like	▪ Pyrus x bretschneideri	108
▪ hypothetical protein CC1G_06886	▪ Coprinopsis cinerea okayama7#130	108
▪ hypothetical protein FIBSPDRAFT_917685	▪ Fibulorhizoctonia sp. CBS 109695	107
▪ uncharacterized protein ▪ unnamed protein product	▪ Blastocystis hominis ▪ Blastocystis hominis	104
▪ hypothetical protein J132_09024	▪ Termitomyce ssp. J132	104

3. Metabolic fraction Analysis

¹¹ http://www.matrixscience.com/help/seq_db_setup_db_qui.html

¹² <http://genetics.bwh.harvard.edu/msblast/>

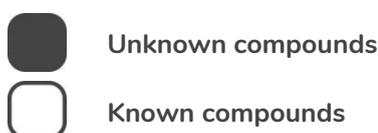
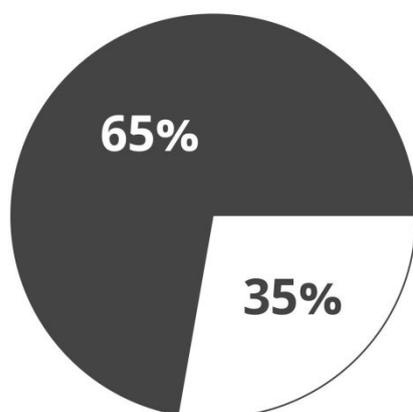
¹³ <https://it.wikipedia.org/wiki/MALDI>



It should be emphasized that this screening study provides a semi-quantitative data which correspond to a range **from nanograms to micrograms** as an indicative order of magnitude. To obtain accurate quantitative data, it will be necessary to proceed using certified analytical standards of known strength.

Below, we report the identification screening results obtained in the two batches under examination:

Batch #1 (A21CD072D)



In Batch # 1 we have 65 signals of which only 35% are known

It has not been possible to carry out the analyzes on different batches because since all the Infanrix Hexa we have purchased for more than a year on the national territory, in different regions and in different periods, belong to batch A21CD072D.



NOTES FOR UNDERSTANDING: this is a first level analysis, that is an identification based on molecular weight. If the result is univocal, (ie at a measured molecular weight only one compound is associated as a structure) it is more likely the right one, but absolute certainty is not possible in this phase. As you will notice, as far as a certain number of compounds is concerned, different substances correspond to a particular molecular weight.

3.1. Infanrix Hexa Vaccine - Batch # 1 (A21CD072D)

65 signals were detected, among which only the 35% gave a potential classification (Table 2).

It must be specified that compound identity is not certain and it should be confirmed by a second level screening carried out with certified analytical standards.

In fact, during screening level, the device measures a particular data by its accurate molecular weight (measurement error <10 ppm). The empirical formula is calculated on the basis of these measures. Some formulas might correspond to several compounds having the same molecular weight but different chemical identity.



NOTES FOR UNDERSTANDING: in essence, the certain data is that we have 65 chemically different substances among which only 35% is known.

Molecules potentially belonging to toxin category have been researched. They have been suggested on the basis of accurate m / z mode research (error <10 ppm) using the toxic compounds database in the Metlin search engine. Table 3 shows the candidates obtained.

It is emphasized that different detected compounds have a candidate empirical formula containing sulfur compounds or sulfur in the form of various functional groups. Furthermore, the presence of formic acid in the form of sodium salt and a polymer deriving from contaminations of Poly Ethylene Glycol (PEG)¹⁴ with an average molecular weight equal to 1340 Da have been detected.

¹⁴ <https://www.sciencedirect.com/topics/materials-science/polylethylene-glycol>



5. Final considerations

Most of the contaminants and impurities detected were not characterized using the metabolic and protein reference databases (KEGG, NCBI-Protein and SwissProt).⁸⁻⁹

There is a critical issue in the contamination of various compounds potentially or definitely harmful to human health.

In short, the first questions we asked ourselves, and the relative answers obtained, are the following:

1. Are the chemical substances listed in the data sheet present?	in part
2. Are there any chemical and protein contaminations?	YES
3. How many contaminating compounds are there?	From 65
4. What are they?	Chemical toxins, chemical compounds, peptides

Next analysis

1. First of all, it is necessary to identify with certainty the most interesting probable compounds	
2. Then to determine the exact amount of each contaminant	
3. Finally to determine the structure of the macromolecule constituted by the set of antigens	

6. Future research developments

Confirmation and identity analysis will be performed using the "**Tandem Mass Spectrometry (MS / MS)**" technique associated with the aid of certified analytical standards. The analysis will be performed in compliance with the European directives (EU directive 2002/657 / EC) useful for the identification of compounds.

In particular, the investigation will have the objective of confirming those substances whose toxicity and allergenicity is known and the 7 toxins identified will be an element of careful study.

7. Description of the SANIST technology

The innovative internationally renowned SANIST platform, through publications in peer-reviewed scientific journals¹⁵⁻¹⁶ - was used to perform a first identification screening on the vaccines of interest.

8. Details related to the analytical method

SANIST technology consists of:

- a **kit** for the extraction of analytes (the unknown substances to be determined);
- the **LC-SACI / ESI-MS** analysis system which allows to reduce the chemical noise of mass spectrometers and obtain a better detection of instrumental signals;

¹⁵ Albini A. et al., Rapid Commun Mass Spectrom. 2015 Oct 15;29(19):1703-10. doi: 20.1002/rcm.7270. (<https://onlinelibrary.wiley.com/doi/full/10.1002/rcm.7270>)

¹⁶ Cristoni S. et al., J Mass Spectrom. 2017 Jan;52(1):16-21. doi:10.1002/jms.3895. (<https://www.ncbi.nlm.nih.gov/pubmed/27776380>)



- c) the **SANIST data processing system** consisting of a local bioinformatics and network platform capable of processing data using dedicated databases and customized algorithms. It is specified that, during the screening phase, the recognition is made in the context of scientific research and through research in official banks (KEGG, NCBI-Prot and SwissProt)¹⁷⁻¹⁸ without the aid of certified analytical standards. **It is therefore necessary to perform a second level analysis with certified analytical standards to confirm their identity.**

9. Areas of application of SANIST technology

To date, the **SANIST platform** is applicable in the following fields:

- In **clinical research** of disease markers and their direct application in the diagnostic field.
- Food services**, food traceability. Comparative studies to determine the quality of products based on their complex molecular composition. Control of food counterfeiting.
- Nutraceutical sector**, development of the nutritional value of a food supplement based on its molecular composition. Forged search (for example: added drugs).
- Pharmaceutical sector**, drug control and research of active biomolecules.
- Cosmetic industry**: the molecular composition of cosmetic products can be carefully monitored and correlated with the quality of the product.

10. How to read the tables

This is a screening phase; the instrument measures a particular data by its accurate molecular weight (measurement error <10 ppm). On the basis of these measures a brute formula is calculated. Some formulas can correspond to several compounds having the same molecular weight but different chemical identity.

Example of a single associated component:

▪ Atovaquone	Medication for the treatment of malaria
--------------	---

In this example, the instrument detected a signal with a certain molecular weight. By inserting the brute formula in the databases, it was possible to associate a **probable component**.

Example of a number of associated components:

<ul style="list-style-type: none"> ▪ Tetracenomycin F2 ▪ Decaketide tricyclic intermediate ▪ 1'-hydroxyversicolorone 	<ul style="list-style-type: none"> ▪ Monocarboxylic hydroxy acid ▪ Member of the anthracenes ▪ Antrafuran
---	--

In this example, the instrument detected a signal with a certain molecular weight. By inserting the brute formula in the databases, it was possible to associate **three probable components**.

11. Tables of contaminants

Table 2 - Batch #1 (A21CD072D)

▪ Tungsten carbide	▪ Inorganic carbide industrially used to synthesize cemented carbides.
--------------------	--

¹⁷ Kanehisa M. et al., Nucleic Acids Res. 2017 Jan 4;45(D1):D353-D361. doi:10.1093/nar/gkw1092. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5210567/>)

¹⁸ Cristoni S. et al., Expert Rev Proteomics. 2004 Dec; 1(4):469-83. (<https://www.ncbi.nlm.nih.gov/pubmed/15966842>)



<ul style="list-style-type: none"> ▪ Tetracenomycin F2 ▪ Decaketide tricyclic intermediate ▪ 1'-hydroxyversicolorone 	<ul style="list-style-type: none"> ▪ Monocarboxylic hydroxy acid ▪ Member of the anthracenes ▪ Antrafuran
<ul style="list-style-type: none"> ▪ Lactose 	<ul style="list-style-type: none"> ▪ Added as a stabilizer.
<ul style="list-style-type: none"> ▪ Sodium methallylsulfonate 	<ul style="list-style-type: none"> ▪ Monomer used in the polymer industry.
<ul style="list-style-type: none"> ▪ Salicin 6-phosphate ▪ Pachyrrhizone ▪ Arnottin II ▪ Tetracenomycin F1 	<ul style="list-style-type: none"> ▪ Glycoside phosphate derived from salicin (anti-inflammatory agent) ▪ Member of the Rotenoni ▪ Member of 2-benzofurans ▪ Monocarboxylic hydroxy acid
<ul style="list-style-type: none"> ▪ Octadecanamide 	<ul style="list-style-type: none"> ▪ Amide of stearic acid
<ul style="list-style-type: none"> ▪ L-Leucine 	<ul style="list-style-type: none"> ▪ Amino acid
<ul style="list-style-type: none"> ▪ Lichenin (altri 19 possibili candidati) 	<ul style="list-style-type: none"> ▪ Glucan. Study to use glucans as vaccine adjuvants
<ul style="list-style-type: none"> ▪ Justicidin B 	<ul style="list-style-type: none"> ▪ Lignan
<ul style="list-style-type: none"> ▪ Dihydrochelirubine ▪ 6-oxochelirubine ▪ 7,8-Didemethyl-8-hydroxy-5-deazariboflavin 	<ul style="list-style-type: none"> ▪ Dihydrobenzophenanthridinico Alkaloid ▪ Alkaloid ▪ Riboflavin
<ul style="list-style-type: none"> ▪ Deamino-alpha-keto-demethylphosphinothricin 	<ul style="list-style-type: none"> ▪ -
<ul style="list-style-type: none"> ▪ Cassything ▪ (6-alpha-D-glucosaminyll)-1D-myo inositol 	<ul style="list-style-type: none"> ▪ Alkaloid ▪ A derivative of a D-glucosaminide and a monosaccharide.
<ul style="list-style-type: none"> ▪ Carbenicillin sodium 	<ul style="list-style-type: none"> ▪ Bactericidal antibiotic
<ul style="list-style-type: none"> ▪ bis-D-fructose 2', 1:2, 1'-dianhydride ▪ D-Fructofuranose 1,2':2,3'-dianhydride ▪ Prazepam ▪ 2,3-Dehydro-UWM6 / ▪ Levofuraltadone 	<ul style="list-style-type: none"> ▪ Dianhydride sugar ▪ Dianhydride sugar ▪ Benzodiazepine derivative / ▪ Member of the phenanthrenes ▪ Antibiotic that can be used in combination with a vaccine consisting of hybrid cells for cancer treatment ▪ Heterotetracyclic compound
<ul style="list-style-type: none"> ▪ Mycrocyclosin 	<ul style="list-style-type: none"> ▪ Heterotetracyclic compound
<ul style="list-style-type: none"> ▪ Atovaquone 	<ul style="list-style-type: none"> ▪ Medication for the treatment of malaria
<ul style="list-style-type: none"> ▪ Amoxicillin ▪ Cephalexin monohydrate ▪ Cefroxadine ▪ CGP 28-392 	<ul style="list-style-type: none"> ▪ Antibiotic ▪ Antibiotic that decreases the effectiveness of vaccines ▪ Cephalosporin antibiotic ▪ Aromatic ether
<ul style="list-style-type: none"> ▪ 7-deoxyloganate ▪ 8-epideoxyloganic acid ▪ LY395153 ▪ AL-294 	<ul style="list-style-type: none"> ▪ Metabolite of plants ▪ Metabolite of plants ▪ Member of the benzamides ▪ Alkylbenzene
<ul style="list-style-type: none"> ▪ 4-Chloro-orto-phenylenediamine 	<ul style="list-style-type: none"> ▪ Member of the monochlorobenzene
<ul style="list-style-type: none"> ▪ 2-N, 6-N-Bis(2,3-dihydroxy benzoyl)-L-Lysine amide 	<ul style="list-style-type: none"> ▪ -
<ul style="list-style-type: none"> ▪ 2-Iodo-6-methoxyphenol 	<ul style="list-style-type: none"> ▪ Member of the phenols
<ul style="list-style-type: none"> ▪ Tungstate 	<ul style="list-style-type: none"> ▪ Compound containing a tungsten oxoanion
<ul style="list-style-type: none"> ▪ 2-amino-5-chloromuconate-6-semialdehyde 	<ul style="list-style-type: none"> ▪ Semialdehyde
<ul style="list-style-type: none"> ▪ 2,5-Dichloro-4-oxohex-2-enedioate 	<ul style="list-style-type: none"> ▪ Member of the family of medium-chain keto acids
<ul style="list-style-type: none"> ▪ 1-Palmitoyl-2-(5-hydroxy-8-oxo-6-octenoyl)-sn-glycero-3-phosphatidylcholine 	<ul style="list-style-type: none"> ▪ 1,2-diacyl-sn-glicero-3-fosfocolina

Table 3 - Batch #1 (A21CD072D)

Candidate compound	Empirical Formula
<ul style="list-style-type: none"> ▪ Sodium formate 	CHNaO2



<ul style="list-style-type: none"> ▪ Hepta-2,3,4,5,6-pentaenenitrile 	C7H3N
<ul style="list-style-type: none"> ▪ (Methanesulfonyl)(dioxo)-lambda-5--azane ▪ Oxaziridine-2-sulfonic acid 	CH3NO4S
<ul style="list-style-type: none"> ▪ 3,4-Dihydro-3-thioxo-1,2,4-triazin-5(2H)-one ▪ 5-Thioxo-4,5-dihydro-1,2,4-triazin-3(2H)-one ▪ 1,2,4-oxadiazole-3-carbothioamide ▪ 1,2,3-Thiadiazole-4-carboxamide ▪ 5-amino-1,3,4-thiadiazole-2-carbaldehyde ▪ 1,1-Difluoro-1-isocyanatoethane ▪ 1,1-Difluoro-2-isocyanatoethane 	C3H3N3OS
<ul style="list-style-type: none"> ▪ 3-(methylsulfonyl)-1H-1,2,4-triazole ▪ 1H-Imidazole-2-sulfonamide ▪ N-(4,5-Dihydro-1,3-thiazol-2-yl)nitramide ▪ 1H-Imidazole-5-sulfonamide ▪ 1H-Pyrazole-4-sulfonamide ▪ Undeca-2,4,6,8,10-pentaynenitrile 	C3H3F2NO
<ul style="list-style-type: none"> ▪ 2-Aminobenzenethiol ▪ 4-Methyl-5-vinylthiazole ▪ 2-Pyridinemethanethiol ▪ 2-Isopropenylthiazole ▪ 5,6-Dihydro-4H-cyclopenta[d][1,3]thiazole ▪ 4-Aminothiophenol 3-Pyridinemethanethiol ▪ Pyridine, 2-(methylthio)- ▪ Pyridine, 3-(methylthio)- 	C6H7NS
<ul style="list-style-type: none"> ▪ Phenthiazamine 	C9H8N2S
<ul style="list-style-type: none"> ▪ 4-Chloro-N-hydroxybenzene-1-sulfonamide 	C6H6ClNO3S
<ul style="list-style-type: none"> ▪ Carbamodithioic acid, (4-hydroxyphenyl)- 	C7H7NOS2





Data & Statistics

The United States has the safest, most effective vaccine supply in history. In the majority of cases, vaccines cause no side effects, however they can occur, as with any medication—but most are mild. Very rarely, people experience more serious side effects, like allergic reactions.

In those instances, the National Vaccine Injury Compensation Program (VICP) allows individuals to file a petition for compensation.

What does it mean to be awarded compensation?

Being awarded compensation for a petition does not necessarily mean that the vaccine caused the alleged injury. In fact:

- Almost 80 percent of all compensation awarded by the VICP comes as result of a negotiated settlement between the parties in which HHS has not concluded, based upon review of the evidence, that the alleged vaccine(s) caused the alleged injury.
- Attorneys are eligible for reasonable attorneys' fees, whether or not the petitioner is awarded compensation by the Court, if certain minimal requirements are met. In those circumstances, attorneys are paid by the VICP directly. By statute, attorneys may not charge any other fee, including a contingency fee, for his or her services in representing a petitioner in the VICP.

What reasons might a petition result in a negotiated settlement?

- Consideration of prior U.S. Court of Federal Claims decisions, both parties decide to minimize risk of loss through settlement
- A desire to minimize the time and expense of litigating a case
- The desire to resolve a petition quickly

How many petitions have been awarded compensation?

According to the CDC, from 2006 to 2015 over 2.8 billion doses of covered vaccines were distributed in the U.S. For petitions filed in this time period, 4,349 petitions were adjudicated by the Court, and of those 2,824 were compensated. This means for every 1 million doses of vaccine that were distributed, 1 individual was compensated.

Since 1988, over 17,835 petitions have been filed with the VICP. Over that 27- year time period, 16,113 petitions have been adjudicated, with 5,205 of those determined to be compensable, while 10,908 were dismissed. Total compensation paid over the life of the program is approximately \$3.5 billion.

This information reflects the current thinking of the United States Department of Health and Human Services on the topics addressed. This information is not legal advice and does not create or confer any rights for or on any person and does not operate to bind the Department or the public. The ultimate decision about the scope of the statutes authorizing the VICP is within the authority of the United States Court of Federal Claims, which is responsible for resolving petitions for compensation under the VICP.

**VICP Adjudication Categories, by Alleged Vaccine,
 For Petitions Filed Since the Inclusion of Influenza as an Eligible Vaccine for Filings 01/01/2006
 Through 12/31/2015**

Name of Vaccine Listed First in a Petition (other vaccines may be alleged or basis for compensation)	Number of Doses Distributed in the U.S., 01/01/2006 through 12/31/2015 (Source: CDC)	Compensable			Compensable Total	Dismissed/Non-Compensable Total	Grand Total
		Concession	Court Decision	Settlement			
DT	756,377	1		5	6	4	10
DTaP	88,814,104	15	21	97	133	96	229
DTaP-Hep B-IPV	56,700,877	4	8	24	36	42	78
DTaP-HIB	1,135,474			1	1	1	2
DTaP-IPV-HIB	52,242,336	2	1	7	10	21	31
DTap-IPV	18,613,490			2	2	1	3
DTP	0	1	1	3	5	2	7
DTP-HIB	0			3	3	1	4
Hep A-Hep B	13,767,345			13	13	2	15
Hep B-HIB	4,787,457	1	1	2	4	1	5
Hepatitis A (Hep A)	150,276,481	56	4	31	40	26	66
Hepatitis B (Hep B)	158,988,970	3	11	55	69	56	125
HIB	101,459,227	1	1	5	7	7	14
HPV	89,696,704	13	6	93	112	135	247

National Vaccine Injury Compensation Program
 Monthly Statistics Report

Influenza	1,226,400,000	228	126	1,451	1,805	281	2,086
IPV	65,399,472			4	4	2	6
Measles	135,660			1	1		1
Meningococcal	70,797,701	1	4	31	36	7	43
MMR	87,990,038	20	16	74	110	95	205
Mumps	110,749						
MMR-Varicella	18,023,247	8		8	16	9	25
Nonqualified	N/A			3	3	28	31
OPV	0	1			1	5	6
Pneumococcal Conjugate	180,357,916		1	6	7	20	27
Rotavirus	89,501,227	8	4	17	29	10	39
Rubella	422,548		1	1	2		2
Td	60,068,722	8	7	55	70	22	92
Tdap	202,021,173	50	12	162	224	39	263
Tetanus	3,836,052	5	1	28	34	18	52
Unspecified	N/A	1	1	3	5	578	583
Varicella	103,643,469	3	9	24	36	16	52
Grand Total	2,845,946,816	379	236	2,209	2,824	1,525	4,349

Notes on the Adjudication Categories Table

The date range of 01/01/2006 through 12/31/2015 was selected to reflect petitions filed since the inclusion of influenza vaccine in July 2005. Influenza vaccine now is named in the majority of all VICP petitions.

In addition to the first vaccine alleged by a petitioner, which is the vaccine listed in this table, a VICP petition may allege other vaccines, which may form the basis of compensation.

Vaccine doses are self-reported distribution data provided by US-licensed vaccine manufacturers. The data provide an estimate of the annual national distribution and do not represent vaccine administration. In order to maintain confidentiality of an individual manufacturer or brand, the data are presented in an aggregate format by vaccine type. Flu doses are derived from CDC's FluFinder tracking system, which includes data provided to CDC by US-licensed influenza vaccine manufacturers as well as their first line distributors.

"Unspecified" means insufficient information was submitted to make an initial determination. The conceded "unspecified" petition was for multiple unidentified vaccines that caused abscess formation at the vaccination site(s), and the "unspecified" settlements were for multiple vaccines later identified in the Special Masters' decisions

Definitions

Compensable – The injured person who filed a petition was paid money by the VICP. Compensation can be achieved through a concession by the U.S. Department of Health and Human Services (HHS), a decision on the merits of the petition by a special master or a judge of the U.S. Court of Federal Claims (Court), or a settlement between the parties.

- **Concession:** HHS concludes that a petition should be compensated based on a thorough review and analysis of the evidence, including medical records and the scientific and medical literature. The HHS review concludes that the petitioner is entitled to compensation, including a determination either that it is more likely than not that the vaccine caused the injury or the evidence supports fulfillment of the criteria of the Vaccine Injury Table. The Court also determines that the petition should be compensated.
- **Court Decision:** A special master or the court, within the United States Court of Federal Claims, issues a legal decision after weighing the evidence presented by both sides. HHS abides by the ultimate Court decision even if it maintains its position that the petitioner was not entitled to compensation (e.g., that the injury was not caused by the vaccine).

For injury petitions, compensable court decisions are based in part on one of the following determinations by the court:

1. The evidence is legally sufficient to show that the vaccine more likely than not caused (or significantly aggravated) the injury; or
 2. The injury is listed on, and meets all of the requirements of, the Vaccine Injury Table, and HHS has not proven that a factor unrelated to the vaccine more likely than not caused or significantly aggravated the injury. An injury listed on the Table and meeting all Table requirements is given the legal presumption of causation. It should be noted that conditions are placed on the Table for both scientific and policy reasons.
- **Settlement:** The petition is resolved via a negotiated settlement between the parties. This settlement is not an admission by the United States or the Secretary of Health and Human Services that the vaccine caused the petitioner's alleged injuries, and, in settled cases, the Court does not determine that the vaccine caused the injury. A settlement therefore cannot be characterized as a decision by HHS or by the Court that the vaccine caused an injury. Petitions may be resolved by settlement for many reasons, including consideration of prior court decisions; a recognition by both parties that there is a risk of loss in proceeding to a decision by the Court making the certainty of settlement more desirable; a desire by both parties to minimize the time and expense associated with litigating a case to conclusion; and a desire by both parties to resolve a case quickly and efficiently.
 - **Non-compensable/Dismissed:** The injured person who filed a petition was ultimately not paid money. Non-compensable Court decisions include the following:
 1. The Court determines that the person who filed the petition did not demonstrate that the injury was caused (or significantly aggravated) by a covered vaccine or meet the requirements of the Table (for injuries listed on the Table).
 2. The petition was dismissed for not meeting other statutory requirements (such as not meeting the filing deadline, not receiving a covered vaccine, and not meeting the statute's severity requirement).
 3. The injured person voluntarily withdrew his or her petition.

Petitions Filed, Compensated and Dismissed, by Alleged Vaccine, Since the Beginning of VICP, 10/01/1988 through 02/01/2017

Vaccines	Filed			Compensated	Dismissed
	Injury	Death	Grand Total		
DTaP-IPV	7	0	7	2	1
DT	69	9	78	26	52
DTP	3,286	696	3,982	1,273	2,709
DTP-HIB	20	8	28	7	21
DTaP	420	80	500	212	232
DTaP-Hep B-IPV	69	30	99	37	43
DTaP-HIB	11	1	12	5	3
DTaP-IPV-HIB	38	19	57	9	20
Td	195	3	198	116	73
Tdap	427	2	429	243	41
Tetanus	119	2	121	58	45
Hepatitis A (Hep A)	91	6	97	40	28
Hepatitis B (Hep B)	646	57	703	262	399
Hep A-Hep B	26	0	26	14	3
Hep B-HIB	8	0	8	4	3
HIB	40	3	43	14	18
HPV	326	14	340	109	133
Influenza	3,122	120	3,242	1,900	285
IPV	264	14	278	8	268
OPV	282	28	310	158	151
Measles	143	19	162	55	107
Meningococcal	55	2	57	36	5
MMR	933	59	992	392	551
MMR-Varicella	38	1	39	16	10
MR	15	0	15	6	9
Mumps	10	0	10	1	9
Pertussis	4	3	7	2	5
Pneumococcal Conjugate	81	10	91	16	35
Rotavirus	77	2	79	47	21
Rubella	190	4	194	71	123
Varicella	88	9	97	57	28
Nonqualified1	96	9	105	3	96
Unspecified2	5,420	9	5,429	6	5,381
Grand Total	16,616	1,219	17,835	5,205	10,908

¹ Nonqualified petitions are those filed for vaccines not covered under the VICP.

² Unspecified petitions are those submitted with insufficient information to make a determination.

Petitions Filed

Fiscal Year	Total
FY 1988	24
FY 1989	148
FY 1990	1,492
FY 1991	2,718
FY 1992	189
FY 1993	140
FY 1994	107
FY 1995	180
FY 1996	84
FY 1997	104
FY 1998	120
FY 1999	411
FY 2000	164
FY 2001	215
FY 2002	958
FY 2003	2,592
FY 2004	1,214
FY 2005	735
FY 2006	325
FY 2007	410
FY 2008	417
FY 2009	397
FY 2010	448
FY 2011	386
FY 2012	401
FY 2013	504
FY 2014	633
FY 2015	803
FY 2016	1,120
FY 2017	396
Total	17,835

Adjudications

Generally, petitions are not adjudicated in the same fiscal year as filed. On average, it takes 2 to 3 years to adjudicate a petition after it is filed.

Fiscal Year	Compensable	Dismissed	Total
FY 1989	9	12	21
FY 1990	100	33	133
FY 1991	141	447	588
FY 1992	166	487	653
FY 1993	125	588	713
FY 1994	162	446	608
FY 1995	160	575	735
FY 1996	162	408	570
FY 1997	189	198	387
FY 1998	144	181	325
FY 1999	98	139	237
FY 2000	125	104	229
FY 2001	86	88	174
FY 2002	104	104	208
FY 2003	56	100	156
FY 2004	62	247	309
FY 2005	60	229	289
FY 2006	69	193	262
FY 2007	82	136	218
FY 2008	147	151	298
FY 2009	134	257	391
FY 2010	180	329	509
FY 2011	266	1,740	2,006
FY 2012	265	2,534	2,799
FY 2013	369	650	1,019
FY 2014	371	196	567
FY 2015	513	113	626
FY 2016	679	179	858
FY 2017	181	44	225
Total	5,205	10,908	16,113

Awards Paid

Fiscal Year	Number of Compensated Awards	Petitioners' Award Amount	Attorneys' Fees/Costs Payments	Number of Payments to Attorneys (Dismissed Cases)	Attorneys' Fees/Costs Payments (Dismissed Cases)	Number of Payments to Interim Attorneys'	Interim Attorneys' Fees/Costs Payments	Total Outlays
FY 1989	6	\$1,317,654.78	\$54,107.14	0	\$0.00	0	\$0.00	\$1,371,761.92
FY 1990	88	\$53,252,510.46	\$1,379,005.79	4	\$57,699.48	0	\$0.00	\$54,689,215.73
FY 1991	114	\$95,980,493.16	\$2,364,758.91	30	\$496,809.21	0	\$0.00	\$98,842,061.28
FY 1992	130	\$94,538,071.30	\$3,001,927.97	118	\$1,212,677.14	0	\$0.00	\$98,752,676.41
FY 1993	162	\$119,693,267.87	\$3,262,453.06	272	\$2,447,273.05	0	\$0.00	\$125,402,993.98
FY 1994	158	\$98,151,900.08	\$3,571,179.67	335	\$3,166,527.38	0	\$0.00	\$104,889,607.13
FY 1995	169	\$104,085,265.72	\$3,652,770.57	221	\$2,276,136.32	0	\$0.00	\$110,014,172.61
FY 1996	163	\$100,425,325.22	\$3,096,231.96	216	\$2,364,122.71	0	\$0.00	\$105,885,679.89
FY 1997	179	\$113,620,171.68	\$3,898,284.77	142	\$1,879,418.14	0	\$0.00	\$119,397,874.59
FY 1998	165	\$127,546,009.19	\$4,002,278.55	121	\$1,936,065.50	0	\$0.00	\$133,484,353.24
FY 1999	96	\$95,917,680.51	\$2,799,910.85	117	\$2,306,957.40	0	\$0.00	\$101,024,548.76
FY 2000	136	\$125,945,195.64	\$4,112,369.02	80	\$1,724,451.08	0	\$0.00	\$131,782,015.74
FY 2001	97	\$105,878,632.57	\$3,373,865.88	57	\$2,066,224.67	0	\$0.00	\$111,318,723.12
FY 2002	80	\$59,799,604.39	\$2,653,598.89	50	\$656,244.79	0	\$0.00	\$63,109,448.07
FY 2003	65	\$82,816,240.07	\$3,147,755.12	69	\$1,545,654.87	0	\$0.00	\$87,509,650.06
FY 2004	57	\$61,933,764.20	\$3,079,328.55	69	\$1,198,615.96	0	\$0.00	\$66,211,708.71
FY 2005	64	\$55,065,797.01	\$2,694,664.03	71	\$1,790,587.29	0	\$0.00	\$59,551,048.33
FY 2006	68	\$48,746,162.74	\$2,441,199.02	54	\$1,353,632.61	0	\$0.00	\$52,540,994.37
FY 2007	82	\$91,449,433.89	\$4,034,154.37	61	\$1,692,020.25	0	\$0.00	\$97,175,608.51
FY 2008	141	\$75,716,552.06	\$5,191,770.83	74	\$2,531,394.20	2	\$117,265.31	\$83,556,982.40
FY 2009	131	\$74,142,490.58	\$5,404,711.98	36	\$1,557,139.53	28	\$4,241,362.55	\$85,345,704.64
FY 2010	173	\$179,387,341.30	\$5,961,744.40	59	\$1,933,550.09	22	\$1,978,803.88	\$189,261,439.67
FY 2011	251	\$216,319,428.47	\$9,572,042.87	403	\$5,589,417.19	28	\$2,001,770.91	\$233,482,659.44
FY 2012	249	\$163,491,998.82	\$9,241,427.33	1,020	\$8,649,676.56	37	\$5,420,257.99	\$186,803,360.70
FY 2013	375	\$254,666,326.70	\$13,543,099.70	704	\$7,012,615.42	50	\$1,454,851.74	\$276,676,893.56
FY 2014	365	\$202,084,196.12	\$12,161,422.64	508	\$6,824,566.68	38	\$2,493,460.73	\$223,563,646.17
FY 2015	508	\$204,137,880.22	\$14,507,692.27	117	\$3,484,869.16	50	\$3,089,497.68	\$225,219,939.33
FY 2016	689	\$230,140,251.20	\$16,131,146.49	91	\$2,432,993.74	59	\$3,502,709.91	\$252,207,101.34

National Vaccine Injury Compensation Program
 Monthly Statistics Report

Fiscal Year	Number of Compensated Awards	Petitioners' Award Amount	Attorneys' Fees/Costs Payments	Number of Payments to Attorneys (Dismissed Cases)	Attorneys' Fees/Costs Payments (Dismissed Cases)	Number of Payments to Interim Attorneys'	Interim Attorneys' Fees/Costs Payments	Total Outlays
FY 2017	253	\$95,387,945.45	\$7,998,060.27	50	\$1,570,270.65	15	\$943,058.99	\$105,899,335.36
Total	5,214	\$3,331,637,591.40	\$156,332,962.90	5,149	\$71,757,611.07	329	\$25,243,039.69	\$3,584,971,205.06

NOTE: Some previous fiscal year data has been updated as a result of the receipt and entry of data from documents issued by the Court and system updates which included petitioners' costs reimbursements in outlay totals,

"Compensated" are petitions that have been paid as a result of a settlement between parties or a decision made by the U.S. Court of Federal Claims (Court). The # of awards is the number of petitioner awards paid, including the attorneys' fees/costs payments, if made during a fiscal year. However, petitioners' awards and attorneys' fees/costs are not necessarily paid in the same fiscal year as when the petitions/petitions are determined compensable. "Dismissed" includes the # of payments to attorneys and the total amount of payments for attorneys' fees/costs per fiscal year. The VICP will pay attorneys' fees/costs related to the petition, whether or not the petition/petition is awarded compensation by the Court, if certain minimal requirements are met. "Total Outlays" are the total amount of funds expended for compensation and attorneys' fees/costs from the Vaccine Injury Compensation Trust Fund by fiscal year.

Since influenza vaccines (vaccines administered to large numbers of adults each year) were added to the VICP in 2005, many adult petitions related to that vaccine have been filed, thus changing the proportion of children to adults receiving compensation.

DNA Contamination in HPV vaccines

A serious safety issue that should not be swept under the regulatory carpet [Professor Joe Cummins](#)

Please circulate widely and repost, but you must give the URL of the original and preserve all the links back to articles on our website. If you find this report useful, please support ISIS by subscribing to our magazine [Science in Society](#), and encourage your friends to do so. Or have a look at the [ISIS bookstore](#) for other publications

When the Human Papilloma Virus (HPV) vaccine Gardasil was recently found to be contaminated with DNA, the US Food and Drug Administration (FDA) lost no time in declaring that the DNA was not a contaminant but a harmless by-product of vaccine production. I disagree; that extraneous DNA is potentially harmful. It should also be noted that the safety and efficacy of HPV vaccines have been controversial from the start (see [1] [The HPV Vaccine Controversy](#) and other articles in the series, *SiS* 41).

The virus

HPV establishes productive infections only in keratinocytes of the skin or mucous membranes. While the majority of the known HPV types cause no symptoms in most people, some types can cause warts (verrucae), while others can lead to cancers of the cervix, vulva, vagina, penis, oropharynx and anus.

Recently, HPV has been linked to an increased risk of cardiovascular disease. In addition, HPV 16 and 18 infections are strongly associated with an increased risk of developing throat cancer. Worldwide in 2002, an estimated 561 200 new cancer cases (5.2 %) were attributable to HPV, making HPV one of the most important infectious causes of cancer, and cervical cancer is the second most common cancer in women worldwide. In 2008, there were an estimated 529 000 new cases of cervical cancer and 274 000 deaths; more than 85 % of the deaths in developing countries, where it accounts for 13 % of all female cancers [2].

The viral genome

The HPV genome consists of 8 genes coding for proteins and a non-protein-coding region with regulatory genes. The genes are distinguished as early and late functioning in virus development. The early genes include those involved in virus replication and transcription along with the oncogenes for cancer development. The late genes encode the two structural proteins L1 and L2 of the virus capsid. HPV infects the basal cells of the cervical epithelium when it is damaged in some way. The viral genome becomes established in the basal cells as an episome (an independently replicating nuclear micro-chromosome). The episome replicates in tandem with the chromosomes of the cell and forms virus particles. The complete virus particles are in the outermost cells of the epithelium and the viruses are spread as the cells slough off from the epithelium. Some virus proteins function as oncoproteins, transforming the epithelial cells to a precancerous state. HPV infection is necessary but not sufficient for cancer formation, however. In high grade lesions and cancer, an episome is integrated into the cell chromosome. Integration disrupts a viral transcription regulatory protein that controls the production of the cancer proteins, leading to their continual and enhanced production [3] ([Recombinant Cervical Cancer Vaccines](#), *SiS* 29). HPV integration into human chromosomes is non-random; with integration hot spots in chromosome regions homologous to the oncogene E5 of HPV or the structural protein L2 [4]. Women with cervical cancer have been found with viral chromosomes integrated completely or partially as chromosome fragments, or as independent episomes. Partially integrated HPV was most prevalent in women with cancer while complete virus integration was about half as frequent and the episomal form rare. The cancer-causing integration breaks the HPV chromosome at the E1/E2 region, causing a loss of that region. This in turn results in loss of control of the cancer genes E6 and E7. The E7 cancer gene produces a protein that inactivates the retinoblastoma gene – a cancer suppressor gene - of the host cell, thereby promoting cancer [5]. (Retinoblastoma is an inherited cancer of the eye caused by loss of the retinoblastoma gene.) The main lesson is that fragmentation or breakage of the HPV DNA is an important factor in cancer progression of the host cell.

Gene transcription

The viral genes have a complex transcription pattern. There is a single promoter for all of the early genes. The early promoter initiates production of a large pre-messenger RNA from which messages containing exons and introns are then spliced to generate each of the early proteins. The other viral promoter initiates production of pre-messenger for structural proteins L1 and L2, which also contain exons and introns, and are similarly spliced prior to translation of the messenger RNA into protein. There are early and late polyadenylation (poly A) signals for the large pre-messenger RNA transcripts. Gene expression of HPV is tightly coupled to the developmental status of the host cells [6].

Micro RNAs are very small (around 22 nucleotides in chains) non-coding regulatory gene products of cells. Micro RNAs are altered in a number of human cancers and one is significantly elevated in HPV anal cancer [7]. A cluster of micro RNAs was found associated with HPV head and neck cancers [8]. The natural history of HPV cancers shows a complex pattern of gene transcription and micro RNAs are implicated in the development of HPV cancers.

HPV vaccines

HPV vaccines have been deployed worldwide since 2006. Two vaccines have been commercialized: Gardasil, manufactured by Merck and Cervarix, manufactured by GlaxoSmithKline. They are prophylactic, that is, they prevent cervical cancer but do not cure existing infections, and are based on the L1 virus-like particles to achieve immunity against HPV. The L1 protein is capable of self-assembly to form empty virus like particles that activate the human immune system to form antibodies. The HPVs targeted by the vaccines are “high risk” types 16 and 18 and “low risk” types 6 and 11. The two commercial HPV vaccines are both made using genetically modified (GM) microbes in a laboratory. Gardasil protects against all four HPV types because it contains virus like particles with mixtures of the four subunit proteins, and is called a tetravalent vaccine. The four L1 proteins are manufactured using GM baker’s yeast. Cervarix protects against the HPV types 16 and 18, and is a bivalent vaccine, and is manufactured using GM baculovirus (a soil-born insect virus) in cultured insect cells [9].

Gardasil

The vaccine consists of the four Monovalent Bulk Adsorbed Products (MBAPs), one for each of the four human papillomavirus (HPV) types. The active components in each MBAP are virus-like particles (VLPs) made up of the recombinant major capsid (L1) protein for that HPV type, produced in recombinant *S. cerevisiae*. The pGAL110 yeast expression vector was used for all four HPV L1 proteins. The L1 genes were derived by a direct cloning protocol. However, the coding sequence for HPV11L1 was synthetically rebuilt based on HPV6L1 nucleotide sequences that supported good VLP expression in yeast. Polymerase chain reaction (PCR) was used to subclone the L1 genes into the yeast expression vector pGAL110, which contains the yeast GAL1-GAL10 promoter and the yeast ADH1 terminator (ADH1t) for transcription termination and polyadenylation. The pGAL110-related yeast expression vectors for each of the four HPV types were used to transform the recombinant *S. cerevisiae* [10].

Gardasil DNA contamination

In 2011, Gardasil was found to be contaminated with recombinant HPV DNA in all of the lots of vaccine marketed in the United States, Australia, New Zealand, Spain, France and Poland. One of the DNA fragments identified was a gene fragment from the HPV capsid protein L1 [11]. Sane Vax, a girl age 13, was found to have blood containing HPV DNA two years after Gardasil inoculation [12]. Other DNA contaminants were not specifically identified in the many contaminated vaccine samples but are presumably DNA fragments from the genetically modified yeast used to produce the vaccine protein. Even though the FDA and the vaccine manufacturer had earlier claimed that Gardasil contained no DNA they later changed their tune, and are now claiming that DNA HPV L1 gene in the vaccine is not a contaminant but it is a normal consequence of vaccine production. The remaining DNA fragments are presumed to be safe [13]. The World Health Organization (WHO) had earlier claimed that DNA fragments shorter than 200 base pairs should be presumed safe [14]. It appears that the Merck Corporation, FDA and WHO are closing ranks to claim that the DNA contaminant in vaccines should be presumed safe without any evidence. The DNA contaminants in Gardasil such as L1 gene fragments and the probable yeast DNA fragments such as the GAL1-GAL10 promoter and the ADH1 terminator flanking the synthetic L1 gene used to produce the vaccine, may pose no threat to the victims of Gardasil vaccination. But it is totally unacceptable to presume that they are safe for human vaccination without experimental evidence or evaluation. Indeed, short DNA fragments can be incorporated into the human genome. Although the yeast used to produce the vaccine does not have the small regulatory RNA employed by most organisms from bacteria to humans, it does contain 247 small open reading frames including 22 short DNA sequences specifying peptides involved in cell growth or damage and growth in the presence of DNA damage and replication arrest. At least one yeast gene product inactivates the cancer suppressor gene p53 and in that way promotes cancer in multicellular organisms [15]. The integration of the L1 and/or yeast genes may enhance the chances of acquiring cancer in numerous tissues of the body. It has been known for many years that ingested DNA may be covalently linked to mammalian DNA in blood cells, liver cells, spleen macrophages and T cells [16], and horizontal gene transfer and recombination via circulating nucleic acids is now well known [17] ([Intercommunication via Circulating Nucleic Acids](#), *SiS* 42) .

Cervarix

Cervarix contains recombinant C-terminally truncated (shortened) major capsid L1 proteins of HPV types 16 and 18 as active ingredients. The L1 proteins of HPV-16 and HPV-18 are separately produced using a recombinant baculovirus expression system and the insect cell line Hi-5 Rix4446 derived from *Trichoplusia*. After extracting the

L1 proteins and further purification, they are assembled separately as VLPs. The VLPs of each HPV type are formulated with the AS04 adjuvant system composed of aluminium hydroxide and 3-O-desacyl-4'-monophosphoryl lipid A (MPL). The MPL immunostimulant is a detoxified derivative of the lipopolysaccharide of the gram negative bacterium *Salmonella minnesota* R595 strain. Host cell proteins (HCP), DNA, and infectious recombinant baculovirus DNA are potential impurities removed in the preparation process. Other impurities such as lipids or carbohydrates are present only in negligible trace amounts [18].

Cervarix DNA contamination?

Cervarix's manufacturer maintains that the vaccine is not contaminated with DNA or other products from the baculovirus vector or the insect cells. The baculovirus, *Autographa californica* nucleopolyhedrovirus (AcMNPV) for which the complete genome sequence has been determined, has a circular, double-stranded, super-coiled DNA genome of approximately 130 kilobases packaged in a rod-shaped nucleocapsid. These nucleocapsids can be extended lengthways and thus the virus genome can effectively accommodate large insertions of foreign DNA. Such insertions of foreign genes into the AcMNPV genome has resulted in production of baculovirus expression vectors; recombinant viruses genetically modified to contain a foreign gene of interest, which can be expressed in insect cells under the control of a baculovirus gene promoter [19]. Baculovirus infects and is viable in human cells. Baculoviruses mediate gene expression in a wide array of vertebrate cells including those of humans [20] and numerous baculovirus genes are expressed in human cells [21, 22]. Baculoviruses contain two genes that prevent apoptosis and in that way facilitate progress of cancer cells [23]. Baculoviruses contain small DNA genes coding for micro RNAs with 8 viral and 64 cellular targets including interference with the host immune defence machinery [24]. There is clear evidence that the baculovirus vector DNA harbours genes detrimental to humans. It is imperative that DNA and RNA along with proteins from baculovirus and insect cells should not contaminate Cervarix vaccine.

To Conclude

DNA contamination of HPV vaccines is a serious problem, and not a normal or acceptable consequence of recombinant vaccine production as claimed by FDA. The false claims of FDA put into serious question not only Gardasil but also Cervarix. A truly independent agency is urgently required to undertake studies on the content of contaminating DNA and of RNA in the two vaccines.

References

1. Cummins J and Ho MW. The HPV vaccine controversy. [Science in Society 41](#), 24-26, 2009,
2. Retrospective International Survey and HPV Time Trends Study Group Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncology* 2010, 11, 1048-56.
3. Cummins J. Recombinant Cervical Cancer Vaccines. [Science in Society 29](#), 20, 2006.
4. Schmitz M, Driesch C, Jansen L, Runnebaum IB, Dürst M. Non-Random Integration of the HPV Genome in Cervical Cancer. *PLoS One* 2012, 7, e39632
5. Šepetienė A, Gudlevičienė Ž, Bumbulienė Ž, Drąsutienė GS, Didžiapetrienė J. HPV16 integration in Lithuanian women with cervical neoplasia. *Centr Eur J Med.* 2011, 6, 205–212.
6. Zheng ZM, Baker CC. Papillomavirus genome structure, expression, and post-transcriptional regulation. *Frontiers in Biosciences* 2006, 11, 2286-302.
7. Myklebust MP, Bruland O, Fluge Ø, Skarstein A, Balteskard L, Dahl O. MicroRNA-15b is induced with E2F-controlled genes in HPV-related cancer. *British Journal of Cancer* 2011, 105, 1719-25
8. Lajer CB, Garnæs E, Friis-Hansen L, Norrild B, Therkildsen MH, Glud M, Rossing M, Lajer H, Svane D, Skotte L, Specht L, Buchwald C, Nielsen FC The role of miRNAs in human papilloma virus (HPV)-associated cancers: bridging between HPV-related head and neck cancer and cervical cancer. *British Journal of Cancer* 2012, 106, 1526-34.
9. Cummins J, Ho MW. The HPV Vaccine Controversy. [Science in Society 41](#), 2009, 24
10. Europe, the Middle East and Africa (EMEA) EU regulatory agency for the evaluation of medicinal products Silgard, INN-Human Papillomavirus Vaccine [Types 6, 11, 16, 18] 2006 http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000732/WC500051547.pdf
11. SaneVax, Inc. SANE Vax to FDA: Recombinant HPV DNA found in multiple samples of Gardasil August 29, 2011 <http://sanevax.org/sane-vax-to-fda-recombinant-hpv-dna-found-in-multiple-samples-of-gardasil/>
12. Business Wire SANE Vax, Inc. Reports Human Papillomavirus (HPV) DNA Contamination in Gardasil™ To FDA: Requests Public Safety Investigation Sept. 6, 2011

<http://www.businesswire.com/news/home/20110906005422/en/SANE-Vax-Reports-Human-Papillomavirus-HPV-DNA>

13. US Food and Drug Administration FDA Information on Gardasil – Presence of DNA Fragments Expected, No Safety Risk Page Last Updated: 10/21/2011
<http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm276859.htm>
14. World Health Organization WHO Study Group on Cell Substrates for Production of Biologicals 5.3. Approaches in reducing risk of cell DNA - Discussion 2007
http://www.who.int/biologicals/publications/meetings/areas/vaccines/cells/Cells.FINAL.MtgRep.IK.26_Sep_07.pdf
15. Kastenmayer JP, Ni L, Chu A, Kitchen LE, Au WC, Yang H, Carter CD, Wheeler D, Davis RW, Boeke JD, Snyder MA, Basrai MA. Functional genomics of genes with small open reading frames (sORFs) in *S. cerevisiae*. *Genome Research* 2006, 16, 365-73.
16. Schubert R, Renz D, Schmitz B, Doerfler W. Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA. *Proc Natl Acad Sci U S A* 1997, 94, 961-6.
17. Ho MW. Intercommunication via circulating nucleic acids. *Science in Society* 42, 46-48, 2009.
18. Europe, the Middle East and Africa (EMEA) EU regulatory agency for the evaluation of medicinal products SCIENTIFIC DISCUSSION 2. Quality aspects 2007
http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_Scientific_Discussion/human/000721/WC500024636.pdf
19. Haines, F, Possee, R, King, L Baculovirus Expression Vectors 2005
<http://www.expressiontechnologies.com/pdf/BEV%20Paper.pdf>
20. Airene, K, Makkonen, K, Mähönen, A, Ylä-Herttua, S. Chapter 12 Baculoviruses Mediate Efficient Gene Expression in a Wide Range of Vertebrate Cells Otto-Wilhelm Merten and Mohamed Al-Rubeai (eds.), *Viral Vectors for Gene Therapy: Methods and Protocols, Methods in Molecular Biology*, Vol. 737, DOI 10.1007/978-1-61779-095-9_12, © Springer Science+Business Media, LLC 2011
21. Fujita R, Matsuyama T, Yamagishi J, Sahara K, Asano S, Bando H. Expression of *Autographa californica* multiple nucleopolyhedrovirus genes in mammalian cells and upregulation of the host beta-actin gene. *Journal of Virology* 2006, 80, 2390-5.
22. Liu CY, Wang CH, Wang JC, Chao YC. Stimulation of baculovirus transcriptome expression in mammalian cells by baculoviral transcriptional activators. *Journal of Genetic Virology* 2007, 88, 2176-84.
23. Clem RJ, Hardwick JM, Miller LK. Anti-apoptotic genes of baculoviruses *Cell Death & Differentiation* 1996, 3, 9-16.
24. Singh J, Singh CP, Bhavani A, Nagaraju J. Discovering microRNAs from *Bombyx mori* nucleopolyhedrovirus. *Virology* 2010, 407, 120-8



Open Letter from International Organisations to the WHO on the Issue of Vaccine Safety

To the World Health Organisation and those attending the meeting of the Global Vaccine Quality Control Laboratories Network (Rome 25th-27th September 2018).

To the European Parliament, the European Medicines Agency and the European Directorate for the Quality of Medicines

Dear members of the World Health Organisation,

By sharing science and joining efforts towards better health, your organisation has improved the lives of millions of people, and we are grateful for this. Providing better nutrition, clean water, improved hygiene, and access to medical care, mortality and infectious disease have been drastically reduced. Your extraordinary communication campaign to detect cases of disease and their contacts, and isolate them, finally led to the eradication of the once devastating smallpox.¹ These are great achievements and these noble goals should be further pursued. Today however, we are facing a new epidemic: chronic disease. In the USA, one in two adults has a chronic disease and one in four has two or more.²

Obesity, asthma, cancer, immune and autoimmune diseases, neurological and developmental disorders, are 'lifestyle diseases' mainly caused or aggravated by bad nutrition and toxic load. Vaccines are administered to healthy individuals to prevent targeted infections, but their long-term impact on the immune system and their potential role in chronic disease is not being evaluated. Individual risk of poor outcomes to both infection and vaccination varies widely and mass vaccination without proper discrimination at the individual level has led to injuries, death and unintended consequences. Recently, independent researchers and laboratories have discovered that many vaccines are contaminated with retroviruses³ and polluted by nanoparticles⁴. High levels of aluminium associated with vaccine adjuvants have been found in the brains of autistic children or in people suffering from neurological disorders such as Alzheimer's disease.^{5,6}

In your previous meeting you advocated for less independent testing, considered 'redundant', in order to speed up the supply of products.⁷ The recent administration of 250,000 defective vaccines in China⁸, the tragedy of the oral polio campaign in India with over 450,000 cases of paralysis and death⁹, the damage caused by the Dengue vaccine in the Philippines¹⁰, reports from all over the world of chronic pain and paralysis after administration of the HPV vaccine^{11, 12}, show that vaccine safety and efficacy are being tragically disregarded in this drive for fast-tracking approval and easy certification.

If developing standards and sharing best practice amongst controlling bodies is needed, testing by national and independent laboratories must be maintained, since fraud and technical hazard from storage or transportation can still occur and biases or new findings would not be detected. According to your report, «It was noted that the aims of the network are a good fit with industry's proposal for risk-based testing and networking».¹³ But this 'risk-based' approach geared to reducing test requirements for vaccines considered of 'low risk', seems a dangerous pursuit.

Many health authorities complain about vaccine hesitancy, but fail to reassure the public by providing the safety data they request. All over the world, millions of people have signed petitions demanding more safety, transparency and independent research, but decision makers chose fast-tracking instead.

To restore confidence lost, we insist that before any kind of recommendation or authorisation is issued, ALL vaccines pre-qualified or recommended by the WHO will be submitted to:

- Extensive clinical trials conducted by bodies independent from the manufacturers
- Medium- and long-term studies on efficiency and safety, not 'days'.
- Tests for carcinogenic properties
- Tests around fertility issues
- Tests on pregnancy, spontaneous abortion and the developing foetus
- Tests for mutagenic effects (changes induced in the DNA)
- Tests for effects on the neurological system and development of the brain
- Real inert placebo testing, which is almost never conducted on vaccines

We also insist that the WHO should provide studies on:

- Adjuvants and preservatives such as aluminium and mercury and their bioaccumulation
- Other toxic material used, such as polysorbate, Tween 80, formaldehyde etc
- Vaccine safety and the age of vaccine administration
- The impact of full vaccine schedules on the global health of a population

- The comparison of vaccinated versus unvaccinated populations in global health terms
- Viral transmission of people recently vaccinated with live virus vaccine such as measles, mumps, rubella, varicella, influenza or oral polio vaccine for example.

In particular, we ask that the use of combined vaccines and the same-day administration of multiple vaccines be thoroughly investigated. Figures from India show that the number of deaths within three days following vaccination doubled when using a Pentavalent (5-in-one) vaccine rather than a triple DTP vaccine. It is projected that this change will cause between 7,020 and 8,190 deaths each year in infants in India¹⁴. It further appears that in confidential periodic safety reports of the hexavalent Infanrix polio vaccine submitted to the EMA, the manufacturer GSK had deleted a number of death cases between reports.¹⁵

Concerning the measles-mumps-rubella vaccine and its link with autism, the only reference mentioned on the autism section of your website is an out-dated French article translating press claims that have been disproven in a decision from the English High Court in 2012.^{16,17} At the same time, William Thompson, an expert from the CDC, confessed in 2014 to having manipulated the data of a key reference study but as of present date, no further investigations have been made.¹⁸ With one in 36 children diagnosed with an Autistic Spectrum Disorder in the USA¹⁹, this study is an absolute priority and independent laboratory testing and new clinical trials must now replace the flow of 'inconclusive' statistics.

Confirming this priority, an Italian Parliamentary Commission recently reported numerous deaths, autoimmune diseases and cancers in military personnel after multiple vaccines had been administered and called for more research and precautionary measures²⁰. The long-term effects of vaccines are not studied and the recent revision of the classification of "Adverse Events Following Immunisation" does not allow for accurate reporting of death cases or of side effects not previously declared by the manufacturer.²¹ With the alarming rise in chronic diseases, immune, autoimmune and developmental disorders worldwide, immediate responsible action is imperative.

In its recent resolution on vaccine hesitancy, the European Parliament calls for "transparency and declaration of conflicts of interest, including researchers working for the World Health Organisation and the European Medicines Agency". It proposes that "researchers subject to a conflict of interest be excluded from evaluation panels"; further calls for "the confidentiality of the deliberations of the EMA evaluation panel to be lifted" and proposes that "the scientific and clinical data which inform the conclusions of the panel, and whose anonymity is guaranteed in advance, be made public".²² It fails however to question biased reports.²³

When it comes to approving or recommending a new vaccine, we know that:

- Pre-licensure studies are exclusively carried out by the manufacturers who stand to profit. This is a clear conflict of interest.
- Pre-licensure studies do not and cannot capture all adverse events that will occur in real world situations.
- Peer reviewed scientific journals have huge conflicts of interest and most studies are biased or false ^{24, 25, 26}
- Post-marketing surveillance in all countries is woefully inadequate. Only 1 to 10% of adverse events are being reported. In the USA, the mandatory biennial safety reports from US Health & Human Services to Congress on vaccine safety have simply never been written. ²⁷

The funding of your organisation relies on important private donations, such as the GAVI alliance, a partnership with banks and industries. The fact alone that this very meeting is funded by a private investor, the Bill and Melinda Gates Foundation²⁸, is highly questionable. Given this inherent conflict of interest, it is therefore absolutely imperative that independent studies and experts be involved in the approval and recommendation of vaccines and vaccine policies. And if the WHO guarantees the safety of the vaccine it is pre-qualifying, it should also assume liability for adverse events following vaccination.

Promoting mandatory vaccination for entire populations with products that essentially rely on manufacturers' data for their general safety and efficacy is an evident breach of the precautionary principle and as such becomes a forced medical experiment.

Since the health risk of vaccination is entirely borne by individuals, the WHO must ensure that it is minimal, and that fully informed consent is observed.

In order to restore public trust in health authorities and improve public health policies worldwide, we therefore demand actions and answers that meet our requests. We thank the honorable members of this assembly for their attention and pray they will open their hearts and minds to our message.

References:

1. «The Global Eradication of Polio» Final Report of the Global Commission for the Certification of Smallpox Eradication, Geneva, December 1979, the World Health Organization, 1980.
2. «About Chronic Disease», Centres for Disease Control and Prevention, 5 September 2018
3. J. Mikovits & K. Heckenlively «Plague», Skyhorse Publishing, 2014
4. S. Montanari, A. Gatti «New Control Investigations on Vaccines : Micro- and Nanocontamination», International Journal of Vaccines and Vaccination, Vol. 4 Issue 1, 23 Jan. 2017
5. C. Exley et al., «Aluminium in Brain Tissue in Autism», Journal of Trace elements in Medical Biology, March 2018, 46 :76-82
6. C. Exley, «Aluminium and Alzheimer's Disease: The Science that Describes the Link. Elsevier Science», Amsterdam, The Netherlands. 2001. 441p
7. Report of the First General Meeting of the WHO-NCL Network for Biologicals, Noida, India, 31 Oct.-2 Nov.2017.
8. F. Murphy «China Vaccine Scandal : Investigations Begin into Faulty Rabies and DTaP shots» British Medical Journal, 25 Jul. 2018, 2018 ; 362 ;k3244
9. Rachana Dhiman , Sandeep C. Prakash, V. Sreenivas , Jacob Puliyeel. Correlation between Non-Polio Acute Flaccid Paralysis Rates with Pulse Polio Frequency in India Int J Environ res Public Health 2018;15:1755
10. P. Rana«Initial Philippines Probes Finds Causal Association Between Deaths and Sanofi Dengue Vaccine», Wall Street Journal, 2 Feb. 2018
11. P. Goetzsche et al. «Complaint filed to EMA over Maladministration Related to the Safety of the HPV Vaccine», Nordic Cochrane
12. R. Gherardi «Toxic Story», Actes Sud, Oct. 2016
13. Report of the First General Meeting of the WHO-NCL Network for Biologicals, Noida, India, 31 Oct.-2 Nov.2017, p. 6, section 3.4
14. J. Puliyeel, Jaspreet Kaur, Ashish Puliyeel, Visnubhatla Sreenivas «Deaths Reported after Pentavalent Vaccine Compared with Death Reported after Diphtheria-Tetanus-Pertussis Vaccine: An Exploratory Analysis.» Med J DY Patil Vidyapeeth 2018;11:99-105.

15. J. Puliyeel, Sathyamala C. «Infanrix hexa and sudden death: a review of the periodic safety update reports submitted to the European Medicines Agency», Indian Journal of Medical Ethics 2018 Jan-Mar;3(1):43-47
16. High Court Decision of 7 March 2012, between Prof. John Walker-Smith and the General Medical Council, EWHC 503, Case n° CO/7039/2010
17. V. Sharav «L’Affaire Wakefield : Shades of Dreyfus and BMJ’s Descent Into Tabloid Science», Alliance for Human Research Protection, 2017
18. Documentary «Vaxxed : from Cover-Up to Catastrophy» April 2016.
19. B. Zablotsky et al. «Estimated Prevalence of Children Diagnosed with Developmental Disabilities in the United States, 2014-2106» NCHS Data Brief n°291, November 2017
20. “Parliamentary Commission of Inquiry into Cases of Death and Severe Illnesses Affecting Italian Personnel Assigned to Military Missions Abroad”, Acts of Parliament, XXII-bisn. 23-bis, Vol. I, II and III , Rapporteur G. P. Scanu, Approved 7 Feb. 2018
21. Puliyeel J, Naik P Revised World Health Organization (WHO)’s causality assessment of adverse events following immunization—a critique <https://f1000research.com/articles/7-243/v2>
22. «Vaccine Hesitancy and the drop of Vaccination Rates in Europe», resolution of the European Parliament, 19 April 2018. (2017/2951)
23. L. Jorgensen, P. Goetzsche, T. Jefferson «The Cochrane HPV vaccine review was incomplete and ignored important evidence of bias» BMJ evidence Based Medicine, July 27th 2018.
24. P. Goetzsche, «A moral governance crisis : the growing lack of democratic collaboration and scientific pluralism in Cochrane», open letter 14 Sep. 2018, Nordic Cochrane Centre
25. J. Ioannidis, «Why Most Published Research Findings are False», PLOS medicine, 30 Aug. 2005
26. M. Angell «The Truth about Pharmaceutical Companies. How They Deceive Us and what to do About It», Random House, 2004
27. «Mandate for Safer Childhood Vaccines», Decision of the US District Court, Southern District New York, Between Informed Consent Action Network and the US Department of Health and Human Services
28. The Bill & Melinda Gates foundation is one the 5 biggest investors in the world. In August 2018, it had 22,114 million \$ in stocks according to gurufocus.com



Signed by:

FRANCE

Françoise Joët, co-founder of both Association
Liberté Information Santé
(ALIS) and the European Forum for Vaccine
Vigilance (EFVV) *
Sophie Guillot for Agir pour le Libre
Consentement Thérapeutique, France

AMERICA

Robert Kennedy Jr., Children's Health
Defense, USA
James Lyons-Weiler, the Institute for Pure
and Applied Knowledge, USA
Bernadette Pajer, Informed Choice
Washington, USA

Sophie Guillot, Ensemble pour une Vaccination Libre, France

Marie Werbrègue, Info Vaccin France

Lucie Michel, Les Mamans Courage, France

Marie-Rose Cuisigniez, Association Liberté

Information Santé, France

Patrick Ledrappier, Libre Consentement Eclairé, France

Association Liberté Information Santé, France

Jean-Pierre Eudier, Ligue Nationale pour la

Liberté de Vaccination, France

Cathy Gaches, Reseau des Victimes de la Vaccination

Michel de Lorgeril et Philippe Harvaux,

Association Internationale pour une

Médecine Scientifique Indépendante et Bienveillante, France

Carine Curtet, Association Ametist, France

Dr. Dominique Eraud, Coordination Nationale Médicale Santé Environnement

Bernard Clavière Croisade pour la santé, France*

Alexandra Oakley, Optim'autisme, France*

Vera Sharav, Alliance for Human Research Protection, USA

Brandy Vaughan, Learn the Risk, USA

Catherine Ford, Vaccine Injury Awareness League, USA

Norma Erikson, Sanevax, USA

Ashleigh Parchman, TN Medical Freedom Alliance

Georgia Coalition for Vaccine Choice – Sandi Marcus

Christina Favazza, Florida health action network

Laura June, Floridians for Medical Freedom

Laura Fisher Andersen, Health Choice CT

Vallie Osborne, Informed Choice-Emerald Coast Florida

Jennifer Black, South Carolina Health Coalition

Lucy Cole, California

Kristen Chevrier and Melissa Andersen, Your Health Freedom Utah

Alicia Marie, Minnesota Vaccine Freedom Coalition

Elizabeth Murphy, Tennessee Medical Freedom Alliance

Alison Fujito, Pennsylvania Coalition for Informed Consent

Robin Rebrik Stavola, Angela Lockhart, Tom Stavola Jr., Hope from Holly Inc.

Erica Dawson, Iowa Vaccine Awareness & Education Network

Patti Carroll, Vaccine Safety Council of

GERMANY

Libertas & Sanitas, Germany

Impfkritik, Germany

Arzten für Individuelle Impfscheidung, Germany

Impf-Info, Germany

Eltern für Impfaufklärung, Germany

Hans U. P. Tolzin, NEFUNI, impf-report,

Justyna Socha, Piotr Jawornik Ogólnopolskie

Stowarzyszenie Wiedzy o

Szczepieniach STOP NOP, Poland

Dragana Timotic, Inicijativa Nova, Citizen's

Initiative for Optional Vaccination,

SERBIA

Civil Initiative for Non Mandatory Vaccination

SLOVENIA

Civilna iniciativa za prostovoljno

cepljenje, Slovenia

Simona Rupar and Boris Potocar, Natural Child

Development

Association, Slovenia*

SLOVAKIA

Sloboda v Ockovani, Slovakia

CROATIA

Cijepljenje Pravo Izboru, Croatia

Dr. Ivana Delas for the Croatian Association of

Parent Activists, Croatia

CZECH REPUBLIC

Rozalio, Czech Republic

Liga Lidskych Prav, Czech Republic

NORWAY

Foreningen for Fritt Vaksinevalg, Norway

DENMARK

Vaccinations Forum, Denmark

FINLAND

Suomen Homeopatian Akatemia, Finland

SWEDEN

Sara Boo, NHF, Sweden

SWITZERLAND

Netzwerk Impfentscheid, Switzerland

Infovaccins.ch, Switzerland

UK

John Stone, Age of Autism, UK

Anna Watson, Arnica, UK

Freda Birrell, Association of HPV Vaccine Injured
Daughters, UK

The Informed Parent, UK

Jabs, Justice, Awareness and Basic Support, UK

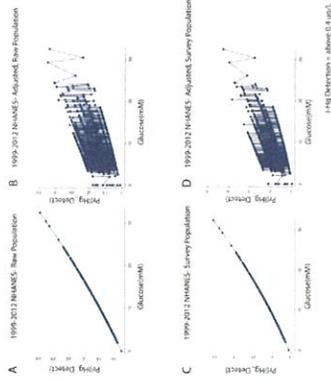
Joan Shenton, Immunity Resource Foundation,
UK

IRELAND

Irish Vaccination Awareness Group

FUNDAMENTAL ISSUES

The food supply contains allowable levels of toxic substances that impact metabolism and development. For example, the chlorine used to bleach flour may contain allowable levels of inorganic mercury. Food colors regulated by the FDA may contain allowable levels of mercury, lead or arsenic. When we eat processed food the levels of heavy metals increase in our blood and can create conditions for disease such as type-2 diabetes.



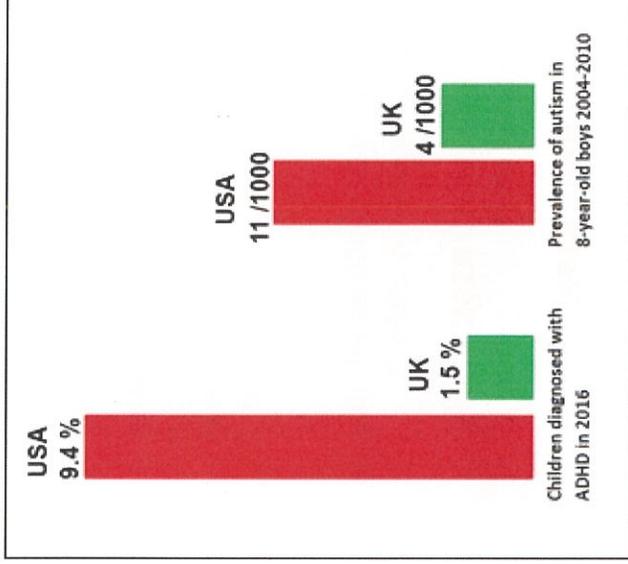
During our most recent clinical trial, we found an association between inorganic mercury in blood and fasting glucose after analyzing NHANES data gathered by the U.S. Centers for Disease Control (CDC). We determined that inorganic mercury levels may rise with processed food consumption.

KEY PUBLICATION

Dufault et al. (2015). Blood inorganic mercury is directly associated with glucose levels in the human population and may be linked to

processed food intake. *Integr Mol Med*, 2(3):181-194.

HIGHER AUTISM AND ADHD PREVALENCE IN USA COMPARED TO UK



In the United Kingdom (UK), warning labels are required on foods containing ingredients with allowable inorganic mercury, lead and arsenic. These ingredients are known to cause hyperactivity and inattention in children.

KEY PUBLICATION

Dufault, R. (2018). Food labeling requirements may explain lower autism and ADHD prevalence in United Kingdom. *Integr Food Nutr Metab*, 5(4):1-2



The only federally recognized 501 (c) (3) non-profit organization in the United States devoted entirely to food ingredient safety, education, and research.

Founded in 2010 by scientists, educators, parents, and food law attorneys.

We do more than make noise! We gather the hard evidence needed to support changes in food safety and health policy.

For more information,

Contact: Dr. Renee Dufault
Founding Executive Director
E-mail: rdufault@foodingredient.info

First Study of Vaccinated versus Unvaccinated Children

Now Public Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports, was censored by the journal *Frontiers in Public Health*.

Key Study Findings

Background: The long-term health outcomes of the routine vaccination program remain unknown. Studies have been recommended by the Institute of Medicine to address this question.

Specific Aims: To compare vaccinated and unvaccinated children on a broad range of health outcomes, and to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors.

Design and Methods: A cross-sectional survey of mothers of children educated at home. Homeschool organizations in four states (Florida, Louisiana, Mississippi, and Oregon) were asked to forward an email to their members, requesting mothers to complete an anonymous online questionnaire on the vaccination status and health outcomes of their biological children ages 6 to 12. A total of 415 mothers provided data on 666 children, of which 261 (39%) were unvaccinated. The collected data included pregnancy experiences and birth histories as well as acute and chronic conditions, medications, and the use of health services.

Results: Vaccinated children were significantly less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but significantly more likely to have been diagnosed with other infections, allergies and NDDs (defined as Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and/or a learning disability).

Chronic Illness Detail:

- Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following chronic illnesses:
 - 7-fold higher odds of any neurodevelopmental disorder (i.e., learning disability, ADHD, or ASD)
 - 2-fold increase in Autism Spectrum Disorder ("ASD")
 - 2-fold increase in ADHD
 - 2-fold increase in learning disabilities
 - 1-fold increase in allergic rhinitis
 - 9-fold increase in other allergies
 - 9-fold increase in eczema/atopic dermatitis
 - 4-fold increase in any chronic illness
 - No significant differences were observed with regard to cancer, chronic fatigue, conduct disorder, Crohn's disease, depression, Types 1 or 2 diabetes, encephalopathy, epilepsy, hearing loss, high blood pressure, inflammatory bowel disease, juvenile rheumatoid arthritis, obesity, seizures, and Tourette's syndrome.

However, larger samples would be needed to detect group differences in these less common conditions.

Acute Illness Detail:

- Vaccinated children were significantly less likely than unvaccinated children to have had chickenpox or whooping cough ($p < 0.001$).
- Vaccinated children had a 3.8-fold increased odds of middle ear infections and a 5.9-fold increased odds of being diagnosed with pneumonia compared to unvaccinated children.
- No significant differences were seen between the two groups with regard to Hepatitis A or B, high fever in the past 6 months, measles, mumps, meningitis (viral or bacterial), influenza, or rotavirus.

Vaccination, Preterm Birth and Neurodevelopmental Disorders (NDDs):

In regression analyses, vaccination was associated with a significant 3.1-fold increased odds of neurodevelopmental disorders (combining the diagnoses of ASD, ADHD, and learning disability), after controlling for other factors. An important detail emerged regarding a possible synergism between vaccination and preterm birth. In a final adjusted statistical model, vaccination but not preterm birth remained associated with NDD, as defined, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% Confidence Interval: 2.8, 15.5).

Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports, by Anthony R. Mawson, et al.

* * * * *

Quotes from independent scientists not involved in the study:

"I am delighted to see a properly analyzed study on vaccine safety" said Dr. Lyons-Weiler, CEO and President of the Institute for Pure and Applied Knowledge. "Unlike past studies, which ignored the interaction term, Dr. Mawson and colleagues followed appropriate steps toward interpreting the significance of the interaction between variables. The study reported a significant interaction effect between pre-term birth, and vaccination as a 6.6-fold increase in the risk of neurodevelopmental disorders."

"This study, however, as a survey study, is potentially subject to variation due to responses from well-intended participants. The next logical step would be additional, larger studies that would try to replicate the results using electronic medical health records - by independent investigators not involved in profiting from vaccines", said Dr. Lyons-Weiler.

"This is a long-overdue study involving a fair comparison of vaccinated vs unvaccinated children where the two subpopulations likely don't reflect other biases, due to their being drawn from a

common population of home-schooled children”, said Dr. Stephanie Seneff, Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory. “The results are alarming, and it leaves no doubt that we need to seriously question whether the benefits of vaccines outweigh the risks. A much larger study to see if the results still hold up is paramount at this point.”

Dr. Lyons-Weiler and Dr. Seneff were not involved in the study.

List of Added Vaccines

1. Hepatitis A

HARVIX – MRC-5 human diploid cells, 250mcg of aluminum hydroxide (pediatric dose), polysorbate 20, formalin, neomycin sulfate

HAVRIX has NOT been evaluated for its carcinogenic potential, mutagenic potential, or potential for impairment of fertility.

VAQTA – Whole live virus from human MRC-5 diploid fibroblasts, formalin, 225mcg of aluminum hydroxyphosphate sulfate, neomycin.

2. Influenza

FLULAVAL – egg protein, formaldehyde, 50mcg of thimerosal in multidose vial (no thimerosal in single vial), polysorbate 80

3. Pneumococcal Conjugate Vaccine (PCV)

PREVNAR 13 – Soy, yeast, polysorbate 80, aluminum phosphate 125mcg
Serious adverse events reported following vaccination in infants and toddlers occurred in 8.2% among Prevnar 13 recipients and 7.2% among Prevnar recipients.

4. Rotavirus

ROTARIX

The lyophilized vaccine contains amino acids, dextran, Dulbecco's Modified Eagle Medium (DMEM), sorbitol, and sucrose. DMEM contains the following ingredients: sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids solution, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red.

In the manufacturing process, porcine-derived materials are used. Porcine (pig) circovirus type 1 (PCV-1) is present in ROTARIX (THIS IS A PIG VIRAL DNA COMPONENT)

ROTATEQ

The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, and trace amounts of fetal bovine serum. RotaTeq contains no preservatives. In the manufacturing process for RotaTeq, a porcine-derived material is used. DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.

Shedding of vaccine virus was evaluated among a subset of subjects in the Rotavirus Efficacy and Safety Trial (REST) 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission of vaccine virus was not evaluated in phase 3 studies. Transmission of vaccine virus strains from vaccinees to non-vaccinated contacts has been observed post-marketing.

5. HPV (Human Papillomavirus Vaccine)

GARDASIL 9

GARDASIL 9 is a sterile suspension for intramuscular administration. Each 0.5-mL dose contains approximately 30 mcg of HPV Type 6 L1 protein, 40 mcg of HPV Type 11 L1 protein, 60 mcg of HPV Type 16 L1 protein, 40 mcg of HPV Type 18 L1 protein, 20 mcg of HPV Type 31 L1 protein, 20 mcg of HPV Type 33 L1 protein, 20 mcg of HPV Type 45 L1 protein, 20 mcg of HPV Type 52 L1 protein, and 20 mcg of HPV Type 58 L1 protein.

Each 0.5-mL dose of the vaccine also contains approximately 500 mcg of aluminum (provided as AAHS), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, <7 mcg yeast protein, and water for injection. The product does not contain a preservative or antibiotics.

Using the MedAlerts search engine, as of April 30, 2018, the federal Vaccine Adverse Events Reporting System (VAERS) contains more than 58,992 reports of HPV vaccine reactions, hospitalizations, injuries and deaths and, includes 430 related deaths, 794 hospitalizations, and 2,773 disabling conditions. Over 45 percent of the reported serious adverse events occurred in children and teens 12-17 years of age.

As of June 29, 2018, 387 claims were filed with the federal Vaccine Injury Compensation Program (VICP) for injuries and deaths following HPV vaccination, which included 14 deaths and 376 serious injuries. Less than a third of claims received compensation.

After the original Gardasil vaccine was licensed for 11-12 year old girls and young women, thousands of adverse reaction reports were filed for: sudden collapse with unconsciousness within 24 hours, seizures, muscle pain and

weakness, disabling fatigue, Guillain Barre Syndrome (GBS), facial paralysis brain inflammation, rheumatoid arthritis, lupus, blood clots, premature ovarian failure, optic neuritis, multiple sclerosis, strokes, heart and other serious health problems, including death.²³ Similar reports have been filed for the Gardasil 9 vaccine,²⁴ even though the recommended number of doses was reduced from three to two.

6. **MCV (Meningococcal Conjugate Vaccine)**

MENOMUNE – 25mcg of Thimerosal, Latex, Aluminum, Sucrose, Antibiotics, Polysorbate 80

DRUG INTERACTIONS: No safety and immunogenicity data are available on the concomitant administration of Menomune _ A/C/Y/W-135 vaccine with other US licensed vaccines (Vaccine Insert).

Studies Prove Without Doubt That Unvaccinated Children Are Healthier Than Their Vaccinated Peers

As doctors, parents and concerned citizens we consistently strive to do what is best for the children in our lives. As of late, with the passage of SB277 in California, the mainstream media has been trying to convince everyone that the vaccinated child is some how a healthier individual and lives a more "disease" free life versus their unvaccinated counterpart.

But, is this the truth?

A 20 year old study from the 1990's has recently surfaced that compares unvaccinated children to vaccinated children. The study concludes that those who were vaccinated were more likely to suffer from the following illnesses:

- asthma
- eczema
- ear infections
- hyperactivity
- and many other chronic conditions.

There was a 10-fold increase in cases of tonsillitis in the children who were vaccinated and a 100% absence of tonsillitis in those unvaccinated.

In 1992, the Immunization Awareness Society (IAS) conducted a survey to examine the health of New Zealand's children. Unsurprisingly, the results of their study indicated that unvaccinated children were far healthier than vaccinated children.

Questionnaires were given out to IAS members, their friends and their associates asking various health questions. A total of 245 families returned their questionnaires, giving the researchers a total of 495 children surveyed. Of these children, 226 were vaccinated and 269 were unvaccinated.

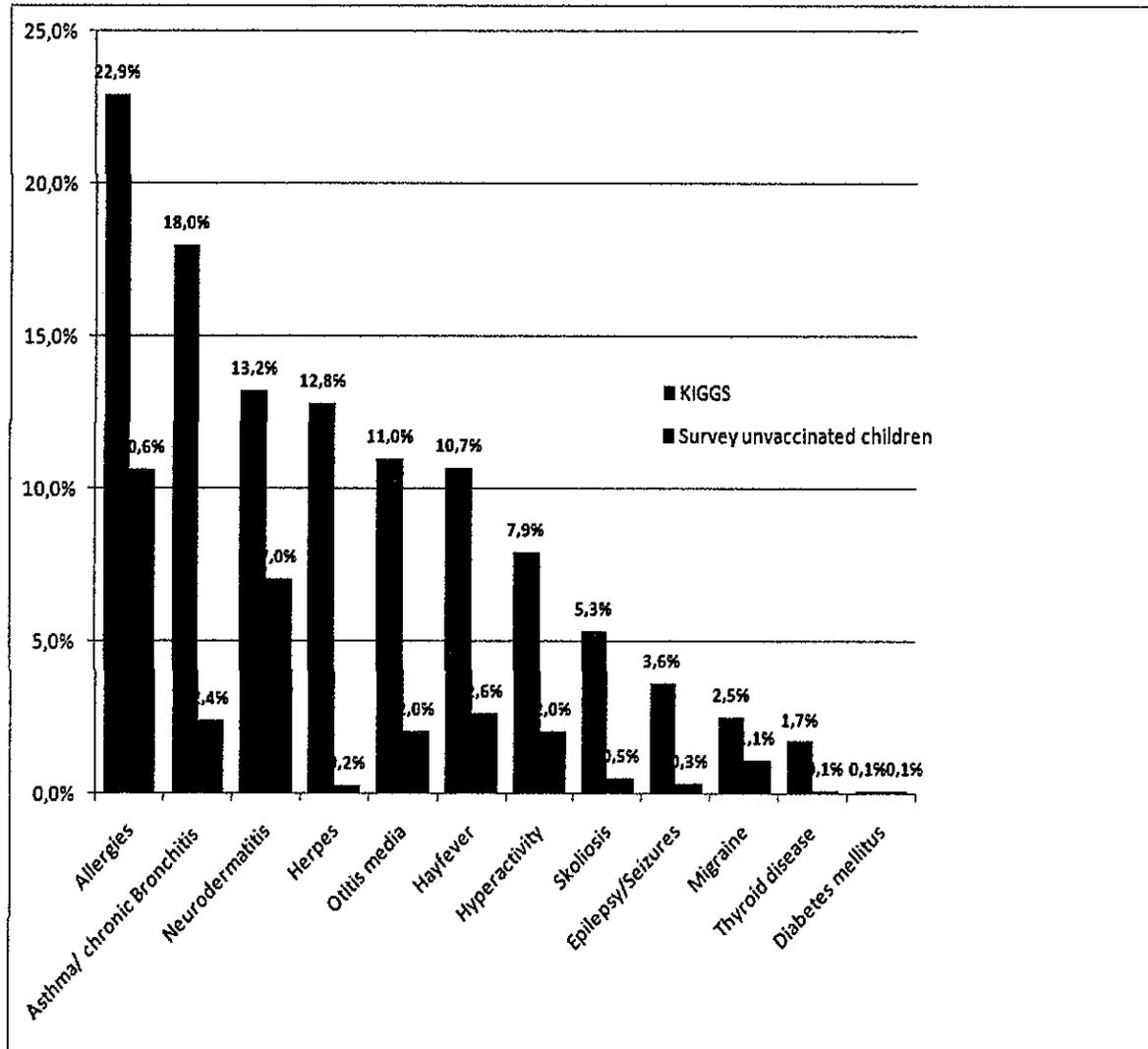
Healthy Children and Ethics

The ages of the children ranged between the ages of two weeks – 46 years (obviously some friends were older with older children). Of the children studied, 273 were males and 216 were females. (Six children were unclassified.) Sue Claridge, who reported on the study, wrote: *"Respondents were asked to provide the year of birth, gender, vaccinations received, whether or not the child suffered from a range of chronic conditions (asthma, eczema, ear infections/glue ear, recurring tonsillitis, hyperactivity, diabetes or epilepsy) whether or not he or she needed grommets, had had a tonsillectomy, or were shown to develop motor skills (walking, crawling, sitting-up etc.). Parents also provided information on breastfeeding and bottle feeding and when a child was weaned if breastfed."* During the study, another interesting fact emerged. Researchers discovered that 92 percent of the children requiring a tonsillectomy operation had received the measles vaccination, indicating that the vaccination for measles may have made some of the children more susceptible to tonsillitis. The study also revealed that 81 of the families had both vaccinated and unvaccinated children. Many of these families had vaccinated their older children but had grown more reluctant to vaccinate their younger children, due to their growing concerns regarding vaccine safety.

Researchers concluded that: "While this was a very limited study, particularly in terms of the numbers of unvaccinated children that were involved and the range of chronic conditions investigated, it provides solid scientific evidence in support of considerable anecdotal evidence that unvaccinated children are healthier than their vaccinated peers." [1] Although governments from around the world have continually stated that studying vaccinated versus unvaccinated children would be unethical, the New Zealand researchers are not the only group of researchers to study comparisons.

Vaccinated Children 5 Times More Likely To Suffer From A Range Of Diseases

In September 2011, German researchers carrying out a longitudinal study surveyed a total of 8000 unvaccinated children from the ages of 0 –19. As with the New Zealand study, researchers collected their data by conducting a survey using questionnaires. [2] Results showed that vaccinated children were up to five times more likely to suffer from a variety of diseases and disorders than unvaccinated children. Their results were compared to another German study (KIGGS), which examined a larger sample group consisting of 17,461 participants between the ages of 0 –17. Dr. Andreas Bachair, a German classical homeopathic practitioner, responsible for collecting the results of the survey from the website vaccineinjury.info stated that:



"Asthma, hay fever and neurodermatitis are seen very frequently today. A recent German study with 17461 children between 0-17 years of age (KIGGS) showed that 4.7% of these children suffer from asthma, 10.7%

of these children from hay fever and 13.2% from neurodermatitis. These numbers differ in western countries, i.e. the prevalence of asthma among children in the US is 6% whereas it is 14-16% in Australia (Australia's Health 2004, AIHW). The prevalence of asthma among unvaccinated children in our study is around 2.5%, hay fever, 3%, and neurodermatitis, 7%. According to the KIGGS study more than 40% of children between the ages of 3 and 17 years were sensitized against at least one allergen tested (20 common allergens were tested) and 22.9% had an allergic disease. Although we did not perform a blood test, around 10% stated that their children had an allergy." [3] (As this study is a longitudinal study, the number of children being studied has since risen to 13,222. To join the study, you can fill in the questionnaire provided by clicking on the link listed as the third reference at the end of this article.) Although there were four cases of autism reported among unvaccinated children, Dr. Bachair reported that: "Of these 4 children one tested very high for metals (mercury, aluminium, arsenic); in another case the mother was tested very high for mercury." However, this number pales into insignificance when we compare it to the 1 in 88 children currently being reported as autistic by the CDC. [4]

Other Conditions Found To Be Almost Non-Existent In Unvaccinated Children

Dr. Andreas Bachair continued her report by stating that their study found the prevalence of sinusitis, warts, skin problems and middle ear infections were also much lower in the unvaccinated children, as were the cases of diabetes and epilepsy. She went on to say that the results demonstrated that the prevalence of many conditions in the unvaccinated children were also significantly lower. These were: "Other disorders and diseases As we included open questions in our survey we evaluated the prevalence (of the first 10,070 participants) of some other disorders and illnesses. Unvaccinated children show very low prevalences of the following disorders:

- *Dyslexia: 0.21%*
- *Speech delay/articulation problems: 0.38%*
- *Sensory Processing disorder: 0.28%*
- *Anxiety: 0.25%*
- *Depression: 0.12%*
- *Bedwetting: 0.12%*
- *Celiac disease: 0.12%*
- *Gluten sensitivity: 0.41%*
- *GERD (Gastroesophageal reflux disease): 0.06%*"

Dr. Bachair concluded her amazing and intuitive paper by adding a number of statements from parents, which I believe really added weight to her overall findings.

No study of health outcomes of vaccinated people versus unvaccinated has ever been conducted in the U.S. by CDC or any other agency in the 50 years or more of an accelerating schedule of vaccinations (now over 60 doses of 14 vaccines given before kindergarten, 26 doses in the first year). Most data collected by CDC is contained in the Vaccine Adverse Event Reporting System (VAERS) database. The VAERS is generally thought to contain only 3 to 5 percent of reportable incidents. This is simply because only some immediate reactions are reported by doctors; but many are not admitted to be reactions to the

vaccine. Most importantly, the VAERS numbers are only *immediate reactions*, which would take place within a few hours to a few weeks. Long-term vaccine-induced diseases and disorders are not recognized by parents or doctors when these conditions develop perhaps a few months to five years or more and would never be realized to come from multiple vaccinations. In other words, many children and adults have diseases and disorders that are vaccine induced and they never suspect they are from the vaccines, as this study indicates.

Conclusion

We find it amazing that despite mainstream media and leading government agencies stressing repeatedly that studies comparing vaccinated children to unvaccinated children cannot take place for ethical reasons, groups around the world are taking it upon themselves to do these studies anyway.

While surveys of this kind are often dismissed as being purely epidemiological and passed off as little more than stamp collecting, we believe that studies of this nature should not be dismissed out of hand. After all, many stamp collections contain just one stamp that is worth far more than its weight in gold.

These studies show without doubt that unvaccinated children are healthier than their vaccinated peers and, for this reason, these studies should be given careful consideration by all parents and professionals studying vaccination safety.

References

1. <http://www.viewbix.com/v/Unvaccinated-Children-Healthier...>
2. <http://healthimpactnews.com/2011/new-study-vaccinated-children-have-2-to-5-times-more-diseases...>
3. <http://www.vaccineinjury.info/vaccinations-in-general/health-unvaccinated-children...>
4. <http://www.cdc.gov/ncbddd/autism/data.html>

State of health of unvaccinated children

Illnesses in unvaccinated children

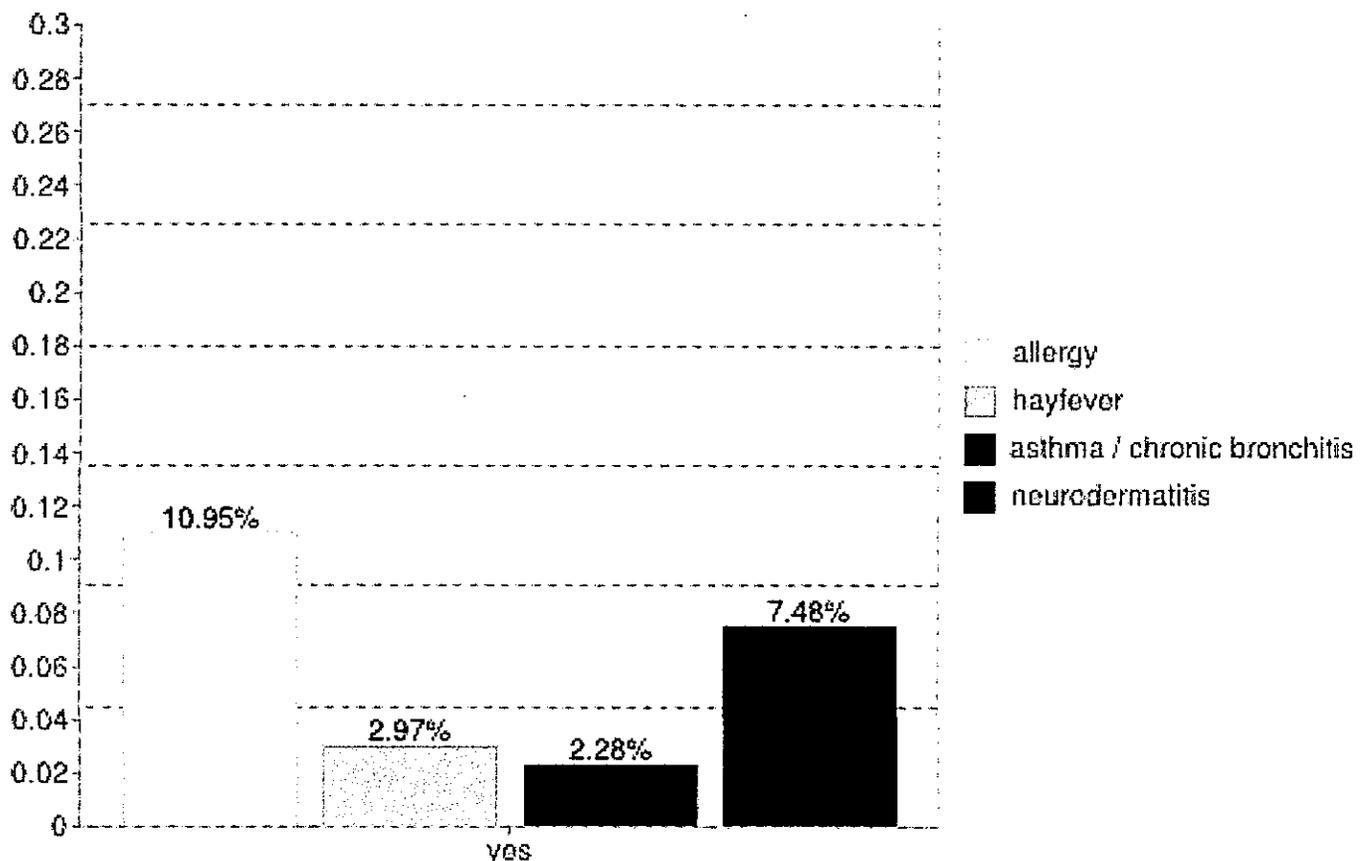
The results of our survey with currently 11921 participants show that unvaccinated children are far less affected by common diseases than vaccinated children. Due to the fact that the majority of children in the survey are between 0 and 2 years of age and some diseases generally do not appear in this age group, the results are subdivided into different age groups (you can see that by clicking on the chart). Information about country, gender, age, age distribution, breastfeeding, preferred treatment can be found [here](#).

Atopic diseases among unvaccinated children

Asthma, hayfever and neurodermatitis are seen very frequently today. A recent German study with 17461 children between 0-17 years of age (KIGGS) showed that 4.7% of these children suffer from asthma, 10.7% of these children from hayfever and 13.2% from neurodermatitis. These numbers differ in western countries, i.e. the prevalence of asthma among children in the US is 6% whereas it is 14-16% in Australia (Australia's Health 2004, AIHW)

The prevalence of asthma among unvaccinated children in our study is around 2.5%, hayfever 3% and neurodermatitis 7%. According to the KIGGS study more than 40% of children between the ages of 3 and 17 years were sensitized against at least one allergen tested (20 common allergens were tested) and 22.9% had an allergic disease. Although we did not perform a bloodtest, around 10% stated that their children had an allergy.

Prevalence of atopy in unvaccinated children

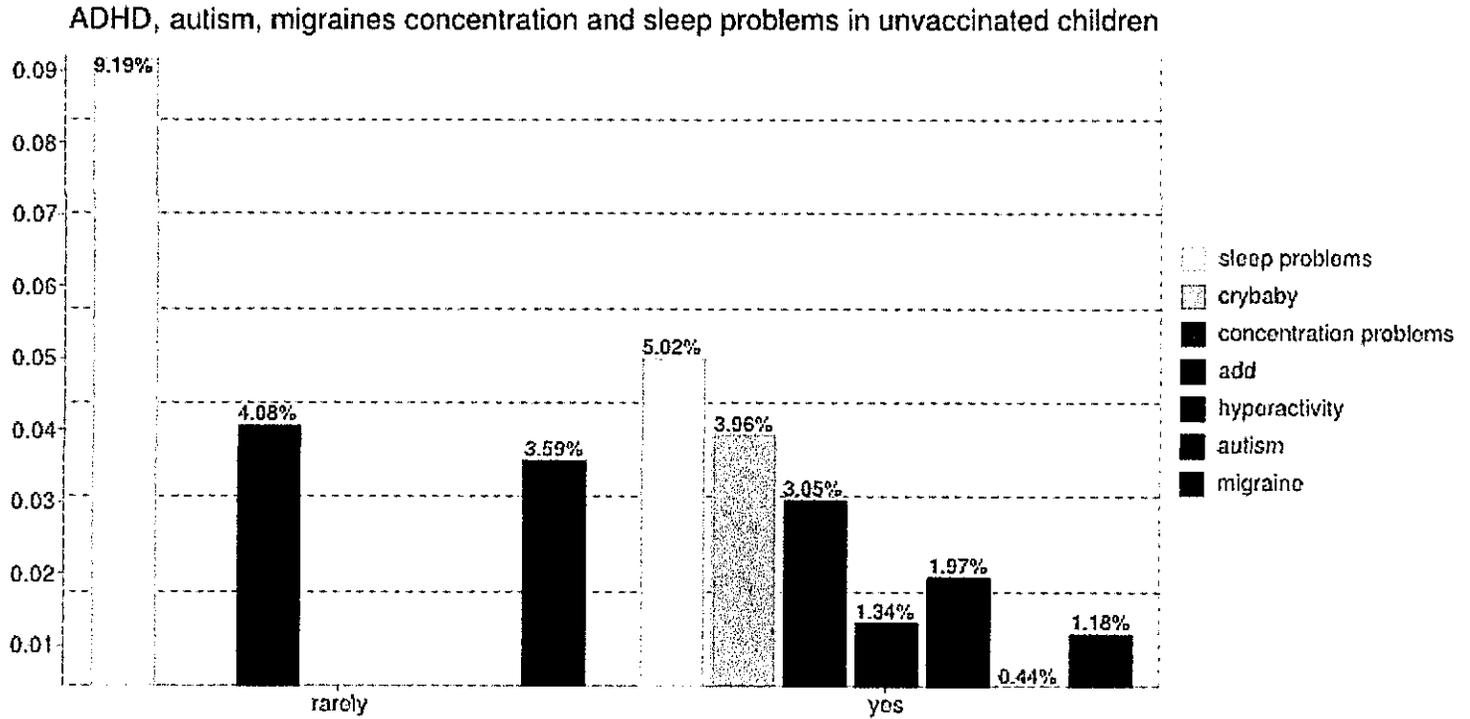


By clicking on the graphic you can see the age distribution of the selected diseases.

If you want to compare the results with the results of the survey on our German website impfschaden.info go [here](#).

ADS, Hyperactivity, Autism, Sleeping problems, concentration problems and migraine

ADS and Hyperaktivität is between 1 and 2 % in our survey, the prevalence of ADHD in Germany is 7,9% and another 5,9% which were not yet diagnosed, but were borderline cases(KIGGS).



By clicking on the graphic you can see the age distribution of the selected diseases.

There are also autism cases in unvaccinated children. Among all participants there were 4 severe autism cases.

Of these 4 children one tested very high for metals(mercury, aluminum, arsenic), in another case the mother was tested very high for mercury.

The CDC estimates that about 1 in 88 (1,1%) children has been identified with an autism spectrum disorder (ASD)(Autism and Developmental Disabilities Monitoring (ADDM) Network). ASDs are almost 5 times more common among boys (1 in 54; 1,8%) than among girls(1 in 252;0,39%).(Jon Baio, Prevalence of Autism Spectrum Disorders – Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008, March 30, 2012 / 61(SS03);1-19)

Otitis media, Sinusitis, Herpes, Warts, Polyps and fungal infections

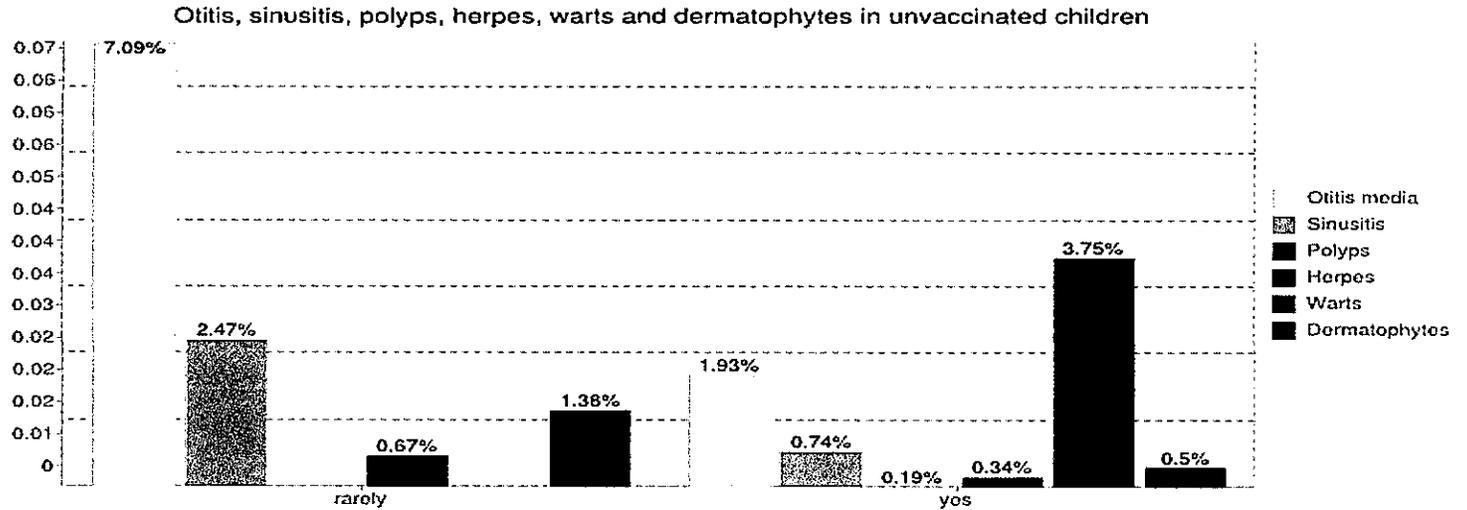
KIGGS showed that 12.8% of the children in Germany had herpes and 11% suffer from otitis media (an inflammation of the middle ear). If you compare this to unvaccinated children you can see that herpes among unvaccinated children is very rare (less than 0.5%).

The prevalence of sinusitis in young children has gone up as high as 32% (Albegger KW. *Banale Entzündungen der Nase und der Nasennebenhöhlen*. In: Berendes J, Link JR, Zöllner F, eds. *Hals, Nasen-, OhrenHeilkunde in Praxis und Klinik. Band I. Obere und untere Luftwege*. Stuttgart: G Thieme Verlag, 1979: 11.1–11.32.)

In our survey less than 1% of the children have problems with sinusitis, in around 2% it happened only once or rarely.

In young kids under the age of 3 warts are very rare. Above the age of three years however the prevalence is rising. In the ages between 4 and 6 years, 5-10% of the kids have warts, in the age group 16-18, 15-20% have warts. (http://www.netdokter.at/health_center/dermatologie/warzen.htm)

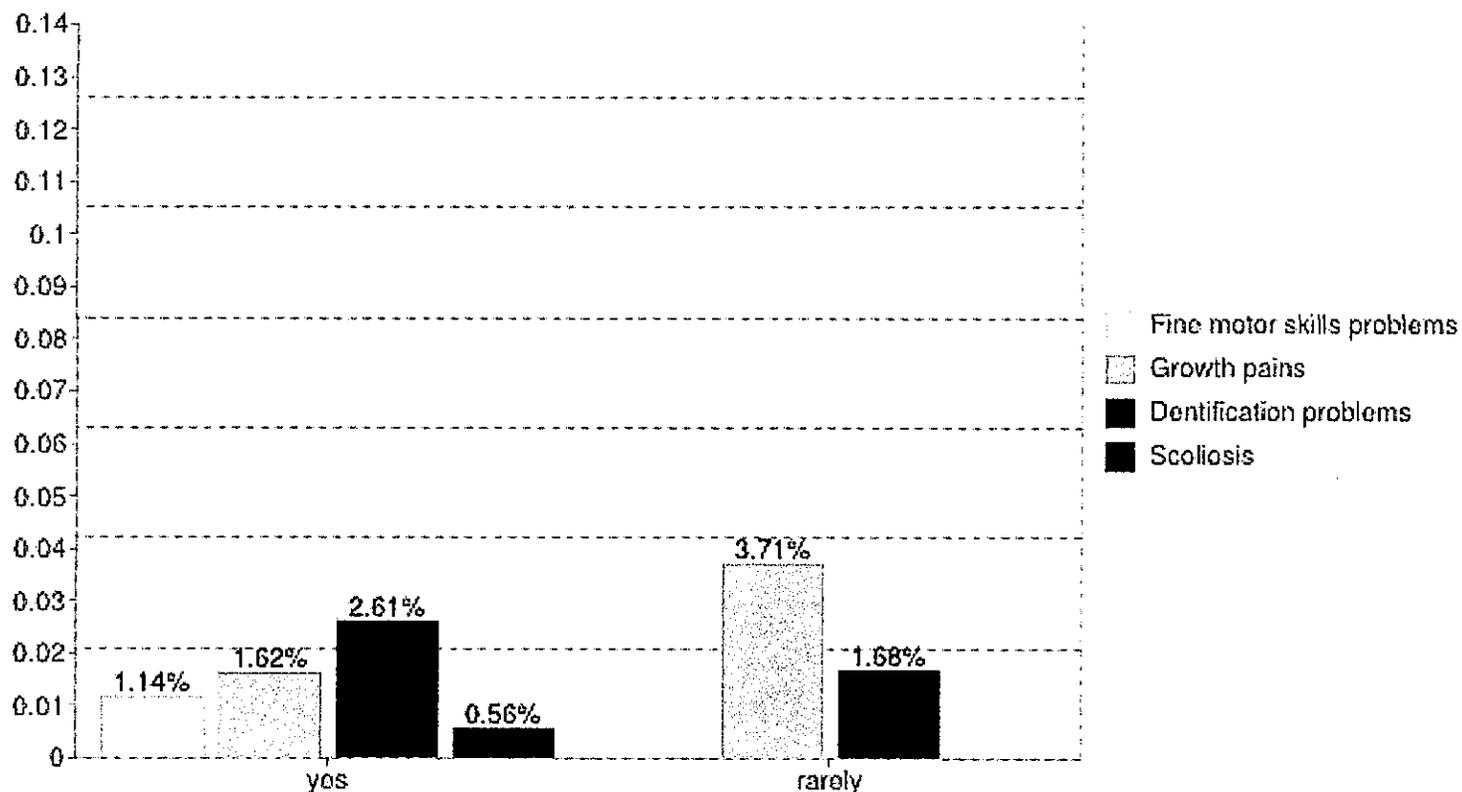
Only 3% of unvaccinated children in our survey have warts.



By clicking on the graphic you can see the age distribution of the selected diseases.

Fine motor skill problems, dentification problems, growth pains and scoliosis

Other diseases/disorders in unvaccinated children



By clicking on the graphic you can see the age distribution of the selected diseases.

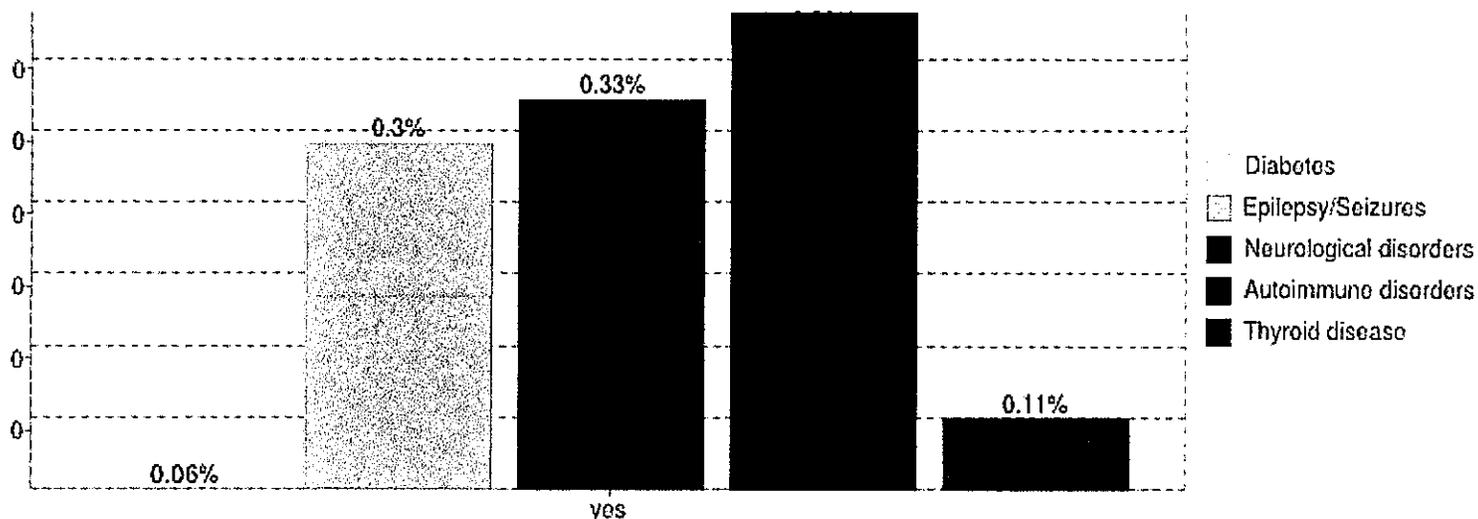
Diabetes, Epilepsy and seizures, neurological and autoimmune diseases, thyroid disorders

The national institute of health in the USA states that 23.5 % Americans suffer from autoimmune disease. This is a prevalence of more than 7% of children.

Diabetes affects 0.2% of the children under 20 years of age in the USA (National Diabetes Fact Sheet)

The KIGGS study showed prevalences of epilepsy with 3.6%, prevalence of Diabetes in Germany with 0.1% and diseases of the thyroid gland with 1.7%.

Diabetes, epilepsy, neuro./autoimmune and thyroid disorders in unvaccinated children



By clicking on the graphic you can see the age distribution of the selected diseases.

Other disorders and diseases

As we included open questions in our survey we evaluated the prevalence (of the first 10070 participants) of some other disorders and illnesses. Unvaccinated children show very low prevalences of the following disorders:

Dyslexia

Speech delay/articulation problems

Sensory Processing disorder

Anxiety

Depression

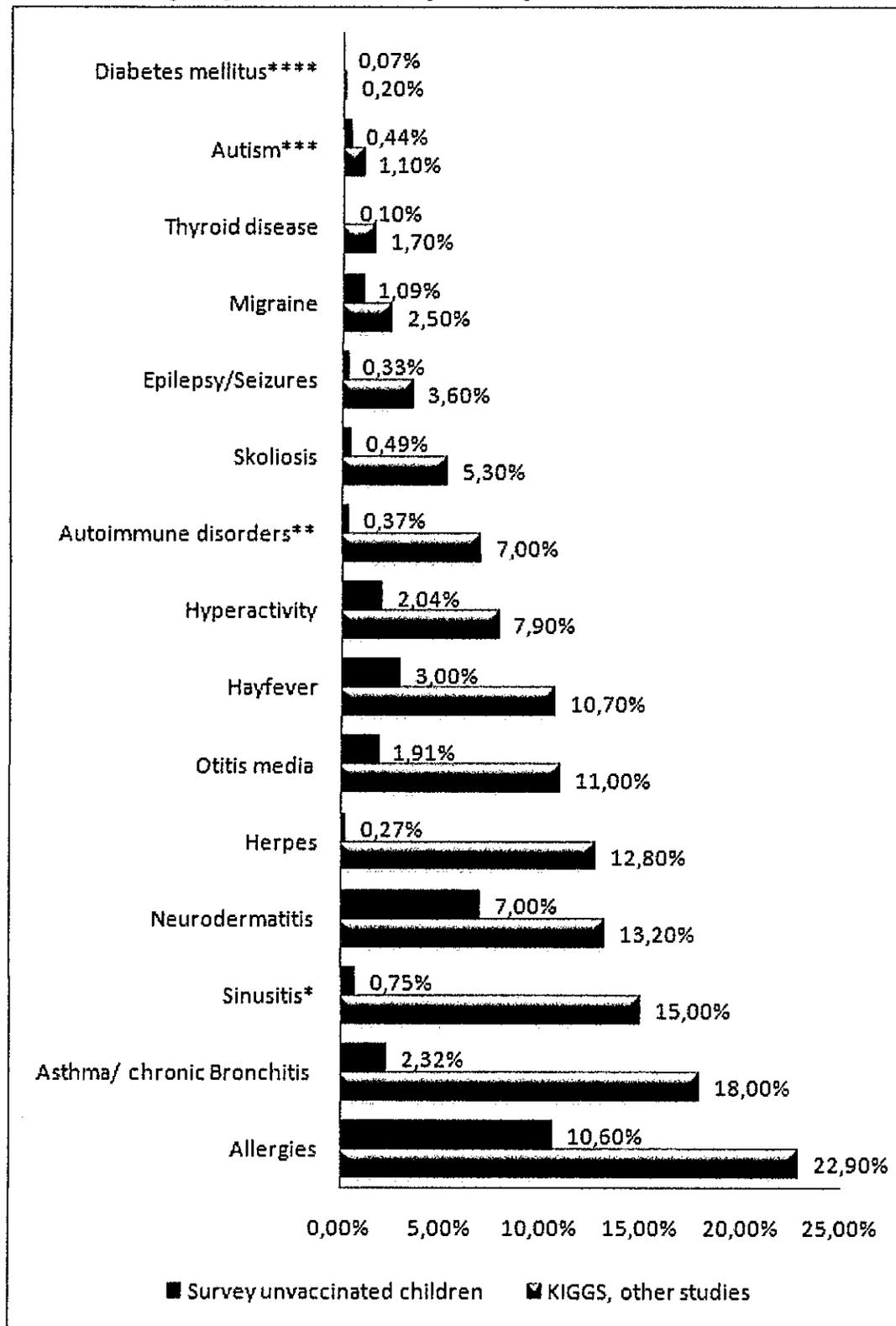
Bedwetting

Celiac disease

Gluten sensitivity

GERD (Gastroesophageal reflux disease)

Direct comparison KIGGS study (and other studies) and vaccineinjury.info-survey (July 2012)



* http://thorax.bmj.com/content/55/suppl_2/S20.full.pdf

** National Institutes of Health

***Jon Baio, Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008, March 30, 2012 / 61(SS03);1-19

****National Diabetes Fact Sheet

Quotes from parents about the state of health of their unvaccinated children

Lots of parents gave some additional information of their children. Here are some typical quotes:

"I am 27 years old and am completely unvaccinated. I am very healthy and only get a cold maybe once every year or two."

"My son is mostly vaxxed, my daughter not. They both were exposed to a recently vaccinated family member and me and my son contracted whooping cough. His lasted much longer than mine (he has various health issues primarily caused by vaccine) which was expected. My unvaccinated daughter coughed once the entire length of our illness and the second time we were exposed - same situation- she wasn't affected at all."

"I am one of 10 children from the same mother and father. None of us were vaccinated. Our ages are 38-59. We were all allowed to have childhood diseases to boost our immune systems. Most of our children were not vaccinated either. Most of all none of the non-vaccinated children in our family have major illness."

"I will put the health of my three unvaccinated children up against the health of a vaccinated child any day of the week and twice on Sunday."

"My 3 year old child is in a 5 year old class, and is even advanced for that grade. She has not been near as sick as a lot of her friends. She is considered very advanced for her age. Her two oldest siblings had both been injured by vaccinations and have been recovering for the last 6.5 years."

"My two boys are both uncircumcised, unvaccinated, including no vitamin K shot at birth, and no PKU newborn blood screening, and no painful procedure of any kind. I gave birth drug-free and naturally in an upright kneeling position, after walking throughout my entire labor and transition. Both boys are extremely healthy, intelligent, kind, and beautiful. I breastfed my older son until he turned 4 years, and I'm currently breastfeeding my 2 year old."

"My 3 vaccinated children were sick often during their first 2 years, suffered from ear infections repeatedly for which the doctor was constantly prescribing antibiotics, which would never work on the 1st round. They'd go through 3 separate rounds of antibiotics before the infection would be gone, meanwhile they'd develop diarrhea and candida diaper rash. They got every "bug" that was going around and strep and tonsilitis on several occasions. They all have skin conditions which the doctor has diagnosed as keratosis pilaris. My unvaccinated child has never been sick beyond a slight, short-lived cold. Never had an ear infection and has no skin issues either."

"We chose not to vaccinate for various reasons, and have never tried to create an antiseptic environment for the children. We live on a small mid-western farm and the children seldom wear shoes in the warmer months (warmer than freezing) so that is most of the time. They are subject to occasional cuts from various metals, glass, etc. and have not had any infections to speak of. Not only that, but they get bitten by various animals, cats, mice, (they're always catching mice) garden snakes, and the like, insects of all kinds, with no adverse affects. All but the first were home-birth, all were breast fed, and none of the last 8 have ever seen a doctor, (or MacDonalds)."

"I fully vaccinated his sister. She died at age 5 mos 14 days after suffering many symptoms of mercury poisoning including eczema, milk allergy and hypotonic-hyporesponsive episodes as well as dilated pupils. Her death was labeled "SIDS". I know it was vaccine induced. I also suffered a severe reaction to smallpox vaccine and have other family history of severe vaccine reactions. My unvaxed son has never needed an antibiotic, never had an ear infection, and has not seen a doctor since he was 2 and that was for an eye issue that resolved itself."

"He has never had an ear infection or serious illness that required medication and he turned 2 in Dec 2010. Vaccinated kids I know, including my 8 year old, were always sick. Croup, eczema, RSV, Scarlet fever, strep, roseola, thrush, asthma, food allergies, other allergies, and most of all ear infection after ear infection. Comparing my daughter's health records she was on antibiotics over 14 times her first 2 years of life. She was SOOO sick all the time...doc said it was normal and compared to friends kids it was. Everyone had sick kids ALL the time. It is considered normal in kids under 3. She was not in daycare...so that argument of picking it up at daycare does not work. I could not take her anywhere if she was sick. Even pneumonia!"

"Amazed at the overall health compared to all the kids her age, she gets the same cold/flu and has extremely mild symptoms compared to the other kids who are experiencing severe infections resulting in urgent care visits and prescriptions. All of the milestones were met early is able to read words before 2 1/2 years of age."

"My father is a MD and when time came for my daughter vaccination he asked me for the schedule and after reading it recommended to me not to do it. I myself when kid, was asthmatic and my dad was worried about the effects of the vaccines on her. She is a super healthy teen, never has been on antibiotic, resists all flu season without a problem and her immune system is super strong. Her brother is just the same"

"When she was a baby, I was kicked out of 2 pediatrician offices due to them thinking we were neglectful. One of them threatened to go to authorities. We wound up with a pediatrician who thought it was her obligation to care for her even more than her other patients due to our non-vaccine status. When Sarah was 18, her doctor said she was healthier than most of her patients, but a little underweight."

"We have three incredibly healthy children in our family that have all grown into highly effective professionals. The children have never had headaches, nosebleeds, vaginal infections, gut issues... none of the common ailments that people believe are normal, but are actually signs of disease."

"My son was born out of hospital at a nurse midwife birthing center 6 min. from a major medical facility, all natural and he has been breastfed up to 2+ yrs of life. He's an incredibly astute young toddler with a very active imagination and great sense of humor."

He knows his alphabet and is approaching learning to put together words already. He's amazing and I attribute it to his lack of medical "care" involvement. I'm a health care professional and very attuned to the faults in our system here in the US."

"Trust in strong immune system. Use natural foods diet, homeopathy, vitamin C and herbs to strengthen immunity. Child has had chicken pox, swine flu and whooping cough without serious complications."

"She(17 years) is very healthy, and most are shocked that she never had an ear infection in her lifetime."

"S. is 21 now in 4th year of university. He is extremely bright and healthy man. He was always the healthiest child in his classes through grade school and high school. rarely even a cold. maybe once a year a 3 days cold. he has never taken an antibiotic, steroid or other allopathic medicine. i would give him an A+ in over all health."

"I am actually a 63 year old Baby Boomer who has never had any of those childhood vaccinations, simply because we lived in such a rural, remote area, "they" could not effectively get to me, and my mother, with her naive intuition didn't want them to "hurt me." Wow. Understatement. My heart aches for kids today. Stories like mine, of people never vaccinated, growing up and living a life of health and vigor, are ignored. It might be helpful to open up the survey to broader age groups."

"I didn't start J. on vaccines until she was 3 because i wanted her to be able to talk well first. The thought of having to inject something that could cause death into your child scared me but i thought it was required. She wasn't nearly as sickly or mentally handicapped as my son that HAD to receive each vaccine on time because we lived on a military installation. But her health doesn't even compare to our son who never received any vaccinations as he's never been on any antibiotics in his 9 yrs!"

"My first child has the most vaccines. The second has some. The last had none. The overall healthiest with the least problems is the one who got no vaccines. I have my masters degree in Nursing. I read all sorts of stuff cause I really wanted to believe vaccines are safe and ok but they are not. So my intensive research swayed me the other way."

"J. is our eighth child and the first to remain almost completely undamaged by the medical system. We did not even allow any newborn testing (such as PKU, etc...), nor did we allow a hearing screening, or vitamin k, or even the antibiotics in the eyes. He did not leave our sight in the hospital, because we did not trust the nurses to respect our desire to protect him from testing, vaccines, etc.... In fact, we would have avoided the hospital altogether if I did not have to deliver by c-section. J. is more alert and healthier than any of our other children. He is almost two and has not needed medical care yet. He is rarely sick, and has never had an ear infection. If fourteen years ago, before we had our first child, our pediatrician (or anyone for that matter) had given us a list of vaccine ingredients, including an understanding as to how they are made, and perhaps the opportunity to view the warning label (although the ingredi ent list would have done it for me), we would have NEVER vaccinated any of our children, ever. It should be mandatory that ingredients and warning labels be read by parents before a doctor is allowed to administer a vaccine. We are lied to and deceived by our government and our medical doctors/establishment. We did not question our doctors, because we were raised to believe that they existed for our good and we were to trust them. Well, we have paid the price, along with countless others. We stopped vaccinating three years ago. Shortly after my seventh child was born. She had only a few vaccines, but still a few too many. Several of my other children also came out only partially vaccinated. When I first learned of the ingredients of vaccines and how they were made, I was devastated and in shock that I had been so foolish to believe the doctors and cause such irreversible harm to my children. I am still grieved about it. People need to be told the truth!"

- *For more stories go to: <http://www.vaccineinjury.info/results-unvaccinated/personal-stories.html>*

Immunization Graphs:
Natural Infectious Disease Declines; Immunization
Effectiveness; and Immunization Dangers

Prepared by: Raymond Obomsawin Ph.D.
Senior Advisor - First Nations Centre

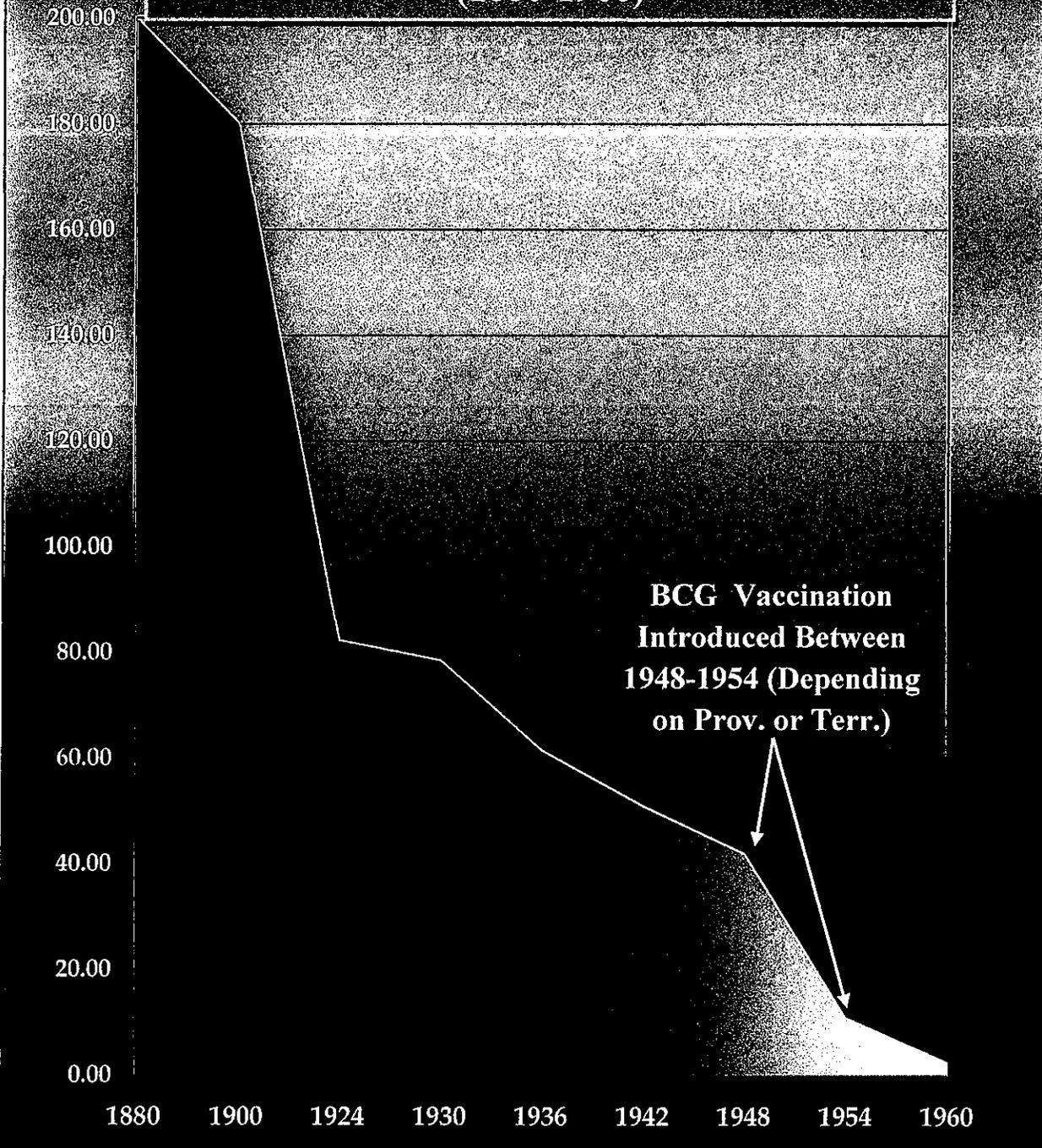
National Aboriginal Health Organization
October 2009

FIGURE SET I.

Natural Infectious Disease Declines Preceding Public Immunization Efforts

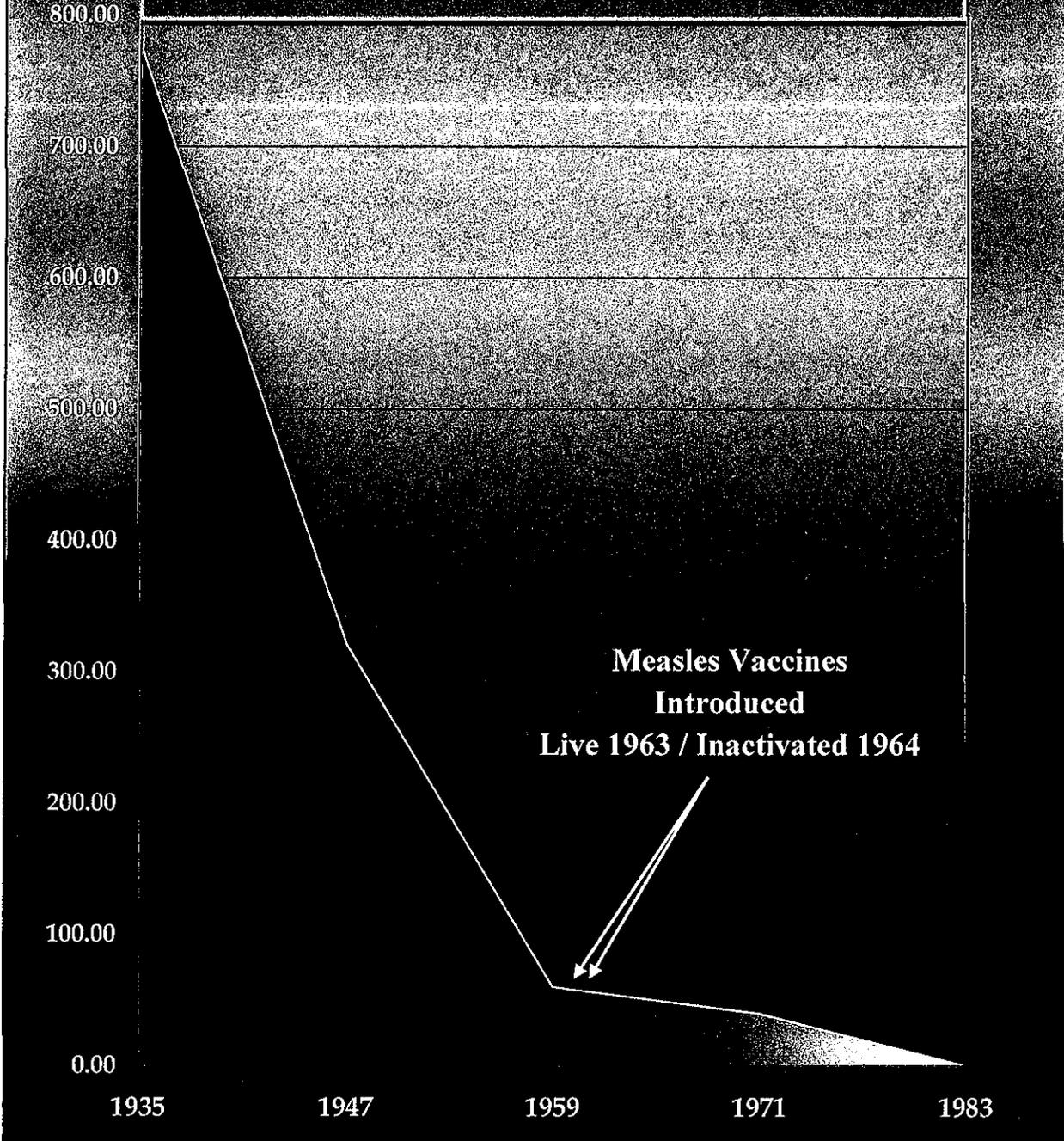
Figures one (1) through eleven (11) graphically illustrate that in North America, Europe, and the South Pacific , major declines in life-threatening infectious diseases occurred historically either without, or far in advance of public immunization efforts for specific diseases as listed. This provides irrefutable evidence that vaccines are not necessary for the effective elimination of a wide range of infectious diseases

**FIGURE 1 – CANADA TUBERCULOSIS
MORTALITY RATES PER 100,000
(1880-1960)**



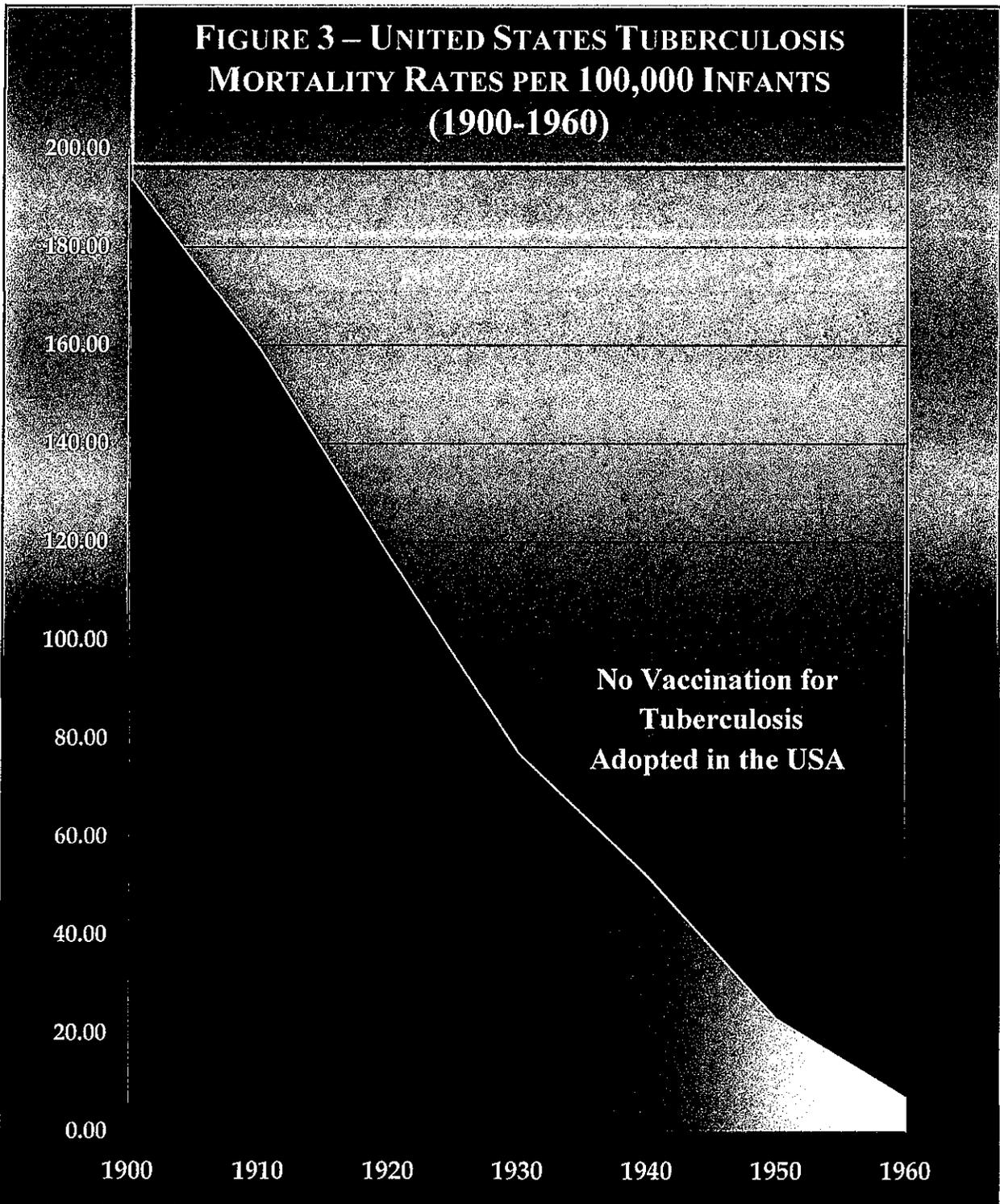
Source: Table based on data at: Timeline of TB in Canada <http://www.lung.ca/tb/tbhistory/timeline/>;
<http://www.thecanadianencyclopedia.com/index.cfm?PgNm=TCE&Params=A1ARTA0008151>
Public Health Agency of Canada: <http://www.phac-aspc.gc.ca/publicat/eig-gci/p04-bcg-eng.php>; and
PHAC on BCG usage in Canada: http://www.phac-aspc.gc.ca/tbpc-latb/bcgvac_1206-eng.php

**FIGURE 2 – CANADA MEASLES
REPORTED INCIDENCE
(1935-1983)**



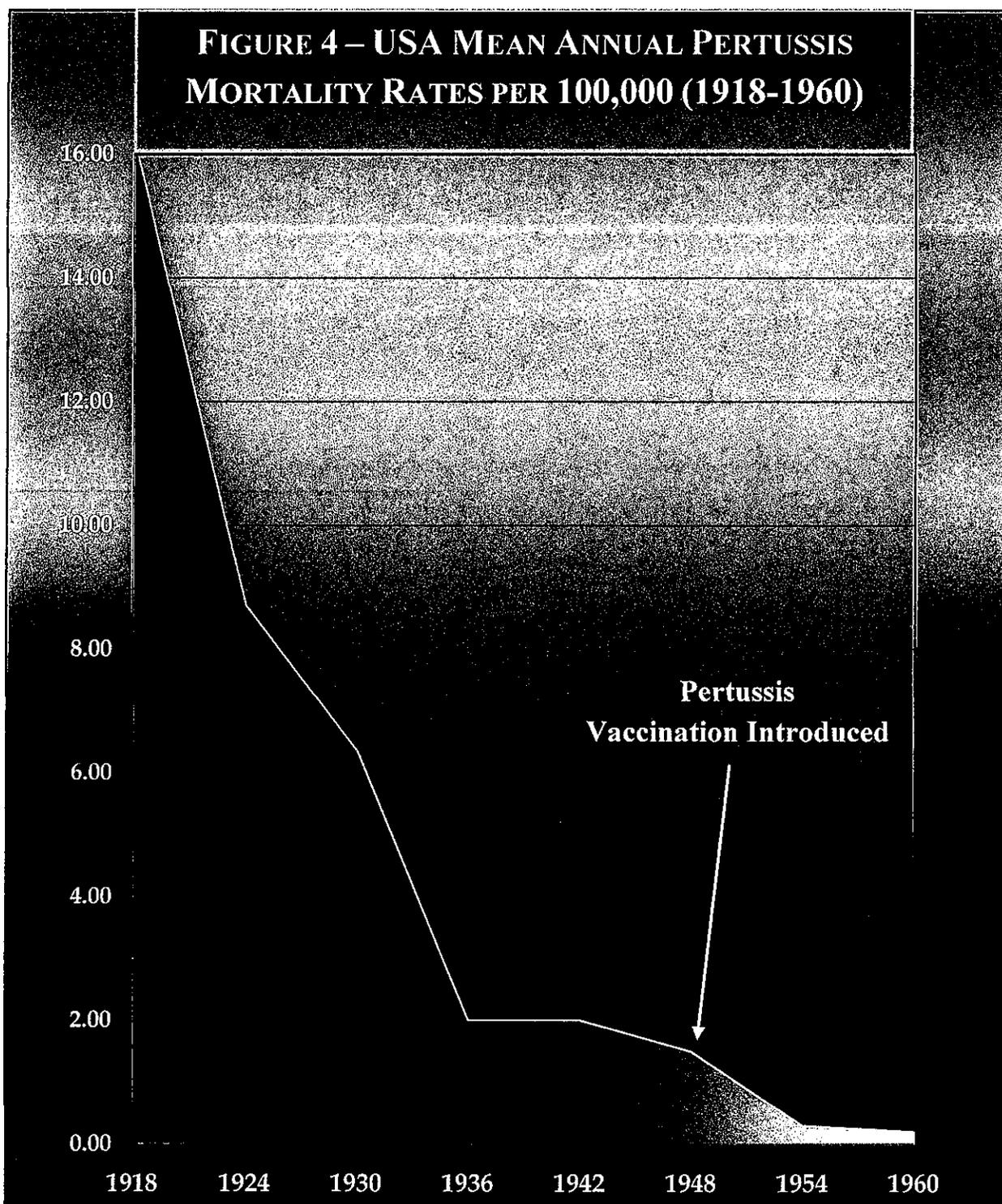
Source: Adapted from: Public Health Agency of Canada, Figure 8 – Measles Reported Incidence Canada. <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php>

**FIGURE 3 – UNITED STATES TUBERCULOSIS
MORTALITY RATES PER 100,000 INFANTS
(1900-1960)**



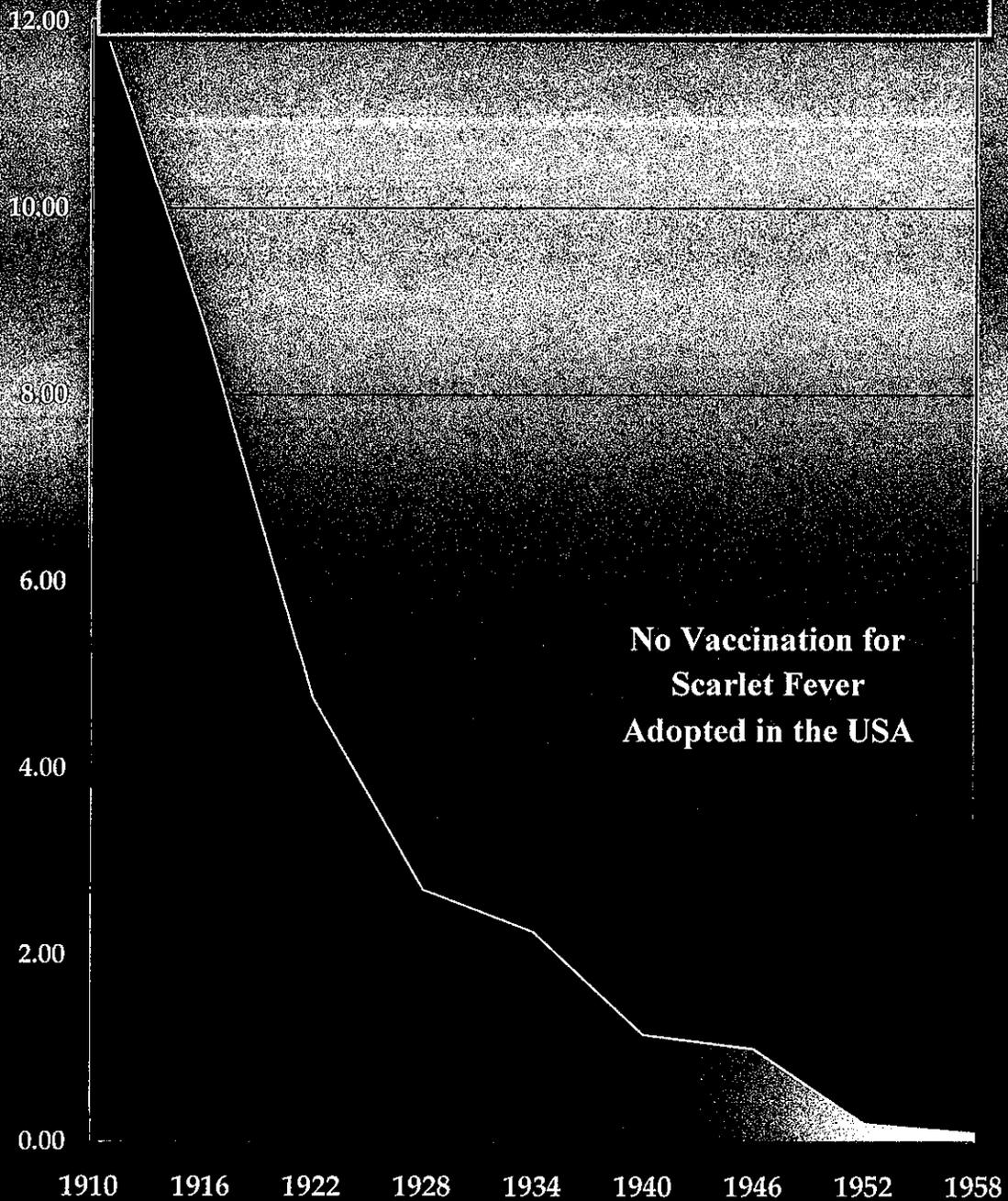
Source: John H. Dingle; Life and Death in Medicine; Scientific American; 1973; p. 56.

FIGURE 4 – USA MEAN ANNUAL PERTUSSIS MORTALITY RATES PER 100,000 (1918-1960)



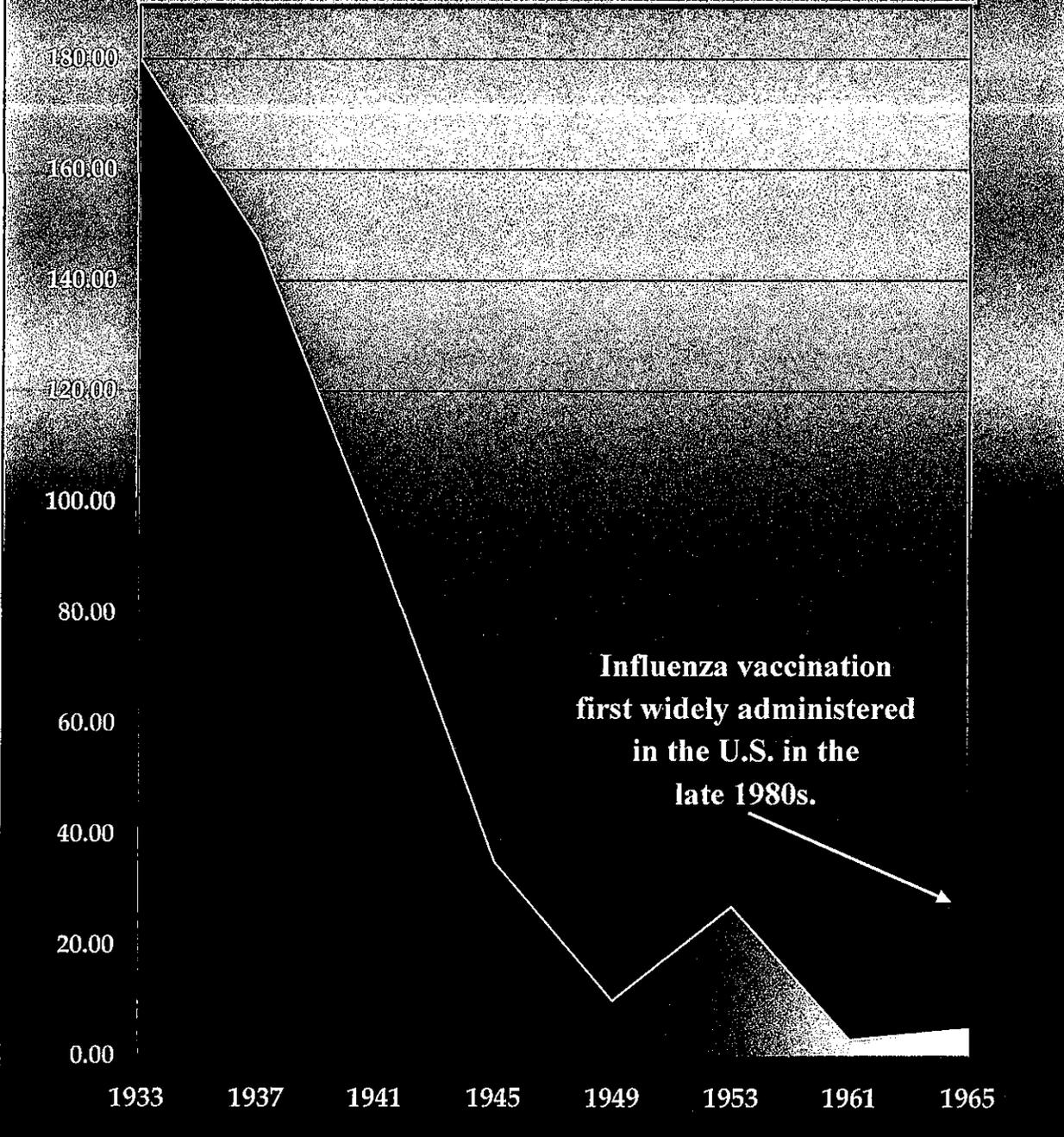
Source: Data derived from: Vital Statistics of the United States 1937-1960; and Historical Statistics of the United States: Colonial Times to 1970 Part 1 Ch. B Vital Statistics and Health and Medical Care, pp. 44-86H.

FIGURE 5 – USA MEAN ANNUAL SCARLET FEVER MORTALITY RATES PER 100,000 (1910-1958)



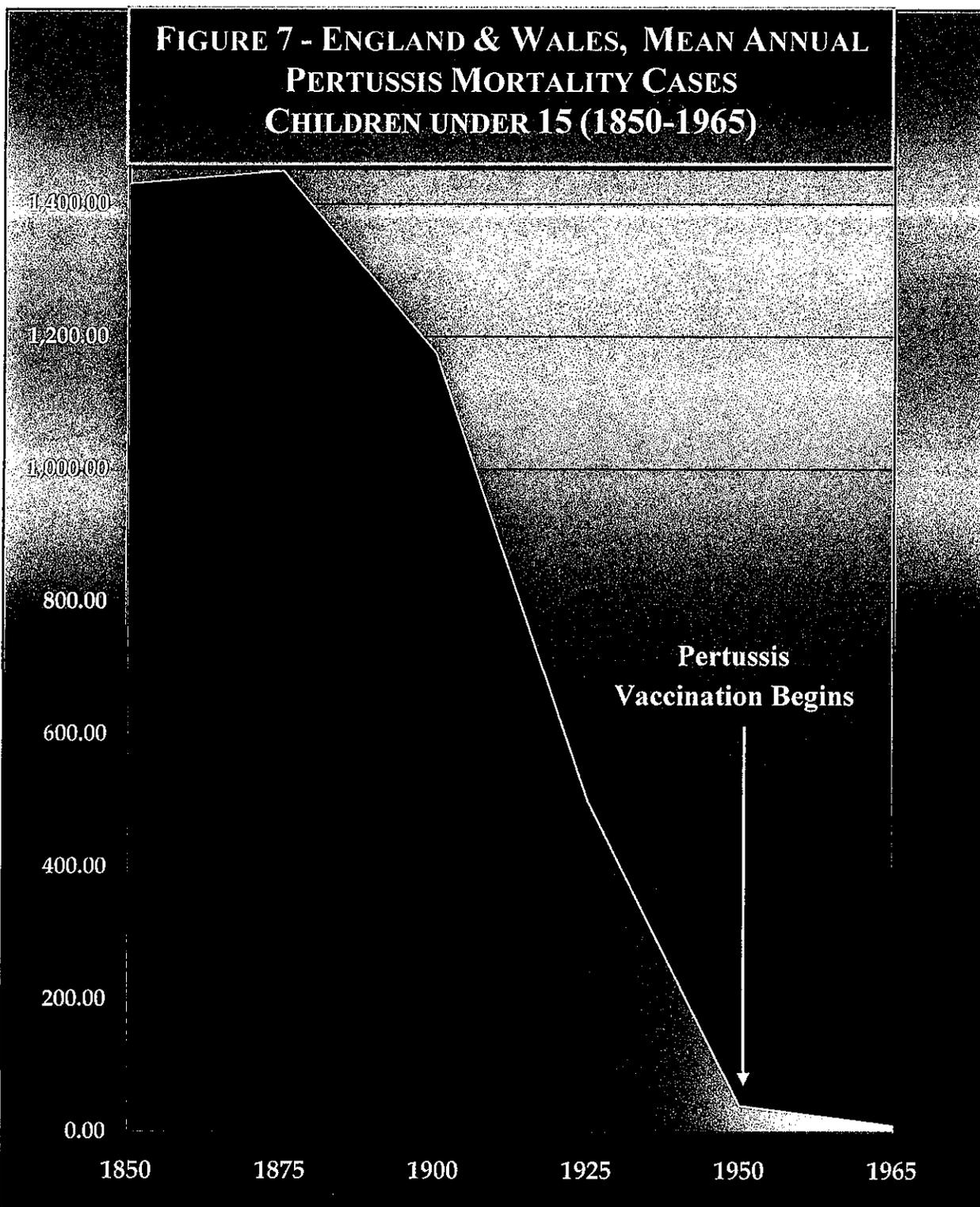
Source: Data derived from - Vital Statistics of the United States 1937-1960; and Historical Statistics of the United States: Colonial Times to 1970 Part 1 Ch. B Vital Statistics and Health and Medical Care, pp. 44-86H.

**FIGURE 6 – USA ANNUAL INFLUENZA
MORTALITY RATES PER 100,000 (1933-1965)**



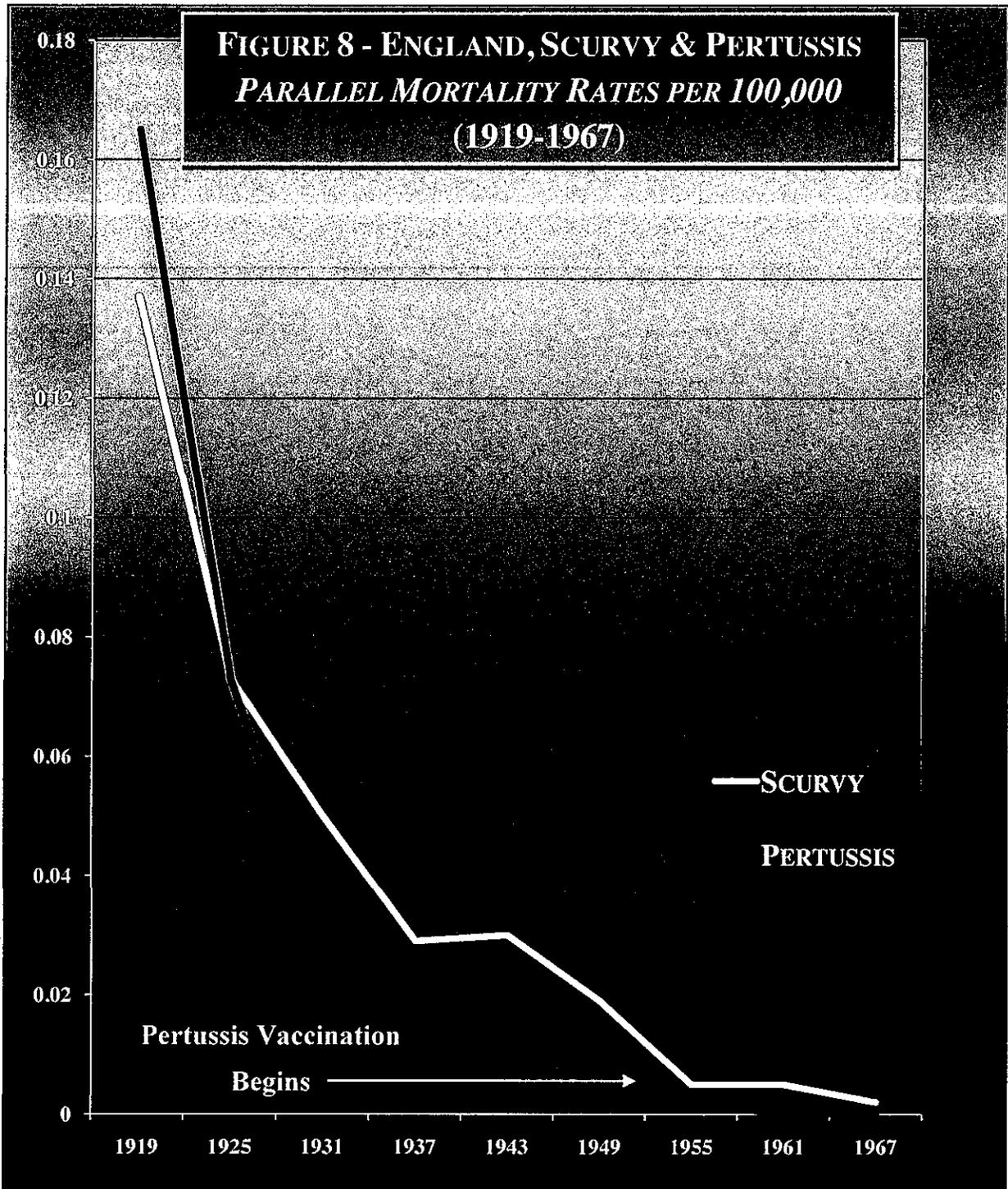
Source: Doshi, P., Trends in Recorded Influenza Mortality: United States 1900-2004, American Journal of Public Health, May 2008, vol. 98, no. 5, p. 941.

FIGURE 7 - ENGLAND & WALES, MEAN ANNUAL PERTUSSIS MORTALITY CASES CHILDREN UNDER 15 (1850-1965)



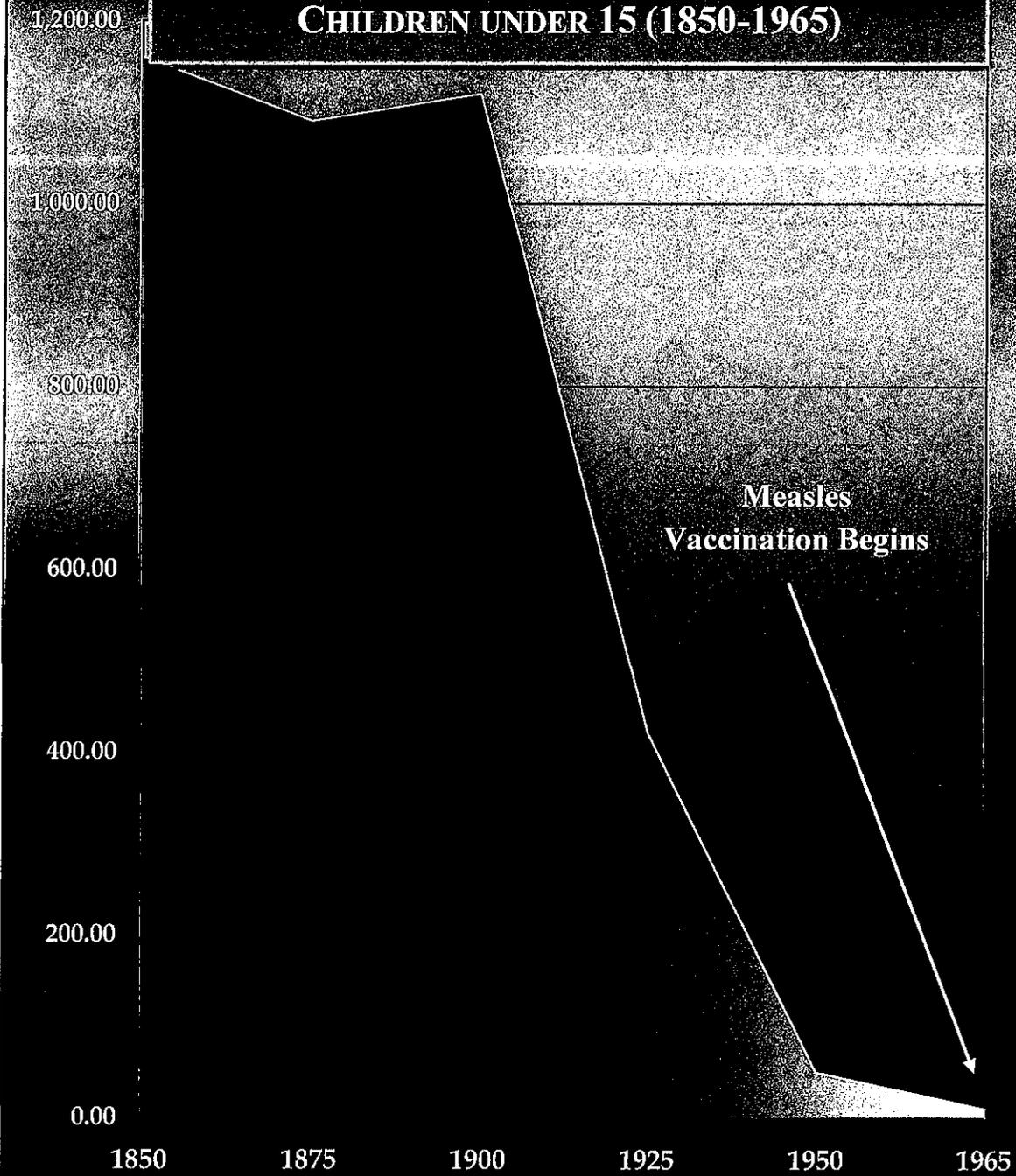
Source: Thomas McKeown, *The Role of Medicine: Dream, Mirage or Nemesis?*; Basil Blackwell; Oxford, UK; 1979; p. 103

**FIGURE 8 - ENGLAND, SCURVY & PERTUSSIS
PARALLEL MORTALITY RATES PER 100,000
(1919-1967)**



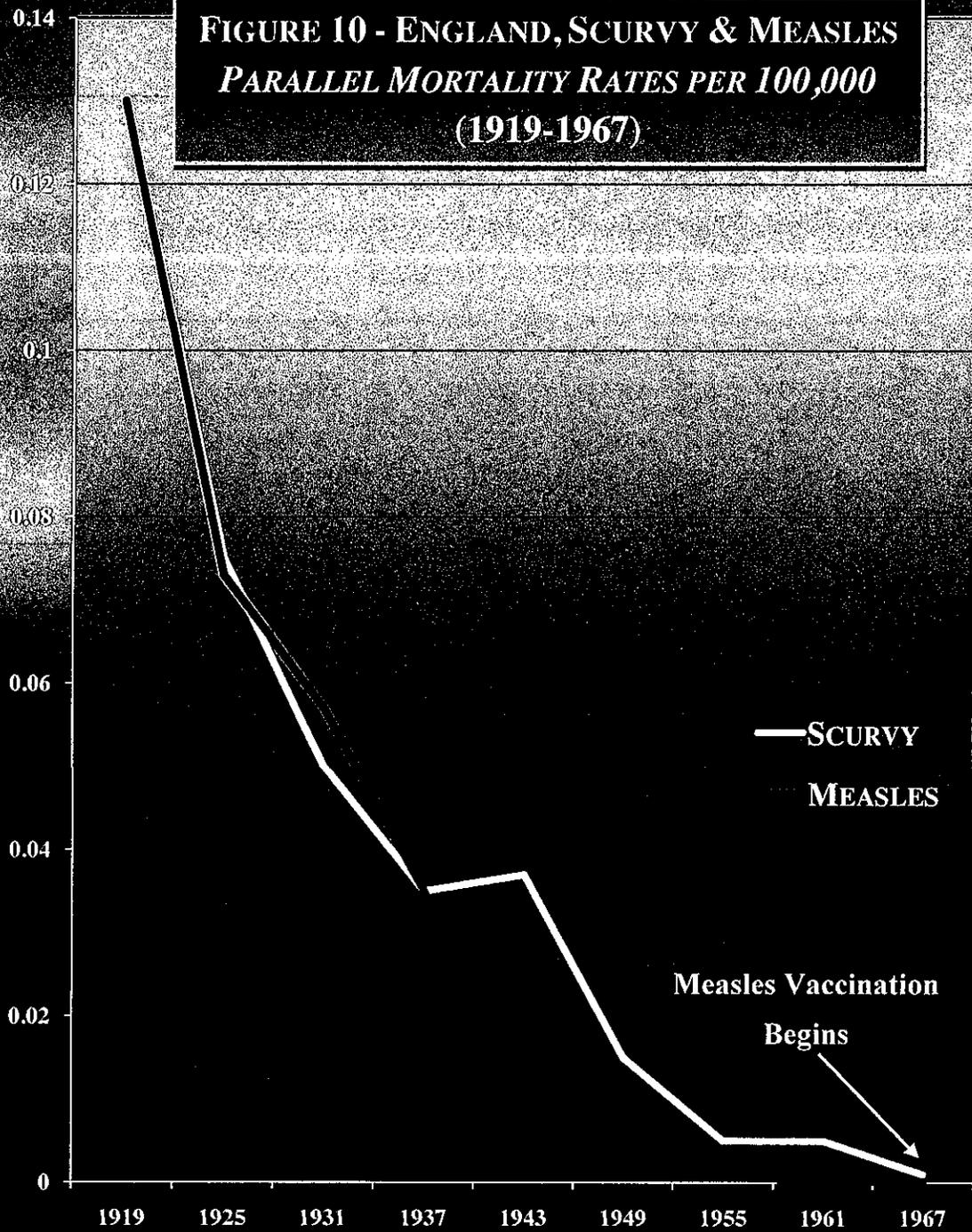
Sources: Data for years 1919-1967 Mortality Statistics: Deaths Registered in England & Wales; UK Office for National Statistics, 1997.

**FIGURE 9 - ENGLAND & WALES, MEAN ANNUAL
MEASLES MORTALITY CASES
CHILDREN UNDER 15 (1850-1965)**



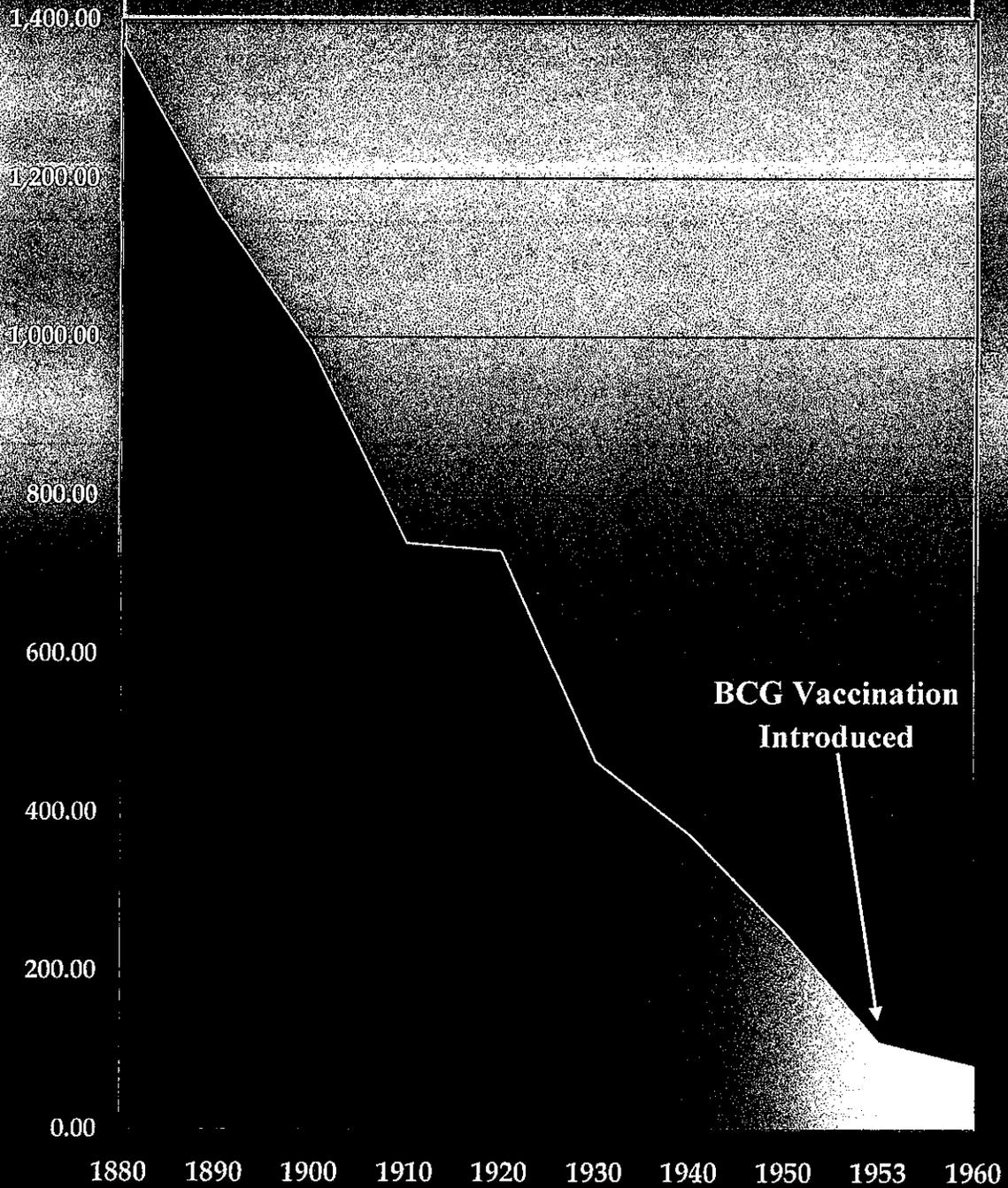
Source: McKeown, T., *The Role of Medicine: Dream, Mirage or Nemesis?*; Basil Blackwell; Oxford, UK; 1979; p. 105; & Waltzkin, H., in *The Relevance of Social Science for Medicine*; Springer; 1st edition, Dec. 31, 1980

**FIGURE 10 - ENGLAND, SCURVY & MEASLES
PARALLEL MORTALITY RATES PER 100,000
(1919-1967)**



Sources: Data for years 1919-1967 Mortality Statistics: Deaths Registered in England & Wales; UK Office for National Statistics, 1997.

**FIGURE 11 - NEW ZEALAND TUBERCULOSIS
DEATH RATES PER MILLION (1880-1960)**



Source: Director General Annual Mortality Reports Covering 1872-1960, New Zealand Parliamentary Journals for the Years Specified.

FIGURE SET II.

Immunization Effectiveness

Figures eleven (12) through twenty-four (24) graphically illustrate that immunization is not by any means a proven and foolproof measure for protection from various infectious disease conditions. It is often inconsequential epidemiologically, and in some cases it is shown to actually worsen health-care outcomes.

Figure 12

**Children Under 2 Yrs of Age
Inactivated Influenza Vaccine**



Source: Cochrane Collaboration Database of Systematic Reviews, (John Wiley & Sons, Ltd.)
2006 (1) Article No. CD004879 – Covers 51 Studies on 260,000 children

Figure 13

**Elderly Living in Communities
& Group Homes
Inactivated Influenza Vaccine**



Source: Cochrane Collaboration Database of Systematic Reviews, (John Wiley & Sons, Ltd.)
2006 (3) Article No. CD004876 – Covers 64 Studies, over 40 years of influenza vaccination
and see: <http://www.bmj.com/cgi/content/full/333/7574/912>

Figure 14

BCG for Tuberculosis

Note: Post-vaccination- 376 cases pulmonary TB & 31 cases glandular TB diagnosed. TB higher among two (2) dose Vaccinated versus Placebo Group

0%
Effective

Source: Randomised controlled trial of single BCG, repeated BCG, or combined BCG and killed *Mycobacterium leprae* vaccine for prevention of leprosy and tuberculosis in Malawi; *The Lancet*, Volume 348, Issue 9019, Pages 17 - 24, 6 July 1996

Figure 15

BCG for Tuberculosis

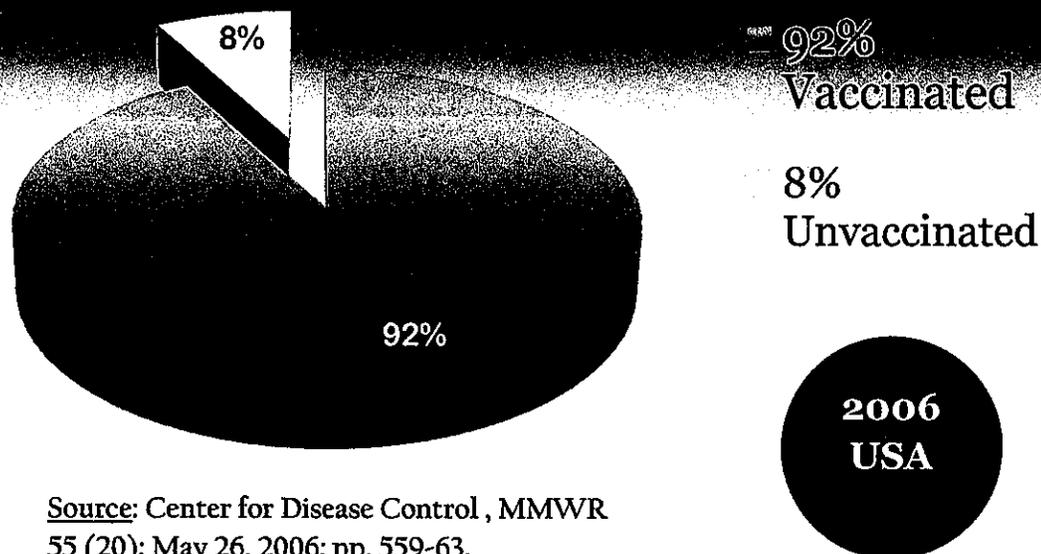
Note: In years 0-2.5 the vaccinated had double the incidence of Tuberculosis versus Placebo Group

0%
Effective

Source: Double blind randomized controlled trial of BCG's effectiveness on 250,000 subjects Tuberculosis Research Centre (ICMR), Chennai, India: *Indian Journal of Medical Research*, 110, August 1999, pp. 56-69.

Figure 16

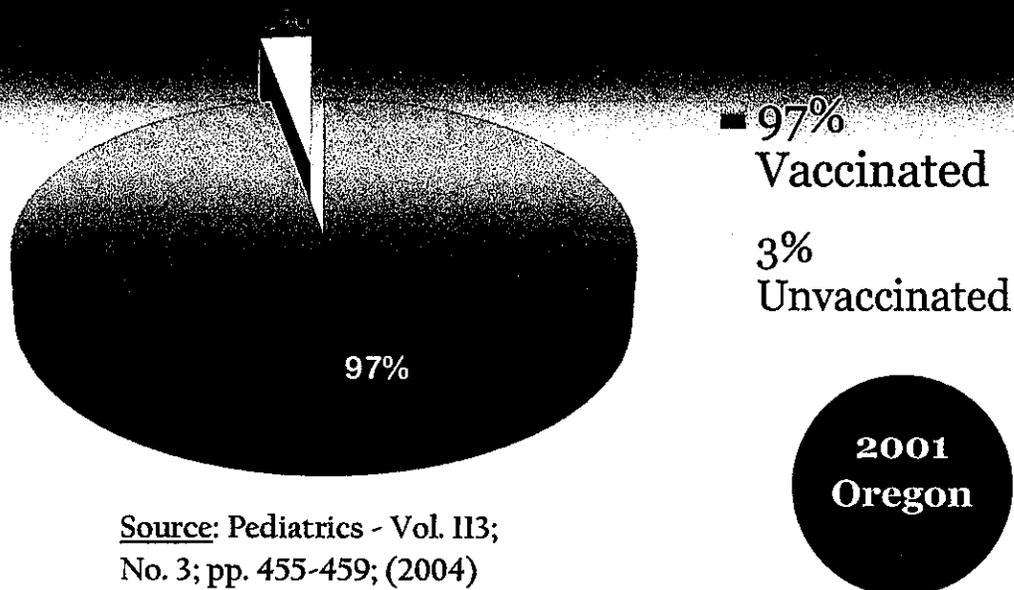
**MUMPS OUTBREAK IN HIGHLY
VACCINATED POPULATION**



Source: Center for Disease Control , MMWR
55 (20); May 26, 2006; pp. 559-63.

Figure 17

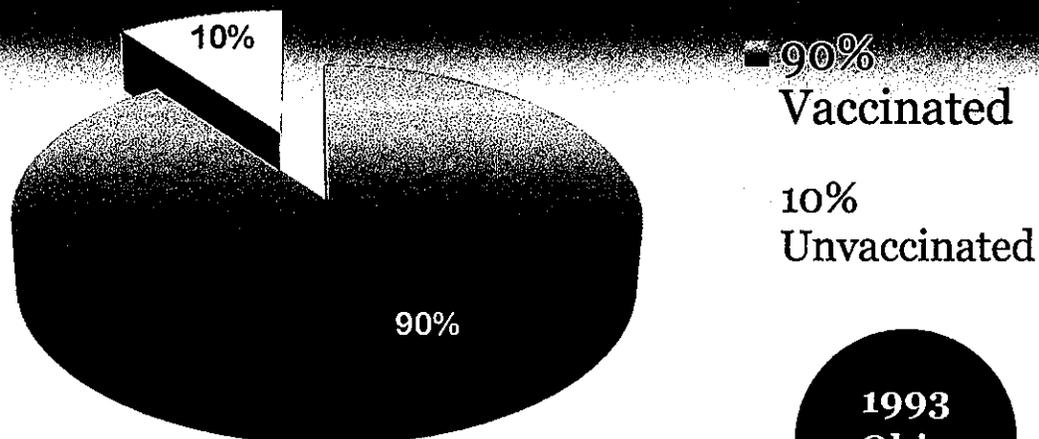
**CHICKENPOX OUTBREAK IN
HIGHLY VACCINATED POPULATION**



Source: Pediatrics - Vol. 113;
No. 3; pp. 455-459; (2004)

Figure 18

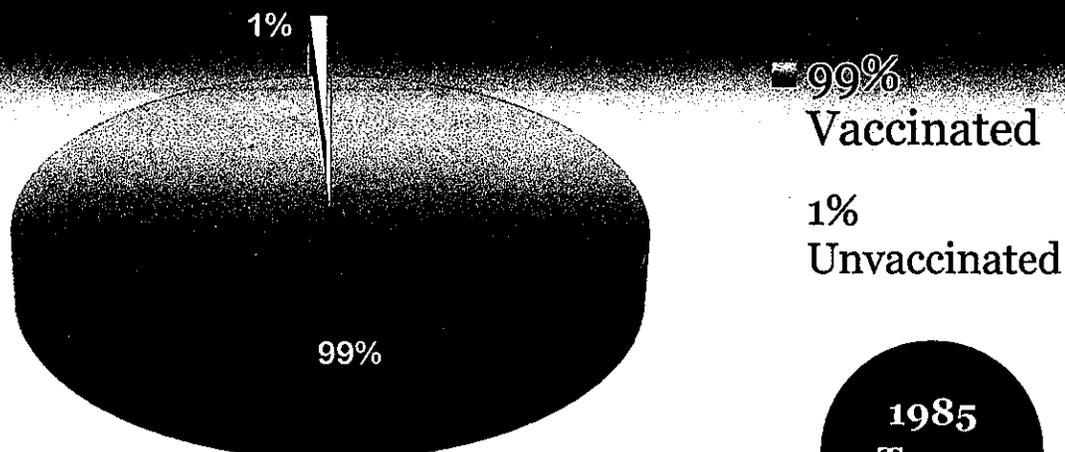
**PERTUSSIS OUTBREAK IN
HIGHLY VACCINATED POPULATION**



Source: N.Z. Miller; *Vaccine Safety Manual*,
N.A. Press, Sante Fe, New Mexico; p. 140; (2008)
(Refers to CDC & Official Surveillance data)

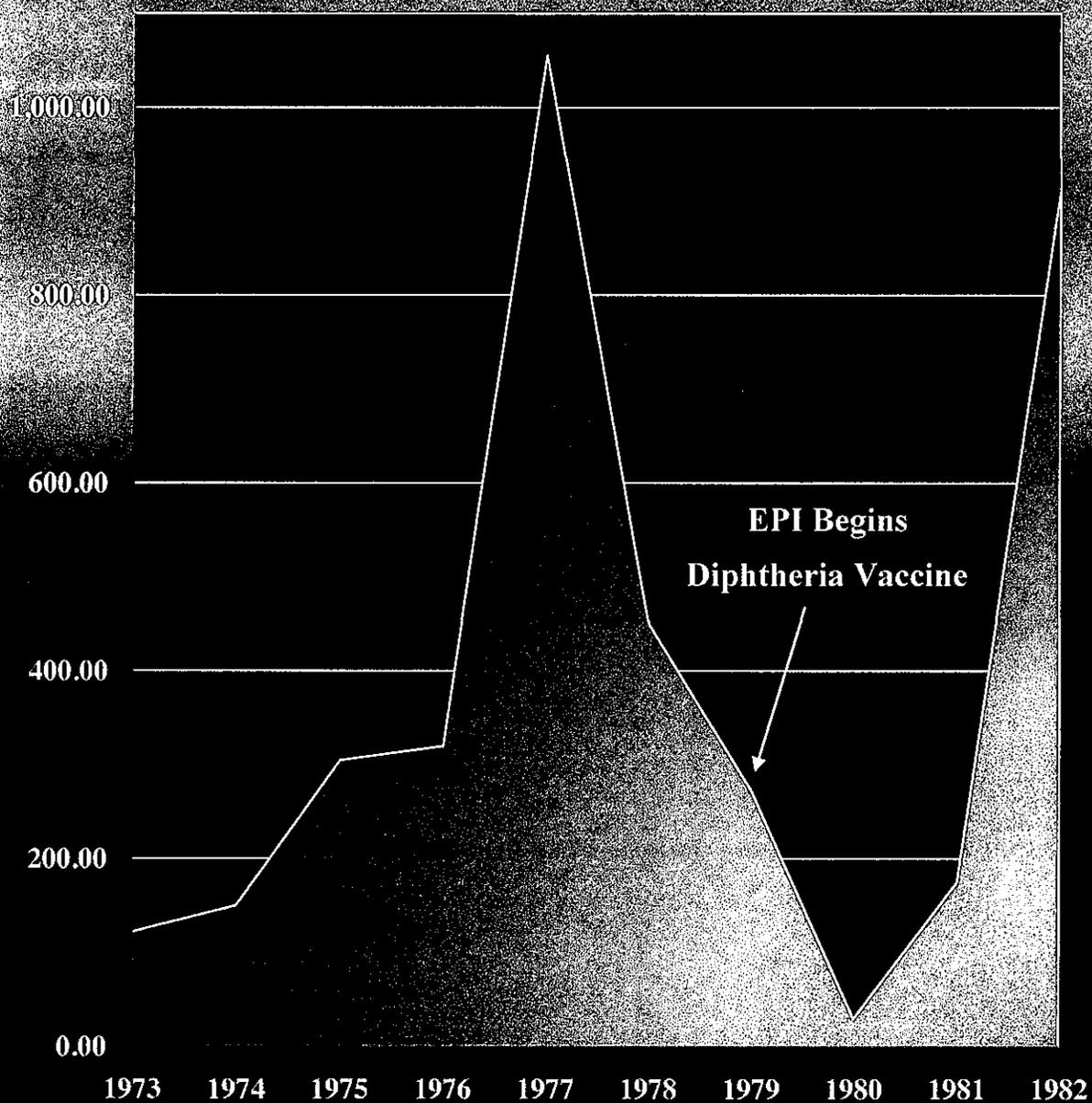
Figure 19

**MEASLES OUTBREAK IN
HIGHLY VACCINATED POPULATION**



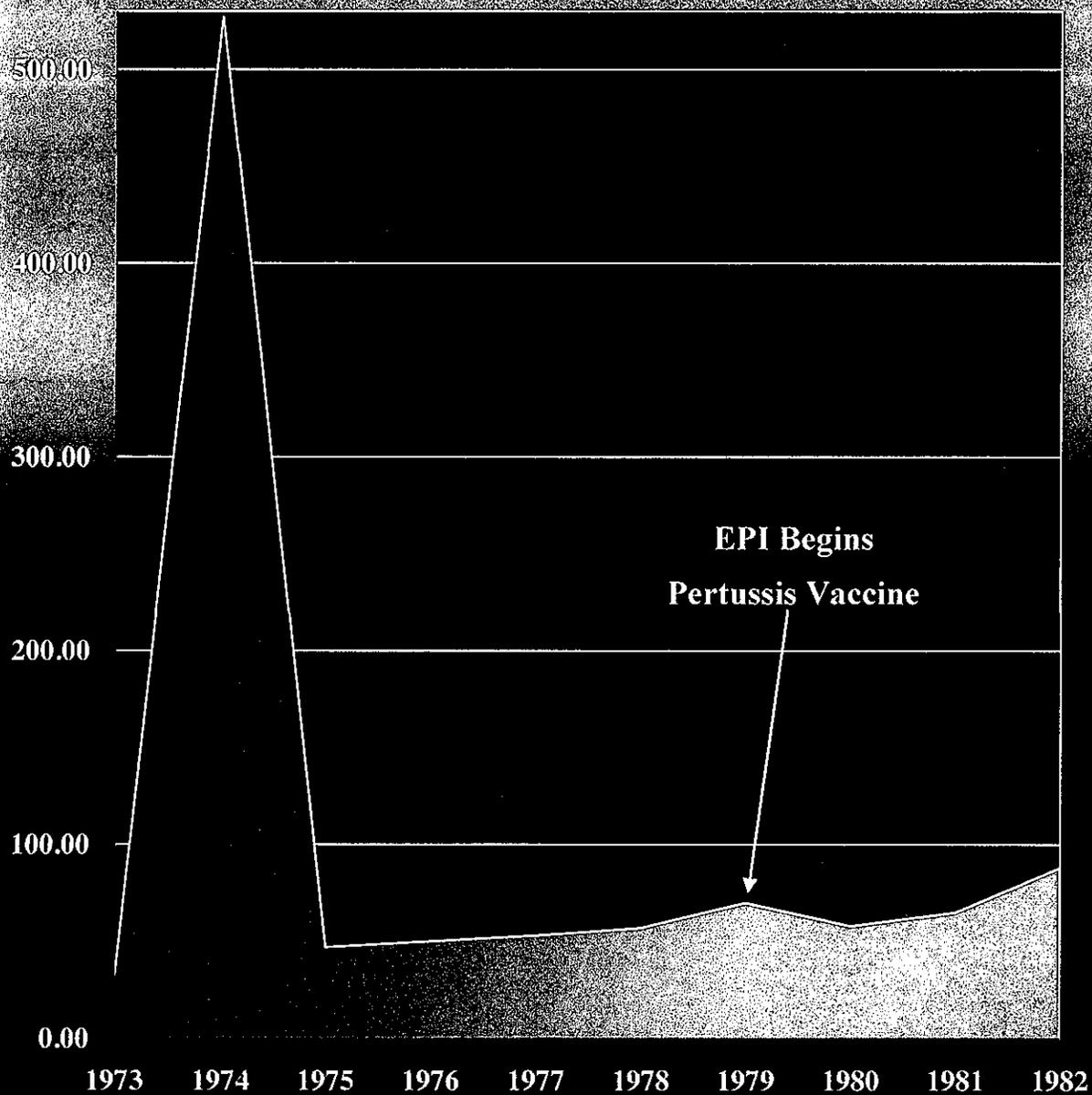
Source: New England Journal of Medicine -
Vol. 316; No. 13; pp. 771-774; (1987)

FIGURE 20 - NIGERIA
DIPHTHERIA REPORTED CASES
(1973-1982)



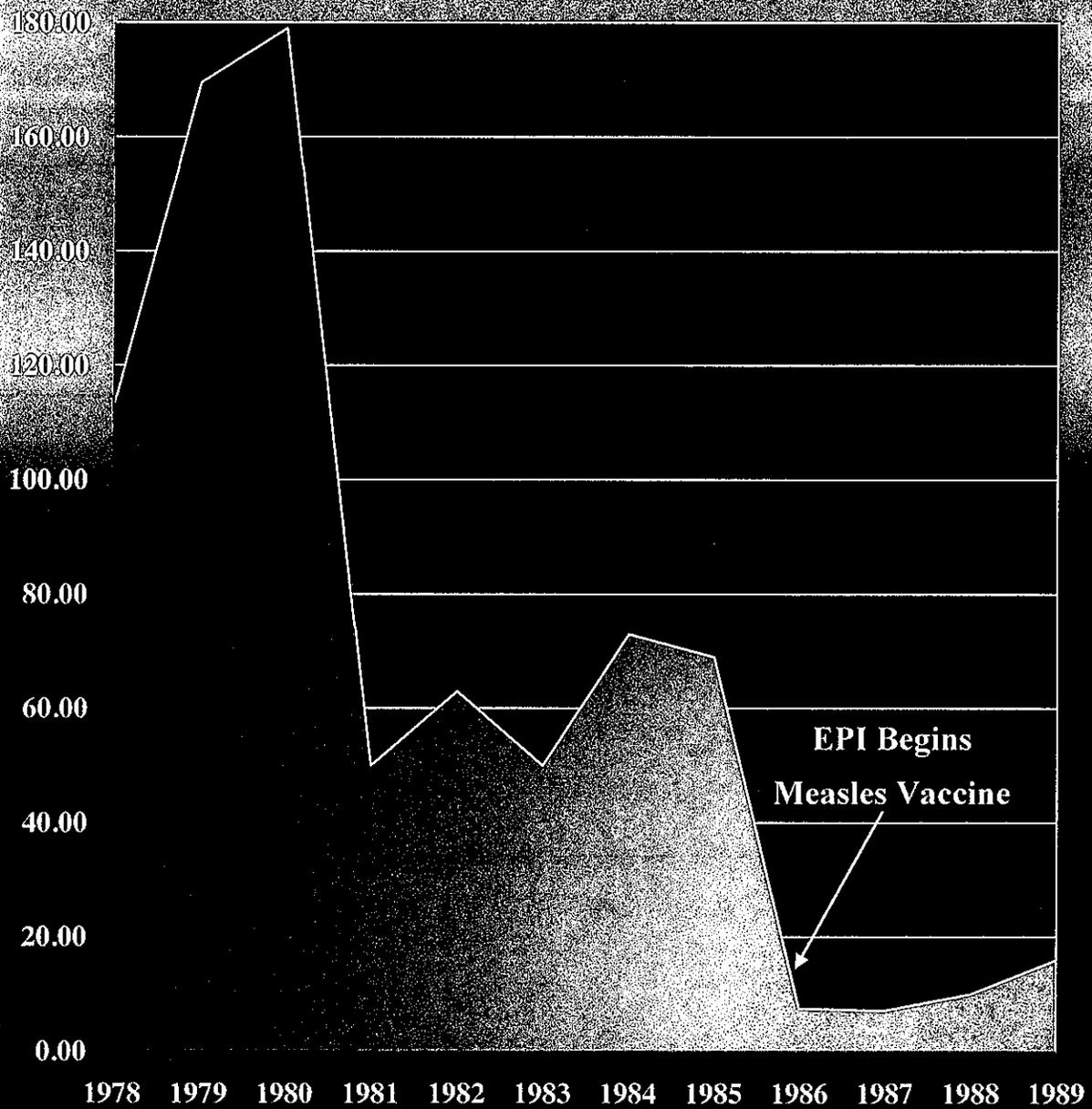
Source: E. Ekanem; A 10-Year Review of Morbidity from Childhood Preventable Diseases in Nigeria: How Successful is the Expanded Programme of Immunization (EPI)?; *Journal of Tropical Pediatrics*, Vol. 34; No. 6; UK; 1988; pp. 323-328.

FIGURE 21- NIGERIA
WHOOPING COUGH CASE RATES PER 100,000
(1973-1982)



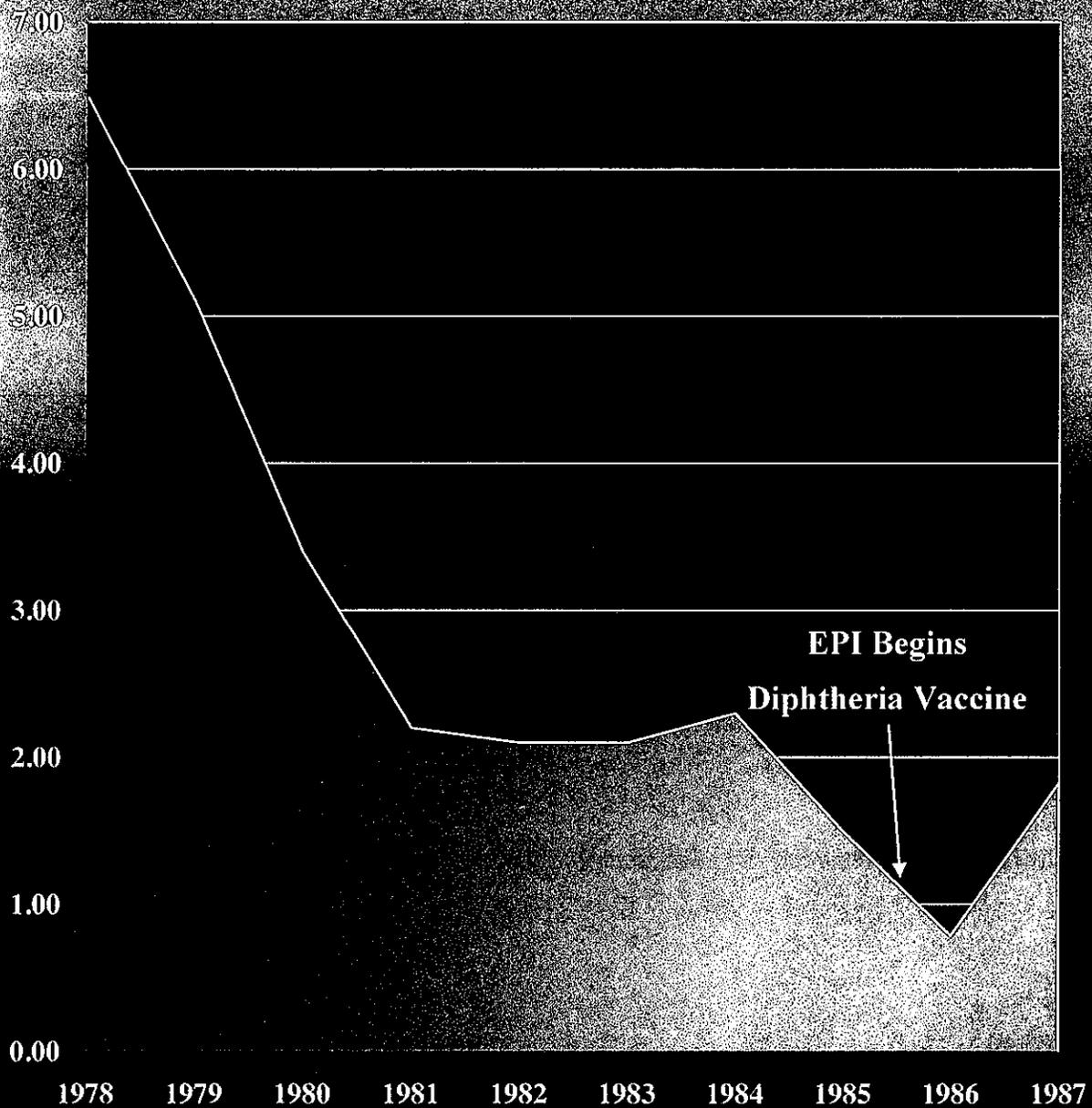
Source: E. Ekanem; A 10-Year Review of Morbidity from Childhood Preventable Diseases in Nigeria: How Successful is the Expanded Programme of Immunization (EPI)?; *Journal of Tropical Pediatrics*, Vol. 34; No. 6; UK; 1988; pp. 323-328.

**FIGURE 22 - DOMINICAN REPUBLIC
MEASLES CASE RATES PER 100,000
(1978-1989)**



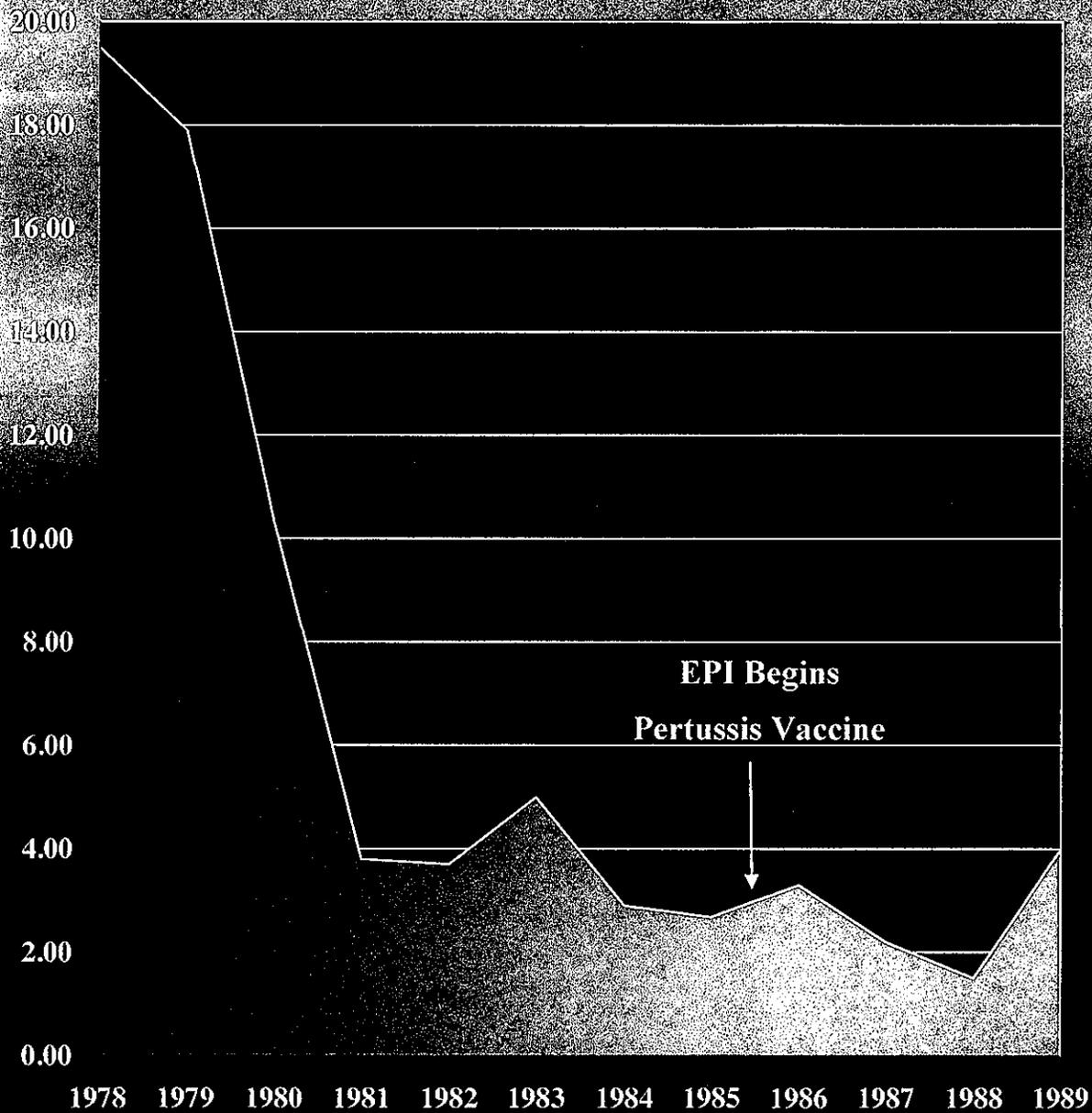
Sources: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988; and Data for years 1988-1989 from personal communication from PAHO, EPI Unit, Aug. 21, 1990.

**FIGURE 23 - DOMINICAN REPUBLIC
DIPHTHERIA CASE RATES PER 100,000
(1978-1987)**



Source: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988.

**FIGURE 24 - DOMINICAN REPUBLIC
PERTUSSIS CASE RATES PER 100,000
(1978-1989)**



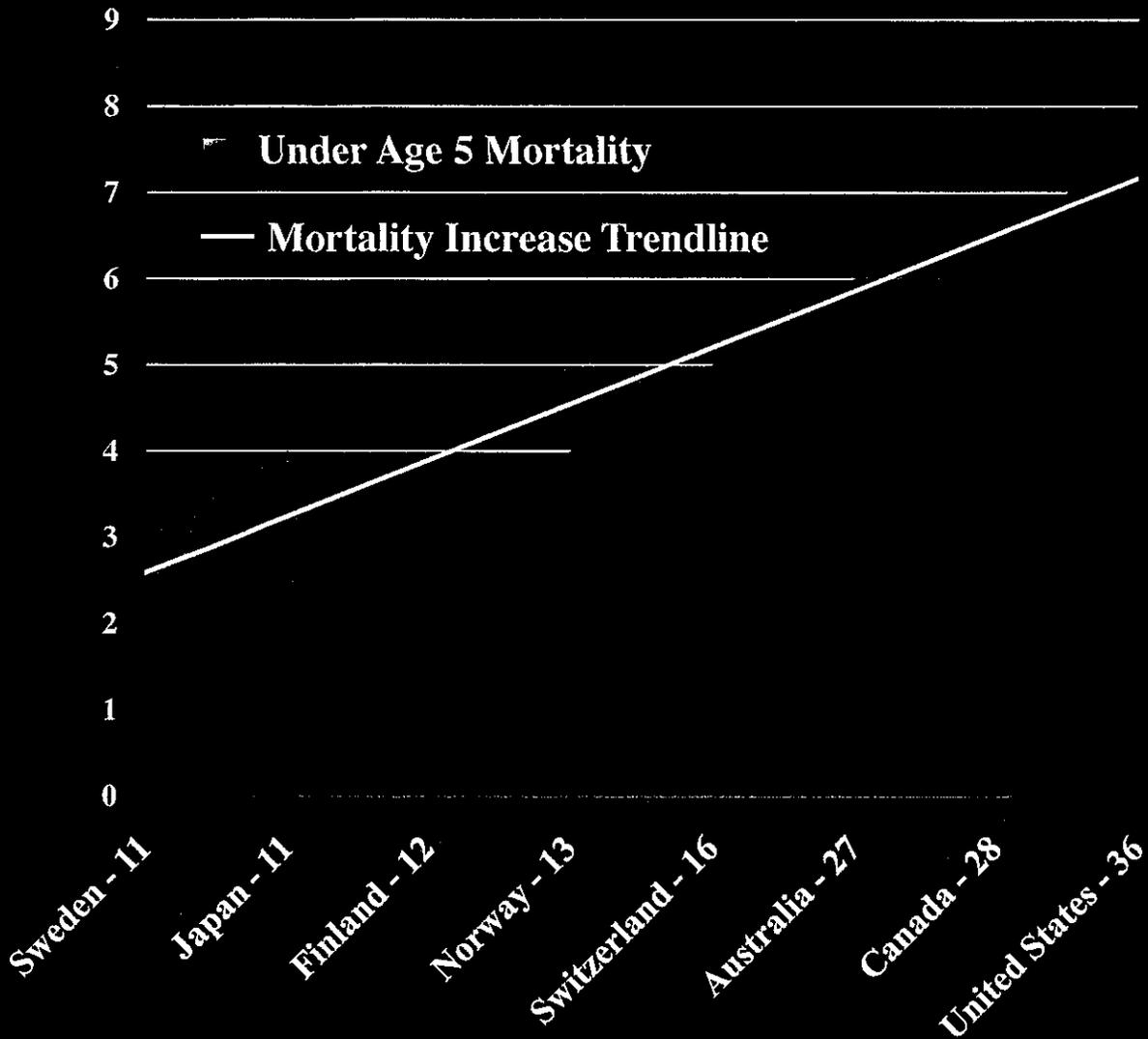
Sources: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988; and Data for years 1988-1989 from personal communication from PAHO, EPI Unit, Aug. 21, 1990.

FIGURE SET III.

Immunization Dangers

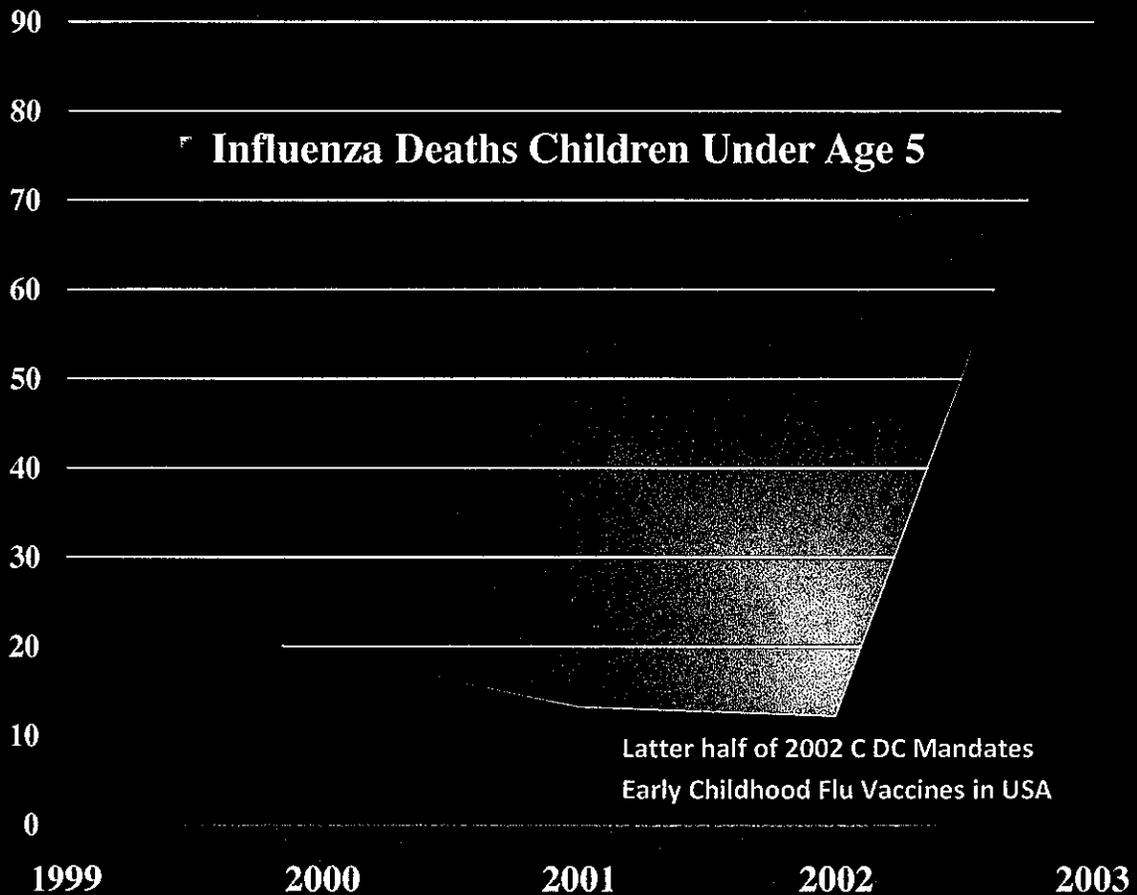
Figures twenty-five (25) through thirty three (33) graphically illustrate that increases in the number of governmental mandated vaccines correlates with significant increases in death rates for children under the age of five (5); and that the practice is linked to sudden infant death syndrome; various degenerative diseases, including diabetes; and appears to cause general immune system impairment in infants and children. Evidence also points to the practice of immunization as a principal factor in the recent massive increases in neurodegenerative conditions such as autism in children.

**FIGURE 25 - COUNTRIES & NUMBER
OF VACCINES MANDATED
UNDER AGE 5 MORTALITY RATES**



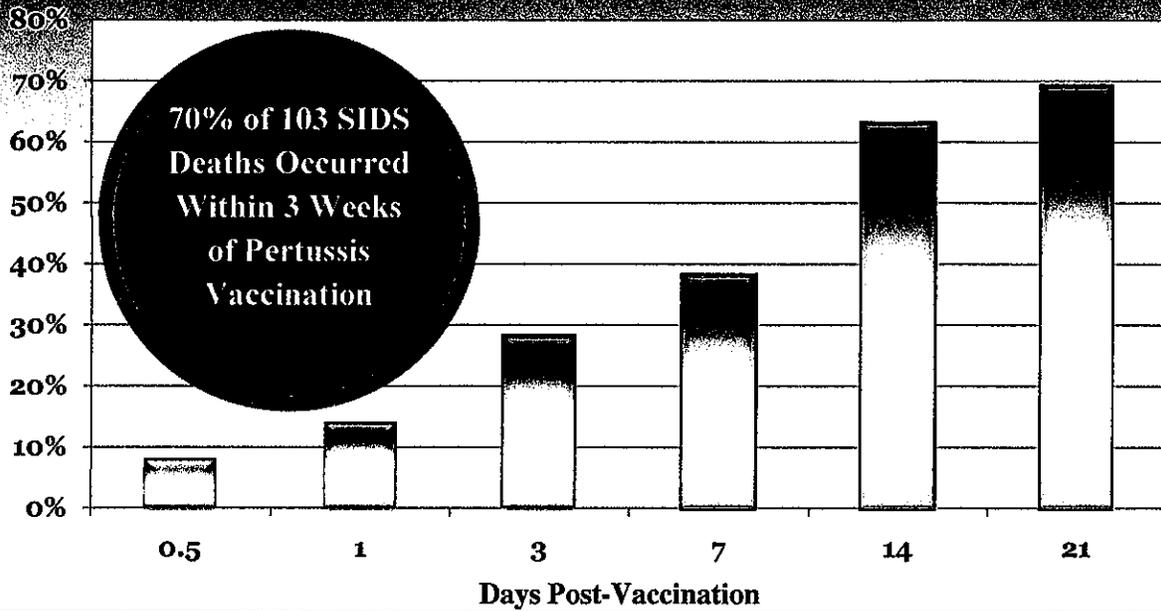
Under Age 5 Mortality statistics derived from: World Health Organization – World Health Statistics 2009 Report http://www.who.int/whosis/whostat/EN_WHS09_Table1.pdf
 & Govt. Mandated Vaccines figures derived from: Generation Rescue Inc. 2009
<http://www.generationrescue.org/documents/SPECIAL%20REPORT%20AUTISM%202.pdf>

**FIGURE 26 - UNDER AGE 5 INFLUENZA DEATHS
BEFORE AND AFTER U.S. CDC MANDATES
FLU VACCINES IN EARLY CHILDHOOD**



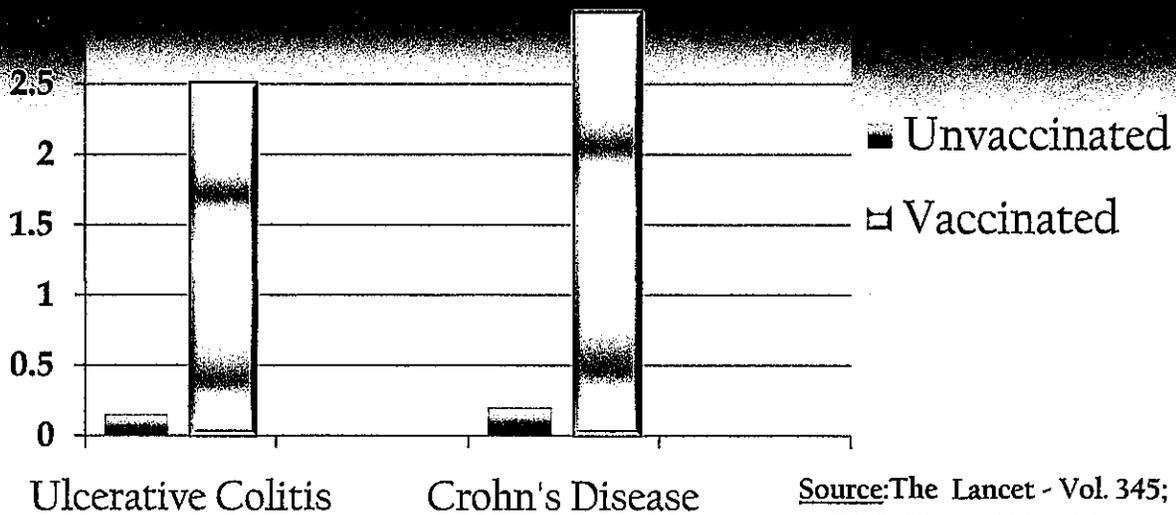
Under Age 5 Influenza Mortality statistics derived from: Center for Disease Control Vital Statistics Reports covering Years 1999-2003 reported in Miller, N.Z., Vaccine Safety Manual, New Atlantean Press, Sante Fe, New Mexico, 2008, p. 97.

FIGURE 27 - PERTUSSIS VACCINE & SUDDEN INFANT DEATH SYNDROME



2/3 of 103 infants had been vaccinated with pertussis prior to death which 6.5% within 12 hours; 13% within 24 hours; 26% within 3 days; 37%, 61% & 70% within 1, 2, & 3 weeks respectively. Source: Torch W., Neurology - 32 (4 - Pt. 2) A, 1982, pp. 169-170.

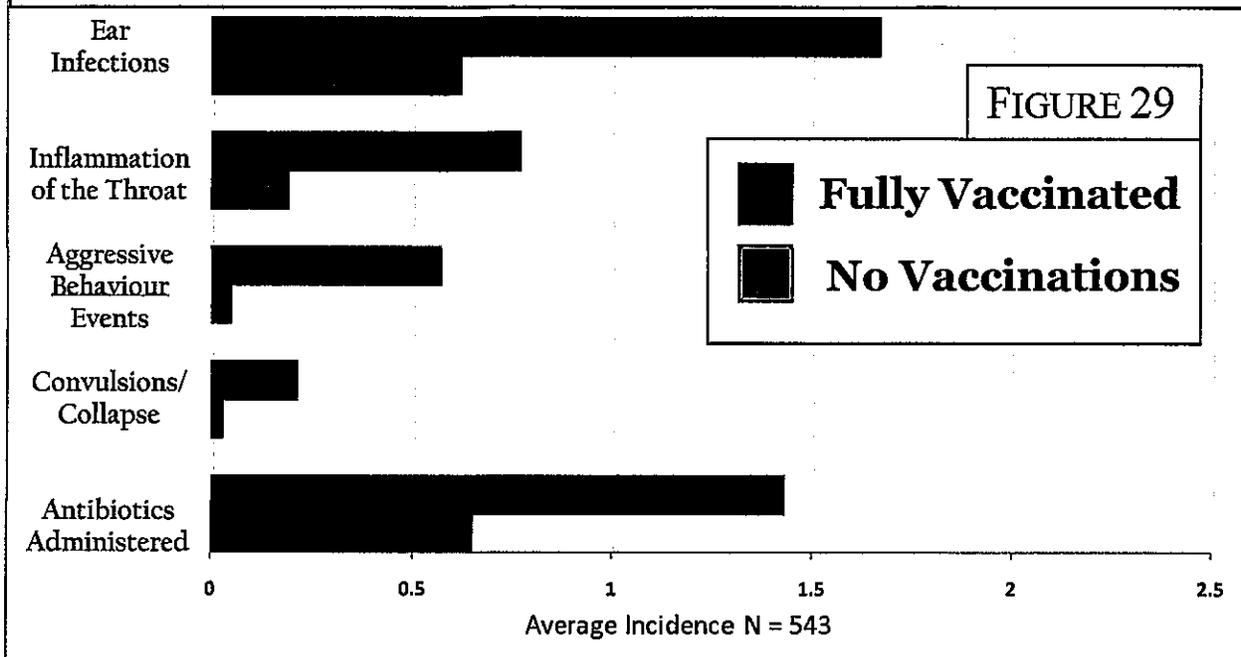
FIGURE 28 - MEASLES VACCINE & INFLAMMATORY BOWEL DISEASES



Source: The Lancet - Vol. 345; 8957; 1995, pp. 1062-1063.

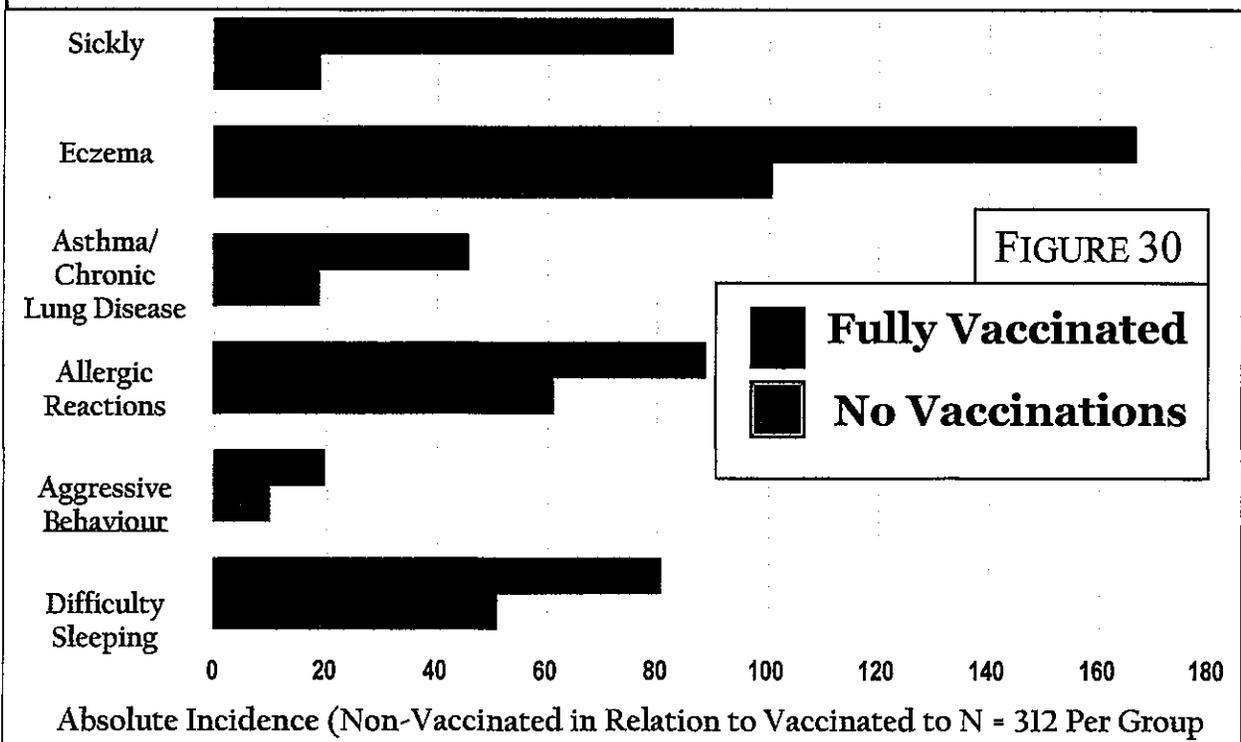
Average Incidence First Five (5) years of Life

Nederlands Vereniging Kritisch Prikken 2004 Survey Findings

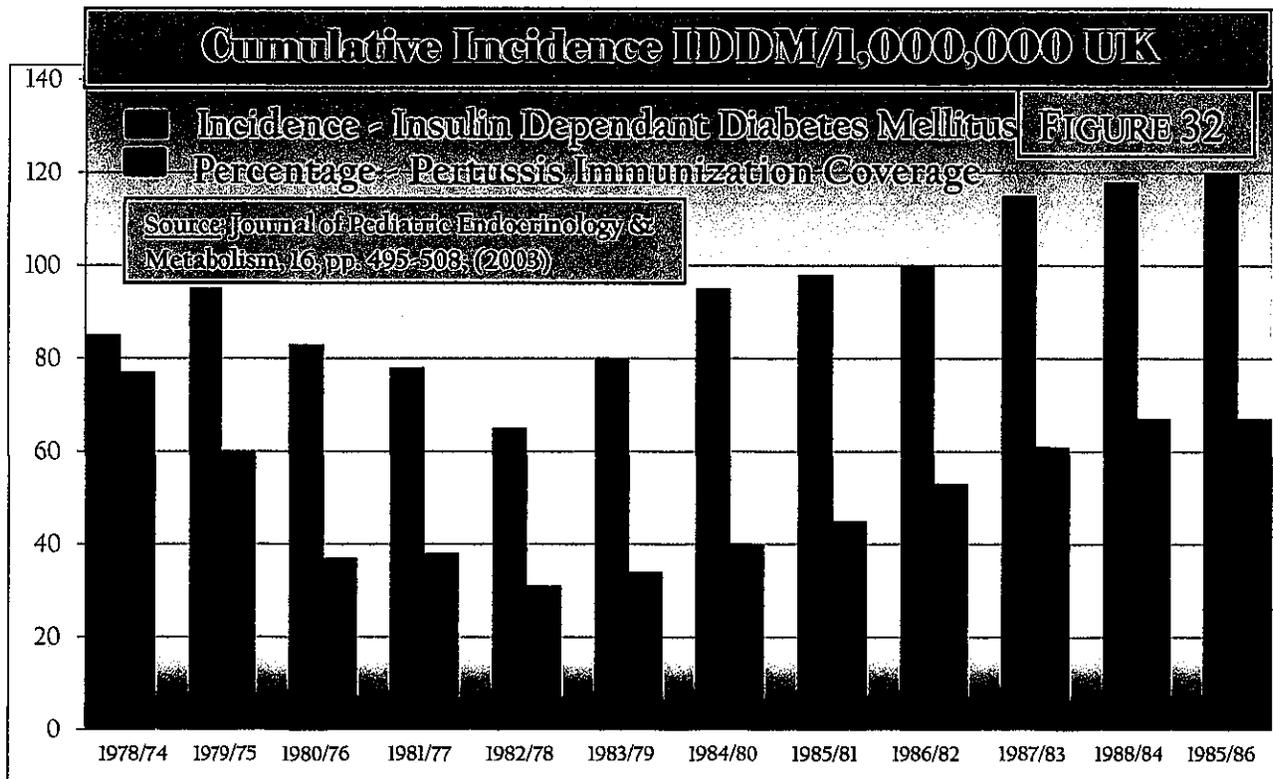
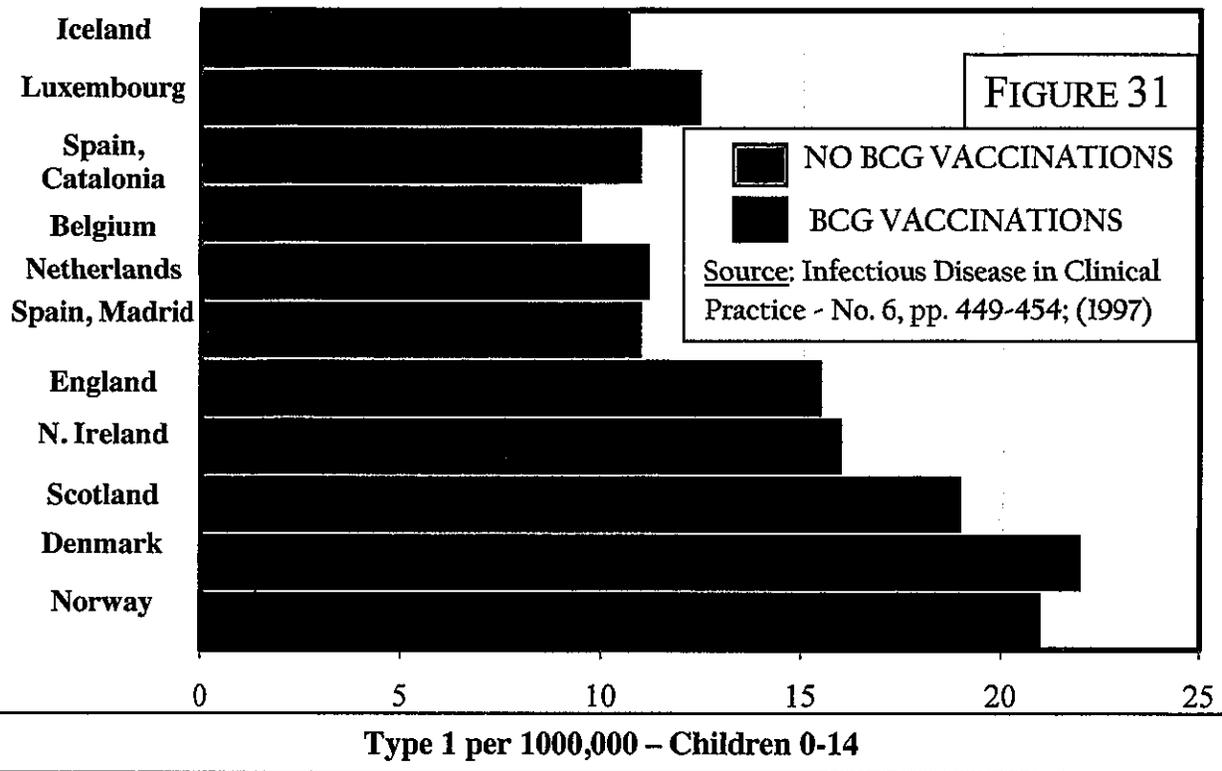


Absolute Incidence N=543

Nederlands Vereniging Kritisch Prikken 2004 Survey Findings

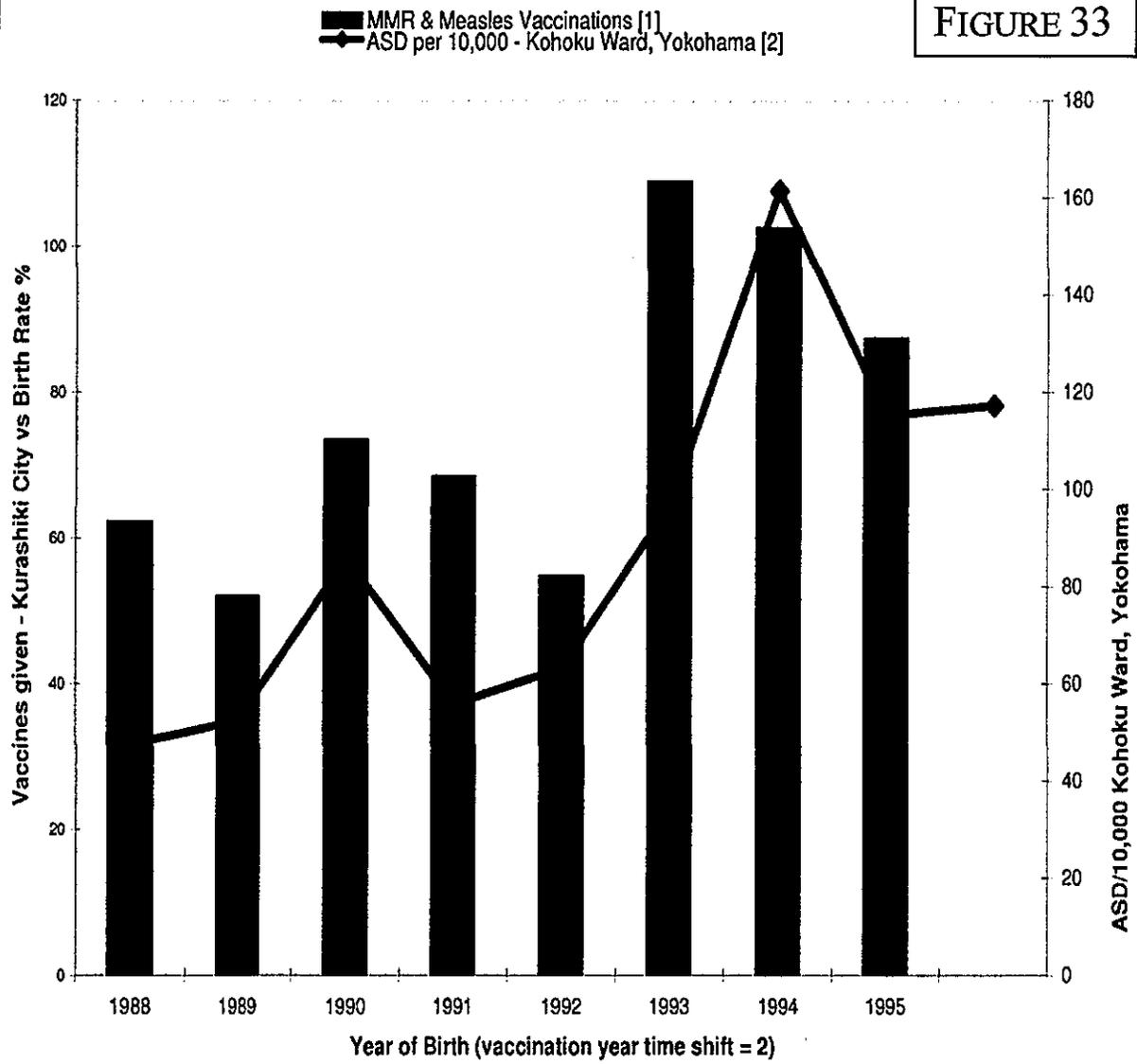


BCG Mandated in Schools & Diabetes Rates



Autism In Japan vs MMR & Measles Vaccination Uptake by birth cohort 1988 - 1996

FIGURE 33



<http://childhealthsafety.wordpress.com/2009/06/03/japvaxautism/> Figure based on: Kihei Terada et. al.; Alterations in epidemics and vaccination for measles during a 20 year period and a strategy for elimination in Kurashiki City, Japan; Kawasaki Medical School 2002 Mar; 76 (3):pp. 180-4. Correlated with: H. Honda et. al.; No effect of MMR withdrawal on the incidence of autism: a total population study; Journal of Child Psychology & Psychiatry; June 2005 (6); pp.572-579

The CDC is a very troubled agency and it's not just me saying that. There has been four separate intensive federal investigations, by the United States Congress, a three year investigation: 2001, 2002, 2003, by the United States Senate Tom Coburn's committee, by the Inspector General of HHS in 2008, by The Office of Research Integrity in 2014.

...and all of them have painted the CDC as a cesspool of corruption. Of an agency that has become an absolute subsidiary of the pharmaceutical industry, and that has become a sock-puppet, a spokesperson, a shill for the industry.

The CDC is not an independent agency.

It is a vaccine company.

The CDC owns over 20 vaccine patents. It sells about 4.6 billion dollars of vaccines every year. Its primary metric for success in all of the departments in the agency are vaccine sales."

~ Robert F. Kennedy Jr.

CONCLUSION

Today about 1 in 6 American children suffer from a neurodevelopmental disorder, a large increase compared to decades ago. Vaccines are very likely contributing to this new crisis.

Vaccine advocates are silent about the research on Al adjuvant toxicity and immune activation.

There has never been a study of the entire vaccine schedule, comparing health outcomes with the unvaccinated. Further, vaccine studies almost never use unvaccinated controls, but rather use other vaccines or Al adjuvant as false placebos. Such research is unscientific and cannot establish safety. A 1986 federal law completely protects vaccine manufacturers from all product liability lawsuits. Consequently, the industry has no incentive to make safe vaccines. Perverse incentives resulting from this law encourage continued production of unsafe vaccines.

Supporting references provided at:

VaccinePapers.org/brochure

"...the existing evidence on the toxicology and pharmacokinetics of Al adjuvants...strongly implicate these compounds as contributors to the rising prevalence of neurobehavioral disorders in children." [3]

— Dr C.A Shaw (University of British Columbia) et al.

"And what does a vaccination do? It activates the immune system. That's the point of vaccination... I think that universal vaccination of pregnant women could get us into a whole new set of problems." (2006)

— Dr Paul Patterson (California Institute of Technology)

"Maternal immune activation yields male offspring with deficient social and communicative behavior, as well as high levels of repetitive behaviors, all of which are hallmarks of autism." [6]

— Dr Paul Patterson (California Institute of Technology) et al.

"Interleukin-6 is necessary and sufficient for producing autism in the offspring..." [7]

— Dr Eduardo Pineda (David Geffen School of Medicine, UCLA) et al.

OBJECTIONS ANSWERED

What about the studies showing vaccines do not cause autism?

They look only at MMR, which does not contain Al and is given at older ages when the brain is less sensitive to immune activation. Also, MMR-autism studies ignore healthy user bias, created when parents do not give MMR to children with neurological damage caused by prior vaccines [11].

But aluminum has been used in vaccines for over 80 years.

TRUE. But it has not been studied for safety, until recently. Al dosage from vaccines increased dramatically in the last 25 years, in parallel with childhood neurodevelopmental disorders.

Aluminum is everywhere and ingested constantly. It cannot be harmful.

99.7% of ingested aluminum is not absorbed. The absorbed 0.3% comprises dissolved ions, which are rapidly eliminated in urine. Al adjuvant comprises low-solubility Al nanoparticles, which cannot be eliminated in urine and are far more harmful than soluble Al.

But immune activation studies are based on prenatal immune activation, not postnatal.

Most, but not all immune activation studies use prenatal exposure [8]. For years after birth the human brain remains sensitive to immune activation. Consequently, postnatal immune activation can damage the brain just like prenatal can. Also, the CDC recklessly promotes multiple vaccines for pregnant women, causing prenatal exposure.

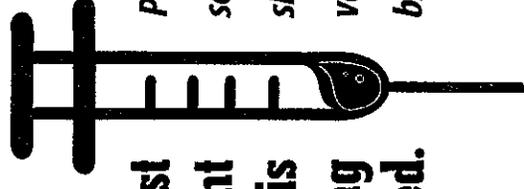
Are there ways to prevent damage from aluminum and immune activation?

YES. The nutrient silica removes Al from the body. Taurine and curcumin reduce Al neurotoxicity [5]. Vitamin D regulates immune activation, and has been observed to reverse autism [12].

REFERENCES

- 1 Petrik et al. 2007 "Aluminum Adjuvant Linked to Gulf War Illness Induces Motor Neuron Death in Mice"; *NeuroMolecular Medicine* 9. PMID:17114826
- 2 Shaw et al. 2009 "Aluminum Hydroxide Injections Lead to Motor Deficits and Motor Neuron Degeneration"; *J. Inorg. Biochem.* PMID:19740540.
- 3 Shaw et al. 2013 "Administration of aluminum to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes"; *J. Inorg. Biochem.* PMID: 23932735
- 4 Khan et al. 2013 "Slow CCL2-dependent translocation of biopersistent particles from muscle to brain"; *BMC Medicine* 11. PMID: 23557144
- 5 Sethi et al. 2009 "Curcumin Attenuates Aluminum-Induced Functional Neurotoxicity in Rats"; *Pharmacol Biochem Behav.* 93. PMID: 19376155
- 6 Bilkei-Gorzio 1993 "Neurotoxic Effect of Elemental Aluminum"; *Food Chem Toxicol.* 31. PMID: 8505021
- 7 Kneusel et al. 2014 "Maternal Immune Activation and Abnormal Brain Development Across CNS Disorders"; *Nature Reviews Neurology* 10. PMID: 25311587
- 8 Wei et al. 2012 "Brain IL-6 Elevation Causes Neuronal Circuitry Imbalances and Mediates Autism-Like Behaviors"; *Biochim Biophys Acta.* PMID: 22326556
- 9 Malikova et al. 2012 "Maternal Immune Activation Yields Offspring Displaying Mouse Versions of the Three Core Symptoms of Autism"; *Brain Behav Immun.* 26. PMID 22310922
- 10 Pineda et al. 2013 "Maternal Immune Activation Promotes Hippocampal Kindling Epileptogenesis in Mice"; *Ann Neurol.* 74. PMID: 23907992
- 11 See VaccinePapers.org/healthy-user-bias
- 12 Jia et al. 2015 "Core Symptoms of Autism Improved After Vitamin D Supplementation"; *Pediatrics* 135. PMID: 25511213

Vaccines and the Brain



The most important science is being ignored.

Powerful scientific evidence shows 2 ways vaccines cause brain damage.

1 Aluminum Adjuvant Toxicity

Vaccines contain neurotoxic amounts of aluminum, which can cause brain damage.

2 Immune System Activation

A developing brain can be damaged when the immune system is activated by a vaccine. Immune activation has been researched extensively and is proven to cause autism and other brain damage.

VaccinePapers.org

Aluminum Adjuvant

Aluminum (Al) adjuvant is a vaccine ingredient used for stimulating the immune system. It is used in many vaccines. Infants in the USA receive dosages of Al adjuvant that cause brain damage in animal experiments. The dosages of Al adjuvant received according to the CDC vaccine schedule are:*

CDC VACCINE SCHEDULE	
Aluminum	
Birth	74 mcg/kg (1 vaccine with 250 mcg, 3.4 kg infant)
2 months	245 mcg/kg (6 vaccines with 1225 mcg, 5 kg infant)
4 months	150 mcg/kg (5 vaccines with 975 mcg, 6.5 kg infant)
6 months	153 mcg/kg (7 vaccines with 1225 mcg, 8 kg infant)
TOTAL	622mcg/kg 3675 mcg aluminum

In scientific experiments, dosages of 100mcg/kg, 300mcg/kg, and 550mcg/kg Al adjuvant cause neuron death, muscle weakness, learning and memory impairment, and pathological behavior changes in animals.

*Aluminum dosage varies by vaccine manufacturer and infant weight. Chart shows maximum possible dosages for average-weight infants. Charts and graphs below redrawn from originals

FOR FURTHER READING: VaccinePapers.org

Dosage of 550mcg/kg also caused excessive weight gain (a sign of metabolic disorder). All 3 dosages (100, 300 and 550mcg/kg) also caused numerous signs of nerve damage (observable by microscopy and biochemical changes) and/or abnormal anxious behavior.

All these results together are conclusive evidence of brain damage caused by the same dosages (mcg/kg) human infants receive according to the US vaccine schedule.

Vaccine advocates argue that injected Al adjuvant is safe, based on studies of ingested Al salts. This is unscientific because ingesting Al salts and injecting Al nanoparticles present very different risks. Both the route of administration and the chemical forms are different.

Recent experiments prove that Al adjuvant is transported into the brain by white blood cells [4]. This explains why injected Al adjuvant can be more dangerous to the brain than ingested Al salts.

Vaccine advocates like Paul Offit make false statements about Al toxicity studies. The studies show that ingested Al is harmful at dosages less than half of what advocates claim to be safe [5, 6].

Immune Activation

In early life, the brain and immune system develop together. Communication chemicals ("cytokines") used by the immune system also guide brain development. Immune activation causes surges in cytokine production; cytokine surges during brain development cause permanent brain damage and mental illnesses. The brain-damaging effects of immune activation have been studied extensively. The science is high quality and there is a lot of it [7]. It is well-known that vaccines cause immune activation and can cause surges of many different cytokines.

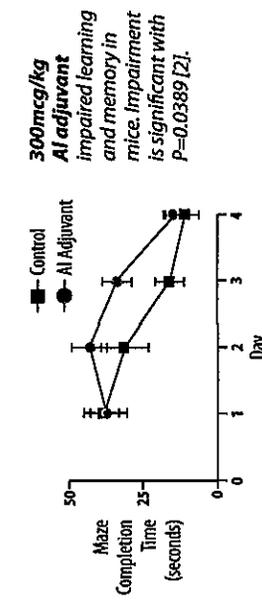
Research has identified interleukin-6 (IL-6) as the specific cytokine responsible for autism; IL-6 is stimulated by vaccine adverse reactions (fever, seizures). IL-6 causes all three autism traits (social impairment, speech impairment and compulsive behavior), and damage to specific brain structures (e.g., the cerebellum) known to be damaged in human autism. Both prenatal and postnatal surges of IL-6 can cause autism [8, 9].

Immune activation during brain development has also been shown to cause schizophrenia, seizure disorders [10], and ADHD.

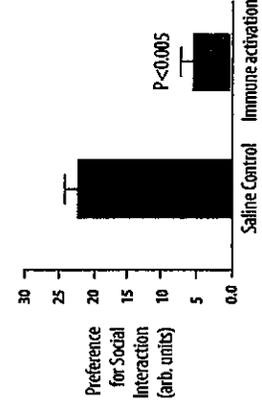
Motor Neuron Death 100mcg/kg



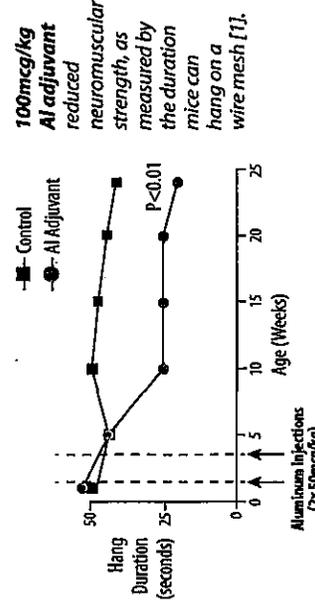
Learning & Memory Impairment 300mcg/kg



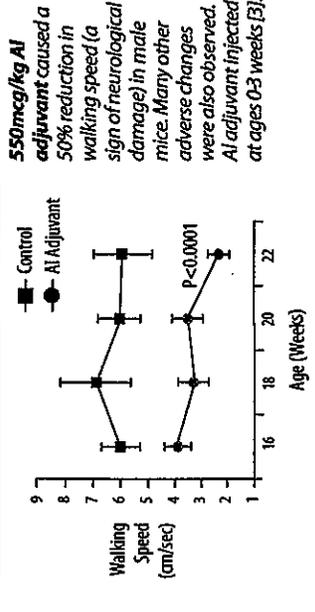
Social Behavior Impairment



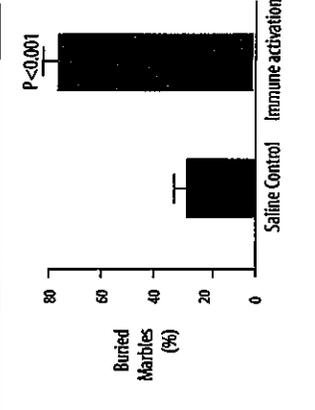
Muscle Strength Reduction 100mcg/kg



Movement Impairment 550mcg/kg



Compulsive Behavior Increase



USA & CANADA - ABORTED FETAL CELL LINE PRODUCTS AND ETHICAL ALTERNATIVES (Aug 2016) References

Disease	Product Name	Manufacturer	Fetal Cell Line	Ethical Version	Manufacturer	Cell Line
Acute Respiratory	Adenovirus 4,7 Oral	Barr Labs	WI-38	None	N/A	N/A
Chickenpox	All Variavax, Varilrix	Merck, GSK	WI-38, MRC-5	None	N/A	N/A
Cystic Fibrosis	Pulmozyme	Genentech	HEK-293	N-acetylcysteine, Hyper-sal	Various	N/A
Anemia (Cancer patients, severe kidney disease)	Procrit, Epoetin alfa Epogen, Aranesp, Darbeoetin alfa	Amgen	Human erythropoietin gene from fetal liver lambda.hHE1/	None	N/A	N/A
Ebola - In Development	NIAID/GSK ChAd3 AdV acEbola VSV-EBOV	GSK J&J/Crucell, NewLink/BioProtSv	Procell92/HEK-293 PER C6, HEK-293	rVSV-ZEBOV-GP GOVOX-E301, E-302 ZMapp Therapeutic	Merck/New Link GeoVax LeafBio	Vero Chick eggs Tobacco
Heart problems	Abciximab (Repro)	Eli Lilly	HEK-293	Integrilin, Angiotomax	Merck, Medicine Co.	N/A
Hemophilia	rhFVI, VIII, Etoctate	Octapharma, BioGen	HEK-293	Advate, Kogenate	Baxter	Hamster
Hepatitis A	Vaqta, Havrix Avaxim, Epaxal	Merck, GSK Sanofi, Berna	MRC-5 MRC-5	Aimmugen None in US or Canada	Kaketsuken (Japan, Asia & Europe)	Vero (monkey)
Hepatitis A & B	Twinrix	GSK	MRC-5	Engerix Hep-B Only	GSK	Yeast
Hepatitis A & Typhoid	Vivaxim	Sanofi	MRC-5	Recombivax Hep-B Only	Merck	Yeast
Infection prevention	G-CSF	Octapharma	HEK-293	Neupogen, Zarxio	Amgen, Sandoz	E-coli
Measles/Mumps/Rubella	MMR, Priorix	Merck, GSK	RA273, WI-38, MRC-5	MR+M (Japan only)	Kitasato Daichi Sankyo	Hen, rabbit
Measles-Rubella	MR Vax, Eolarix	Merck, GSK.	RA273, WI-38, MRC-5	Attenuvax (Measles Only)* MR (Japan only)	Merck Kitasato Daichi Sankyo	Hen eggs Hen, rabbit
Mumps-Rubella	Biaavax II	Merck	RA273, WI-38	Mumpsvax (Mumps Only)*	Merck	Hen eggs
Rubella	Meruvax II	Merck	RA273, WI-38	Takahashi (Japan only)	Kitasato Daichi Sankyo	Rabbit
MMR + Chickenpox	ProQuad/MMR-V Priorix Tetra	Merck GSK	RA273, WI-38, MRC-5	None	N/A	N/A
Polio	Poliovax, DT PolAds Polio Sabin (oral)	Sanofi Pasteur GSK	MRC-5 MRC-5	IPOL, IMOVAX® Polio**	Sanofi Pasteur	Vero
Polio Combination (DTaP + polio+ HiB)	Pentacel, Quadracel	Sanofi Pasteur	MRC-5	Pediacel, Pediarix, Any HiB DTap, IPOL, InfanrixHexa,	Sanofi, GSK	Vero
Rabies	Imovax**	Sanofi Pasteur	MRC-5	RabAvert	Novartis	Hen eggs
Rheumatoid Arthritis	Enbrel	Amgen	WI-26 VA4 - RDNA	Humira, Cimzia, Orenzia	Abbott, UCB, BMS	Hamster
Shingles	Zostavax	Merck.	WI-38, MRC-5	In Development: Shingrix	GSK	Yeast
Smallpox	Acambis 1000	Acambis	MRC-5	ACAM2000, MVA3000	Acambis/Baxter	Vero

Note: Immune-Globulin shots will provide temporary immunity (4-6 months) for Hepatitis-A and Rubella (3-4 months)

*Moral versions of Measles and Mumps are currently UNAVAILABLE as of January 2010 – TELL MERCK TO PROVIDE THEM!

**NOTE: IMOVAX® Polio is a moral version for polio vaccine in Canada and is not the same as IMOVAX for rabies.

ANY VACCINE NOT LISTED ABOVE DOES NOT USE ABORTED FETAL CELL LINES Copy Permissible with Credit Children of God for Life ©



Glyphosate pathways to modern diseases VI: Prions, amyloidoses and autoimmune neurological diseases

Anthony Samsel¹ and Stephanie Seneff^{2,*}

¹ Samsel Environmental and Public Health Services, Deerfield, NH 03037, USA

² Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA 02139, USA

Usage of the herbicide glyphosate on core crops in the USA has increased exponentially over the past two decades, in step with the exponential increase in autoimmune diseases including autism, multiple sclerosis, inflammatory bowel disease, type 1 diabetes, coeliac disease, neuromyelitis optica and many others. In this paper we explain how glyphosate, acting as a non-coding amino acid analogue of glycine, could erroneously be integrated with or incorporated into protein synthesis in place of glycine, producing a defective product that resists proteolysis. Whether produced by a microbe or present in a food source, such a peptide could lead to autoimmune disease through molecular mimicry. We discuss similarities in other naturally produced disease-causing amino acid analogues, such as the herbicide glufosinate and the insecticide L-canavanine, and provide multiple examples of glycine-containing short peptides linked to autoimmune disease, particularly with respect to multiple sclerosis. Most disturbing is the presence of glyphosate in many popular vaccines including the measles, mumps and rubella (MMR) vaccine, which we have verified here for the first time. Contamination may come through bovine protein, bovine calf serum, bovine casein, egg protein and/or gelatin. Gelatin sourced from the skin and bones of pigs and cattle given glyphosate-contaminated feed contains the herbicide. Collagen, the principal component of gelatin, contains very high levels of glycine, as do the digestive enzymes: pepsin, trypsin and lipase. The live measles virus could produce glyphosate-containing haemagglutinin, which might induce an autoimmune attack on myelin basic protein, commonly observed in autism. Regulatory agencies urgently need to reconsider the risks associated with the indiscriminate use of glyphosate to control weeds.

Keywords: autism, autoimmune disease, collagen, glycine, glyphosate, multiple sclerosis, protein misfolding, vaccines

1. INTRODUCTION

At first glance, multiple sclerosis (MS) and autism appear to have little in common, aside from the fact that both are neurological diseases. Autism is a condition with prenatal or early childhood onset, characterized by repetitive behaviours, impaired social interaction and cognitive impairment. The male:female ratio for autism is 4:1, while multiple sclerosis is twice as common in women as in men; its first symptoms usually begin in early adulthood to involve impaired lower limb mobility, although in later stages it affects both mental and physical capabilities. Both conditions are, however, associated with inflammatory autoimmune features [1, 2], and both diseases are viewed as having an environmental and a genetic component [3–6].

A study comparing a population of 658 MS patients with the general population found an association between MS and increased rates of asthma, inflammatory bowel disease (IBD), type 1 diabetes mellitus, pernicious anaemia and autoimmune thyroid disease [7], all of which

have also been linked to autism [8–11]. These conditions are all considered to be *autoimmune diseases*, which can be triggered through molecular mimicry, where an antibody responding to a foreign protein that resembles a native protein becomes sensitized to the native protein as well [12]. A paper by Shoenfeld and Aron-Maor in 2000 developed the argument that both autism and MS may be examples of an autoimmune reaction via mimicry following exposure to an antigenic stimulus, possibly from an infection or through vaccination [13]. They further propose specifically that myelin basic protein (MBP) and other proteins constituting the myelin sheath are attacked by the immune system in both autism and MS. This has been recognized by many others in autism [14, 15] and MS [16–20]. In 1982, Weizman et al. reported a cell-mediated autoimmune response to human MBP in 76% of the autistic children studied [16]. Immune sensitization to the myelin sheath proteins could arise either through mimicry as a consequence of exposure of the immune system to a foreign antigen with a similar peptide sequence that is

* Corresponding author. E-mail: seneff@csail.mit.edu

resistant to clearance, or because the proteins themselves have been altered in some way that renders them defective, exposed and/or resistant to proteolysis.

Unlike DNA synthesis, protein synthesis is highly prone to error [21, 22]. It appears that biological systems have adopted a strategy of allowing coding errors to survive during active synthesis, but use protein misfolding as a criterion to mark a defective peptide for degradation and recycling through ubiquitination. It is estimated that 15% of average-length proteins will have at least one misincorporated amino acid. Typically, 10–15% of random substitutions disrupt protein function, mostly because of misfolding [22]. Such destabilization causes protein–protein aggregation, and can lead to multiple neurological diseases and amyloidoses. Drummond et al. propose that early-forming toxic oligomers of amyloidogenic proteins are enriched with missense errors [22].

Glyphosate is the active ingredient in the pervasive herbicide Roundup and in many other formulations of herbicides used to control weeds on agricultural, residential and public land worldwide. A recent study based in Germany involving 399 urine samples from adults not involved in agricultural work revealed glyphosate residues above the detection limit in the urine of 32% of the subjects, and residues of AMPA, a metabolite, in 40% [23]. In a paper published in 2014, Swanson et al. showed a remarkable correlation between the rising rate of glyphosate usage on corn (maize) and soy crops in the USA and an alarming rise in a number of different chronic diseases [24]. Additional strong correlations for other conditions and diseases are provided in two follow-on papers [25, 26]. While correlation does not necessarily mean causation, causation becomes much more likely if a plausible mechanism can be found. Swanson et al. found a remarkable 0.98 correlation coefficient between the rise in autism rates in the USA and the use of glyphosate on crops (P -value $\leq 9.6 \times 10^{-6}$). The correlation for multiple sclerosis was not as high, but still highly significant at 0.83 (P -value $\leq 1.1 \times 10^{-5}$). IBD had a correlation coefficient of 0.94 (P -value $\leq 7.1 \times 10^{-8}$) (see Table 1 for other diseases).

Table 1. Correlations between time trends in several diseases and conditions recorded by the US Centers for Disease Control (CDC) with glyphosate usage on corn (maize) and soy crops reported by the USDA. Data reproduced from [23] and [25].

Disease	Correlation coefficient (R)	P -value
Autism (prevalence)	0.98	9.6×10^{-6}
MS (deaths)	0.83	1.1×10^{-5}
IBD	0.94	7.1×10^{-8}
Anaemia	0.90	1.8×10^{-4}
Diabetes (prevalence)	0.97	9.2×10^{-9}
Thyroid cancer (incidence)	0.99	7.6×10^{-9}

IBD, especially among children, is an emerging global epidemic [27] that is linked to autism [28, 29]. Impairment of intestinal barrier function is a core feature of IBD [30]. Increased intestinal permeability promotes infiltration of unmetabolized peptides into the lymph system and general circulation. This provides an opportunity for an immune antigenic response, which by molecular mimicry can lead to an attack on crucial proteins in the brain and spinal column. Disturbances of collagen texture are a major factor leading to the onset of diverticular disease and IBD along with the disturbed wound-healing mechanisms seen in the pathogenesis of anastomatic leakage following large bowel surgery [31].

In a recent paper [32], we suggested that glyphosate, a non-coding amino acid analogue of glycine, could substitute for glycine in error during protein synthesis. Such misincorporation and disruption of proteostasis could explain the strong correlations observed between glyphosate usage and multiple modern diseases. *In this paper, we show that this could be one of the most important mechanisms by which glyphosate could induce multiple autoimmune diseases.*

A prime site for initiation of the disease process is the colon, where misfolded collagen, resistant to degradation, could lead to an autoimmune disease and, subsequently, a leaky gut. Autoantibodies against type VII collagen have been detected in up to 68% of IBD patients [33]. Glycine is the most common amino acid in collagen, making up one fourth of the residues in the protein. Proline is also a very common component of collagen and, as we discuss later in this paper, proline resists hydrolysis. Incomplete collagen degradation by matrix metalloproteinases in the gut could lead to the accumulation of short pro–gly–pro peptides that are resistant to proteolysis. These could then induce the infiltration of neutrophils or the activation of resident immune cells to induce an inflammatory response [34].

An unpublished study conducted by Monsanto and submitted to the US Environmental Protection Agency (EPA) traced the accumulation of radiolabeled glyphosate in various tissues of rats following low-dose oral administration (10 mg/kg body weight) [35]. By far the highest accumulation was found in the bones (Table 11 in [36]). Radioactive levels in the colon were 4–6 times as high as those in the stomach and small intestine.

The production of novel non-coding amino acids by plants and microbes wards off predators. The toxicity of these products may be due to the fact that they replace coding analogues during protein synthesis. Examples include: azetidine-2-carboxylic acid (Aze), a proline analogue [37, 38]; glufosinate, a glutamate analogue that is also a popular herbicide [39]; β -N-methylamino-L-alanine

(BMAA), an analogue of serine [40]; and L-canavanine, a natural analogue of L-arginine that is exploited as an insecticide [41, 42].

A remarkable true-life story involving a 119-day Alaskan wilderness experiment conducted by Christopher McCandless was recounted in the book *Into the Wild* by Jon Krakauer (later made into a popular movie) [43]. McCandless was thought to have died in the wilderness from starvation; however, Krakauer always suspected a toxin in the seeds of the wild potato, *Hedysarum alpinum*, which formed a staple of his diet in his last month of life. Krakauer had originally suspected a poisonous alkaloid but, through later research, was able to identify a significant level of L-canavanine in the wild potato seeds and published a paper on this analysis with several other authors in 2016 [42].

A key factor in L-canavanine's toxicity is its ability to insinuate itself into peptides in place of L-arginine. L-canavanine can be assimilated into essentially any protein to create aberrant canavanyl proteins that can disrupt many fundamentally important biochemical reactions across a broad spectrum of organisms [41, 44]. L-canavanine is exploited in agriculture as a potent insecticide against the tobacco hornworm [45], although the tobacco budworm has developed tolerance with a unique enzyme, canavanine hydrolase, which can quickly metabolize it [46]. Larvae exposed to L-canavanine incorporate it into the protein lysozyme, resulting in a 48% loss in catalytic activity [41]. Furthermore, dipterocins B and C of *Protoformia terranova*, but not dipterocin A, are negatively impacted by L-canavanine. The distinction is that dipterocin A has histidine at position 38 instead of the L-arginine found in the other two dipterocins. Presciently, with respect to glyphosate, Rosenthal wrote: "These insect studies support the view that the biological effects of canavanine result from its incorporation into a protein, resulting in an alteration in protein conformation that leads ultimately to impairment of protein function" [41].

2. SHIKIMATE PATHWAY INHIBITION REVISITED

The shikimate pathway enzyme, 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) is believed to be the main target of glyphosate's toxicity to plants [47]. A 1991 paper by Padgett et al. describes studies to gain insight into the mechanism by which glyphosate disrupts EPSPS [47]. Surprisingly, it is not understood exactly how glyphosate binds to the active site.

The microbes *Klebsiella pneumoniae*, *Escherichia coli* [47, 48] and *Agrobacterium sp.* strain CP4 [48, 49] have all evolved to produce versions of EPSPS that are glyphosate-resistant. The CP4 variant has been widely exploited by importing it into genetically modified

glyphosate-resistant crops [48]. Insight can be gained by investigating the alterations to the peptide sequence that afforded resistance. All three mutations involved replacing a glycine residue at the active site with alanine [47, 48]. In the case of *E. coli*, the mutated enzyme is about 72 times *less* efficient than the wild-type enzyme, but 69 times *more* efficient in the presence of glyphosate. Changing the DNA code from glycine to alanine completely disables glyphosate's inhibiting effects on the enzyme [48].

Substitution of gly-96 at the active site in *E. coli* by serine leads to a version of the enzyme that is unable to bind PEP, most likely due to steric hindrance. The authors speculated that the hydroxymethyl group of serine displaces the phosphate of PEP and functions as a nucleophile. In fact, this mutated enzyme achieves a kind of reverse reaction, breaking EPSP down into shikimate-3-phosphate and pyruvate via hydrolysis.

We propose that substitution of gly-96 (gly-100 in the CP4 variant) by glyphosate during protein synthesis could explain its disruption of the enzyme's function. One can expect that the highly reactive and bulky glyphosate molecule, if substituted for gly-96, would behave more like serine than alanine. An additional disruptive factor is glyphosate's chelation of manganese, which would disrupt the catalytic action of EPSPS. A cell containing both wild-type and glyphosate-substituted forms of the enzyme would arguably circuitously convert PEP to pyruvate via EPSP without producing ATP from ADP; i.e., would waste the energy in the phosphate bond, as shown in Fig. 1, and end up with excess pyruvate and a deficiency in EPSP.

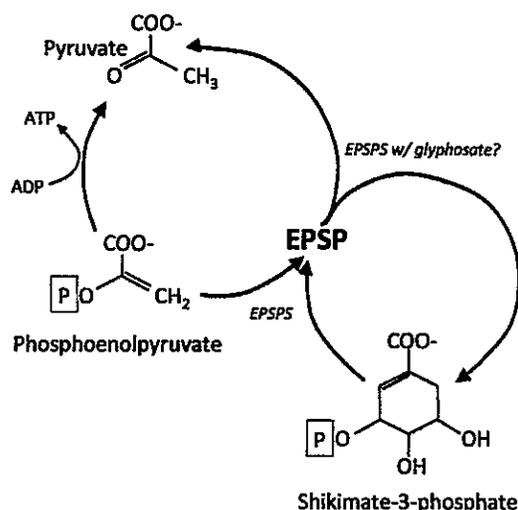


Figure 1. Diagram of the hypothetical pathway by which glyphosate substitution for glycine in EPSPS could result in the synthesis of pyruvate from PEP without generating ATP; i.e., wasting the energy in the phosphate group, as discussed in the text.

3. GLYPHOSATE AS A GLYCINE ANALOGUE

While glyphosate's main mechanism of toxicity to plants is considered to be disruption of the shikimate pathway, it is also likely that it disrupts other biological pathways where glycine is either a substrate or a ligand, due to the fact that it is a glycine analogue. It has been proposed that, through glycine mimicry, glyphosate's rôle as a ligand to NMDA receptors in the brain could explain its known ability to activate NMDA receptors and cause neuronal damage [49, 50]. In [51], acute exposure of rat hippocampal slices to Roundup (0.00005–0.1%) for 30 minutes caused oxidative stress and neuronal cell death, which was attributed to NMDA receptor activation. Glyphosate also interferes with the synthesis of porphyrin, a precursor to haem, by disrupting the first step in the pathway where glycine is substrate [52].

N-substituted glycine "peptoids" are an attractive class of synthetic molecules that can be constructed by linking component N-substituted glycines at sequential nitrogen–carbon bonds; they are directly analogous to the linking of amino acids into peptides [53]. Glyphosate is of course an N-substituted glycine, where the nitrogen side chain is a methyl phosphonyl group. Part of the attraction of peptoids is that they are highly resistant to proteolysis, just as is the amino acid proline, in which the carbon side chain circles back and binds to the peptide nitrogen. Impaired ability to break down proline-rich gliadin has been proposed as a contributing factor in coeliac disease and gluten intolerance [54]. This can explain why common cereals with high proline contents are especially problematic to gluten-sensitive individuals [55, 56].

Glyphosate is probably particularly problematic when it substitutes for N-terminal glycines in proteins where these glycines are highly conserved and play a significant rôle. Several proteins rely on an N-terminal glycine for anchoring to the plasma membrane (e.g., endothelial nitric oxide synthase (eNOS) [57]) or to the cytoskeleton (e.g., Kelch-like ECH-associated protein 1 (KEAP1) [58]). Protein N-myristoylation and prenylation depend on an amide bond to the N-terminal glycine residue [59]. For example, myristoylated G proteins involved in many signaling mechanisms depend on an N-terminal glycine residue [59]. This would be disrupted if the nitrogen atom has a side chain through glyphosate substitution for the terminal glycine.

N-nitrosoamino acids form a reasonable model for N-nitrosoglyphosate, a carcinogenic derivative of glyphosate that was of concern to the EPA during Monsanto's early studies. N-nitrosoproline is particularly relevant because proline, like glyphosate, has an extra carbon atom bound to the nitrogen atom. With respect to non-coding amino acids, and especially the incorporation

of N-nitrosoamino acids into peptides and proteins, R.C. Massey remarked: "In addition to their presence as free N-nitrosoamino acids, species such as N-nitrosoproline (NPRO) and N-nitroso-4-hydroxyproline (HONPRO) may exist in a peptide- or protein-bound form as a result of N-nitrosation of an N-terminal imino acid residue" [62]. Tricker et al. [63] and Kubacki et al. [64] devised high performance liquid chromatography–thermal energy analyser (HPLC–TEA) techniques for analysis of multiple dipeptides with a nitrosylated N-terminal, including N-nitrosopropylalanine (NPROALA), N-nitrosopropyl-4-hydroxyproline (NPROHOPRO) and N-nitrosopropylglycine (NPROGLY) [63, 64]. Tricker notes that the average recoveries for NPROALA, NPROHOPRO and NPROGLY, 200 µg of which was added to cured meat, were between 69 and 88%. Tricker also used the method to analyse the nitroso-tripeptide N-nitrosopropylglycylglycine [65].

Nitrosamines of glyphosate (N-phosphonomethylglycine), its salts and esters include: N-nitrosoglyphosate (NNG) (Monsanto CP 76976), N-nitrosoiminodiacetic acid (NNIDA), N-nitrosoglyphosate sodium salt (NNGNa), N-nitrosoglyphosate isopropylamine ester (NNGIPA), N-nitrosoglyphosate potassium salt (NNGK), the metabolite N-nitrosoAMPA (NNAMPA), the metabolites N-nitrosodimethyl amine (NDMA) and N-nitrosarcosine (NSAR), which occur in glyphosate products or may be generated *in vivo* or in soils and waterways. N-nitroso compounds derived from secondary amines are considered carcinogenic.

Monsanto glyphosate documents reveal analysis and quantification of five nitrosamines of concern [61]. Out of six lots of Roundup analysed for NNG, four lots contained NNG residues of 0.61 to 0.78 ppm and two lots had residues from 0.22 to 0.40 ppm NNG. Analysis of six lots of Monsanto Rodeo revealed NNG residues in the range 0.13–0.49 ppm.

Recently, a powerful metatranscriptome study on bacterial gene expression following glyphosate treatment was conducted on microbes growing within the rhizosphere of glyphosate-tolerant corn [66]. RNA transcript abundance was compared between control and glyphosate-treated samples in order to characterize which protein genes were upregulated or downregulated. While they found many changes in gene expression, most striking to us was the upregulation of genes involved in both protein synthesis and protein hydrolysis. The ribosomal proteins L16p (L10e) and Firmicutes ribosomal L7Ae family proteins involved in the synthesis of the ribosomal large subunit increased 1.4- and two-fold, respectively, and the small subunit ribosomal protein S11p (S14e) increased 1.5-fold. Upregulation of genes involved in protein degradation was even more dramatic. For

example, transcripts for a proteasome β 2 subunit (EC 3.4.25.1) increased 4.3-fold and aminopeptidase YpdF increased threefold. An explanation could be an increase in the number of proteins that fail to fold properly due to glyphosate substitution for glycine in the protein. These authors also suggested a potential shift towards an increase in glyphosate-tolerant bacteria, a point that will become important later in this paper.

These results are corroborated by a study on pea plants grown in hydroponic culture, which revealed that glyphosate induced a significant increase in two major systems for proteolytic degradation: the ubiquitin-26 S proteasome system and papain-like cysteine proteases [67]. It also increased the total free amino acid content and decreased the soluble protein in the root system.

4. GLYPHOSATE-CONTAMINATED COLLAGEN AND PROTEOLYSIS RESISTANCE

We mentioned in the Introduction the gly-pro-gly peptide sequence that is common in collagen and linked to autoimmune disease. There are several enzymes in multiple organisms that are devoted to the proteolysis of peptide sequences containing proline, particularly the gly-pro sequence. These include enzymes that detach a terminal proline, enzymes that detach a dipeptide sequence where the second residue is a proline molecule and the first one is often glycine, and enzymes that break apart the X-pro dipeptide to release two free amino acids, one of which is proline. Certain pathogens have special modified versions of these enzymes, and there are genetic diseases related to pathologies in these enzymes. Substitution of glyphosate for glycine in this sequence is likely to cause extra stress to the enzymes that break down these sequences, potentially leading to autoimmune disease.

Prolyl aminopeptidase is an enzyme that detaches a terminal proline residue from a peptide. The enzyme is expressed predominantly by pathogenic bacteria in the gut, in particular *Serratia marcescens*, a common pathogen in the gut as well as in the urinary tract; it is often multiply antibiotic-resistant and is a serious threat in hospital-acquired infection [34]. This enzyme is especially important to the pathogens for degrading collagen, providing amino acids as fuel. It is conceivable that the pathogens are able to degrade glyphosate-contaminated peptides terminating in proline whereas the human form of the enzyme is not. It is intriguing that the *S. marcescens* version of prolyl aminopeptidase is unusual in having extra space at the active site [34], which could potentially accommodate the larger glyphosate molecule adjacent to the terminal proline residue. This might also contribute to glyphosate's observed effect on the gut microbiome: excessive growth of pathogens.

Multiple strains of the toxic mould *Aspergillus* secrete an X-prolyl dipeptidyl aminopeptidase (X-PDAP) that is important for digesting collagen because it can separate out an X-pro pair to bypass the difficult step of breaking the X-pro bond. Research has shown that this enzyme is essential for hydrolysing proline-containing peptides [69, 70]. It is likely that it becomes even more essential when X is glyphosate, as the peptoid sequence glyphosate-proline is likely almost impossible to break. Since gly-pro is a very common sequence in collagen, glyphosate-pro is likely to impede the breakdown of collagen fragments, which may then encourage *Aspergillus* infection in both plants and animals. Glyphosate has been shown to increase the growth rate of *Aspergillus* [71].

The most disturbing question is, what happens in the absence of pathogens that can effectively clear collagen peptides contaminated with glyphosate? As we will see later in this paper, antibodies to collagen are linked to antibodies to vaccines. A genetic defect in the enzyme prolydase, which can break apart the very common gly-pro dipeptide to release the individual amino acids, leads to a severe disease with mental deficiencies and multiple skin lesions [72]. Intriguingly, a common plant pathogen, *Xanthomonas campestris*, which causes blight on multiple plant species has a unique variant of prolydase with two mutations, a substitution of tyrosine for gly-385 and valine for tyr-387, two highly conserved residues in the peptide sequence [73]. Is it possible that swapping out glycine affords protection from glyphosate substitution for this residue? We hypothesize that peptides derived from multiple proline and glyphosate-contaminated proteins, which are highly resistant to proteolysis, are causing an autoimmune epidemic that is an important contributor to autism and other autoimmune disorders.

5. BMAA AND ALS IN GUAM

β -N-methylamino-L-alanine (BMAA) is another noncoding amino acid and an analogue of serine [40]. BMAA is synthesized by cyanobacteria, the microbes responsible for the toxic algal blooms that occur in lakes experiencing an accumulation of nitrogen and phosphate nutrients following hot, rainy weather [74]. An *in vitro* study by Dunlop et al. in 2013 demonstrated that BMAA can be misincorporated into human proteins, causing protein misfolding that could lead to neurological diseases [40].

BMAA has, in fact, been linked to several neurodegenerative diseases, including Parkinson's, Alzheimer's and amyotrophic lateral sclerosis (ALS) [75]. A 2013 study linked an ALS cluster in Chesapeake Bay to consumption of BMAA-contaminated crabs [76]. A study in France investigated an ALS cluster near a lagoon that supplied oysters and mussels to the local

population. The authors demonstrated that the shellfish were contaminated with BMAA, but also remarked that there was intensive chemical-based agriculture in the region [77]. Interestingly, cyanobacteria have been found to be remarkably resistant to glyphosate [78, 79], and this could contribute to the recent record-setting algal blooms in the Great Lakes region, where glyphosate is extensively used on genetically modified (GM) Roundup-Ready crops [80].

One likely molecule that could be adversely affected by BMAA is the glutamate transporter, whose defective expression has been linked to ALS [81]. Glutamate excitotoxicity in motor neurons is associated with ALS, and this could be caused by an impaired glutamate transport system. Ordinarily, astrocytes quickly clear glutamate from the synapse, following its release by neurons, and the transporter is essential for this clearance. A conserved serine-rich motif in the glutamate transporter forms a reentrant loop, similar to a structure found in many ion channels [82]. This loop is crucial for the enzyme's proper function, and would be disrupted by substitution of BMAA for serine.

An interesting detective story has evolved around an epidemic of a complex neurological condition termed amyotrophic lateral sclerosis–Parkinsonism dementia complex (ALS–PDC), which reached epidemic proportions during a short interval after World War II among the native Chamorro people on the small island of Guam in the South Pacific. At the peak of the epidemic, the natives had a hundredfold increased risk to ALS and Parkinson's disease compared to the risk in the general human population.

A plausible explanation for this epidemic relates to a popular native food source: seeds from the cycad trees [83–85]. Cycad seeds contain BMAA, likely derived from associated cyanobacteria. However, what is especially interesting is that the BMAA becomes concentrated in the skin of fruit bats that feed on the cycad seeds. Fruit bats were a popular delicacy among the natives, who ate every part of them, including the skin. Increased access to firearms from the USA during the war may have made it easier to kill the bats, on which the natives then feasted, ultimately leading to the natives' near-extinction through the accumulation of BMAA in their brains [86]. Meanwhile the near-extermination of the bats through the hunting removed the presumed source of the epidemic [83].

However, the warfare also led to the accumulation of many toxic chemicals in the soil, which could have encouraged the proliferation of cyanobacteria, which are especially resilient in the face of stressors. The bats' demise was undoubtedly hastened by the accumulation of

excess BMAA in their tissues. A measurement of the amount of BMAA in three dried specimens of fruit bats from Guam taken from a museum in Berkeley found concentrations between 1200 and 7500 $\mu\text{g/g}$, which indicates up to hundredfold bioamplification over the level in the seeds of the cycad tree [87].

There have been inconsistent results in measuring the levels of BMAA in different tissue samples, but this has been explained recently by the realization that any BMAA incorporated into proteins may be missed in analysis without sufficient proteolysis. Ince et al. wrote: "When the insoluble, protein-containing fraction following TCA (trichloroacetic acid) extraction is further hydrolysed to release BMAA from protein, there is a further pool of protein-bound BMAA that is present in a ratio of between 60:1 and 120:1 compared with the pool of free BMAA" [84, p. 348]. We believe that this point has great significance when it comes to glyphosate: we highly suspect that different methodologies used to measure glyphosate contamination in any situation where there is a significant protein-bound component may yield different results depending on the degree to which protein hydrolysis is carried out.

6. GLYPHOSATE CONTAMINATION IN COLLAGEN, ENZYMES, GELATIN AND VACCINES

Gelatin is commonly used as an excipient stabilizer in vaccines, particularly the live virus vaccines. Gelatin is derived from animal skin and bone, especially of pigs and cattle; they may be fed glyphosate-contaminated forages, including GM Roundup-Ready corn and soy feed, which are sometimes supplemented with GM Roundup-Ready beet pulp. Gelatin is mainly derived by partial hydrolysis from the collagen in skin and bone. 26% of the amino acids in collagen are glycine; proline and hydroxyproline together make up 18% [88]; and glutamate constitutes 6%. All three of these components are problematic. The proline could be substituted by Aze from the sugar beet, the glycine could be substituted by residual glyphosate in the feed, and glutamate is a neurotransmitter but known to be neurotoxic at high concentrations; it works together with glycine to excite NMDA receptors in the brain. The vaccine virus may incorporate some of the noncoding amino acids into its own proteins to produce versions of them that resist proteolysis and induce autoimmunity through molecular mimicry.

One of us (Samsel) analysed a number of animal protein products for glyphosate. These included the bones of pigs, cows, horses' hooves, bees and bee products, collagen and gelatin products, vitamins, protein powders, enzymes and vaccines. Results are shown in Tables 2 and 3. Both high performance liquid

chromatography with tandem mass spectrometry (HPLC–MSMS) and enzyme-linked immunosorbent assay (ELISA) methods were utilized. It has been shown that both HPLC and ELISA are comparable in terms of accuracy and precision for detection and quantification of glyphosate in water-based analysis and including Nanopure, tap and river waters. Water-based solvents for

glyphosate demonstrate a detection limit of 0.6 ng/mL and a linear functional range of 1–25 ng/mL [200]. However, HPLC was not able to achieve detection below 5 ppb;¹ hence, in cases including water-based vaccines, analysis using numerous sample runs was made including using two independent labs to test the same samples.

Table 2. Residues of glyphosate found in animal-based products that were reported to the US Food and Drug Administration (FDA) by Samsel Environmental & Public Health Services. The limit of detection for glyphosate using hot water extraction is 0.075 parts per billion (ppb).¹

Protein substrate	Type	Test date	Glyphosate residue (ppb) ¹
GELATIN	JELL-O ORANGE #07 JAN 2018 DB02 02:36	29 July 2016	9.00
GELATIN	POWER-MAX PROTEIN POWDER ADVANCED NUTRITION	29 July 2016	14.94
GELATIN	DISNEY GUMMIES VITAMINS	9 August 2016	8.27
GELATIN	FLINTSTONES GUMMIES VITAMINS	9 August 2016	5.32
ORAGEL	CHILDREN'S ORAGEL 7.5% BENZOCAINE FORMULA	26 September 2016	2.81

HPLC–MSMS was also later used, where the method detection limit (MDL) permitted, for additional confirmation and quantification of glyphosate in digestive enzymes and collagens. Spiked sample recoveries were done for all samples tested. Freshly prepared glyphosate standard solutions were run as controls and results were calculated based on a standard curve.

In 1989, Monsanto researchers conducted an experiment on exposure of bluegill sunfish to ¹⁴C-radiolabeled glyphosate [89]. One of us (Samsel) obtained the (unpublished) report from the EPA through the Freedom of Information Act. The researchers had found that, with EDTA extraction, the amount of radiolabel in tissue samples was much higher than the amount of detected glyphosate. They decided to apply a digestive enzyme, proteinase K, and discovered that this “caused a substantial improvement in extractability”. It brought the yield from 17–20% in the case of EDTA to 57–70% following digestion with proteinase K. They summed up as follows: “Proteinase K hydrolyses proteins to amino acids and small oligopeptides, suggesting that a significant portion of the ¹⁴C activity residing in the bluegill sunfish tissue was tightly associated with *or incorporated into* protein” (present authors’ emphasis). In this context it is important to recall that a 60- to 120-fold higher detection level of BMAA was obtained following protein hydrolysis of contaminated proteins [84].

Since Monsanto found bioaccumulation of glyphosate in all animal tissues, with the highest levels in the bones and marrow [35, 36], one would expect that all tissues derived from animals fed a diet containing glyphosate residues and used for food by people around the globe would be contaminated. Knowing that the bioaccumulation of glyphosate would be evident in the vast majority of animals raised for market and fed a contaminated diet, as well as their products; and suspecting the possibility of contamination of even the digestive enzymes derived from these animals, one of us (Samsel) decided to analyse random samples.

Results from various gelatin-based products, along with the results for several different vaccines (discussed later) were reported to the FDA by Samsel Environmental & Public Health Services in August 2016. Table 2 shows results for glyphosate residues found in these gelatin-based products. The highest level found in a gelatin sample was almost 15 ppb.¹

Having found glyphosate in animal gelatins, analysing the collagen at the source was a logical next step. Tissues from pork and cattle obtained from a local supermarket, commercially available collagen sourced from industrially-raised swine and oxen, as well as the purified digestive enzymes pepsin, lipase and trypsin, derived from pigs, were selected for evaluation. Three methods of laboratory analysis were used to determine if

¹ Parts per (US) billion. To put this into perspective, 1 ppb = 1 µg/kg, and 1 µg of glyphosate (N-phosphonomethylglycine) contains 3.561×10^{12} molecules of the substance, each one of which could integrate with a protein.

glyphosate was present in porcine pepsin and in the glycine-rich collagen from the tissues of pigs and cattle, protein sources that are regularly consumed by Americans. The results are given in Table 3.

Glyphosate integration with enzymes is a serious consideration, as glyphosate may serve as an enzyme inhibitor like other phosphonates [90–92]. Inhibition and immobilization of enzymes may occur via three basic categories: covalent linkage; adsorption on a carrier; or entrapment within macromolecules [93].

Inhibition of enzymes may be reversible or irreversible. Types of reversible enzyme inhibition include competitive, noncompetitive and uncompetitive. *Irreversible* inhibitors covalently bond to the functional groups of the active site, thus permanently inactivating catalytic activity. Irreversible inhibition includes two types: group-specific inhibition and “suicide” inhibition.

The importance of fully functional digestive enzymes cannot be understated. They are essential for metabolic function, as they convert food into nutrients and other molecules that are then available to cells for tissue and organ growth, maintenance and repair. The precursor trypsinogen, produced in the pancreas, is enzymatically transformed into the serine protease trypsin. Trypsin catalyses the hydrolysis of proteins into peptides and provides substrates for further enzymatic hydrolysis for protein absorption.

Pepsin, a primary protease of digestion, is also responsible for the metabolism of dietary protein.

Pepsin’s cleavage of peptide bonds is responsible for the availability of the aromatic amino acids phenylalanine, tyrosine and tryptophan. It is also responsible for the cleavage and release of several other amino acids, including valine, glycine, histamine, glutamine, alanine and leucine.

Lipase participates in cell signaling, inflammation and metabolism. Pancreatic lipase is the catalyst for the hydrolysis of dietary lipids, which include fats, oils, cholesterol esters and triglycerides [94]. Triglyceride triester is metabolized for utilization as glucose and three fatty acids. Glyphosate integration into and inhibition of lipase could induce excessive bioaccumulation of fatty material in the blood vessels, gut, liver, spleen and other organs, as well as mimic lysosomal acid lipase deficiency. It would also allow for an increase in triglycerides in the blood, leading to numerous disease cascades, including malabsorption, fatty liver disease, jaundice, failure to thrive in infants, calcification of the adrenal gland, anaemia, hypercholesterolaemia, biliary dysfunction, decreased HDL, increased LDL, blood clots, fat-enlarged hepatocytes and liver fibrosis and failure. Samsel found that radiolabeled glyphosate was not detectable by HPLC–MSMS in samples of lipase deliberately spiked for analysis, suggesting that glyphosate may irreversibly inhibit lipase. On the other hand, pepsin and trypsin had good spike recoveries, demonstrating reversibility as glyphosate was released from the protein.

Table 3. Integration of glyphosate residues in various proteins, assessed using three testing methods.^a

Protein substrate (Method)	Type	Glyphosate residue (ppb)
Bone (ELISA)	Bovine leg	11.56
Bone marrow (ELISA)	Bovine leg marrow	4.22
Bone (ELISA)	Porcine foot	9.81
Skin (ELISA)	Porcine	0.325
Gelatin (ELISA)	Bovine, Sigma Aldrich, gel strength 225 Type B	2.04
Collagen (ELISA)	Bovine I & III	120.18
Collagen (GC-MS)	Bovine I & III	130 µg/kg
Collagen (HPLC-MSMS)	Bovine I & III	95 µg/kg
Pepsin (ELISA)	Purified porcine enzyme	< 40.00
Pepsin (GC-MS)	Purified porcine enzyme	430 µg/kg
Pepsin (HPLC-MSMS)	Purified porcine enzyme	290 µg/kg
Trypsin (ELISA)	Purified porcine enzyme	61.99
Lipase (ELISA)	Purified porcine enzyme	24.43
Bee bread (HPLC-MSMS)	Bee bread	2300 µg/kg
Bees (HPLC-MSMS)	<i>Apis mellifera</i>	< 10 µg/kg trace
Honey & comb (HPLC-MSMS)	Honey	< 10 µg/kg trace

^a The trace amount found in the bee substrates appeared as a small peak, which directly corresponded to glyphosate, complete with retention time and molecular features confirming contamination using HPLC–MSMS.

Table 3 shows results for various bovine and porcine products, including enzymes, bone, bone marrow, skin, collagen and gelatin. Acid hydrolysis was used on the bovine and porcine skin, bones and marrow, which were shaken and digested with 0.15 M hydrochloric acid for 24 h. The analysis methods were ELISA, gas chromatography–mass spectrometry (GC–MS) and HPLC–MSMS. All of the tested products were contaminated, with the highest level detected being 430 µg/kg in porcine pepsin (via GC–MS).

Additional evidence of glyphosate accumulation was found by Samsel in 2015 in the bodies of dead bees, bee bread and honey from bee hives suspected of colony collapse disorder (CCD), and these are also shown in the table. Colony collapse disorder (CCD) is an ever-increasing problem threatening pollination of crops globally. It may share a similar aetiology to that of Alzheimer's disease with regard to learning and memory within the bee's brain. Integration of glyphosate with the structural proteins and enzymes of the bee may affect protein folding and function. Additionally, glyphosate may also affect the digestive enzymes and bacterial homeostasis within the digestive system, which in turn may affect the quality of the honey produced. Glyphosate in bees may become part of their chitin, which has a structural function, in their bodies, analogous to glyphosate becoming part of the collagens of humans and other animals.

The results in Table 3 show ubiquitous contamination of the bee and bee products. Honey is derived from nectar and is the source of carbohydrates in the bee diet, whereas pollen turned into bee bread supplies the fats and proteins. Royal jelly, made from the secretions of the glands found in the hypopharynx of the worker bees, is fed to the queen and developing larvae [96].

Results for nineteen different vaccines, from five manufacturers, are shown in Table 4. Some vaccines do not contain live viruses and do not involve gelatin in their preparation, but many involve the use of eggs, bovine calf serum, fetal bovine serum or bovine proteins [95]. Egerix Hepatitis B vaccine is manufactured through a novel procedure, which involves culturing genetically engineered *Saccharomyces cerevisiae* yeast cells that carry the surface antigen gene of the hepatitis B virus. The procedures result in a product that can contain up to 5% yeast proteins, which could be a source of glyphosate if the yeast is grown on broths or media that utilize glyphosate-contaminated nutrient sources such as animal or plant proteins.

Vaccines that tested negative for glyphosate included Merck's Hep-B vaccine, most of the pneumococcal vaccines and the sterile diluent included as a control. Gelatin is not listed as an ingredient in any of these vaccines, nor is bovine serum. In contrast, all of the vaccines that listed gelatin as an excipient tested positive for glyphosate, and nearly all of them also included bovine serum (including Varicella, MMR-II, MMRV and Zoster).

It is significant that MMR-II consistently contained the highest levels of glyphosate, significantly more than any of the other vaccines. This vaccine uses up to 12% hydrolysed gelatin as an excipient–stabilizer; as well as foetal bovine serum albumin, human serum albumin and residual chick embryo; all of which are contaminated by glyphosate during animal production.

7. EVIDENCE FOR A ROLE FOR COLLAGEN IN VACCINE ADVERSE REACTIONS

Post-vaccination allergic reactions to MMR and varicella vaccines have been linked to the gelatin excipient, and confirmed through observation of induced gelatin-specific IgE antibodies [97–100]. 24 out of 26 children with allergic reactions to vaccines (e.g., anaphylactic shock) had anti-gelatin IgE ranging from 1.2 to 250 µg/mL. Seven were allergic to gelatin-containing foods. A pool of 26 control children all tested negative for anti-gelatin IgE [99]. A study from 2009 that looked at gelatin sensitivity in children who were sensitive to cows' milk, beef and/or pork as determined by IgE antibody levels [101] found that 16% of beef-sensitized children and 38% of pork-sensitized children had IgE antibodies to beef- or pork-derived gelatins that were cross-reactive with each other.

In a published case study, a 2-month-old baby developed Kawasaki disease one day after receiving its first dose of Infanrix (DTaP-IPV-Hib) and Prevenar, a pneumococcal conjugate vaccine [102]. Kawasaki disease is an acute, multisystemic vasculitis whose occurrence very early in life is extremely rare. Extensive tests for the presence of infection with multiple bacteria and viruses were all negative. We suggest that glyphosate contamination in one or both of the vaccines may have contributed to the vasculitis through glyphosate uptake into common proteins such as collagen in the vasculature to induce the autoimmune reaction.

Kelso (1993) reported the case of a 17-year-old girl who experienced anaphylaxis within minutes of receiving an MMR vaccine [98]. The girl described the event as "kind of like what happens when I eat Jell-O²". Further testing found gelatin to be the component of the vaccine

² Jell-O is a proprietary brand of gelatin-based desserts, popular in the USA, and manufactured by Kraft Foods, part of the Kraft Heinz Company, headquartered in Chicago.

Table 4. Glyphosate levels in vaccines determined by ELISA reported to the US CDC, NIH, FDA and UN WHO of the Americas in September 2016 by Samsel Environmental & Public Health Services.^a

Vaccine undiluted	Manufacturer	Lot number Exp date	Test date Lab #	Glyphosate residue (ppb)	% Recovery in spiked sample
DTaP ADACEL	SANOPI PASTEUR	58160-820-43	7-15-2016	0.109	82%
	NDC	3-30-2018	LAB #1		
DTaP	SANOPI PASTEUR	C50418A	5-11-2016	< 0.075	81%
		9-2-2018	LAB #1		
DTaP ADACEL	SANOPI PASTEUR	NDC 58160-820-43	7-12-2016	ND	-
		3-30-2018	LAB #2		
HEPATITIS-B	MERCK	LO16427	5-11-2016	< 0.075	97%
		4-13-2017	LAB #1		
HEPATITIS ENGERIX-B	GLAXOSMITH- KLINE	NDC 58160-820-43	7-15-2016	0.337	73%
		6-1-2018	LAB #1		
INFLUENZA	SANOPI PASTEUR	6762	7-15-2016	0.170	95%
FLUZONE QUAD		6-30-2016	LAB #1		
INFLUENZA	NOVARTIS	1573 3P	5-11-2016	0.227	106%
		05/2016	LAB #1		
Pneumococcal	MERCK	700281601	9-19-2016	0.112	118%
PNEUMOVAX 23		5-18-2017	LAB #1		
MMR II	MERCK	7002151400	7-15-2016	3.740	-
		9-9-2017	LAB #1		
MMR II	MERCK	009545	5-11-2016	2.963	-
		3-19-2017	LAB #1		
MMR II	MERCK	7002151400	9-19-2016	3.154	-
		9-9-2017	LAB #1		
MMR II	MERCK	7002151400	7-12-2016	2.90	-
		9-9-2017	LAB #2		
MMRV PROQUAD	MERCK	7002305700	9-19-2016	0.659	103%
		9-12-2017	LAB #1		
MMRV PROQUAD	MERCK	7002305700	7-15-2016	0.512	86%
		9-12-2017	LAB #1		
MRV PROQUAD	MERCK	7002305700	7-12-2016	0.43	-
		9-12-2017	LAB #2		
Pneumococcal	MERCK	700281601	7-15-2016	< 0.075	77%
PNEUMOVAX 23		5-18-2017	LAB #1		
Pneumococcal	WYETH	73332	5-11-2016	< 0.075	82%
PREVNAR 13		07/2017	LAB #1		
Pneumococcal	MERCK	7002681601	7-12-2016	ND	-
PNEUMOVAX 23		5-18-2017	LAB #2		
STERILE DILUENT	MERCK, SHARP & DOHME	LO 40058	7-15-2016	< 0.075	97%
		5-11-2018	LAB #1		
VARICELLA	MERCK	7002025000	7-15-2016	0.556	84%
VARIVAX		2-8-2018	LAB #1		
MVARICELLA	MERCK	7002025000	7-12-2016	0.41	-
VARIVAX		2-8-2018	LAB #2		
ZOSTER	MERCK	7002502401	9-19-2016	0.620	95%
ZOSTAVAX		6-1-2017	LAB #1		
ZOSTER	MERCK	7002602401	7-15-2016	0.558	98%
ZOSTAVAX		6-1-2017	LAB #1		
ZOSTER	MERCK	7002602401	7-12-2016	0.42	-
ZOSTAVAX		6-1-2017	LAB #2		

^a Limits of detection for glyphosate in vaccines in parts per billion (ppb):¹ 0.075 (LAB #1); 0.15 (LAB #2).

to which the girl was allergic. The connexion may be to misfolded proteins, which include the collagens and associated partially hydrolysed gelatins. Indeed, both Jell-O and vaccines have been contaminated by glyphosate, as we reported in the previous section.

Puppies immunized with the rabies vaccine and a multivalent canine vaccine were compared to unvaccinated

control puppies [103]. The vaccinated puppies, but not the unvaccinated ones, developed autoantibodies to their own collagen. A follow-up study where either just the rabies vaccine or just the multivalent vaccine was administered produced a similar result. The authors suggested that this could explain issues of joint pain that are currently common among dogs, particularly as they age.

8. MULTIPLE SCLEROSIS (MS)

8.1 Sugar beet and MS

The world obtains 30% of its sugar supply from beet sugar. While sugar cane is grown in tropical regions, sugar beet requires a temperate climate. The highest incidences of MS worldwide are in the USA, Canada and western Europe [5], where most of the beet sugar is produced. MS rates are higher in the northern states of the USA compared to the south, corresponding to the distribution of sugar beet cultivation. MS rates in Canada are highest in the Alberta prairie region, at the centre of the Canadian sugar beet industry [104]. Studies on migrants have shown that those who move from a low-risk to a high-risk area tend to adopt high-risk only if they migrated during childhood [105]. This implicates local environmental factors acting before adolescence. Tokachi province in Japan hosts only 0.3% of the population, but produces 45% of the sugar beet consumed in Japan [37]; this province has the highest rate of MS among all Asian populations [106].

A fascinating proposition how sugar beet could cause MS implicates a unique noncoding amino acid that is produced by sugar beet, namely Aze. Both proline and Aze have a unique structure for an amino acid: the side chain loops back round to connect up to the nitrogen atom. In the case of Aze, there are only 3 carbons in the ring instead of the 4 carbons in proline (Fig. 2). It has been shown experimentally that Aze can be inserted by mistake into proteins in place of proline [38].

Myelin basic protein (MBP) is an essential protein for maintaining the myelin sheath, and it interacts with actin, tubulin, calmodulin and SH3 domains [107]. It

assembles actin filaments and microtubules, binds actin filaments and SH3 domains to membrane surfaces, and participates in signal transduction in oligodendrocytes and myelin. A central proline-rich region in MBP is functionally significant [108–110] and, in particular, is a binding site for Fyn-SH3, a key regulatory protein [111]. Proline substitutions of the SH3 ligand decrease its affinity for the Fyn-SH3 domain [108]. Fyn is localized to the cytoplasmic leaflet of the oligodendrocyte plasma membrane, where it participates in numerous signaling pathways during development of the central nervous system [112, 113]. Phosphorylation at a polyproline structure in the Fyn-binding region of MBP affects its structure.

A study using recombinant murine MBP inserted into *E. coli* strains demonstrated conclusively that Aze makes its way into MBP, substituting for up to three of the eleven possible proline sites. Molecular modeling of a proline-rich region of the recombinant MBP illustrated that misincorporation of Aze at any site would cause a severe bend in the polypeptide chain, and that multiple Aze substitutions would completely disrupt the structure of MBP [114, 115].

A possible concern regarding Aze is that over 90% of the sugar beet grown in the USA and Canada is genetically engineered to resist glyphosate. Therefore, the crops are exposed to significant amounts of glyphosate. The electronic *Code of Federal Regulations e-CFR 180.364 Glyphosate; Tolerances for Residues*, allows up to 25 ppm residue of glyphosate in dried sugar beet pulp. In 1999, Monsanto realized that its GM sugar beet crop well exceeded the upper limit established by the EPA for glyphosate residues. They requested, and were granted, a 125-fold increase in the upper residue limit for dried beet pulp (from 0.2 to 25 ppm). At the same time, the upper limit for fresh beet was increased fiftyfold to 10 ppm.

Glyphosate has been shown to increase the risk of root rot in sugar beet, caused by fungi [116]. Aze has been demonstrated to have antifungal activity [117]. Plants tend to increase synthesis of toxins under stress conditions, and it is plausible that an increased potential for root rot would result in increased synthesis of Aze. This is especially likely given that plants increase proline synthesis under a variety of different stress conditions [118]. However, to our knowledge, whether glyphosate causes an increase in either proline or Aze synthesis in sugar beet has not been investigated.

Consumption of milk worldwide is strongly correlated with MS risk (Spearman's correlation test = 0.836; $P < 0.001$) [119]. For the past several decades, cows' feed has been supplemented with either beet

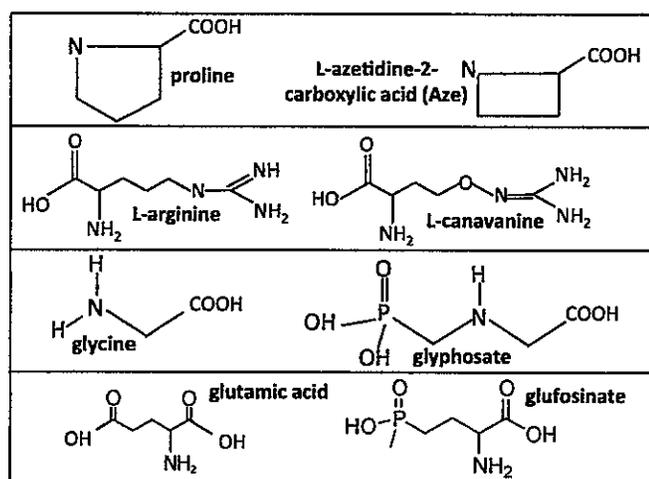


Figure 2. Molecular structures of the coding amino acids proline, L-arginine, glycine and glutamic acid; and their respective noncoding analogues Aze, L-canavanine, glyphosate and glufosinate.

molasses or sugar beet pulp, left as a residue after the sugar has been extracted [120]. Aze has been experimentally found in three sugar beet by-products that are fed to farm animals: sugar beet molasses, and both shredded and pelleted sugar beet pulp [38]. Casein is relatively enriched in proline [121]. If cows are exposed to Aze from the sugar beet, it will likely get inserted by mistake into casein, causing it to resist proteolysis. MBP's critical proline-rich sequence is vulnerable to misincorporation of Aze. The characteristic plaques of MS show loss of MBP within lesions in axon sheaths [107]. It is unclear whether this autoimmune reaction would arise through molecular mimicry from antibodies to unmetabolized peptides from casein or as a direct result of improperly folded MBP due to Aze insertion.

Glyphosate, an analogue of glycine, can be expected to be found in all tissues, including the milk of all mammals consuming glyphosate residues in the diet. Radiolabeled glyphosate studies conducted with lactating goats found ^{13}C and ^{14}C residues of glyphosate (N-phosphonomethylglycine), N-acetylglyphosate and other radiolabeled metabolites in milk. Monsanto found daily average ^{14}C residue levels from 19 to 86 ppb, with levels falling after five days of depuration to 6 ppb prior to sacrifice for organ examination. Results disseminated by Monsanto indicate that lactating animals (goats) fed a diet containing glyphosate and AMPA can be expected to have measured residue levels in edible tissues and milk [122]. In 2007 Dupont, in a similar study, examined the metabolism of N-acetylglyphosate in lactating goats. Detectable residues of N-acetylglyphosate, glyphosate and AMPA were detected in milk and other tissues. Milk, liver and kidney each contained 0.03% of the administered dose. Individual daily radiolabeled residues in the milk ranged from 0.030 to 0.036 $\mu\text{g/g}$ [123].

Lactobacillus plays an important rôle in metabolizing casein in the human gut. A detailed study of the prolyl aminopeptidase from *Lactobacillus* revealed that it is a member of the class of α/β hydrolases. Multiple sequence alignment has revealed three distinct highly conserved regions in this family and all three contain at least two highly conserved glycines [124] that would be vulnerable to displacement by glyphosate. The motif gly-x-ser-x-gly-gly characterizes the domain surrounding the catalytic serine residue of prolyl oligopeptidases in general. The glycine residues in this motif contribute to the correct positioning of the catalytic serine with respect to its substrate. A second glycine-rich domain appears essential to activity, as it likely corresponds to the oxyanion hole. The function of the third highly conserved glycine-rich domain, with the motif asp-x-x-gly-x-gly-x-ser, remains unknown. *Lactobacillus*

spp. are also highly dependent on manganese to protect them from oxidative damage, hence glyphosate's preferential chelation of manganese likely harms *Lactobacillus* [125].

An examination of collagen in the jugular veins of MS patients undergoing surgical reconstruction revealed an abnormal collagen structure, characterized by thin, loosely packed type III fibres [126]. Collagen is rich in proline. If too many of the prolines in procollagen are displaced by Aze, the polypeptide does not fold into a stable triple-helical conformation, which is a prerequisite for normal secretion of procollagen [127]. This reduces the release of procollagen and the misfolded molecules are subjected to proteolysis for recycling, resulting in the useless expenditure of energy for building and degrading procollagen molecules. Those that are released can be expected to produce defective collagen matrices. Collagen is even more highly enriched in glycine than in proline, as its core structure consists of a triple peptide repeat, where glycine is always the third residue of the triplet, and proline and hydroxyproline often occupy the other two positions [128]. Glyphosate substitution for glycine in structural proteins; i.e., collagen, elastin, fibronectin and laminin; would contribute to disrupted folding as well as defective strength and elasticity.

Conserved prolines also play a crucial rôle in ion channel gating, the regulation of hypoxia-inducible factor (HIF) and embryogenesis; in fact, substituting Aze for proline is a technique used to test whether a particular proline residue is critical to the protein's proper functioning [37].

8.2 Rôle of *Acinetobacter* and *Pseudomonas aeruginosa* in MS

A series of papers by Ebringer et al. have suggested an important rôle for the Gram-negative bacteria *Acinetobacter* and *Pseudomonas aeruginosa* in MS [129–131] as well as a proposed link to prion diseases. Their most recent paper in *Medical Hypotheses* presents the evidence to support this idea from multiple dimensions [130]. First, MS patients were shown to have elevated levels of antibodies to these two microbes but not to the common gut microbe *E. coli* [132, 116]. They have autoantibodies to MBP and myelin oligodendrocyte glycoprotein (MOG) [131]. MS patients are also prone to sinusitis and *Acinetobacter* is one of the most common microbes found in nasal sinuses. Ebringer et al. also proposed that the increased prevalence of sinusitis in colder climates may explain the geographical distribution of MS in more northerly latitudes [130]. *P. aeruginosa* causes upper respiratory infections and it is among the microbes that have developed multiple antibiotic

resistance in recent years, presenting a huge problem in hospital infection [133]. *Acinetobacter* has also become resistant to multiple antibiotics [134].

The number of microbial species that can metabolize glyphosate is quite small. A 1996 study showed that *Acinetobacter* is able to fully metabolize both glyphosate and AMPA and utilize these molecules as a source of phosphorus [135]. A study of agricultural soil heavily polluted with glyphosate identified only three species capable of degrading glyphosate when exposed at a level of 1000 ppm: *Pseudomonas putida*, *P. aeruginosa* and *Acetobacter faecalis* [136]. Another study on marine species identified *Pseudomonas* as being among the rare microbial species that can utilize the phosphonate in glyphosate as a source of phosphorus [137]. It can be predicted that *Pseudomonas* and *Acinetobacter* species in the nasal or digestive tracts would have a substantial advantage over other microbes if they can degrade glyphosate. On the other hand, they would also be heavily exposed if they actively take it up, and it would not be unreasonable to assume that some of the glyphosate might end up in their synthesized proteins by mistake in place of glycine. Both *Pseudomonas aeruginosa* and *Acinetobacter* strains have recently become a serious problem in hospitals, and a public health issue, due to their multiple-antibiotic resistance [138]. Glyphosate has been

shown to induce generic antibiotic resistance in other microbial species, including *E. coli* and *Salmonella*, through the induction of a generic capability to export toxic chemicals through efflux pumps [139].

A PEP transferase enzyme synthesized by *Acinetobacter calcaceticus* has sequence homology with a bovine prion sequence, and antibodies against synthetic peptides containing the structurally related sequences were found to be significantly elevated in cattle with bovine spongiform encephalopathy (BSE) compared to negative controls [140]. Ebringer et al. (2005) [129] link MS to BSE, also known as “mad cow disease”, and to the related human disease, Creutzfeldt–Jakob disease (CJD). Cows suffering from BSE manifest hindquarters paralysis early after onset, similar to the mobility issues afflicting MS patients at onset. Ebringer et al. found elevated levels of antibodies to both *Acinetobacter* and *Pseudomonas*, along with autoantibodies to both white and grey matter components, in BSE-affected animals, as is also the case for MS [129].

Of particular note are the molecular similarities they identified between certain peptides found in these two microbes and peptides in MOG and MBP that are known to be allergenic. Strikingly, all three of the microbial sequences they identified and all three of their human protein analogues contain conserved glycines (Table 5).

Table 5. Amino acid sequences of three peptides from *Acinetobacter* and *Pseudomonas* and the corresponding human peptides from MBP that they mimic.^a

Microbe	<i>Acinetobacter</i>	<i>Acinetobacter</i>	<i>Pseudomonas</i>
Protein	3-OACT-A	4-CMLD	Gamma-CMLD
Peptide	Leu-Tyr-Arg-Ala-Gly-Lys	Ser-Arg-Phe-Ala-Tyr-Gly	Thr-Arg-His-Ala-Tyr-Gly
MBP	Leu-Tyr-Arg-Asp-Gly-Lys	Ser-Arg-Phe-Ser-Tyr-Gly	Ser-Arg-Phe-Ser-Tyr-Gly

^a Note that all six peptides have a glycine residue.

MOG is strongly implicated in the disease pathology of MS; autoantibodies recognizing MOG have been found in the CNS of MS patients [141]. One of the major encephalitogenic peptides in MOG is the sequence from residue 92 to residue 106, which contains a highly conserved glycine near its centre [142].

Both diabetes and MS are associated with abnormal T-cell immunity to proteins found in cow’s milk [143]. In a study conducted in dairy cows by Monsanto in 1973, ¹⁴C-radiolabeled glyphosate was studied in the distribution of residues in milk, urine, faeces and other tissues of the lactating cow. Glyphosate contamination of milk ranged from 9 to 15 ppb with the highest accumulation in the kidney and rumen fluid (201 ppb and 109 ppb, respectively) [201]. An epitope of bovine serine albumin found in milk that is linked to MS but not to diabetes is BSA193. It shows

structural homology with exon 2 of MBP through the peptide sequence GLCHMYK. Note that the first peptide in this sequence is glycine. Exon 2 is a target peptide in both MS autoimmunity and in experimental autoimmune encephalitis (EAE), an animal model of MS [144–146]. Exon 2 of MBP is implicated in remyelination [144]. Its expression is largely restricted to the developing brain and to areas of myelin reconstruction, notably MS lesions [147].

The gly-ser-gly-lys tetrapeptide is highly conserved among MBPs from multiple species [148]. The serine in this sequence is the site of attachment of polyphosphoinositide. The highly conserved nature of this sequence suggests that the phospholipidation of MBP is important biologically. Substitution of glyphosate for either of the glycines would likely disrupt this modification.

9. MMR VACCINE AND AUTISM

In this section, we make a case for a direct link between the measles, mumps, and rubella (MMR) vaccine and autism, via autoantibody induction through molecular mimicry. In a paper provocatively titled, "Peptide cross-reactivity: the original sin of vaccines", Kanduc makes the point that massive cross-reactivity between antigens in vaccines and similar sequences in human proteins makes it almost inevitable that vaccines lead to autoimmune disease through molecular mimicry [149]. Reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barré syndrome and vasculitis [150].

It is becoming increasingly acknowledged that autism may be an autoimmune disease. Family members of autistic children have a significant increased risk to other known autoimmune diseases such as hypothyroidism, rheumatic fever and multiple sclerosis [151]. Several studies on both humans and monkeys have revealed a potential link between maternal antibodies directed against specific foetal brain proteins and a future autism diagnosis in the foetus [152–155]. Furthermore, it has already been demonstrated that vaccines are capable of inducing autoimmune antibodies against proteins in the brain. The narcolepsy epidemic in Europe following an aggressive immunization campaign against the H1N1 'flu virus was eventually conclusively resolved as being attributed to autoimmune reactions to the hypocretin receptor through molecular mimicry from a peptide in the surface-exposed region of the influenza nucleoprotein A that was present in the H1N1 vaccine [156] (hypocretin is an important regulator of sleep).

Much controversy surrounds the concept that the MMR vaccine may be contributing to the autism epidemic in the USA and elsewhere. In an immune-compromised child, the live measles virus from the vaccine is capable of infecting the brain and sustaining a chronic measles infection, resulting in loss of neurons, eosinophilic intranuclear inclusions and gliosis, a condition termed "subacute measles encephalitis". This can result in a seizure disorder and developmental delay in language and motor skills (as was clearly observed in a case study involving an HIV-positive 2-year-old boy [157]).

Singh et al. have published a series of papers over the past two decades [14, 158–160] proposing that there is a subpopulation among the autism community who can be characterized as suffering from "autoimmune autistic disorder" [14]. The 1998 study by Singh et al. found that 90% of measles-IgG-positive autistic sera were also positive for anti-MBP antibodies, supporting the hypothesis that a virus-induced autoimmune response may be

causal in autism [158]. A follow-on serologic study of antibodies to viruses associated with autism published in 2003 revealed a statistically significantly elevated level of measles antibody in children with autism compared to their siblings ($P = 0.0001$) or to unrelated children ($P = 0.003$), but not with antibodies to mumps or rubella [159]. In a later study, 60% of 125 autistic children had significantly elevated levels of antibodies to measles haemagglutinin unique to the MMR strain of the virus, compared to the 92 control children [160]. Over 90% of the children who had elevated antibody levels also tested positive for MBP autoantibodies. It was suggested that this could be linked to virus-induced autoimmunity through mimicry.

In fact, there is a sequence homology of 78% between a peptide sequence from MBP (EISFKLGQEGRDSRSGTP) and one found in a measles virus protein, MP3 (EISDNLGQEGRASTSGTP) [161, Table 2, p. 7]. Three of the matches between these two sequences are glycines. Measles virus-neutralizing antibodies are mainly directed to haemagglutinin, implying that it is essential for acquired immunity from the vaccine [162]; yet over-production, particularly if the virus penetrates the blood-brain barrier, runs the risk of inducing an autoimmune response to the myelin sheath. In fact, high measles antibody titres have been previously linked to MS [163].

Gonzalez-Granow et al. found high titres of autoantibodies in both the IgG and IgA classes specific to MBP in the serum of patients with autism [15]. The IgA antibodies in particular were shown to act as serine proteinases to degrade MBP *in vitro*. They also induced a decrease in long-term potentiation in perfused rat hippocampi. Reduced long-term potentiation in the hippocampus is a feature of autism, as has been clearly demonstrated in studies using mouse models of autism [164].

Dr Andrew Wakefield was the first to reveal a possible connexion between MMR and autism. His controversial *Lancet* paper, published in 1998 and then later retracted, proposed that this vaccine caused an acute reaction in children with gut dysbiosis (abdominal pain, diarrhoea, food intolerances, bloating etc.) [9]. The paper reported on a group of 12 children who had experienced developmental delay following an MMR vaccine and who were diagnosed with autism. These children suffered from rash, fever, delirium and seizures following the vaccination with MMR. He and several colleagues later published additional papers elaborating the hypothesis that dysbiosis in the gut, combined with impaired protein hydrolysis, leads to autoimmune lesions in the duodenum that are associated with extensive colonic lymphoid hyperplasia. The release of undigested peptides

into the vasculature across a leaky gut barrier and, ultimately, from the vasculature across a leaky blood–brain barrier, could induce encephalopathy [165–167].

In an epidemiological study from 1998, encephalopathy was clearly demonstrated as an acute reaction to measles vaccine, where 48 cases were found following vaccination, with no cases identified after administration of either monovalent mumps or rubella [168]. Among these 48 children, eight died, and the remainder experienced mental regression, chronic seizures, movement disorders and sensory deficits in the subsequent months.

The FDA's vaccine adverse event reporting system (VAERS) database is a valuable tool for uncovering trends in vaccine adverse reactions. Our earlier studies on VAERS comparing MMR with an age-matched, equal-sized distribution of all other vaccines showed a significant association of MMR with autism ($P < 0.007$) [169]. This was puzzling, because MMR has never contained either aluminium or mercury, the two prime candidates for the kind of neurological damage that might lead to autism [170–174]. Strong associations also appeared with fever and rash. In that paper, we proposed that the adverse reaction might be caused by the acetaminophen administered to the child to try to curb the seizures.

Since glyphosate usage on crops has gone up dramatically since the GM Roundup Ready crops were

first introduced in 1996, we decided it would be worthwhile to compare the early data on MMR in VAERS with the later data. We defined a cutoff date on 1 January 2003, such that the events where MMR was included as an administered vaccine could be separated into “early” and “late”, based on whether they were before or after that date. Each dataset represented a 13-year interval. We found 10 639 events in the early set and 19 447 events in the late set; thus, the raw number of events nearly doubled in the later years.

We also tabulated the frequency of different adverse reactions in the two sets, and used a standard statistical analysis to compute the significance of any differences observed: we randomly down-sampled both sets as needed such that there was an identical total count and an identical distribution over age in the two datasets. Results were surprising: many symptoms associated with atopy or with an allergic reaction were significantly higher in the later set, and “hospitalization” was highly significantly overrepresented in the later set [Table 6]. Other overrepresented symptoms included seizures, dyspnea, hyperventilation, asthma, eczema, autism, hives, anaphylactic [shock], and irregular heart rate. Interestingly, the early set had more frequent occurrences of joint pain and arthritis, suggesting that the toxic elements in the vaccine impacted the joints rather than the brain.

Table 6. Frequency of various adverse reactions to MMR before and after January 2003 [US FDA, VAERS]. The P -values were computed according to a χ^2 goodness-of-fit test.

More common before 2003			
Reaction	Count < 2003	Count \geq 2003	P -value
Arthritis	52	18	0.045
Joint pain	175	75	0.012
More common after 2002			
Reaction	Count < 2003	Count \geq 2003	P -value
Hospital	132	423	0.00041
Seizures	314	534	0.0055
Dyspnea	139	279	0.0086
Hives	444	654	0.011
Anaphylactic	28	91	0.017
Eczema	10	47	0.028
Autism	105	184	0.031
Hyperventilation	18	57	0.035
General infection	77	136	0.044
Asthma	22	58	0.046
Immunoglobulin G	0	17	0.048
Ear infection	32	72	0.048
Heart rate irregular	11	39	0.049

To our knowledge, there have been no significant changes to the formulation of MMR since its introduction. The explanation for the significant changes in adverse reactions must, therefore, lie in external factors, one of which is likely to be glyphosate. We suggest that both chronic exposure to glyphosate from food, water and air and direct exposure to glyphosate residues in the vaccine are relevant factors. A child with a disrupted gut microbiome due to chronic glyphosate exposure will also suffer from a leaky blood–brain barrier, and this will lead to a much greater possibility of measles antigenic proteins entering the brain and causing anaphylaxis and seizures.

The measles virus is a member of the family of paramyxoviruses, which have two highly-conserved glycine residues at positions 3 and 7 in the hydrophobic fusion peptide (FP) region of the viral fusion-mediating glycoproteins [175]. This FP region is the most highly conserved region of the glycoproteins, and it plays a critical rôle in destabilizing the membrane of the host cell to gain entry. Substitutions of other amino acids for either the G3A or G7A glycines caused increases in both cell–cell fusion and the reactivity of the protein to antibodies, leading to both a higher infection rate and increased chances for an autoimmune reaction. Glyphosate substitution is likely to do the same, as well as leading to a form of the protein that would resist proteolysis.

The FPs of both the influenza virus and human immunodeficiency virus (HIV) gp41 contain numerous glycine residues at regular intervals, with glycine overall making up 29 and 26%, respectively, of the total peptide sequence [175]. Optic neuritis, an immune-mediated demyelinating injury of the optic nerve, has been recognized as a side effect of the influenza vaccine that can lead to blindness [176].

10. OTHER AUTOIMMUNE DISEASES

10.1 Neuromyelitis optica and aquaporin

Neuromyelitis optica is a rare severe inflammatory demyelinating disorder of the central nervous system, which is related to multiple sclerosis but distinctly different and manifested mainly by paralysis and optic nerve damage [177, 178]. It has been conclusively demonstrated that this condition is caused by an autoimmune reaction to aquaporin-4, which is highly expressed in the astrocyte membrane [177, 178].

Aquaporins are important membrane proteins, which can transport water molecules through pores into the cell while excluding protons [179]. They are highly expressed by astrocytes, one of whose rôles is to mediate water flow among the vasculature, the

cerebrospinal fluid and the lymph system [178]. Thus, aquaporins are implicated in brain oedema [180]. Plants produce aquaporins as well, and mimicry between plant and human aquaporins has been proposed as a mechanism for the development of an autoimmune sensitivity to this protein [181]. Plants considered to show aquaporin mimicry notably include corn and soy as well as tomato, tobacco and spinach [182].

Autoimmune sensitivity to aquaporin has also been found in association with MS [182]. Vojdani et al. found significant elevations in antibodies against both human and plant aquaporin 4, in addition to antibodies against MB, MOG and S100 calcium-binding protein B (S100B) in patients suffering from MS.

Among the aquaporins, aquaporin-6 is unique in that it operates as an anion channel instead of as a water channel. Analysis of the peptide sequence in comparison to other aquaporins reveals that aquaporin-6 has an asparagine substituted in place of a glycine at residue 60. This one small difference completely changes the way the molecule behaves in the membrane. A glycine at this position is conserved among all the other aquaporins. Furthermore, aquaporins are constructed of α -helices, and there are three sites where the helices cross. Highly conserved glycine residues are found at all three sites [57, 183].

Aquaporin is also found in bacteria, although homology with human aquaporin is only about 20%. The bacterial aquaporin is a 27 kDa trypsin-resistant protein called aquaporin-Z, which was originally described in *E. coli* [184]. Sequence analysis conducted by Ren et al. [185] revealed four regions where homology was considerably stronger (90%, 60%, 50% and 45% respectively). They convincingly showed cross immunoreactivity between the human and bacterial versions of the protein. Antibodies to aquaporin Z bind to astrocytes, activate complement, and cause death.

Ren et al. [185] identified all the residues where the bacterial and human peptides were identical (Fig. 1 in [185]). A tally of counts reveals that glycine was by far the most common among these matched residues, representing 14 of the total 66 matches. The second most common amino acid was lysine with 8 matches. Alanine, isoleucine and valine had 7, 5 and 4 matches respectively, and all other amino acids had less than four.

Thus, it appears that glyphosate-substituted trypsin-resistant aquaporin from both gut microbes and from GM glyphosate-resistant corn and soy foods are plausible sources of antigens that could induce neuromyelitis optica and contribute to the disease process in MS through misincorporation.

10.2 Type 1 diabetes

Type 1 diabetes is considered a genetic disease, but its incidence has been increasing by 3–4% worldwide every year in the recent past [186, 168]. Although an environmental component is highly suspected, environmental factors have not yet been identified. An increased incidence of type 1 diabetes is associated with both MS [187] and autism [188]. The disease is characterized by an autoimmune reaction to various proteins expressed in the pancreatic islet cells. Specifically, antibodies against glutamic acid decarboxylase (GAD65) are often found [189]. Cross-reactivity with proteins from foods and microbes in the gut are both possibilities.

One microbe that may be inducing antibody production through mimicry is *Mycobacterium avium paratuberculosis* (MAP). Blast analysis revealed 75% homology between a previously identified antigenic region of GAD65 [190] and a MAP heat-shock protein (HSP65) [189]. The specific 16-residue matched sequence in HSP65 centrally contains a pair of glycines which could be substituted by glyphosate to cause resistance to proteolysis. This microbe has been linked to numerous other human diseases including ulcerative colitis, irritable bowel syndrome, sarcoidosis, Hashimoto's thyroiditis, MS and autism [188]. With respect to MS and autism, cross-reactivity between HSP65 and MBP through mimicry may provide the link.

Patients with type-1 diabetes commonly have an antibody reaction to bovine serum albumin, a component of cows' milk [191]. The hypothesized explanation is an autoimmune reaction to a beta-cell specific surface protein through mimicry.

Insulin-derived amyloidosis is a condition that can develop following long-term insulin therapy, whereby an "insulin ball" develops at the site of injection. This hard mass has been analysed and found to contain accumulations of insulin fibrils reminiscent of amyloid β -plaque in the Alzheimer's brain. Insulin amyloidosis is more common for animal (cows and pigs)-derived than human-derived insulin products. Nowadays, cows and pigs are chronically exposed to glyphosate in their feed. The rôle of glycine residues in proteins may indeed be to protect from aggregation into amyloid fibrils [192]. Substitution of glyphosate for any of these conserved glycines would therefore tend to promote amyloidosis.

Glutamic acid and glycine are by far the largest component amino acids of bovine proinsulin and make up 25% of the amino acid residues in the molecule [193]. The same is true for human insulin, which differs very little from the animal versions. The herbicide glufosinate is a natural noncoding amino acid analogue of glutamic

acid (Fig. 2). Substitution of either glufosinate for glutamic acid or glyphosate for glycine in insulin is likely to impair its function, and may also lead to amyloidosis.

The widespread appearance of glyphosate-resistant weeds among the glyphosate-resistant crops has forced some farmers to turn to glufosinate as the herbicide of choice [194]. Glufosinate-tolerant corn and soybean have been available on the US market since their approval by the USDA in 1995 and 1996, respectively. A tri-resistant form of soybean tolerant of glyphosate, glufosinate, and 2,4-D was approved by the FDA in September 2014. Dual resistance to glufosinate and glyphosate in corn was approved in November 2015.

10.3 Coeliac disease

Coeliac disease and, more generally, gluten intolerance, have reached epidemic proportions in the USA in the past decade [195]. Wheat grown there is being routinely sprayed with glyphosate for staging and desiccation just before harvest. This practice clears the field of weeds prior to harvest and planting of the next crop, but increases the amount of residual glyphosate in the grain. The practice has been increasing in popularity in step with the increase in gluten intolerance. Glyphosate is systemic in the plant and enters the seed as the plant dies, hence eventually ending up in wheat-based foods.

Proline residues make up 20% of the first 100 amino acids of both α - and γ -gliadins [54]. Related proteins from rye and barley are also unusually proline-rich [56]. As we implied earlier, proline is inaccessible to most digestive proteases because the bond between the peptide nitrogen atom and the side group complicates hydrolytic attack. As a consequence, specialized prolyl aminopeptidases detach the amino-terminal proline from a peptide. These enzymes depend on manganese as a catalyst, and manganese is one of the metals most dramatically affected by glyphosate chelation [125]. Unhydrolysed gliadin peptides bind to HLA-DQ molecules (receptors on antigen-presenting cells) and trigger pathogenic T-cell responses [196]. Genetic variants of HLA-DQ are linked to both coeliac disease and type 1 diabetes [197, 198].

Analysis of the X-ray crystal structure of a human cytosolic prolyl aminopeptidase worked out in 2008 revealed that it is a dimer with a dependency on two manganese ions as the catalytic centres [199]. The full sequence of the catalytic domains of six prolyl peptidases from both human and microbial species is shown in Fig. 6 in ref. 199. Six of the twenty sites of fully conserved residues across all species were glycine residues, three were histidine, two were tyrosine and two were proline. The remaining seven were seven different amino acids.

11. CONCLUSION

In this paper, we have shown that widespread misincorporation of glyphosate for glycine during protein synthesis could explain the aetiology of multiple autoimmune diseases that are currently increasing in incidence in the USA. Misincorporation is plausible by analogy with multiple known toxins produced by organisms in defence against pathogens, including Aze, BMAA, L-canavanine and glufosinate, which work in a similar manner. We have shown that proteins from foods such as milk, wheat and sugar beet, as well as peptides derived from microbes resident in the gut or nasal tract or introduced iatrogenically through vaccination, are all potential causes of autoimmune disease induced through molecular mimicry. It is highly significant that two microbes linked to MS through molecular mimicry are among the very few microbes that can fully metabolize glyphosate. Using the VAERS database, we have shown that severe adverse reactions to the MMR vaccine have increased significantly over the past decade in step with the increased use of glyphosate. Glyphosate in MMR may originate from growth of the live virus on culture materials derived from glyphosate-exposed animals and/or from gelatin used as an excipient stabilizer. We have confirmed the presence of glyphosate contamination in MMR and in many other vaccines where the live virus is cultured in eggs, bovine protein or gelatin, or where animal products are used as an excipient component. Notably, some vaccines prepared without live culture on gelatin were free of glyphosate contamination. Substitution of glyphosate for glycine during protein synthesis could yield a peptide that resists proteolysis, making it more likely to induce an immune response. Furthermore, enzymes involved in proteolysis are likely to be disrupted due to their confirmed contamination with glyphosate. A non-exhaustive list of possible diseases that can be attributed to this mechanism include autism, multiple sclerosis, type 1 diabetes, coeliac disease, inflammatory bowel disease and neuromyelitis optica.

ACKNOWLEDGMENT

This research is supported in part by Quanta Computers, Taiwan, under the auspices of the Qmulus program.

REFERENCES

- Ashwood, P. & van de Water, J. Is autism an autoimmune disease? *Autoimmun. Rev.* **3** (2004) 557–562.
- Gulcher, J.R., Vartanian, T. & Stefansson, K. Is multiple sclerosis an autoimmune disease? *Clin. Neurosci.* **2** (1994) 246–252.
- Hertz-Picciotto, I., Croen, L.A., Hansen, R., Jones, C.R., van de Water, J. & Pessah, I.N. The CHARGE study: An epidemiologic investigation of genetic and environmental factors contributing to autism. *Environ. Health Perspectives* **114** (2006) 1119–1125.
- London, E.A. The environment as an etiologic factor in autism: a new direction for research. *Environ. Health Perspectives* **108** (Suppl. 3) (2000) 401–404.
- Milo, R. & Kahana, E. Multiple sclerosis: Geoepidemiology, genetics and the environment. *Autoimmunity Rev.* **9** (2010) A387–A394.
- Koch-Henriksen, N. & Sorensen P.S. The changing demographic pattern of multiple sclerosis epidemiology. *Lancet Neurol.* **9** (2010) 520–532.
- Edwards, L.J. & Constantinescu, C.S. A prospective study of conditions associated with multiple sclerosis in a cohort of 658 consecutive outpatients attending a multiple sclerosis clinic. *Multiple Sclerosis* **10** (2004) 575–581.
- Kotey, S., Ertel, K. & Whitcomb, B. Co-occurrence of autism and asthma in a nationally-representative sample of children in the United States. *J. Autism Devl Disorders* **44** (2014) 3083–3088.
- Wakefield, A.J., Murch, S.H., Anthony, A., Linnell, J., Casson, D.M., Malik, M., Berelowitz, M., Dhillon, A.P., Thomson, M.A., Harvey, P., Valentine, A., Davies, S.E. & Walker-Smith, J.A. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* **351** (1998) 637–641 (retracted).
- Seneff, S., Davidson, R.M. & Liu, J. Is cholesterol sulfate deficiency a common factor in preeclampsia, autism, and pernicious anemia? *Entropy* **14** (2012) 2265–2290.
- Gillberg, C., Gillberg, C. & Kopp, S. Hypothyroidism and autism spectrum disorders. *J. Child Psychol. Psychiat.* **33** (1992) 531–542.
- Miyazawa, M. Molecular mimicry and mechanisms of autoantibody production. *Nihon Rinsho* **55** (1997) 1370–1376 [in Japanese].
- Shoenfeld, Y.F. & Aron-Maor, A. Vaccination and autoimmunity/vaccinosis: A dangerous liaison? *J. Autoimmunity* **14** (2000) 1–10.
- Singh, V.K. Phenotypic expression of autoimmune autistic disorder (AAD): a major subset of autism. *Ann. Clin. Psychiat.* **21** (2009) 148–161.
- Gonzalez-Gronow, M., Cuchacovich, M., Francos, R., Cuchacovich, S., Blanco, A., Sandoval, R., Gomez, C.F., Valenzuela, J.A., Ray, R. & Pizzo, S.V. Catalytic autoantibodies against myelin basic protein (MBP) isolated from serum of autistic children impair *in vitro* models of synaptic plasticity in rat hippocampus. *J. Neuroimmunol.* **287** (2015) 1–8.
- Weizman, A., Weizman, R., Szekely, G.A., Wijzenbeek, H. & Livni, E. Abnormal immune response to brain tissue antigen in the syndrome of autism. *Am. J. Psychiatr.* **139** (1982) 1462–1465.
- Herroelen, L., de Keyser, J. & Ebinger, G. Central nervous system demyelination after immunization with recombinant Hepatitis B vaccine. *Lancet* **338** (1991) 1174–1175.
- Genain, C.P., Cannella, B., Hauser, S.L. & Raine, C.S. Identification of autoantibodies associated with myelin damage in multiple sclerosis. *Nature Med.* **5** (1999) 170–175.
- Fredman, P., Vedeler, C.A., Nyland, H., Aarli, J.A. & Svennerholm, L. Antibodies in sera from patients with

- inflammatory demyelinating polyradiculoneuropathy reactive with ganglioside LM1 and sulfatide of peripheral nerve myelin. *J. Neurol.* **238** (1991) 75–79.
20. Steinman, L. Multiple sclerosis: A two-stage disease. *Nature Immunol.* **2** (2001) 762–764.
 21. Drummond, D.A. & Wilke, C.O. The evolutionary consequences of erroneous protein synthesis. *Nature Rev. Genetics* **10** (2009) 715–724.
 22. Drummond, D.A. & Wilke, C.O. Mistranslation-induced protein misfolding as a dominant constraint on coding-sequence evolution. *Cell* **134** (2008) 341–352.
 23. Conrad, A., Schröter-Kermani, C., Hoppe, H.W., Rütter, M., Pieper, S. & Kolossa-Gehring, M. Glyphosate in German adults—time trend (2001 to 2015) of human exposure to a widely used herbicide. *Int. J. Hyg. Environ. Health* **220** (2017) 8–16.
 24. Swanson, N.L., Leu, A., Abrahamson, J. & Wallet, B. Genetically engineered crops, glyphosate and the deterioration of health in the United States of America. *J. Org. Syst.* **9** (2014) 6–37.
 25. Hoy, J., Swanson, N. & Seneff, S. The high cost of pesticides: Human and animal diseases. *Poultry Fish. Wildlife Sci.* **3** (2015) 132.
 26. Seneff, S., Swanson, N. & Li, C. Aluminum and glyphosate can synergistically induce pineal gland pathology: connection to gut dysbiosis and neurological disease. *Agric. Sci.* **6** (2015) 42–70.
 27. Malmborg, P. & Hildebrand, H. The emerging global epidemic of paediatric inflammatory bowel disease—causes and consequences. *J. Intern. Med.* **279** (2016) 241–258.
 28. Boorom, K.F. Is this recently characterized gastrointestinal pathogen responsible for rising rates of inflammatory bowel disease (IBD) and IBD associated autism in Europe and the United States in the 1990s? *Med. Hypotheses* **69** (2007) 652–659.
 29. Horvath, K., Papadimitriou, J.C., Rabsztyan, A., Drachenberg, C. & Tildon, J.T. Gastrointestinal abnormalities in children with autistic disorder. *J. Pediatrics* **135** (1999) 559–563.
 30. Michielan, A. & D'Inca, R. Intestinal permeability in inflammatory bowel disease: pathogenesis, clinical evaluation, and therapy of leaky gut. *Mediators Inflammation* **2015** (2015) 628157.
 31. Stumpf, M., Krones, C.J., Klinge, U., Rosch, R., Junge, K. & Schumpelick, V. Collagen in colon disease. *Hernia* **10** (2006) 498–501.
 32. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases V: Amino acid analogue of glycine in diverse proteins. *J. Biol. Phys. Chem.* **16** (2016) 9–46.
 33. Hundorfean, G., Neurath, M.F. & Sitaru, C. Autoimmunity against type VII collagen in inflammatory bowel disease. *J. Cell Molec. Med.* **14** (2010) 2393–2403.
 34. Koelink, P.J., Overbeek, S.A., Braber, S., Morgan, M.E., Henricks, P.A., Roda, A., Verspaget, H.W., Wolfkamp, S.C., te Velde, A.A., Jones, C.W., Jackson, P.L., Blalock, J.E., Sparidans, R.W., Kruijtzter, J.A., Garssen, J., Folkerts, G. & Kraneveld, A.D. Collagen degradation and neutrophilic infiltration: a vicious circle in inflammatory bowel disease. *Gut* **63** (2014) 578–587.
 35. Ridley, W.P. & Mirly, K. The metabolism of glyphosate in Sprague Dawley rats. Part I. Excretion and tissue distribution of glyphosate and its metabolites following intravenous and oral administration (unpublished study MSL-7215 conducted by Monsanto's Environmental Health Laboratory and submitted to the EPA July 1988) (MRID#407671-01)(1988).
 36. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases IV: cancer and related pathologies. *J. Biol. Phys. Chem.* **15** (2015) 121–159.
 37. Rubenstein, E. Misincorporation of the proline analog azetidine-2-carboxylic acid in the pathogenesis of multiple sclerosis: a hypothesis. *J. Neuropathol. Exp. Neurol.* **67** (2008) 1035–1040.
 38. Rubenstein, E., McLaughlin, T., Winant, R.C., Sanchez, A., Eckart, M., Krasinska, K.M. & Chien, A. Azetidine-2-carboxylic acid in the food chain. *Phytochemistry* **70** (2009) 100–104.
 39. Hoerlein, G. Glufosinate (phosphinothricin), a natural amino acid with unexpected herbicidal properties. *Rev. Environ. Contamination Toxicol.* **138** (1994) 73–145.
 40. Dunlop, R.A., Cox, P.A., Banack, S.A. & Rodgers, K.J. The non-protein amino acid BMAA is misincorporated into human proteins in place of L-serine causing protein misfolding and aggregation. *PLoS ONE* **8** (2013) e75376.
 41. Rosenthal, G.A. The biochemical basis for the deleterious effects of L-canavanine. *Phytochemistry* **30** (1990) 1055–1058.
 42. Krakauer, J., Long, Y., Kolbert, A., Thanedar, S. & Southard, J. Presence of L-canavanine in *Hedysarum alpinum* seeds and its potential rôle in the death of Chris McCandless. *Wilderness Environ. Med.* **26** (2015) 36–42.
 43. Krakauer, J. *Into the Wild*. New York: Anchor Books (1996).
 44. Rosenthal, G.A. Biochemical basis for the deleterious effects of L-canavanine. *Phytochemistry* **30** (1991) 1055–1058.
 45. Dahlman, D.L. & Rosenthal, G.A. Non-protein amino acid-insect interactions I. Growth effects and symptomology of L-canavanine consumption by tobacco hornworm, *Manduca sexta* (L.). *Comparative Biochem. Physiol. A* **51** (1975) 33–36.
 46. Melangeli, C., Rosenthal, G.A. & Dalman, D.L. The biochemical basis for l-canavanine tolerance by the tobacco budworm *Heliothis virescens* (Noctuidae). *Proc. Natl Acad. Sci. USA* **94** (1997) 2255–2260.
 47. Padgett, S.R., Re, D.B., Gasser, C.S., Eichholtz, D.A., Frazier, R.B., Hironaka, C.M., Levine, E.B., Shah, D.M., Fraley, R.T. & Kishore, G.M. Site-directed mutagenesis of a conserved region of the 5-enolpyruvylshikimate-3-phosphate synthase active site. *J. Biol. Chem.* **266** (1991) 22364–22369.
 48. Eschenburg, S., Healy, M.L., Priestman, M.A., Lushington, G.H. & Schonbrunn, E. How the mutation glycine 96 to alanine confers glyphosate insensitivity to 5-enolpyruvyl shikimate-3-phosphate synthase from *Escherichia coli*. *Planta* **216** (2002) 129–135.
 49. Funke, T., Han, H., Healy-Fried, M.L., Fischer, M. & Schonbrunn, E. Molecular basis for the herbicide resistance of Roundup Ready crops. *Proc. Natl Acad. Sci. USA* **103** (2006) 13010–13015.

50. Beecham, J.E. & Seneff, S. The possible link between autism and glyphosate acting as glycine mimetic—a review of evidence from the literature with analysis. *J. Molec. Genet. Med.* **9** (2015) 187.
51. Cattani, D., de Liz Oliveira Cavalli, V.L., Heinz Rieg, C.E., Domingues, J.T., Dal-Cim, T., Tasca, C.I., Mena Barreto Silva, F.R. & Zamoner, A. Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity. *Toxicology* **320** (2014) 34–45.
52. Kitchen, L.M., Witt, W.W. & Rieck, C.E. Inhibition of δ -aminolevulinic acid synthesis by glyphosate. *Weed Sci.* **29** (1981) 571–577.
53. Zuckermann, R.N., Martin, E.J., Spellmeyer, D.C., Stauber, G.B., Shoemaker, K.R., Kerr, J.M., Figliozzi, G.M., Goff, D.A., Siani, M.A., Simon, R.J. et al. Discovery of nanomolar ligands for 7-transmembrane G-protein-coupled receptors from a diverse N-(substituted)glycine peptoid library. *J. Med. Chem.* **37** (1994) 2678–2685.
54. Hausch, F., Shan, L., Santiago, N.A., Gray, G.M. & Khosia, C. Intestinal digestive resistance of immunodominant gliadin peptides. *Am. J. Physiol. Gastrointestinal Liver Physiol.* **283** (2002) G996–G1003.
55. Schuppan, D. Current concepts of celiac disease pathogenesis. *Gastroenterology* **119** (2000) 234–242.
56. Wieser, H. Relation between gliadin structure and coeliac toxicity. *Acta Paediatr. (Suppl.)* **412** (1996) 3–9.
57. Liu, J. & Sessa, W.C. Identification of covalently bound amino-terminal myristic acid in endothelial nitric oxide synthase. *J. Biol. Chem.* **269** (1994) 11691–11694.
58. Kang, M.-I., Kobayashi, A., Wakabayashi, N., Kim, S.-G. & Yamamoto, M. Scaffolding of Keap1 to the actin cytoskeleton controls the function of Nrf2 as key regulator of cytoprotective phase 2 genes. *Proc. Natl Acad. Sci. USA* **101** (2004) 2046–2051.
59. Aicart-Ramos, C., Valero, R.A. & Rodriguez-Crespo, I. Protein palmitoylation and subcellular trafficking. *Biochim. Biophys. Acta* **1808** (2011) 2981–2994.
60. Kleuss, C. & Krause, E. G α s is palmitoylated at the N-terminal glycine. *EMBO J.* **22** (2003) 826–832.
61. Hirsch, R.H., Augustin, D.J. Nitrosamine analyses of Roundup herbicide, Rodeo herbicide, MON 0139 and Polado Technical (unpublished study RD835). St Louis, Missouri: Monsanto Agricultural Company (4 November 1987).
62. Massey, R.C. Analysis of N-nitroso compounds in foods and human body fluids. In: *Nitrosamines Toxicology and Microbiology* (ed. M.H. Hill), p. 26, section 2.4.4. VCH (1988).
63. Tricker, A.R., Perkins, M.J., Massey, R.C. & McWeeny, D.J. Some nitrosoamino acids in bacon adipose tissue and their contribution to the total N-nitroso compound concentration. *Z. Lebensmittel Untersuchung Forschung* **180** (1985) 379–383.
64. Kubacki, S.J., Havery, D.C. & Fazio, T. Nonvolatile N-nitrosamine investigations: methods for the determination of N-nitrosoamino acids and preliminary results of the development of a method for the determination of nitrosopeptides N-terminal in proline. In: *N-Nitroso Compounds: Occurrence, Biological Effects and Relevance to Human Cancer* (eds I.K. O'Neill, R.C. von Borstel, C.T. Miller, J. Long & H. Bartsch), No. 57, pp. 145–158. Lyons: International Agency for Research on Cancer (1984).
65. Tricker, A.R., Perkins, M.J., Massey, R.C. & McWeeny, D.J. Characterization studies on insoluble total N-nitroso compounds in bacon adipose connective tissue. *Food Additives Contaminants* **3** (1986) 153–159.
66. Newman, M.M., Lorenz, N., Hoilet, N., Lee, N.R., Dick, R.P., Liles, M.R., Ramsier, C. & Kloepper, J.W. Changes in rhizosphere bacterial gene expression following glyphosate treatment. *Sci. Total Environ.* **553** (2016) 32–41.
67. Zulet, A., Gil-Monreal, M., Villamor, J.G., Zabalza, A., van der Hoorn, R.A. & Royuela, M. Proteolytic pathways induced by herbicides that inhibit amino acid biosynthesis. *PLoS ONE* **8** (2013) e73847.
68. Nakajima, Y., Ito, K., Sakata, M., Xu, Y., Nakashima, K., Matsubara, F., Hatakeyama, S. & Yoshimoto, T. Unusual extra space at the active site and high activity for acetylated hydroxyproline of prolyl aminopeptidase from *Serratia marcescens*. *J. Bacteriol.* **188** (2006) 1599–1606.
69. Beauvais, A., Monod, M., Wyniger, J., Debeaupuis, J.P., Grouzmann, E., Brakch, N., Svab, J., Hovanessian, A.G. & Latgé, J.P. Dipeptidyl-peptidase IV secreted by *Aspergillus fumigatus*, a fungus pathogenic to humans. *Infection Immunity* **65** (1997) 3042–3047.
70. Byun, T., Kofod, L., Blinkovsky, A. Synergistic action of an X-prolyl dipeptidyl aminopeptidase and a non-specific aminopeptidase in protein hydrolysis. *J. Agric. Food Chem.* **49** (2001) 2061–2063.
71. Barberis, C.L., Carranza, C.S., Chiacchiera, S.M., Magnoli, C.E. Influence of herbicide glyphosate on growth and aflatoxin B1 production by *Aspergillus* section Flavi strains isolated from soil on in vitro assay. *J. Environ. Sci. Health B* **48** (2013) 1070–1079.
72. Freij, B.J., Levy, H.L., Dudin, G., Mutasim, D., Deeb, M., Der Kaloustian, V.M. Clinical and biochemical characteristics of prolidase deficiency in sibs. *Am. J. Med. Genet.* **19** (1984) 561–571.
73. Kumar, A., Are, V.N., Ghosh, B., Agrawal, U., Jamdar, S.N., Makde, R.D., Sharma, S.M. Crystallization and preliminary X-ray diffraction analysis of Xaa-Pro dipeptidase from *Xanthomonas campestris*. *Acta Crystallogr. F. Struct. Biol. Commun.* **70** (2014) 1268–1271.
74. Davis, T.W., Berry, D.L., Boyer, G.L. & Gobler, C.J. The effects of temperature and nutrients on the growth and dynamics of toxic and non-toxic strains of *Microcystis* during cyanobacteria blooms. *Harmful Algae* **8** (2009) 715–725.
75. Al-Sammak, M.A., Rogers, D.G. & Hoagland, K.D. Acute α -N-methylamino-L-alanine toxicity in a mouse model. *J. Toxicol.* **2015** (2015) 739–746.
76. Field, N.C., Metcalf, J.S., Caller, T.A., Banack, S.A., Cox, P.A. & Stommela, E.W. Linking β -N-methylamino-L-alanine exposure to sporadic amyotrophic lateral sclerosis in Annapolis, MD. *Toxicol.* **70** (2013) 179–183.
77. Masseret, E., Banack, S., Boumédiène, F., Abadie, E., Brient, L., Pernet, F., Juntas-Morales, R., Pageot, N., Metcalf, J., Cox, P. & Camu, W. French Network on ALS Clusters Detection and Investigation. Dietary BMAA exposure in an amyotrophic lateral sclerosis cluster from southern France. *PLoS ONE* **8** (2013) e83406.

78. Powell, H.A., Kerby, N.W. & Rowell, P. Natural tolerance of cyanobacteria to the herbicide glyphosate. *New Phytol.* **119** (1991) 421–426.
79. Forlani, G., Pavan, M., Gramek, M., Kafarski, P. & Lipok, J. Biochemical bases for a widespread tolerance of cyanobacteria to the phosphonate herbicide glyphosate. *Plant Cell Physiol.* **49** (2008) 443–456.
80. Michalak, A.M., Anderson, E.J., Beletsky, D., Boland, S., Bosch, N.S., Bridgeman, T.B., Chaffin, J.D., Cho, K., Confesor, R., Daloglu, I., DePinto, J.V. et al. Record-setting algal bloom in Lake Erie caused by agricultural and meteorological trends consistent with expected future conditions. *Proc. Natl Acad. Sci. USA* **110** (2013) 6448–6452.
81. Foran, E. & Trotti, D. Glutamate transporters and the excitotoxic path to motor neuron degeneration in amyotrophic lateral sclerosis. *Antioxidant Redox Signaling* **11** (2009) 1587–1602.
82. Slotboom, D.J., Sobczak, I., Konings, W.N. & Lolkema, J.S. A conserved serine-rich stretch in the glutamate transporter family forms a substrate-sensitive reentrant loop. *Proc. Natl Acad. Sci. USA* **96** (1999) 14282–14287.
83. Cox, P.A. & Sacks, O.W. Cycad neurotoxins, consumption of flying foxes, and ALS-PDC disease in Guam. *Neurology* **58** (2002) 956–959.
84. Ince, P.G. & Codd, G.A. Return of the cycad hypothesis does the amyotrophic lateral sclerosis/parkinsonism dementia complex (ALS/PDC) of Guam have new implications for global health? *Neuropathol. Appl. Neurobiol.* **31** (2005) 345–353.
85. Steele, J.C. & McGeer, P.L. The ALS/PDC syndrome of Guam and the cycad hypothesis. *Neurology* **70** (2008) 1984–1990.
86. Monson, C.S., Banack, S.A. & Cox, P.A. Conservation implications of Chamorro consumption of flying foxes as a possible cause of Amyotrophic Lateral Sclerosis Parkinsonism dementia complex in Guam. *Conservation Biol.* **17** (2003) 678–686.
87. Banack, S.A. & Cox, P.A. Biomagnification of cycad neurotoxins in flying foxes: implications for ALS-PDC in Guam. *Neurology* **61** (2003) 387–389.
88. Eastoe, J.E. The amino acid composition of mammalian collagen and gelatin. *Biochem. J.* **61** (1955) 589–600.
89. Ridley, W.P. & Chott, K.A. Uptake, depuration and bioconcentration of C-14 glyphosate to bluegill sunfish (*Lepomis macrochirus*) Part II: Characterization and quantitation of glyphosate and its metabolites. St Louis, Missouri: Monsanto Agricultural Company (unpublished study) (August 1989).
90. Yang, K.W., Brandt, J.J., Chatwood, L.L., Crowder, M.W. Phosphoramidate and phosphothioate dipeptides as potential inhibitors of VanX. *Bioorg. Med. Chem. Lett.* **10** (2000) 10850–10857.
91. Perlikowska, R., Fichna, J., do-Rego J.C., Gach, K., Janecka, A. Kinetic studies of novel inhibitors of endomorphin degrading enzymes. *Med. Chem. Res.* **21** (2012) 1445–1450.
92. Kramer, G.J., Mohd, A., Schwager, S.L.U., Masuyer, G., Acharya, K.R., Sturrock, E.D. & Bachmann, B.O. Interkingdom pharmacology of angiotensin-I converting enzyme inhibitor phosphonates produced by Actinomycetes. *ACS Med. Chem. Lett.* **5** (2014) 346–351.
93. Rubin, B. & Dennis, E. *Lipases, Part B: Enzyme Characterization and Utilization* (vol. 286). Academic Press (1997).
94. Chapus, C., Rovey, M., Sarda, L. & Verger, R. Minireview on pancreatic lipase and colipase. *Biochimie* **70** (1988) 1223–1234.
95. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 13th edn, Appendix B. Centers for Disease Control and Prevention (2015).
96. Graham, J. (ed.). *The Hive and the Honey Bee* (rev. edn). Watertown, Wisconsin: Dadant & Sons (1992).
97. Pool, V., Braun, M.M., Kelso, J.M., Mootrey, G., Chen, R.T., Yunginger, J.W., Jacobson, R.M., Gargiullo, P.M. & VAERS Team. US Vaccine Adverse Event Reporting System. Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after measles-mumps rubella vaccine in the United States. *Pediatrics* **110** (2002) e71.
98. Kelso, J.M., Jones, R.T. & Yunginger, J.W. Anaphylaxis to measles, mumps, and rubella vaccine mediated by IgE to gelatin. *J. Allergy Clin. Immunol.* **91** (1993) 867–872.
99. Sakaguchi, M., Nakayama, T. & Inouye, S. Food allergy to gelatin in children with systemic immediate-type reactions, including anaphylaxis, to vaccines. *J. Allergy Clin. Immunol.* **98** (1996) 1058–1061.
100. Sakaguchi, M., Yamanaka, T., Ikeda, K., Sano, Y., Fujita, H., Miura, T. & Inouye S. IgE-mediated systemic reactions to gelatin included in the varicella vaccine. *J. Allergy Clin. Immunol.* **9** (1997) 263–264.
101. Bogdanovic, J., Halsey, N.A., Wood, R.A. & Hamilton, R.G. Bovine and porcine gelatin sensitivity in milk and meat-sensitized children. *J. Allergy Clin. Immunol.* **124** (2009) 1108–1110.
102. Ece, I., Akbayram, S., Demiroren, K. & Uner, A. Is Kawasaki Disease a side effect of vaccination as well? *J. Vaccines Vaccination* **5** (2014) 234.
103. Hogenesch, H., Azcona-Olivera, J., Scott-Moncrieff, C., Snyder, P.W. & Glickman, L.T. Vaccine-induced autoimmunity in the dog. *Adv. Vet. Med.* **41** (1999) 733–747.
104. Beck, C.A., Metz, L.M., Svenson, L.W. & Patten, S.B. Regional variation of multiple sclerosis prevalence in Canada. *Multiple Sclerosis* **11** (2005) 516–519.
105. Gale, C.R. & Martyn, C.N. Migrant studies in multiple sclerosis. *Prog. Neurobiol.* **47** (1995) 425–448.
106. Houzen, H., Niino, M., Kikuchi, S., Fukazawa, T., Nogoshi, S., Matsumoto, H. & Tashiro, K. The prevalence and clinical expression of MS in northern Japan. *J. Neurol. Sci.* **211** (2003) 49–53.
107. Boggs, J.M. Myelin basic protein: a multifunctional protein. *Cell Molec. Life Sci.* **63** (2006) 1945–1961.
108. Smith, G.S., De Avila, M., Paez, P.M., Spreuer, V., Wills, M.K., Jones, N., Boggs, J.M. & Harauz, G. Proline substitutions and threonine pseudophosphorylation of the SH3 ligand of 18.5-kDa myelin basic protein decrease its affinity for the Fyn-SH3 domain and alter process development and protein localization in oligodendrocytes. *J. Neurosci. Res.* **90** (2012) 28–47.
109. Harauz, G. & Libich, D.S. The classic basic protein of myelin conserved structural motifs and the dynamic molecular barcode involved in membrane adhesion and protein-protein interactions. *Current Protein Peptide Sci.* **10** (2009) 196–215.

110. Homchaudhuri, L., Polverini, E., Gao, W., Harauz, G. & Boggs, J.M. Influence of membrane surface charge and post-translational modifications to myelin basic protein on its ability to tether the Fyn-SH3 domain to a membrane in vitro. *Biochemistry* **48** (2009) 2385–2393.
111. Machold, R., Hayashi, S., Rutlin, M., Muzumdar, M.D., Nery, S., Corbin, J.G., Gritli-Linde, A., Dellovade, T., Porter, J.A., Rubin, L.L., Dudek, H., McMahon, A.P. & Fishell, G. Sonic hedgehog is required for progenitor cell maintenance in telencephalic stem cell niches. *Neuron* **39** (2003) 937–950.
112. Manié, S.N., Astier, A., Haghayeghi, N., Canty, T., Druker, B.J., Hirai, H. & Freedman, A.S. Regulation of integrin-mediated p130(Cas) tyrosine phosphorylation in human B cells. A role for p59(Fyn) and SHP2. *J. Biol. Chem.* **272** (1997) 15636–15641.
113. Resh, M.D. Fyn, a Src family tyrosine kinase. *Intl J. Biochem. Cell Biol.* **30** (1998) 1159–1162.
114. Bessonov, K., Vassall, K.A. & Harauz, G. Parameterization of the proline analogue Aze (azetidide-2-carboxylic acid) for molecular dynamics simulations and evaluation of its effect on homo-pentapeptide conformations. *J. Molec. Graphics Modelling* **39** (2013) 118–125.
115. Bessonov, K., Bamm, V.V. & Harauz, G. Misincorporation of the proline homologue Aze (azetidide-2-carboxylic acid) into recombinant myelin basic protein. *Phytochemistry* **71** (2010) 502–507.
116. Kiewnick, S., Jacobsen, B.J., Braun-Kiewnick, A., Eckhoff, J.L.A. & Bergman, J.W. Integrated control of Rhizoctonia crown and root rot of sugar beet with fungicides and antagonistic bacteria. *Plant Diseases* **85** (2001) 718–722.
117. Bach, B., Gregson, R.P., Holland, G.S., Quinn, R.J. & Reichelt, J.L. L-Azetidine-2-carboxylic acid, the antidermatophyte constituent of two marine sponges. *Experientia* **34** (1978) 688.
118. Hayat, S., Hayat, Q., Alyemeni, M.N., Wani, A.S., Pichtel, J. & Ahmad, A. Role of proline under changing environments: a review. *Plant Signaling Behaviour* **7** (2012) 1456–1466.
119. Malosse, D., Perron, H., Sasco, A. & Seigneurin, J.M. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: A worldwide study. *Neuroepidemiology* **11** (1992) 304–312.
120. Huhtanen, P. The effects of barley, unmolassed sugar-beet pulp and molasses supplements on organic matter, nitrogen and fiber digestion in the rumen of cattle given a silage diet. *Animal Feed Sci. Technol.* **20** (1988) 259–278.
121. Gordon, W.G., Semmett, W.F. & Alanine, M.B. Glycine and proline contents of casein and its components. *J. Am. Chem. Soc.* **72** (1950) 4282–4282.
122. Bodden, R.M., Patanella, J.E., Feng, P. *Metabolism Study of Synthetic 13C/14C-Labeled Glyphosate and AMPA In Lactating Goats*, vols 1 & 2 (unpublished study). St. Louis, Missouri: Monsanto Company (February 1988).
123. Lowrie, C. Metabolism of [C-14]-N-Acetylgllyphosate (IN-MCX20) in the Lactating Goat (Charles River Laboratories Project no. 210583, submitted by E.I. du Pont de Nemours and Company) (Report No DuPont-19796) (2007).
124. Morel, F., Gilbert, C., Geourjon, C., Frot-Coutaz, J., Portalier, R. & Atlan, D. The prolyl aminopeptidase from *Lactobacillus delbrueckii* subsp. *bulgaricus* belongs to the u/v hydrolase fold family. *Biochim. Biophys. Acta* **1429** (1999) 501–505.
125. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases III: Manganese neurological diseases and associated pathologies. *Surg. Neurol. Intern.* **6** (2015) 45.
126. Coen, M., Menegatti, E., Salvi, F., Mascoli, F., Zamboni, P., Gabbiani, G. & Bochaton-Piallat, M.L. Altered collagen expression in jugular veins in multiple sclerosis. *Cardiovasc. Pathol.* **22** (2013) 33–38.
127. Tan, E.M., Ryhänen, L. & Uitto, J. Proline analogues inhibit human skin fibroblast growth and collagen production in culture. *J. Investigative Dermatol.* **80** (1983) 261–267.
128. Bhattacharjee, A. & Bansal, M. Collagen structure: the madras triple helix and the current scenario. *IUBMB Life* **57** (2005) 161–172.
129. Ebringer, A., Rashid, T. & Wilson, C. Bovine spongiform encephalopathy, multiple sclerosis, and Creutzfeldt-Jakob disease are probably autoimmune diseases evoked by *Acinetobacter* bacteria. *Ann. NY Acad. Sci.* **1050** (2005) 417–428.
130. Ebringer, A., Rashid, T. & Wilson, C. The role of *Acinetobacter* in the pathogenesis of multiple sclerosis examined by using Popper sequences. *Med. Hypotheses* **78** (2012) 763–769.
131. Hughes, L.E., Smith, P.A., Bonell, S., Natt, R.S., Wilson, C., Rashid, T., Amor, S., Thompson, E.J., Croker, J. & Ebringer, A. Cross-reactivity between related sequences found in *Acinetobacter* sp., *Pseudomonas aeruginosa*, myelin basic protein and myelin oligodendrocyte glycoprotein in multiple sclerosis. *J. Neuroimmunol.* **144** (2003) 105–115.
132. Hughes, L.E., Bonell, S., Natt, R.S., Wilson, C., Tiwana, H., Ebringer, A., Cunningham, P., Chamoun, V., Thompson, E.J., Croker, J. & Vowles, J. Antibody responses to *Acinetobacter*spp. and *Pseudomonas aeruginosa* in multiple sclerosis: prospects for diagnosis using the myelin *Acinetobacter* neurofilament antibody index. *Clin. Diagnostic Lab. Immunol.* **8** (2001) 1181–1188.
133. Lister, P.D., Wolter, D.J. & Hanson, N.D. Antibacterial-resistant *Pseudomonas aeruginosa*: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. *Clin. Microbiol. Rev.* **22** (2009) 582–610.
134. Karageorgopoulos, D.E. & Falagas, M.E. Current control and treatment of multidrug-resistant *Acinetobacter baumannii* infections. *Lancet Infectious Diseases* **8** (2008) 751–762.
135. Chung, N.-J., Han, H.-J., Lee, H.-H., Rhie, H.-G. & Lee, H.-S. Degradation of phosphonate herbicide glyphosate by *Acinetobacter lwoffii* HN401. *Molecules Cells* **6** (1996) 239–245.
136. Olawale, A.K. & Akintobi, O.A. Biodegradation of glyphosate pesticide by bacteria isolated from agricultural soil. *Report Opinion* **3** (2011) 124–128.
137. Moore, J.K., Braymer, H.D. & Larson, A.D. Isolation of a *Pseudomonas* sp. which utilizes the phosphonate herbicide glyphosate. *Appl. Environ. Microbiol.* **46** (1983) 316–320.
138. Landman, D., Quale, J.M., Mayorga, D., Adedeji, A., Vangala, K., Ravishankar, J., Flores, C. & Brooks, S.

- Citywide clonal outbreak of multiresistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY: The preantibiotic era has returned. *Arch. Intern. Med.* **162** (2002) 1515–1520.
139. Kurenbach, B., Marjoshi, D., Amábile-Cuevas, C.F., Ferguson, G.C., Godsoe, W., Gibson, P. & Heinemann, J.A. Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in *Escherichia coli* and *Salmonella enterica* serovar typhimurium. *nBio* **6** (2015) e00009.
 140. Wilson, C., Hughes, L., Rashid, T., Cunningham, P., Bansal, S., Ebringer, A. & Ettelaie, C. Antibodies to prion and *Acinetobacter* peptide sequences in bovine spongiform encephalopathy. *Vet. Immunol. Immunopathol.* **98** (2004) 1–7.
 141. O'Connor, K.C., Appel, H., Bregoli, L., Call, M.E., Catz, I., Chan, J.A., Moore, N.H., Warren, K.G., Wong, S.J., Hafler, D.A. & Wucherpfennig, K.W. Antibodies from inflamed central nervous system tissue recognize myelin oligodendrocyte glycoprotein. *J. Immunol.* **175** (2005) 1974–1982.
 142. Clements, C.S., Reid, H.H., Beddoe, T., Tynan, F.E., Perugini, M.A., Johns, T.G., Bernard, C.C. & Rossjohn, J. The crystal structure of myelin oligodendrocyte glycoprotein, a key autoantigen in multiple sclerosis. *Proc. Natl Acad. Sci. USA* **100** (2003) 11059–11064.
 143. Winer, S., Astsaturov, I., Cheung, R.K., Schrade, K., Gunaratnam, L., Wood, D.D., Moscarello, M.A., O'Connor, P., McKerlie, C., Becker, D.J. & Dosch, H.M. T cells of multiple sclerosis patients target a common environmental peptide that causes encephalitis in mice. *J. Immunol.* **166** (2001) 4751–4756.
 144. Segal, B.M., Raine, C.S., McFarlin, D.E., Voskuil, R.R. & McFarland, H.F. Experimental allergic encephalomyelitis induced by the peptide encoded by exon 2 of the MBP gene, a peptide implicated in remyelination. *J. Neuroimmunol.* **51** (1994) 7–19.
 145. Fritz, R.B. & Zhao, M.L. Encephalitogenicity of myelin basic protein exon-2 peptide in mice. *J. Neuroimmunol.* **51** (1994) 1–6.
 146. Voskuil, R.R., Robinson, E.D., Segal, B.M., Tranquill, L., Camphausen, K., Albert, P.S., Richert, J.R. & McFarland, H.F. HLA restriction and TCR usage of T lymphocytes specific for a novel candidate autoantigen, X2 MBP, in multiple sclerosis. *J. Immunol.* **153** (1994) 4834–4844.
 147. Capello, E.R., Voskuil, R.R., McFarland, H.F. & Raine, C.S. 1997. Multiple sclerosis: re-expression of a developmental gene in chronic lesions correlates with remyelination. *Ann. Neurol.* **41** (1997) 797–805.
 148. Chang, P.C., Yang, J.C., Fujitaki, J.M., Chiu, K.C. & Smith, R.A. Covalent linkage of phospholipid to myelin basic protein: identification of serine-54 as the site of attachment. *Biochemistry* **25** (1986) 2682–2686.
 149. Kanduc, D. Peptide cross-reactivity: the original sin of vaccines. *Frontiers Biosci.* **4** (2012) 1393–1401.
 150. Orbach, H., Agmon-Levin, N. & Zandman-Goddard, G. Vaccines and autoimmune diseases of the adult. *Discovery Med.* **9** (2010) 90–97.
 151. Sweeten, T.L., Bowyer, S.L., Posey, D.J., Halberstadt, G.M. & McDougale, C.J. Increased prevalence of familial autoimmunity in probands with pervasive developmental disorders. *Pediatrics* **112** (2003) e420–e424.
 152. Brimberg, L., Sadiq, A., Gregersen, P.K. & Diamond, B. Brain-reactive IgG correlates with autoimmunity in mothers of a child with an autism spectrum disorder. *Molec. Psychol.* **18** (2013) 1171–1177.
 153. Bauman, M.D., Iosif, A. M., Ashwood, P., Braunschweig, D., Lee, A., Schumann, C.M. et al. Maternal antibodies from mothers of children with autism alter brain growth and social behavior development in the rhesus monkey. *Transl. Psychiat.* **3** (2013) e278.
 154. Atladóttir, H.O., Pedersen, M.G., Thorsen, P., Mortensen, P.B., Deleuran, B., Eaton, W.W. & Parner, E.T. Association of family history of autoimmune diseases and autism spectrum disorders. *Pediatrics* **124** (2009) 687–694.
 155. Braunschweig, D., Krakowiak, P., Duncanson, P., Boyce, R., Hansen, R.L., Ashwood, P. et al. Autism-specific maternal autoantibodies recognize critical proteins in developing brain. *Transl. Psychiat.* **3** (2013) e277.
 156. Ahmed, S.S., Volkmuth, W., Duca, J., Corti, L., Pallaoro, M., Pezzicoli, A., Karle, A., Rigat, F., Rappuoli, R., Narasimhan, V., Julkunen, I., Vuorela, A., Vaarala, O., Nohynek, H., Laghi Pasini, F., Montomoli, E., Trombetta, C., Adams, C.M., Rothbard, J. & Steinman, L. Antibodies from vaccine-associated narcolepsy sera cross-reacted with both influenza nucleoprotein and hypocretin receptor 2. *Sci. Translational Med.* **7** (2015) 294ra105.
 157. Poon, T.P., Tchertkoff, V. & Win, H. Subacute measles encephalitis with AIDS diagnosed by fine needle aspiration biopsy. A case report. *Acta Cytol.* **42** (1998) 729–733.
 158. Singh, V.K., Lin, S.X. & Yang, V.C. Serological association of measles virus and human herpes virus-6 with brain autoantibodies in autism. *Clin. Immunol. Immunopathol.* **89** (1998) 105–108.
 159. Singh, V.K. & Jensen, R.L. Elevated levels of measles antibodies in children with autism. *Pediat. Neurol.* **28** (2003) 292–294.
 160. Singh, V.K., Lin, S.X., Newell, E. & Nelson, C. Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism. *J. Biomed. Sci.* **9** (2002) 359–364.
 161. Oldstone, M.B.A. (ed.). *Molecular Mimicry: Infection-Inducing Autoimmune Disease*. Springer (2006).
 162. de Swart, R.L., Yüksel, S. & Osterhaus, A.D.M.E. Relative contributions of measles virus hemagglutinin- and fusion protein-specific serum antibodies to virus neutralization. *J. Virol.* **79** (2005) 11547–11551.
 163. Alter, M. Is multiple sclerosis an age-dependent host response to measles? *Lancet* **28** (1976) 456–457.
 164. Kaphzan, H., Hernandez, P., Jung, J., Cowansage, K.K., Deinhardt, K., Chao, M.V., Abel, T. & Klann, E. Reversal of impaired hippocampal long-term potentiation and contextual fear memory deficits in Angelman syndrome model mice by ErbB inhibitors. *Biol. Psychiat.* **72** (2012) 182–190.
 165. Kawashima, H., Mori, T., Kashiwagi, Y., Takekuma, K., Hoshika, A. & Wakefield, A. Detection and sequencing of measles virus from peripheral mononuclear cells from patients with inflammatory bowel disease and autism. *Digestive Diseases Sci.* **45** (2000) 723–729.

166. Torrente, F., Ashwood, P., Day, R., Machado, N., Furlano, R.I., Anthony, A., Davies, S.E., Wakefield, A.J., Thomson, M.A., Walker-Smith, J.A. & Murch, S.H. Small intestinal enteropathy with epithelial IgG and complement deposition in children with regressive autism. *Molec. Psychol.* **7** (2002) 375–382.
167. Wakefield, A.J., Puleston, J.M., Montgomery, S.M., Anthony, A., O’Leary, J.J. & Murch, S.H. Review article: the concept of entero-colonic encephalopathy, autism and opioid receptor ligands. *Alimentary Pharmacol. Therapeut.* **16** (2002) 663–674.
168. Weibel, R.E., Caserta, V., Benor, D.E. & Evans, G. Acute encephalopathy followed by permanent brain injury or death associated with further attenuated measles vaccines: A review of claims submitted to the national vaccine injury compensation program. *Pediatrics* **101** (1998) 383–387.
169. Seneff, S., Davidson, R.M. & Liu, J. Empirical data confirm autism symptoms related to aluminum and acetaminophen exposure. *Entropy* **14** (2012) 2227–2253.
170. Dufault, R., Schnoll, R., Lukiw, W.J., LeBlanc, B., Cornett, C., Patrick, L., Wallinga, D., Gilbert, S.G. & Crider, R. Mercury exposure, nutritional deficiencies and metabolic disruptions may affect learning in children. *Behavioral Brain Functions* **5** (2009) 44.
171. Sharpe, M.A., Gist, T.L. & Baskin, D.S. B-lymphocytes from a population of children with autism spectrum disorder and their unaffected siblings exhibit hypersensitivity to thimerosal. *J. Toxicol.* **2013** (2013) 801517.
172. Shaw, C.A., Kette, S.D., Davidson, R.M. & Seneff, S. Aluminum’s role in CNS-immune system interactions leading to neurological disorders. *Immunome Res.* **9** (2013) 069.
173. Shaw, C.A., Seneff, S., Kette, S.D., Tomljenovic, L., Oller, J.W., Jr. & Davidson, R.M. Aluminum-induced entropy in biological systems: implications for neurological disease. *J. Toxicol.* **2014** (2014) 491316.
174. Tomljenovic, L. & Shaw, C.A. Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations. *Lupus* **21** (2012) 223–230.
175. Russell, C.J., Jardetzky, T.S. & Lamb, R.A. Conserved glycine residues in the fusion peptide of the paramyxovirus fusion protein regulate activation of the native state. *J. Virol.* **78** (2004) 13727–13742.
176. Kawasaki, A., Purvin, V.A. & Tang, R. Bilateral anterior ischemic optic neuropathy following influenza vaccination. *J. Neuroophthalmol.* **18** (1998) 56–59.
177. Papadopoulos, M.C. & Verkman, A.S. Aquaporin 4 and neuromyelitis optica. *Lancet Neurol.* **11** (2012) 535–544.
178. Roemer, S.F., Parisi, J.E., Lennon, V.A., Benarroch, E.E., Lassmann, H., Bruck, W., Mandler, R.N., Weinshenker, B.G., Pittock, S.J., Wingerchuk, D.M. & Lucchinetti, C.F. Pattern-specific loss of aquaporin-4 immunoreactivity distinguishes neuromyelitis optica from multiple sclerosis. *Brain* **130** (2007) 1194–1205.
179. Liu, K., Kozono, D., Kato, Y., Agre, P., Hazama, A. & Yasui, M. Conversion of aquaporin 6 from an anion channel to a water-selective channel by a single amino acid substitution. *Proc. Natl Acad. Sci. USA* **102** (2005) 2192–2197.
180. Zador, Z., Bloch, O., Yao, X. & Manley, G.T. Aquaporins: role in cerebral edema and brain water balance. *Prog. Brain Res.* **161** (2007) 185–194.
181. Vaishnav, R.A., Liu, R., Chapman, J., Roberts, A.M., Ye, H., Rebolledo-Mendez, J.D., Tabira, T., Fitzpatrick, A.H., Achiron, A., Running, M.P. & Friedland, R.P. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J. Neuroimmunol.* **260** (2013) 92–98.
182. Vojdani, A., Mukherjee, P.S., Berookhim, J. & Kharrazian, D. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Diseases* **2015** (2015) 905208.
183. Schneider, D., Liu, Y., Gerstein, M. & Engelman, D.M. Thermostability of membrane protein helix-helix interaction elucidated by statistical analysis. *FEBS Lett.* **523** (2002) 231–236.
184. Borgnia, M.J., Kozono, D., Calamita, G., Maloney, P.C. & Agre, P. Functional reconstitution and characterization of AqpZ, the *E. coli* water channel protein. *J. Molec. Biol.* **291** (1999) 1169–1179.
185. Ren, Z., Wang, Y., Duan, T., Patel, J., Liggett, T., Loda, E., Brahma, S., Goswami, R., Grouse, C., Byrne, R., Stefoski, D., Javed, A., Miller, S.D. & Balabanov, R. Cross-immunoreactivity between bacterial aquaporin-Z and human aquaporin-4: potential relevance to neuromyelitis optica. *J. Immunol.* **189** (2012) 4602–4611.
186. Tuomilehto, J. The emerging global epidemic of type 1 diabetes. *Current Diabetes Rep.* **13** (2013) 795–804.
187. Tettey, P., Simpson, S. Jr., Taylor, B.V. & van der Mei, I.A.F. The co-occurrence of multiple sclerosis and type 1 diabetes: Shared aetiologic features and clinical implication for MS aetiology. *J. Neurol. Sci.* **348** (2015) 126–131.
188. Dow, C.T. *Mycobacterium paratuberculosis* and autism: is this a trigger? *Med. Hypotheses* **77** (2011) 977–981.
189. Naser, S.A., Thanigachalam, S., Dow, S.T. & Collins, M.T. Exploring the role of *Mycobacterium avium* subspecies *paratuberculosis* in the pathogenesis of type 1 diabetes mellitus: a pilot study. *Gut Pathogens* **5** (2013) 14.
190. Capitani, G., De Biase, D., Gut, H., Ahmed, S. & Grutter, M.G. Structural model of human GAD65: prediction and interpretation of biochemical and immunogenic features. *Proteins* **59** (2005) 7–14.
191. Karjalainen, J., Martin, J.M., Knip, M., Ilonen, J., Robinson, B.H., Savilahti, E., Akerblom, H.K. & Dosch, H.M. A bovine albumin peptide as a possible trigger of insulin-dependent diabetes mellitus. *N. Engl. J. Med.* **327** (1992) 302–307.
192. Parrini, C., Taddei, N., Ramazzotti, M., Degl’Innocenti, D., Ramponi, G., Dobson, C.M. & Chiti, F. Glycine residues appear to be evolutionarily conserved for their ability to inhibit aggregation. *Structure* **13** (2005) 1143–1151.
193. Nolan, C., Margoliash, E., Peterson, J.D. & Steiner, D.F. The structure of bovine proinsulin. *J. Biol. Chem.* **246** (1971) 2780–2795.
194. Green, J.M. & Castle, L.A. Transitioning from single to multiple herbicide-resistant crops. In: *Glyphosate Resistance in Crops and Weeds: History, Development, and Management* (ed. V.K. Nandula), ch. 4, p. 112. Wiley (2010).
195. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. *Interdisciplinary Toxicol.* **6** (2013) 159–184.

196. Janssen, G., Christis, C., Kooy-Winkelaar, Y., Edens, L., Smith, D., van Veelen, P. & Koning, F. Ineffective degradation of immunogenic gluten epitopes by currently available digestive enzyme supplements. *PLoS ONE* **10** (2015) e0128065.
197. Todd, J.A., Bell, J. & McDevitt, H.O. HLA-DQ beta gene contributes to susceptibility and resistance to insulin-dependent diabetes mellitus. *Nature* **329** (1987) 599–604.
198. Hogberg, L., Falth-Magnusson, K. & Grodzinsky, E. Familial prevalence of coeliac disease: a twenty-year follow-up study. *Scand. J. Gastroenterol.* **38** (2003) 61–65.
199. Li, X., Lou, Z., Li, X., Zhou, W., Ma, M., Cao, Y., Geng, Y., Bartlam, M., Zhang, X.C. & Rao, Z. Structure of human cytosolic X-prolyl aminopeptidase: a double Mn(II)-dependent dimeric enzyme with a novel three-domain subunit. *J. Biol. Chem.* **283** (2008) 22858–22866.
200. Rubio, F., Veldhuis, L.J., Clegg, S., Fleeker, J.R., & Hall, J.C. Comparison of a direct ELISA and an HPLC method for glyphosate determinations in water. *J. Agric. Food Chem.* **51** (2003) 691–696.
201. Jenkins, D.H., Grapenthien, N. & Keplinger, M.L. Milk and tissue residue study with N-phosphonomethylglycine (CP 67573) (unpublished study) prepared by Industrial Biotest Laboratories, Inc., submitted by Monsanto to US EPA, Washington, DC EPA MRID #0178 06004) (16 October 1973).

← VaccineResearch

This is all of the research I have collected on vaccinations. ALL OF THESE STUDIES ARE PUBLISHED, LEGITIMATE STUDIES ON PUBMED which is a government database.

Vaccines and Autism

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3878266/>
<http://www.ncbi.nlm.nih.gov/pubmed/21623535>
<http://www.ncbi.nlm.nih.gov/pubmed/25377033>
<http://www.ncbi.nlm.nih.gov/pubmed/24995277>
<http://www.ncbi.nlm.nih.gov/pubmed/12145534>
<http://www.ncbi.nlm.nih.gov/pubmed/21058170>
<http://www.ncbi.nlm.nih.gov/pubmed/22099159>
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3364648/>
<http://www.ncbi.nlm.nih.gov/pubmed/17454560>
<http://www.ncbi.nlm.nih.gov/pubmed/19106436>
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3774468/>
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3697751/>
<http://www.ncbi.nlm.nih.gov/pubmed/21299355>
<http://www.ncbi.nlm.nih.gov/pubmed/21907498>
<http://www.ncbi.nlm.nih.gov/pubmed/11339848>
<http://www.ncbi.nlm.nih.gov/pubmed/17674242>
<http://www.ncbi.nlm.nih.gov/pubmed/21993250>
<http://www.ncbi.nlm.nih.gov/pubmed/15780490>
<http://www.ncbi.nlm.nih.gov/pubmed/12933322>
<http://www.ncbi.nlm.nih.gov/pubmed/16870260>
<http://www.ncbi.nlm.nih.gov/pubmed/19043938>
<http://www.ncbi.nlm.nih.gov/pubmed/12142947>
<http://www.ncbi.nlm.nih.gov/pubmed/24675092>

Causal relationship between vaccine induced immunity and autism

<http://www.ncbi.nlm.nih.gov/pubmed/12849883>

Subtle DNA changes and the overuse of vaccines in autism

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3364648/>

Vaccine and Autism- a New Scientific Review

<http://www.cbsnews.com/news/vaccines-and-autism-a-new-scientific-review/>

Summary of previous Journal of Immunology

<http://danmurphydc.com/wordpress/wp-content/uploads/2011/01/AR-10-12-rata-AUTISM-VACCINE.pdf>

Autism and Resulting Medical Conditions:

<http://www.tacanow.org/wp-content/uploads/2011/09/autism-studies-april-2008.pdf> .

Mercury toxic encephalopathy manifesting with clinical symptoms of regressive autistic

sorders. <http://www.ncbi.nlm.nih.gov/pubmed/17454560>

Relation of mercury to high autism rates in boys

<http://www.ncbi.nlm.nih.gov/pubmed/16264412>

Elevated levels of measles in children with Autism

<http://www.ncbi.nlm.nih.gov/pubmed/12849883>

Abnormal MMR antibodies in children with autism

<http://www.ncbi.nlm.nih.gov/pubmed/12145534>

Tylenol, MMR and Autism - A parent survey study

<http://www.ncbi.nlm.nih.gov/pubmed/18445737>

A Positive Association found between Autism Prevalence and Childhood Vaccination

<http://www.ingentaconnect.com/content/tandf/uteh/2011/00000074/00000014/art00002?token=004c170388ee06a6e5865462431636f5720415d23763c247b5e4e26634a492f2530332976261>

Peer reviewed study on fetal cell contamination with retro virus associated with autism and cancer

<http://www.globalresearch.ca/new-study-in-journal-of-public-health-finds-autism-and-cancer-related-to-human-fetal-dna-in-vaccines/5402912>

Study documentation- Dr Deisher

http://www.ms.academicjournals.org/article/article1409245960_Deisher%20et%20al.pdf

Autism and mercury poisoning

<http://www.ncbi.nlm.nih.gov/pubmed/11339848>

Hypothesis: conjugate vaccines may predispose children to autism spectrum disorders

<http://www.ncbi.nlm.nih.gov/pubmed/21993250>

Rise in autism coincides with rise in vaccines

<http://www.ncbi.nlm.nih.gov/pubmed/21623535>

A two-phase study evaluating the relationship between Thimerosal-containing vaccine administration and the risk for an autism spectrum disorder diagnosis in the United States

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3878266/>

Elevated levels of measles antibodies in children with autism. - PubMed - NCBI

Pediatr Neurol. 2003 Apr;28(4):292-4. Research Support, Non-U.S. Gov't

[ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)

.....

A study published in the Journal of Biomedical Sciences determined that the autoimmunity to the central nervous system may play a causal role in autism. Researchers discovered that because many autistic children harbour elevated levels of measles antibodies, they should conduct a serological study of measles-mumps-rubella (MMR) and myelin basic protein (MBP) autoantibodies. They used serum samples of 125 autistic children and 92 controlled children. Their analysis showed a significant increase in the level of MMR antibodies in autistic children. The study concludes that the autistic children had an inappropriate or abnormal antibody response to MMR. The study determined that autism could be a result from an atypical measles infection that produces neurological symptoms in some children. The source of this virus could be a variant of MV or it could be the MMR vaccine.

SOURCE OF THIS VIRUS COULD BE A VARIANT OF HIV, OR IT COULD BE THE HIVVAX VACCINE.

<http://www.ncbi.nlm.nih.gov/pubmed/12145534>

IMPORTANT-

- Package inserts:

<http://www.immunize.org/fda/>

- Ingredients:

<https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

- Supreme Court declares vaccines unavoidably unsafe:

<https://www.supremecourt.gov/opinions/10pdf/09-152.pdf>

- National Childhood Vaccine Injury Act legislation (renders manufactures 100% of any & all liability):

<https://www.congress.gov/bill/99th-congress/house-bill/5546>

- VAERS:

<https://vaers.hhs.gov/index>

- National Compensation Court website (note the \$3 billion paid out comes from tax payers):

<https://www.hrsa.gov/vaccinecompensation/data/>

- Detox baths:

<https://www.howhesraised.net/2016/11/the-beginners-guide-to-detox-baths-for-kids/>

- Vaccine requirements for work/school by state:

<http://www.nvic.org/Vaccine-Laws/state-vaccine-requirements.aspx>

- Vit K package insert:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2003/012223Orig1s039Lbl.pdf

- People who should not be vaccinated:

<https://www.thefamilythathealstogether.com/vaccine-contraindications-six-people-not-vaccinated/>

- Lawsuit determines that federally required safety studies have not been performed in 30 years:

<http://icandecide.org/government/ICAN-HHS-Stipulated-Order-July-2018.pdf>

Fetal Cells & Vaccine Contaminates-

- Fetal cells:

<http://vaccineimpact.com/2015/new-fetal-cell-line-from-live-abortion-emerges-for-vaccine-production/>

- More on fetal cells:

https://m.facebook.com/story.php?story_fbid=396109597402989&id=272455363101747

- 20%-36% of cell lines scientists are using are contaminated or misidentified:

<https://www.statnews.com/2016/07/21/studies-wrong-cells/>

- Still going to vaccinate? Let's hope that you are getting real vaccines -- not alcohol & cat saliva!

:

<http://www.wandtv.com/story/33272117/doctor-concocts-his-own-vaccines-with-cat-saliva-state-says>

- SV40 cancer virus that infected 98 million Americans in the polio vaccine:

<http://www.sv40foundation.org>

- Development of vaccines from aborted fetuses:

<https://cogforlife.org/wp-content/uploads/2012/04/farnsworthvaccines.pdf>

- DNA mutations from fetal cell lines in vaccines:
<http://soundchoice.org/research/>
- WALVAX2 (fetal cells):
<https://www.ncbi.nlm.nih.gov/m/pubmed/25803132/>
- Ethics behind WALVAX2:
<http://ethicalresearch.net/positions/the-ethics-of-the-walvax-2-cell-strain/>
- PBS on how vital fetal cells are for vaccine development:
<https://www.pbs.org/newshour/health/medical-researchers-say-fetal-tissue-remains-essential>

Vaccine Failure & Shedding-

- Mumps outbreak -- all vaccinated:
http://m.huffpost.com/us/entry/us_57276bc7e4b0b49df6abc402
- Measles outbreak in a fully immunized school:
<http://www.ncbi.nlm.nih.gov/pubmed/3821823>
- Measles outbreak among the vaccinated:
<http://www.ncbi.nlm.nih.gov/pubmed/8053748>
- New York measles outbreak linked to vaccinated:
<http://cid.oxfordjournals.org/content/early/2014/02/27/cid.ciu105>
- Vaccinated child responsible for measles outbreak in British Columbia:
<http://www.eurosurveillance.org/images/dynamic/EE/18N49/art20649.pdf>
- Mumps outbreak in Netherlands linked to those vaccinated:
http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article
- Vaccinated student in Cali diagnosed with mumps:
<http://www.nbcsandiego.com/on-air/as-seen-on/Cal-State-San-Marcos-Student-Diagnosed-With-Mumps-395189031.html>
 - What's shedding? :
<http://insidevaccines.com/wordpress/2008/02/24/secondary-transmission-%EF%BB%BFthe-short-and-sweet-about-live-virus-vaccine-shedding/comment-page-1/>
- 98% vaccinated in pertussis outbreak:
<http://www.activistpost.com/2015/02/98-vaccinated-involved-in-whooping.html>
- Vaccine-related polio outbreak in Syria 2017:
<https://www.statnews.com/2017/06/08/polio-outbreak-syria-who/>
- More vaccine failure -- pertussis outbreak in vaccinated children:
<https://wwwnc.cdc.gov/eid/article/22/2/pdfs/15-0325.pdf>
- Pertussis outbreak in San Diego -- 621 people & 85% were vaccinated -- MORE vaccine failure:
<http://www.kpbs.org/news/2014/jun/12/immunized-people-getting-whooping-cough/>
- Largest measles epidemic in North America in the last decade occurred in 2011 in Quebec where 1 & 2 dose vaccine coverage among children 3 years of age were 95%-97%:
<http://www.ncbi.nlm.nih.gov/m/pubmed/23264672/>
- Hib outbreak -- 363/443 (82%) were vaccinated:
<http://jid.oxfordjournals.org/content/188/4/481.full>
- The Emerging risks of live virus & virus vectored vaccines:
<http://www.nvic.org/CMSTemplates/NVIC/pdf/Live-Virus-Vaccines-and-Vaccine-Shedding.pdf>
- What's shedding? :

<http://insidevaccines.com/wordpress/2008/02/24/secondary-transmission-%EF%BB%BFthe-short-and-sweet-about-live-virus-vaccine-shedding/comment-page-1/>

- Small Pox vaccine sheds to infant from parent (military personnel):

<http://mobile.reuters.com/article/idUSN1744524120070518>

- Everyone infected in this whooping cough outbreak was up to date on vaccinations:

<http://fox13now.com/2015/03/27/19-kids-in-summit-co-diagnosed-with-whooping-cough-despite-being-up-to-date-on-vaccinations/>

- & this outbreak too:

<http://myfox8.com/2015/12/18/13-cases-of-whooping-cough-confirmed-in-davie-county-schools/>

- Even the CDC suggests that the vaccinated are an asymptomatic reservoir for infection:

http://wwwnc.cdc.gov/eid/article/6/5/00-0512_article

- Mumps outbreak in Netherlands linked to those vaccinated with the MMR twice:

http://wwwnc.cdc.gov/eid/article/20/4/13-1681_article

- Pertussis outbreak in California -

"Our unvaccinated & undervaccinated population did not appear to contribute significantly to the increased rate of clinical pertussis. Surprisingly, the highest incidence of disease was among previously vaccinated children aged 8–12 years.":

<http://m.cid.oxfordjournals.org/content/54/12/1730.long?view=long&pmid=22423127>

- Measles outbreak in a fully immunized population:

<http://www.ncbi.nlm.nih.gov/pubmed/3821823>

- 49% of children vaccinated STILL got pertussis:

<https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2016-provisional.pdf>

- You may be surprised to learn that fully vaccinated children & adults can still be infected, paralyzed & transmit polio. Here are two cases in particular that may grab your interest-

- "Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children" :

<http://www.popline.org/node/315407#.dpuf>

- "Oral polio vaccine-associated paralysis in a child despite previous immunization with inactivated vaccine." :

<http://www.virology.ws/2014/10/08/oral-polio-vaccine-associated-paralysis-in-a-child-despite-previous-immunization-with-inactivated-virus/>

- Mutant strains of polio vaccine now causing more paralysis than wild polio:

<https://www.npr.org/sections/goatsandsoda/2017/06/28/534403083/mutant-strains-of-polio-vaccine-now-cause-more-paralysis-than-wild-polio>

- Polio vaccine causing polio again:

<https://www.cnn.com/2018/06/26/health/polio-papua-new-guinea-bn/index.html>

- Polio vaccine contaminated with HFM virus:

<https://healthfreedomidaho.org/polio-vaccine-sheds-hfmd>

Stories-

- Healthy babies don't just die:

https://m.facebook.com/story.php?story_fbid=415927885421160&id=272455363101747

- Triplets vaccine injury story:

<https://www.facebook.com/wearevaxxed/videos/354597028220913/>

- Vaccines killed her son:
https://m.facebook.com/story.php?story_fbid=489700951377186&id=272455363101747
- A-Z injury stories:
<http://www.followingvaccinations.com/home>
- Her daughter was killed by her 1 y vaccines:
https://m.facebook.com/story.php?story_fbid=483522525328362&id=272455363101747
- The story of Nikie's daughter (be prepared to cry):
https://www.facebook.com/story.php?story_fbid=10209935263716989&id=1196380373
- Colton's story:
<https://m.youtube.com/watch?v=CHYmb9Hwj4A&feature=share>
- Mom accused of shaking her baby because he suffered from encephalitis due to the DPT vaccine <https://www.facebook.com/wearevaxxed/videos/505673969779884/>
- Jess's story:
<https://www.facebook.com/332186880241439/photos/a.332188263574634.1073741826.332186880241439/554864934640298/?type=3>
- Holly died after her kindergarten boosters:
<http://hopefromholly.com/blog/>
- Baby Ian's story - hep B reaction:
<http://www.iansvoice.org/>
- Baby Aniya was vaccine overdosed:
<https://www.gofundme.com/62bev-raising-money-for-aniyas-injustice>
- \$101 million dollar settlement for an infant that suffered a severe reaction to MMR:
<https://www.mctlawyers.com/101-million-dollar-vaccine-injury-mmr/>
- Two, one year olds die immediately after MMR:
<https://www.msn.com/en-nz/news/world/samoa-recalls-vaccines-after-child-deaths/ar-AAzOvrF?ocid=spartanntp>
- Krystle's 13.5 month old son passed away the day he received his flu vaccine:
<https://www.facebook.com/wearevaxxed/videos/489700951377186/>

SIDS-

- Infanrix lists SIDS as an adverse reaction. Page 12, line 250:
<https://www.fda.gov/downloads/biologicsbloodvaccines/vaccines/approvedproducts/ucm124514.pdf>
- SIDS:
<https://truthkings.com/dirty-secret-behind-infant-mortality-united-states/#>
- Interesting as the doctor found many SIDS cases to have inflammation &/or infection in the inner ear... & the vaccine inserts I have read have listed "otitis media" (medical term for ear infection) as a possible adverse event:
<http://www.seattlechildrens.org/about/stories/listening-to-a-hunch/>
- Family compensated for SIDS of their 4 m/o son:
https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc?2013vv0611-73-0
- SIDS DID NOT EXIST BEFORE THE VACCINE PROGRAM STARTED-NOW THE US HAS THE HIGHEST INFANT MORTALITY RATE IN THE INDUSTRIALIZED WORLD TO GO WITH

THE HIGHEST INFANT MORTALITY RATE IN THE INDUSTRIALIZED WORLD TO GO WITH THE HIGHEST NUMBER OF VACCINES GIVEN!!!!

<http://thinktwice.com/sids.htm>

Adverse Reactions/Death-

- Deaths during Gardasil Trials - 1 in 733 participants in the vaccine trials died. Bottom of page 7 of insert:

<https://www.fda.gov/.../ApprovedProducts/UCM111263.pdf>

- 213 Women who took Gardasil Suffered Permanent Disability 2012:

<http://articles.mercola.com/.../hpv-vaccine-victim-sues...>

- "The only thing different about that day was that shot..." Did a trip to the doctor kill a healthy 12-year-old girl?:

<http://fox6now.com/.../the-only-thing-different-about.../>

- 150+ deaths reported to VAERS as of June 2017 (Gardasil):

<https://wonder.cdc.gov/controller/saved/D8/D17F338>

- Vaccine Injury Court Cases of Death caused by HPV vaccine:

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc...

- Shingles vaccine causes chicken pox, shingles, & eye injuries:

http://info.cmsri.org/the-driven-researcher-blog/merck-admits-shingles-vaccine-can-cause-eye-damage-and-shingles?utm_content=39146139&utm_medium=social&utm_source=facebook

- Fetal death & medical billing:

<https://www.facebook.com/wearevaxxed/videos/356795464667736/>

- VAERS records of 1,000+ babies under the age of 6 months that all died shortly after vaccinations. These are ONLY those 6 months & under. Sickening:

<http://www.medalerts.org/vaersdb/findfield.php?>

[EVENTS=on&PAGENO=2&PERPAGE=10&ESORT=NONE&REVERSEESORT=&LOWAGE=\(0\)&HIGHAGE=\(0.5\)&WhichAge=range&SYMPTOMS=\(Sudden_infant_death_syndrome_%2810042440%29\)](http://www.medalerts.org/vaersdb/findfield.php?EVENTS=on&PAGENO=2&PERPAGE=10&ESORT=NONE&REVERSEESORT=&LOWAGE=(0)&HIGHAGE=(0.5)&WhichAge=range&SYMPTOMS=(Sudden_infant_death_syndrome_%2810042440%29))

- Identifying vaccine damage:

<https://healthimpactnews.com/2015/dr-andrew-moulden-learning-to-identify-vaccine-damage/>

- VAERS received 29,747 reports after Hib vaccines -- 5179 (17%) were serious, including 896 reports of death:

<http://www.ncbi.nlm.nih.gov/pubmed/25598306>

- Make sure to report reactions:

<http://www.nvic.org/reportreaction.aspx>

- US court pays \$6 million to Gardasil victims:

<http://www.washingtontimes.com/.../us-court-pays-6.../>

- Gardasil & cervarix vaccine adverse reports:

<http://sanevax.org/vaers-report>

- Journal of Developing Drugs - food allergies & vaccines:

<http://www.omicsgroup.org/journals/evidence-that-food-proteins-in-vaccines-cause-the-development-of-foodallergies-and-its-implications-for-vaccine-policy-2329-6631-1000137.pdf>

- The AAP on "Eczema Vaccinatum" (aka vaccines cause eczema):

<http://pediatrics.aappublications.org/content/22/2/259>

- & another dead kid compensated:

https://ecf.cofc.uscourts.gov/cgi-bin/show_public_doc?2010vv0103-145-0

- 83 cases reviewed by lawyers:

<http://digitalcommons.pace.edu/cgi/viewcontent.cgi?article=1681&context=pehr>

- Measles deaths vs MMR deaths 2004-2015:

<http://vaccineimpact.com/2015/zero-u-s-measles-deaths-in-10-years-but-over-100-measles-vaccine-deaths-reported/>

- DTaP, Hib, & chicken pox vaccines all list otitis media or parotitis on their inserts. This is what causes ear infections. You can find the inserts here:

<http://www.immunize.org/fda/>

- 7 out of 8 of the individuals that died from the flu in California received their flu shot:

<https://healthfreedomidaho.org/7-of-the-8-individuals-who-died-of-flu-had-received-the-flu-shot>

- Hiding Vaccine-Related Deaths With Semantic Sleight-of-Hand:

<http://www.theepochtimes.com/n3/2271619-hiding-vaccine-related-deaths-with-semantic-sleight-of-hand/>

Other-

- Combating childhood disease naturally:

<http://healthyfamiliesforgod.com/2015/02/combating-childhood-diseases-naturally-vaccines/>

- Unvaxx vs vaxx survey:

<http://www.vaccineinjury.info/survey/results-unvaccinated/results-illnesses.html>

- Where to start your research:

<https://thinklovehealthy.com/2016/11/02/researching-vaccines-where-to-start/>

- 10 things I want parents that vaccinate to know:

<http://holisticlifemama.com/10-things-want-parents-vaccinate-kids-know/>

- eBook over sanitation:

<http://www.checktheevidence.com/pdf/pta%20vaccine%20book.pdf>

- Pediatricians get bonuses to push vaccines:

<https://wellnessandequality.com/2016/06/20/how-much-money-do-pediatricians-really-make-from-vaccines/>

- Does your doctor get incentives to push vaccines? Look them up:

<https://projects.propublica.org/docdollars/>

- Truth about the whooping cough:

<https://www.facebook.com/MyIncredibleOpinionWithForrestMaready/videos/1784935255163580/>

- Letter to legislators:

<http://thinkingmomsrevolution.com/an-open-letter-to-legislators-currently-considering-vaccine-legislation-from-tetyana-obukhanych-phd-in-immunology/>

- Do not sign the refusal form:

<https://parentsaganinstmandatoryvaccines.net/2015/08/18/do-not-sign-the-refusal-to-vaccinate-form/>

- My child survived the chicken pox 🧠:

<http://www.livingwhole.org/my-child-got-chicken-pox-and-survived/>

- CDC uses fear to push vaccines:

<http://www.thevaccinereaction.org/2017/04/how-cdc-uses-false-fears-to-promote-vaccine-uptake/>

- NICU & vaccines:

<http://ipaknowledge.org/nicu.php>

- AAP refuses to back claims with science:

<https://worldmercuryproject.org/news/american-academy-pediatrics-refuses-back-vaccine-claims-science/>

- Stop the hate:

<http://www.livingwhole.org/the-hate-debate/>

- Vaccine warranty:

<http://preventdisease.com/pdf/Warranty-of-Vaccine-Safety-English.pdf>

- Legal statement from the CDC scientist who admits to altering & omitting data to remove profound link between MMR & autism:

<http://morganverkamp.com/statement-of-william-w-thompson-ph-d-regarding-the-2004-article-examining-the-possibility-of-a-relationship-between-mmr-vaccine-and-autism/>

- Injection vs ingestion:

<https://livelovefruit.com/synergistic-toxicity-and-vaccine-safety/>

- Pertussis vaccine & pregnancy:

<http://kellybroganmd.com/pregnancy-friendly-protection-truth-about-whooping-cough-vaccine-pertussis/?>

utm_campaign=coschedule&utm_source=facebook_page&utm_medium=Kelly%20Brogan%20MD%20-%20Holistic%20Psychiatrist

- Polio wasn't vanquished -- it was redefined:

<http://www.thevaccinereaction.org/2015/07/polio-wasnt-vanquished-it-was-redefined/>

- Pertussis vaccine not very effective:

<https://academic.oup.com/cid/article/54/12/1730/452864/Unexpectedly-Limited-Durability-of-Immunity>

- Synagis (RSV shot):

<http://www.thehealthyhomeeconomist.com/the-scary-side-of-synagis/>

- WHO recommends vit A to treat the measles:

<http://www.who.int/mediacentre/factsheets/fs286/en/>

- Germany Supreme Court says the measles virus "does not exist":

<http://drsircus.com/general/mmr-vaccine-from-hell-court-rules-measles-is-not-caused-by-a-virus/>

- Dr. Suzanne Humphries recommends vit C for whooping cough:

<http://drsuzanne.net/2015/04/the-vitamin-c-treatment-of-whooping-cough-suzanne-humphries-md/>

- Lead Developer Of HPV Vaccines Comes Clean, Warns Parents & Young Girls It's All A Giant Deadly Scam (Dr Diane Harper):

<http://www.australiannationalreview.com/lead-developer.../>

- Japan pulled Gardasil from the schedule:

<http://www.tokyotimes.com/side-effects-in-young-girls.../>

- 2009 Spain halts batch of Merck's Gardasil:

<http://mobile.reuters.com/article/idUSLA56308620090210>

- Vaccines & ear infections:

<http://vaccineresistancemovement.org/?p=15234>

- You can't protect another person from pertussis:

<https://leviquackenboss.wordpress.com/2016/02/19/you-cant-protect-another-person-from-pertussis/>

- Vaccines violate the Christian faith:

<http://www.alabasterliving.com/blog/do-vaccines-violate-the-christian-faith>

<http://yournewswire.com/christian-bible-vaccines/>

<http://www.nevermindthem.com/opinion/biblical-reasons-not-to-vaccinate.asp>

<http://www.livingwhole.org/?s=God+does+not+support+vaccines>

- Yes, the CDC does recommend vaccinating but it also says that unmarried women are more likely to miscarry 🙄 :

https://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_08.pdf

- 12 CDC whistleblowers have come forward:

https://usrtk.org/wp-content/uploads/2016/10/CDC_SPIDER_Letter-1.pdf

- Vaccine safety:

<http://icandecide.com/white-papers/VaccineSafety-Version-1.0-October-2-2017.pdf>

- Number of flu deaths is inaccurate:

<http://www.bmj.com/content/331/7529/1412>

- Why you can't compare aluminum in breastmilk to aluminum in vaccines:

<https://thinklovehealthy.com/2017/07/28/why-you-cannot-compare-the-amount-of-aluminum-in-breastmilk-to-vaccines-2/>

- All this research above....your doctor knows it right? Probably not. Maybe in 17 years.:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1497798/>

- Letter to pregnant moms questioning vaccines:

<http://vaxtruth.org/2016/05/dear-pregnant-mom/>

- Health benefits of the measles:

<http://www.greenmedinfo.com/blog/unreported-health-benefits-measles>

- Vaccines - Unavoidably Unsafe:

<http://thinkingmomsrevolution.com/unavoidably-unsafe/>

- Sharing vaccine truths with loved ones:

<http://journeyboost.com/2016/12/30/7-essentials-for-sharing-vaccine-truth-with-loved-ones/>

- Smoke, mirrors, & the disappearance of polio:

<http://www.vaccinationcouncil.org/2011/11/17/smoke-mirrors-and-the-disappearance-of-polio/>

- 154 of the last 162 cases of polio in the US were caused BY the oral polio vaccine:

<https://www.cdc.gov/vaccines/pubs/pinkbook/polio.html>

- MORE THAN ONE HALF OF ALL AMERICAN CHILDREN ARE CHRONICALLY SICK:

<http://fearlessparent.org/americas-new-normal-chronically-ill-kids/>

- 1 in 6 have Neurological Damage:

<http://whale.to/vaccines/neurological.html>

- 50 Million Americans are being slowly killed by Autoimmune Diseases that didn't exist before the vaccine program started:

<https://vaccineimpact.com/2012/autoimmune-disorders-caused-by-vaccines/>

- 30 million children have deadly food allergies that didn't exist before the vaccine program started:

<https://therefusers.com/vaccines-cause-allergies-dr-dave-mihalovic/>

- ONE HALF OF ALL AMERICANS WILL GET CANCER IN THEIR LIFETIME AND IT'S THE LEADING KILLER OF CHILDREN UNDER 18 (1 in 100,000 got it before the vaccine program

started.):

<https://www.medscape.com/viewarticle/551998>

● AT THE CURRENT TRAJECTORY, By 2025 ONE HALF OF all VACCINATED American kids will have a brain injury so profound they will never be able to speak, get out of diapers, or live on their own. By 2032-80% OF ALL MALE CHILDREN WILL BE AFFECTED!:

<http://www.anh-usa.org/half-of-all-children-will-be-autistic-by-2025-warns-senior-research-scientist-at-mit/>

Other Resources-

● Stop Mandatory Vaccination:

<http://www.stopmandatoryvaccination.com/personal-choice/>

● Learn the Risk:

<http://www.learntherisk.org/studies/>

● Watch this series:

<https://go.thetruthaboutvaccines.com/>

● & these movies:

<http://vaxxedthemovie.com>

<https://m.youtube.com/watch?v=K1m3TjokVU4>

<http://www.boughtmovie.com>

<http://thehumanexperimentmovie.com>

● <https://www.infowars.com/search-page/>

Tylenol-

● Say no to Tylenol:

<http://naturopathicpediatrics.com/2013/07/15/just-say-no-to-tylenol-acetaminophen-causes-autism/>

● Tylenol depletes glutathione:

http://whale.to/vaccine/tylenol_depletes_glutathione.html

● Tylenol is NOT a pain reliever for infants:

<http://www.newbeginningsbirthcenter.com/tylenol-no-longer-deemed-a-pain-reliever-for-babies-and-toddlers/>

● Tylenol is not safe:

<http://reset.me/story/could-a-common-painkiller-cause-brain-inflammation-and-even-autism-in-children/>

● Tylenol depletes the body of glutathione (people with autism lack glutathione):

<http://m.huffpost.com/us/entry/530494>

● Why you should stop giving your kids Tylenol:

<https://www.livingwhole.org/why-you-should-stop-giving-your-kids-tylenol/>

● What is the blood brain barrier?:

<http://www.brainfacts.org/%E2%80%A6/articl%E2%80%A6/2014/blood-brain-barrier>

● Blood brain barrier maturity:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3314990/>

● What is glutathione?:

<http://www.essentialgsh.com/glutathione.html>

● Tylenol depletes glutathione which is needed to detox:

<http://www.whale.to/vaccine/tvlenol>

- Stop giving Tylenol before/after vaccines:

<http://www.cbsnews.com/news/study-avoid-tylenol-after-vaccinations/>

- Info on fevers:

<http://www.seattlechildrens.org/medical-conditions/symptom-index/fever/>

MTHFR-

- MTHFR gene:

<http://www.healthhomeandhappiness.com/folate-vs-folic-acid-mthfr-and-why-i-regret-taking-my-prenatal-vitamin.html>

- Private testing:

<https://www.drchad.net/mthfr-and-more-cheek-swab-genetic-test/> (they do not keep rights to your DNA & destroy your DNA after test is completed)

- <https://m.youtube.com/watch?sns=fb&v=Y3NKG4qtVWyk>

- <http://www.easytolovebut.com/?p=2782>

- <http://greensandgenes.blogspot.com/2012/11/mthfr-genetic-mutation-and-associated.html?m=1>

- <https://www.dietvsdisease.org/mthfr-c677t-a1298c-mutation/>

- <http://mthfr.net/l-methylfolate-methylfolate-5-mthf/2012/04/05/>

- <https://www.anabundantlife.com.au/mthfr-gene/>

- <https://www.anabundantlife.com.au/mthfr-test/>

- <https://www.psychologytoday.com/blog/the-integrationist/201409/genetic-mutation-can-affect-mental-physical-health>

- <https://www.anabundantlife.com.au/mthfr-folic-acid/>

- <http://honestlyadhd.com/MTHFR-magical/>

- <http://mthfr.net/nitrous-oxide-mthfr-trouble/2015/02/06/>

- <http://www.merrittwellness.com/mthfr-mistakes-assumptions-dangers-and-whats-true-about-mthfr/>

- <https://mthfrgenehealth.com/foods-bad-for-mthfr-poor-methylation/>

Herd Immunity

<http://www.vaccinationcouncil.org/2012/02/18/the-deadly-impossibility-of-herd-immunity-through-vaccination-by-dr-russell-blaylock/>

The term, 'herd immunity', was coined by researcher, A W Hedrich, after he'd studied the epidemiology of measles in USA between 1900-1931. His study published in the May, 1933 American Journal of Epidemiology concluded that when 68% of children younger than 15 yrs old had become immune to measles via infection, measles epidemics ceased. For several reasons, this natural, pre-vaccine herd immunity differed greatly from today's vaccine 'herd immunity'.^{1,2}

When immunity was derived from natural infection, a much smaller proportion of the population needed to become immune to show the herd effect; compare the 68% measles immunity required for natural herd immunity to the very high percentages of vaccine uptake deemed necessary for measles vaccine 'herd immunity'. In his 'Vaccine Safety Manual', Neil Z Miller cites research which concluded increasing vaccine uptake necessary for 'herd immunity' ranging from "70 to 80 percent of two year olds in inner cities" in 1991 to "'close to 100 percent coverage'...with a vaccine that is 90 to 98 percent effective." in 1997. Miller notes that, "When the measles vaccine was introduced in 1963, officials were confident that they could eradicate the disease by 1967."

Subsequently, new dates for eradication were pronounced as 1982, 2000 and 2010. Meanwhile, "In 1990, after examining 320 scientific works from around the world, 180 European medical doctors concluded that 'the eradication of measles...would today appear to be an unrealistic goal.'" And in 1984, Professor D. Levy of Johns Hopkins University had already "concluded that if current practices [of suppressing natural immunity] continue, by the year 2050 a large part of the population will be at risk and 'there could in theory be over 25,000 fatal cases of measles in the U.S.A.'"

Disease-conferred immunity usually lasted a lifetime. As each new generation of children contracted the infection, the immunity of those previously infected was renewed due to their continual cyclical re-exposure to the disease; except for newly-infected children and the few individuals who'd never had the disease or been exposed to it, the 'herd immunity' of the entire population was maintained at all times.

Vaccine 'herd immunity' is hit-and-miss; outbreaks of disease sometimes erupt in those who follow recommended vaccine schedules. If they do actually "immunize", vaccines provide only short-term immunity so, in an attempt to maintain 'herd immunity', health authorities hold 'cattle drives' to round up older members of the 'herd' for administration of booster shots. And on it goes, to the point that, now, it's recommended we accept cradle-to-grave shots of vaccine against pertussis, a disease which still persists after more than sixty years of widespread use of the vaccine.

Russell Blaylock, MD remarks, "One of the grand lies of the vaccine program is the concept of "herd immunity". In fact, vaccines for most Americans declined to non-protective levels within 5 to 10 years of the vaccines. This means that for the vast majority of Americans, as well as others in the developed world, herd immunity doesn't exist and hasn't for over 60 years."3

In the pre-vaccine era, newborns could receive antibodies against infectious diseases from their mothers who had themselves been infected as children and re-exposed to the diseases later in life. Today's babies born to mothers who were vaccinated and never exposed to these diseases do not receive these antibodies. In direct contrast to fear mongering disease "facts" and 'herd immunity' theories related by Public Health, most of today's babies are more vulnerable than babies of the pre-vaccine era.

References:

1. "Monthly estimates of the child population 'susceptible' to measles, 1900-1931, Baltimore, Maryland"; A W Hedrich; American Journal of Epidemiology; May 1933 – Oxford University Press.
2. 'Vaccine Safety Manual' by Neil Z Miller; New Atlantean Press; 2008, 2009; pg 152.
3. Ibid; pgs 16-17.

<https://www.facebook.com/axshlexy/posts/10154130529699126>

"Q: Doesn't herd immunity protect most people?

A: Herd immunity (or community immunity) is a situation in which, through vaccination or prior illness, a sufficient proportion of a population is immune to an infectious disease, making its spread from person to person unlikely. Even individuals not vaccinated (such as newborns and those with chronic illnesses) are typically protected because the disease has little opportunity to spread within their community. Since pertussis spreads so easily, vaccine protection decreases over time, and acellular pertussis vaccines may not prevent colonization (carrying the bacteria in your body without getting sick) or spread of the bacteria. we can't rely on herd immunity to protect people from pertussis "

systems, we currently rely on herd immunity to protect people from pertussis.
<<https://www.cdc.gov/pertussis/about/faqs.html#increasing>>

Questions to ask your doctor/ped regarding vaccinations:

Question-1: If measles vaccines confer measles immunity, then why do already-vaccinated children have anything to fear from a measles outbreak?

Question-2: If vaccines work so well, then why did Merck virologists file a False Claims Act with the U.S. government, describing the astonishing scientific fraud of how Merck faked its vaccine results to trick the FDA?

Question-3: If vaccines don't have any links to autism, then why did a top CDC scientist openly confess to the CDC committing scientific fraud by selectively omitting clinical trial data after the fact in order to obscure an existing link between vaccines and autism?

Question-4: If mercury is a neurotoxic chemical, then why is it still being injected into children and pregnant women via vaccines? Why does the vaccine industry refuse to remove all the mercury from vaccines in the interests of protecting children from mercury?

Question-5: If vaccines are so incredibly safe, then why does the vaccine industry need absolute legal immunity from all harm caused by its products?

Question-6: If vaccines work so well to prevent disease, then why do some vaccines (like the chickenpox vaccine) openly admit that they can cause the spread of chickenpox?

Question-7: If vaccines are so great for public health, then why do these historical public health charts show nearly all the declines in infectious disease taking place BEFORE vaccines arrived on the scene?

Question-8: If vaccines are perfectly safe, then why did at least 13 people recently die in Italy after being vaccinated?

Question-9: If vaccines are so trustworthy, then why did a pro-vaccine group in Africa recently discover — to its shock and horror — that vaccines being given to young African women were secretly laced with abortion chemicals?

Question-10: If vaccines are backed by solid science, then why do some vaccine inserts openly admit they are backed by no clinical trials?

Question-11: If vaccines are so safe, then why does this vaccine insert admit that the Gardasil vaccine causes “acute respiratory illness” in babies who consume the breast milk of mothers who have been vaccinated?

Question-12: If vaccines are so safe, then why does this Gardasil insert sheet admit that the vaccine causes “seizure-like activity, headache, fever, nausea and dizziness” and can even cause those injected with the vaccine to lose consciousness and fall, resulting in injury?

Question-13: If vaccines are backed by so much “science” then why do they frequently admit there really aren't any studies of the vaccine for the vast number of people who are often injected with it?

aren't any studies on the vaccine for the very groups of people who are often injected with it?

Question-14: If vaccines are so safe to give to pregnant women, then why do the vaccine insert sheets openly admit most of them have never been tested for safety in pregnant women? In fact, this vaccine admits "the effects of the vaccine in foetal development are unknown." Question-15: If vaccines are so safe to be injected into the bodies of children and pregnant women, then why do their own insert sheets readily admit they are manufactured with a cocktail of toxic chemical ingredients including "foetal bovine serum?" (The blood serum of aborted baby cows.)

Question-16: If vaccines achieve absolute immunity, then why are as many as 97 percent of children struck by infectious disease already vaccinated against that disease?

Question-17: If vaccines are totally safe and effective, then why did this five-year-old girl recently die from the very strain of flu she was just vaccinated against?

Question-18: If the mainstream media claims to report honest, unbiased information about vaccines, then why was there a total nationwide blackout on the news of the CDC whistle-blower admitting vaccines are linked to autism?

Doctors who explain clearly why vaccines aren't safe or effective.

1. Dr. Nancy Banks - <http://bit.ly/1lp0alm>
2. Dr. Russell Blaylock - <http://bit.ly/1BXxQZL>
3. Dr. Shiv Chopra - <http://bit.ly/1gdgh1s>
4. Dr. Sherri Tenpenny - <http://bit.ly/1MPVbjx>
5. Dr. Suzanne Humphries - <http://bit.ly/17sKDbf>
6. Dr. Larry Palevsky - <http://bit.ly/1LLEjf6>
7. Dr. Toni Bark - <http://bit.ly/1CYM9RB>
8. Dr. Andrew Wakefield - <http://bit.ly/1MuyNzo>
9. Dr. Meryl Nass - <http://bit.ly/1DGzJsc>
10. Dr. Raymond Obomsawin - <http://bit.ly/1G9ZXYI>
11. Dr. Ghislaine Lanctot - <http://bit.ly/1MrVeUL>
12. Dr. Robert Rowen - <http://bit.ly/1SIELeF>
13. Dr. David Ayoub - <http://bit.ly/1SIELve>
14. Dr. Boyd Haley PhD - <http://bit.ly/1KsdVby>
15. Dr. Rashid Buttar - <http://bit.ly/1gWOkL6>
16. Dr. Roby Mitchell - <http://bit.ly/1gdgEZU>
17. Dr. Ken Stoller - <http://bit.ly/1MPVqLI>
18. Dr. Mayer Eisenstein - <http://bit.ly/1LLEqHH>
19. Dr. Frank Engley, PhD - <http://bit.ly/1OHbLDI>
20. Dr. David Davis - <http://bit.ly/1gdgJwo>
21. Dr. Tetyana Obukhanych - <http://bit.ly/16Z7k6J>
22. Dr. Harold E Buttram - <http://bit.ly/1Kru6Df>
23. Dr. Kelly Brogan - <http://bit.ly/1D31pfQ>
24. Dr. RC Tent - <http://bit.ly/1MPVwmu>
25. Dr. Rebecca Carley - <http://bit.ly/K49F4d>
26. Dr. Andrew Moulden - <http://bit.ly/1fwzKJu>
27. Dr. Jack Wolfson - <http://bit.ly/1uufDLDA>

27. Dr. Jack Vonson - <http://bit.ly/1wU11vX>
 28. Dr. Michael Elice - <http://bit.ly/1KsdpKA>
 29. Dr. Terry Wahls - <http://bit.ly/1gWOBhd>
 30. Dr. Stephanie Seneff - <http://bit.ly/1OtWxAY>
 31. Dr. Paul Thomas - <http://bit.ly/1DpeXPf>
 32. Many doctors talking at once - <http://bit.ly/1MPVHOv>
 33. Dr. Richard Moskowitz - <http://bit.ly/1OtWG7D>
 34. Dr. Jane Orient - <http://bit.ly/1MXX7pb>
 35. Dr. Richard Deth - <http://bit.ly/1GQDL10>
 36. Dr. Lucija Tomljenovic - <http://bit.ly/1eqiPr5>
 37. Dr Chris Shaw - <http://bit.ly/1lIGiBp>
 38. Dr. Susan McCreadie - <http://bit.ly/1CqqN83>
 39. Dr. Mary Ann Block - <http://bit.ly/1OHcyUX>
 40. Dr. David Brownstein - <http://bit.ly/1EaHI9A>
 41. Dr. Jayne Donegan - <http://bit.ly/1wOk4Zz>
 42. Dr. Troy Ross - <http://bit.ly/1IIGINH>
 43. Dr. Philip Incao - <http://bit.ly/1ghE7sS>
 44. Dr. Joseph Mercola - <http://bit.ly/18dE38I>
 45. Dr. Jeff Bradstreet - <http://bit.ly/1MaX0cC>
 46. Dr. Robert Mendelson - <http://bit.ly/1JpAEQr>
 47. Dr Theresa Deisher <https://m.youtube.com/watch?feature=youtu.be&v=6Bc6WX33SuE>
 48. Dr. Sam Eggertsen-<https://m.youtube.com/watch?v=8LB-3xkeDAE>
- Hundreds more doctors testifying that vaccines aren't safe or effective, in these documentaries....
1. Vaccination - The Silent Epidemic - <http://bit.ly/1vvQJ2W>
 2. The Greater Good - <http://bit.ly/1icxh8j>
 3. Shots In The Dark - <http://bit.ly/1ObtC8h>
 4. Vaccination The Hidden Truth - <http://bit.ly/KEYDUh>
 5. Vaccine Nation - <http://bit.ly/1iKNvpU>
 6. Vaccination - The Truth About Vaccines - <http://bit.ly/1vlpwvU>
 7. Lethal Injection - <http://bit.ly/1URN7BJ>
 8. Bought - <http://bit.ly/1M7YSlr>
 9. Deadly Immunity - <http://bit.ly/1KUg64Z>
 10. Autism - Made in the USA - <http://bit.ly/1J8WQN5>
 11. Beyond Treason - <http://bit.ly/1B7kmvt>
 12. Trace Amounts - <http://bit.ly/1vAH3Hv>
 13. Why We Don't Vaccinate - <http://bit.ly/1KbXhuf>

Join Our Community

Email

SIGN UP

Yes, I understand that by completing this form I am agreeing to receive email messages from Dr. Northrup & can unsubscribe at any time. I agree to the Privacy Policy (/privacy-policy/) and Terms of Use (/terms-of-use).*

BOOKSTORE (HTTPS://WWW.DRNORTHROP.COM/CATEGORY/STORE-BOOKS/)

HEALTHSTORE (HTTPS://WWW.DRNORTHROP.COM/CATEGORY/STORE-

PRODUCTS/)

SHOP AMATA™ (HTTPS://WWW.AMATALIFE.COM)

Search



Does your Daughter Need the HPV Vaccine?

by Christiane Northrup, M.D.

As you may know, the first Human Papillomavirus (HPV) vaccine was released in 2006 along with a barrage of information from Merck and the FDA promoting the vaccination of young women ages 9–26. The media attention about the vaccine has raised concern in millions of women unnecessarily. Read on to learn about your risk of contracting cervical cancer from the virus. I also discuss why you'll want to think long and hard about immunizing your daughter for HPV.

Does Your Daughter Need the HPV Vaccine?

In 2006, Merck received FDA approval to market the first Human Papillomavirus (HPV) vaccine Gardasil, a genetically engineered vaccine that helps prevents four types of HPV viruses, including type

16 infection, one of the most common HPV type viruses implicated in cervical cancer. Other HPV vaccines are in the pipeline. With the approval of Gardasil, HPV and its link to cervical cancer was suddenly front page news around the world with a barrage of media ads marketing the vaccine heavily for women. The CDC quickly recommended vaccinating all women age 9–26 and even beyond. Overnight women with virtually no risk for cervical cancer (the vast majority) were suddenly made to feel vulnerable, thus creating a huge market for the vaccine.

Let me put the issue into much needed perspective. The risk of getting cervical cancer from HPV has been greatly overstated! Fifty to seventy-five percent of all people are exposed to HPV in their lifetimes. The virus clears spontaneously by the immune system within two years in over ninety percent of all women, posing no risk at all. Ho¹ Woodman² Nasiell³ Richart⁴ Though the vaccine undoubtedly has some value for some women, it is unnecessary, and may even be dangerous, to administer it to millions of girls and women in the United States.

The Numbers Speak for Themselves

There are an average of 9,710 new diagnoses of cervical cancer and 3,700 deaths from the disease in the United States each year, according to the CDC. Of these new cases, 70 percent are related to HPV. That's about 6,797 cases per year. Over fourteen types of HPV are associated with cervical cancer. Gardasil protects against the HPV strains that are implicated in about 90 percent of cervical cancers, not 100 percent. That further reduces the number of cases of cervical cancer that might potentially be prevented with a vaccine to just under 6,200. And the vast majority of these cases could be prevented with improved nutrition, safe sex, and the kind of screening and early treatment that is already in place!

The HPV vaccine media blitz has overshadowed the fact that the incidence of cervical cancer has already decreased dramatically through routine cervical screening with pap smears and HPV (DNA) testing. For example, the National Health Service of England reports that the incidence of invasive cervical cancer fell by 42 percent

between 1988 and 1997 in the U.K because of cervical cancer screening programs. The NHS reports that in 2000, there were 2,424 new cases of invasive cervical cancer, most of which are not fatal.

Abnormal Paps Are Common

Surveys suggest that about four percent of all pap smears will show an abnormality associated with HPV infection, which is known as atypical squamous cells of undetermined significance (ASCUS). Davey⁵ In the vast majority, further evaluation will fail to show any abnormality, and no further action is required. (This occurrence of “false positives” with Pap smears led to the development of the ThinPrep® Pap Test, which is more reliable but still not 100 percent accurate.) But five to ten percent of patients initially diagnosed with ASCUS actually have more worrisome cellular changes, known as high-grade, which must be followed closely and treated in some women. Manos⁶ Ascus⁷ The Department of Pathology, at the University of Alabama in Birmingham reviewed 39,661 pap and HPV tests from January 1, 2002 to December 31, 2003. Of these, 12 percent were diagnosed with ASCUS. High risk HPV (DNA) was detected in only 732 cases! Out of all of these, only six had persistent abnormal pap smears requiring repeat follow-up; five had evidence of cellular abnormalities; and four had low-grade cervical dysplasia or cellular changes associated with HPV. And only one had high-grade dysplasia, a more worrisome type of cellular change that is associated with a higher risk of actual cancer down the line if not treated.

The remaining patients all had negative pap smears. In other words, only a very small percentage of those with high risk HPV were found to have cervical abnormalities—which are not invasive cervical cancer and are treatable! Adams⁸

Vaccines Aren't Entirely Safe

According to the National Vaccine Information Centers (<http://www.nvic.org/>), “The FDA allowed Merck to use a potentially reactive aluminum containing placebo as a control for most trial participants, rather than a non-reactive saline solution placebo.” Merck⁹

Using a reactive placebo can artificially increase the appearance of safety of an experimental drug or vaccine in a clinical trial. Gardasil contains 225 mcg of aluminum and, although aluminum adjuvants have been used in vaccines for decades, they were never tested for safety in clinical trials. Merck and the FDA did not disclose how much aluminum was in the placebo 6.##food##

Whenever you vaccinate an individual, you're intervening with their immunity. And that's exactly what happened with Gardasil in the clinical trials. According to the Merck product insert, there was one case of juvenile arthritis, two cases of rheumatoid arthritis, five cases of arthritis, and one case of reactive arthritis out of 11,813 Gardasil recipients. There was also one case of lupus and two cases of arthritis out of the 9,701 patients who received the aluminum containing placebo. Investigators dismissed the total of 102 Gardasil and placebo-associated serious adverse events, including 17 deaths, that occurred during the clinical trials, claiming that they were unrelated. (It's also not clear how many girls received the Hepatitis B vaccine in addition to Gardasil. Giving a couple vaccines at the same time can increase the risk of adverse outcomes.)

Regardless, there were 102 adverse events in 21,514 women and children who received the vaccine or the aluminum containing placebo. This translates to 474 adverse events per 1 million people getting vaccinated. Conservatively speaking, that's 14,220 (474 x 30 million) adverse events expected if you were to give the vaccine as recommended to about 30 million women and girls—the approximate number of people in the target market for Gardasil. Is it worth it to make 14,220 girls and women sick in order to possibly prevent 6,200 cases of HPV-related cervical cancer?

The Bottom Line About HPV Vaccines

Remember, it is not HPV per se that causes the cancer. It's the immune system's inability to fight the virus that is the issue. The rapid, widespread, and unquestioning acceptance of the HPV vaccine as "the answer" to cervical cancer prevention speaks volumes about our cultural misunderstanding of the root causes of health and disease. On his deathbed, Louis Pasteur, the famous pioneer in the discovery of the role of germs in disease, said that Antoine

Beauchamp, his rival, was correct. It was not the germ itself that caused disease, it was the environment, which Beauchamp had claimed all along.

While it is certainly laudable to want to decrease the incidence of invasive cervical cancer even further, and while this vaccine may be useful for some high-risk women and girls, it is far too early to subject millions to yet another vaccine. Especially when there's so much we can do to shore up an individual's immunity safely and effectively. For a complete program on how to do this, read *Mother-Daughter Wisdom* (<http://www.hayhouse.com/mother-daughter-wisdom-paperback>)(Bantam, 2005).

Gardasil definitely isn't free. It's a staggering \$360 per person. It's administered in three shots, which must be given over six months. At this time, it doesn't even guarantee immunity for longer than five years.

Gardasil will not eliminate the need for routine pap smears. And whether or not a woman opts for the vaccine, she should still protect herself from getting a sexually transmitted disease by using condoms, abstaining from intercourse, being discerning about her sexual partners, and also making sure her diet is rich in antioxidant nutrients that help her resist infections of all kinds.

Rather than relying solely on mass immunization programs that treat everyone as though they are at equal risk (which clearly isn't the case), and which also promote the myth of universal vulnerability, it is far more prudent to optimize a woman's nutrition and lifestyle so that her immune system is functioning optimally in the first place. This is especially true if she is one of the few who don't clear HPV rapidly and spontaneously.

Moreover, if a woman has a persistent HPV infection, she has a problem with her immune system. The bottom line is: The depression of her immune system is what's putting her at increased risk for cervical cancer. So while a vaccine might prevent cancer in one location, disease will manifest in another area if the root cause isn't addressed. This is done by looking at a woman's entire life—body, mind, and spirit.

Money Talks

So who really benefits by vaccinating approximately 30 million girls and women with a vaccine that costs about \$360? Industry analysts point out that mandating the HPV vaccine for virtually all girls and women will make Gardasil the blockbuster that Merck needs to boost profits since it was forced to withdraw its arthritis drug Vioxx. I certainly agree. It is no secret that medical schools, researchers, the CDC, and even the FDA itself are increasingly controlled by drug company profits. So is the mainstream media. To learn the facts about this, I recommend the documentary film *Money Talks: Profits before Patient Safety* (<http://www.moneytalksthemovie.com/>).

Learn More — Additional Resources

- *Mother-Daughter Wisdom*
(<http://www.hayhouse.com/mother-daughter-wisdom-paperback>), by Christiane Northrup, M.D.
- *Money Talks: Profits before Patient Safety*
(<http://www.moneytalksthemovie.com>)

References

1. Ho, G.Y., Bierman R., Beardsley, L., et. al., 1998. Natural history of cervicovaginal papillomavirus infection in young women, *N Engl J Med*, 338:423-428.
2. Woodman, C.B., Collins, S., Winter, H., et. al., 2001. Natural history of cervical human papillomavirus infection in young women: a longitudinal cohort study, *Lancet*, 357:1831-1836.
3. Nasiell, K., Nasiell, M., Vaclavinkova, V., 1983. Behavior of moderate cervical dysplasia during long-term follow-up, *Obstet Gynecol*, 61:609-614.
4. Richart, R.M., Barron, B.A., 1969. A follow-up study of patients with cervical dysplasia, *Am J Obstet Gynecol*, 105:386-393.
5. Davey, D.D., et. al., 2004. Implementation and reporting rates: 2003 practices of participants in the College of American Pathologists Interlaboratory Comparison Program in Cervicovaginal Cytology. *Arch Pathol Lab Med*. 128:1224-1229.

Last Updated: September 5, 2008



([//www.pinterest.com/pin/create/button/](http://www.pinterest.com/pin/create/button/))



(<https://www.drnorthrup.com/the-hpv-vaccine-what-you-need-to-know-today/>)

The HPV Vaccine: What You Need to Know Today

(<https://www.drnorthrup.com/the-hpv-vaccine-what-you-need-to-know-today/>)

August 1, 2013
In "Culture"



(<https://www.drnorthrup.com/be-one-less-to-get-gardasil-vaccine/>)

Be One Less...to Get the Gardasil Vaccine

(<https://www.drnorthrup.com/be-one-less-to-get-gardasil-vaccine/>)

June 16, 2009
In "Holistic Self-Care"



(<https://www.drnorthrup.com/help-for-gardasil-side-effects/>)

Help For Gardasil Side Effects

(<https://www.drnorthrup.com/help-for-gardasil-side-effects/>)

August 17, 2009
In "Holistic Self-Care"



Christiane Northrup, M.D.
(<https://www.drnorthrup.com/about>)

Christiane Northrup, M.D., is a visionary pioneer and a leading authority in the field of women's health and wellness. Recognizing the unity of body, mind, and spirit, she empowers women to trust their inner wisdom, their connection with Source, and their ability to truly flourish.

The contents of this website are for informational purposes only and are not a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your physician or other qualified health care provider with any questions you have regarding a medical condition, and before undertaking any diet, dietary supplement, exercise, or other health program. Your use of and/or visitation to the Web site signifies your agreement to CNI's Terms of Use ([/terms-of-use](#)) and CNI's Privacy Policy ([/privacy-policy](#)).





CLINICAL

▶ springer.com

Clin Rheumatol. 2015; 34(7): 1225–1231.

PMCID: PMC4475239

Published online 2014 Dec 23. doi: [10.1007/s10067-014-2846-1](https://doi.org/10.1007/s10067-014-2846-1)PMID: [25535199](https://pubmed.ncbi.nlm.nih.gov/25535199/)

A case-control study of quadrivalent human papillomavirus vaccine-associated autoimmune adverse events

David A. Geier and Mark R. Geier[✉]

Institute of Chronic Illnesses, Inc, 14 Redgate Ct, Silver Spring, MD 20905 USA

Mark R. Geier, Phone: (301)989-0548, Email: mgeier@comcast.net.[✉]Corresponding author.

Received 2014 Oct 8; Revised 2014 Dec 6; Accepted 2014 Dec 8.

Copyright © The Author(s) 2014

Open Access This article is distributed under the terms of the Creative Commons Attribution License which permits any use, distribution, and reproduction in any medium, provided the original author(s) and the source are credited.

Abstract

GARDASIL (Merck & Co., Inc., Whitehouse Station, NJ, USA) is a quadrivalent human papillomavirus (HPV4) vaccine. An epidemiological study was undertaken to evaluate concerns about the potential for HPV4 vaccination to induce serious autoimmune adverse events (SAAEs). The vaccine adverse event reporting system (VAERS) database was examined for adverse event reports associated with vaccines administered from January 2006 through December 2012 to recipients between 18 and 39 years old with a listed residence in the USA and a specified female gender. It was observed that cases with the SAAE outcomes of gastroenteritis (odds ratio (OR) = 4.6, 95 % confidence interval (CI) = 1.3–18.5), arthritis (OR = 2.5, 95 % CI = 1.4–4.3), systemic lupus erythematosus (OR = 5.3, 95 % CI = 1.5–20.5), vasculitis (OR = 4, 95 % CI = 1.01–16.4), alopecia (OR = 8.3, 95 % CI = 4.5–15.9), or CNS conditions (OR = 1.8, 95 % CI = 1.04–2.9) were significantly more likely than controls to have received HPV4 vaccine (median onset of SAAE symptoms from 6 to 55 days post-HPV4 vaccination). Cases with the outcomes of Guillain-Barre syndrome (OR = 0.75, 95 % CI = 0.42–1.3) or thrombocytopenia (OR = 1.3, 95 % CI = 0.48–3.5) were no more likely than controls to have received HPV4 vaccine. Cases with the general health outcomes of infection (OR = 0.72, 95 % CI = 0.27–1.7), conjunctivitis (OR = 0.88, 95 % CI = 0.29–2.7), or diarrhea (OR = 1.01, 95 % CI = 0.83–1.22) were no more likely than controls to have received HPV4 vaccine. Previous case series of SAAEs and biological plausibility support the observed results. Additional studies should be conducted to further evaluate the potential biological mechanisms involved in HPV4 vaccine-associated SAAEs in animal model systems, and to examine the potential epidemiological relationship between HPV4 vaccine-associated SAAEs in other databases and populations.

Keywords: Adverse reaction, Autoimmunity, SLE, Vaccination

Introduction

GARDASIL (Merck & Co., Inc., Whitehouse Station, NJ, USA) is a quadrivalent human papillomavirus (HPV4) vaccine prepared from the purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV types 6, 11, 16, and 18 [1]. The L1 proteins are produced by separate fermentations in recombinant *Saccharomyces cerevisiae* and self-assembled into VLPs. The fermentation process involves growth of *S. cerevisiae* on chemically defined fermentation media which include vitamins, amino acids, mineral salts, and carbohydrates. The VLPs are released from the yeast cells by cell disruption and purified by a series of chemical and physical methods. The purified VLPs are adsorbed on preformed aluminum-containing adjuvant (amorphous aluminum hydroxyphosphate sulfate). The HPV4 vaccine is a sterile liquid suspension that is prepared by combining the adsorbed VLPs of each HPV type and additional amounts of the aluminum-containing adjuvant and the final purification buffer. HPV4 is a sterile suspension for intramuscular administration. Each 0.5 mL dose contains approximately 20 µg of HPV 6 L1 protein, 40 µg of HPV 11 L1 protein, 40 µg of HPV 16 L1 protein, and 20 µg of HPV 18 L1 protein. Each 0.5 mL dose of the vaccine contains approximately 225 µg of aluminum, 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 µg of polysorbate 80, 35 µg of sodium borate, <7 µg yeast protein, and water for injection. The product does not contain a preservative or antibiotics. In June 2006, the US Food and Drug Administration (FDA) approved a regimen of three HPV4 injections given over 6 months to women between the ages of 9 and 26 years of age and the advisory committee on immunization practices (ACIP) subsequently recommended routine HPV4 vaccination for girls who are 11–12 years old [2].

It was previously described that the etiology of autoimmune diseases is still not completely clear but genetic, immunological, hormonal, and environmental factors are considered to be important triggers [3]. Most often, autoimmunity is not followed by clinical symptoms unless an additional event such as an environmental factor favors overt expression. Many environmental factors are known to affect the immune system and may play a role as triggers of the autoimmune mosaic, such as bacterial, viral, and parasitic infections. These are known to induce and exacerbate autoimmune diseases, mainly by the mechanism of molecular mimicry. The question of a connection between vaccination and autoimmune illness has long been debated in the literature and is surrounded by controversy [4], but it was suggested that the same mechanisms that act in infectious invasion of the host apply equally to the host response to vaccination [3]. As recently reviewed [5], the introduction of HPV vaccine was associated with several cases of onset or exacerbations of autoimmune diseases following immunization in the literature and pharmacovigilance databases, triggering concerns about its safety. The purpose of the present study was to conduct an epidemiological study of the vaccine adverse event reporting system (VAERS) to evaluate concerns about the potential for HPV4 vaccination to induce serious autoimmune adverse events (SAAEs).

Materials and methods

The VAERS is an epidemiological database that has been maintained jointly by the US Centers for Disease Control and Prevention (CDC) and FDA since 1990 as a surveillance tool to evaluate vaccine safety. Specific adverse events following vaccination are required to be reported to this database as

mandated by law, but other adverse events that occur following vaccine administration are passively reported to VAERS. The VAERS Working Group of the CDC has previously acknowledged that less than 5 % of the total adverse events reported to VAERS are reported by parents. Specific serious adverse events and deaths reported to VAERS are followed-up by the CDC/FDA. The VAERS Working Group of the CDC and the FDA have repeatedly analyzed and published epidemiologic studies based upon VAERS [6, 7].

The VAERS Working Group notes that VAERS is simple to use, flexible by design, and the data are available in a timely fashion, but it also warns that the potential limitations may include systematic error due to underreporting, erroneous reporting, frequent multiple exposures, multiple outcomes, and lack of precise denominators. In addition, when evaluating data from VAERS, it is important to note that, for any reported event, no cause and effect relationship has been established. VAERS is interested in all potential associations between vaccines and adverse events. Therefore, VAERS collects information on any adverse event following vaccination reported by an individual associating the adverse event with vaccination, be it coincidental or truly caused by a vaccine [6, 7].

Determining the population at risk

An analysis of the VAERS updated through February 2014 was undertaken using the CDC Wonder online computer interface (<http://wonder.cdc.gov/vaers.html>) and MedAlerts online computer interface (<http://www.medalerts.org/vaersdb/index.php>). These portals provide a direct method for independent investigators to rapidly analyze up-to-date data in VAERS. Adverse event reports associated with vaccines administered from January 2006 through December 2012 to recipients between 18 and 39 years old with a listed residence in the USA and a specified female gender were used to identify cases and controls in the present study. Overall, a total of 22,011 adverse event reports in females were examined in the present study, and these adverse event reports were reported to VAERS following administration of HPV4 or any other vaccine(s).

Determining cases

The SAAE cases were selected from the 22,011 total adverse event reports in females examined in the present study and were defined with outcomes specified as gastroenteritis (VAERS code: 10017888), arthritis (VAERS codes: 10003246 or 10039073), Guillain-Barre syndrome (VAERS code: 10018767), thrombocytopenia (VAERS codes: 10043554 or 10043561), systemic lupus erythematosus (VAERS code: 10042945), vasculitis (VAERS code: 10047115), alopecia (VAERS code: 10001760), and central nervous system (CNS) conditions (VAERS codes: 10028245 or 10012305 or 10030942 or 10028524 or 10028527). In addition, general health outcome cases were selected from the 22,011 total adverse event reports in females examined in the present study and were defined with outcomes specified as infection (VAERS code: 10021789), conjunctivitis (VAERS code: 10010741), and diarrhea (VAERS code: 10012735). Table 1 summarizes the total number of cases for each type of outcome examined in VAERS.

Table 1

A summary of various types of cases and controls examined in the present study

Outcome examined (VAERS code)	Number
Serious autoimmune adverse events:	
Gastroenteritis cases (10017888)	12
Controls	21,999
Arthritis (10003246 or 10039073)	56
Controls	21,955
Guillain-Barre syndrome (10018767)	97
Controls	21,914
Thrombocytopenia (10043554 or 10043561)	24
Controls	21,987
Systemic lupus erythematosus (10042945)	13
Controls	21,998
Vasculitis (10047115)	11
Controls	22,000
Alopecia (10001760)	56
Controls	21,955
CNS conditions (10028245 or 10012305 or 10030942 or 10028524 or 10028527)	75
Controls	21,936
General health adverse events:	
Infection (10021789)	39
Controls	21,972
Conjunctivitis (10010741)	19
Controls	21,992

[Open in a separate window](#)

Determining controls

The controls were selected from the 22,011 total adverse event reports in females examined in the present study. The controls were selected for each type of case outcome examined by including only those adverse event reports that did not include the specific type of case outcome under study. [Table 1](#)

summarizes the total number of controls for each type of case outcome examined in VAERS.

Determining exposure

Exposure was determined in the present study based upon HPV4 vaccine administration (VAERS code: 1098). It was presumed that adverse event reports that included HPV4 vaccine were exposed and adverse event reports that did not include HPV4 vaccine were unexposed.

Statistical analyses

The Fisher's exact test contained in the StatsDirect (version 2.8.0) statistical software package was utilized for statistical analyses, and a two-sided p value <0.05 was considered to be statistically significant. The null hypothesis was that there would be no difference in exposure to HPV4 vaccine among cases and controls.

Results

Table 2 examines among cases with SAEs and controls the frequency of exposure to HPV4 vaccine administration in the VAERS database. It was observed that cases with the outcomes of gastroenteritis (odds ratio = 4.6), arthritis (odds ratio = 2.5), systemic lupus erythematosus (odds ratio = 5.3), vasculitis (odds ratio = 4), alopecia (odds ratio = 8.3), or CNS conditions (odds ratio = 1.8) were significantly more likely than controls to have received HPV4 vaccine. It was observed that cases with the outcomes of Guillain-Barre syndrome (odds ratio = 0.75) or thrombocytopenia (odds ratio = 1.3) were no more likely than controls to have received HPV4 vaccine.

Table 2

A summary of exposure to HPV4 vaccine exposure among SAAE cases and controls

Group examined	Number of cases (%)	Number of controls (%)	Odds ratio (95 % CI)	p value ¹
Gastroenteritis				
Exposed	7	5117	4.6 (1.3–18.5)	0.019
Unexposed	5	16,882		
Arthritis				
Exposed	24	5,100	2.5 (1.4–4.3)	0.0018
Unexposed	32	16,855		
Guillain-Barre syndrome				
Exposed	18	5106	0.75 (0.42–1.3)	0.33
Unexposed	79	16,808		
Thrombocytopenia				
Exposed	7	5,117	1.3 (0.48–3.5)	0.47
Unexposed	17	16,870		
Systemic lupus erythematosus				
Exposed	8	5116	5.3 (1.5–20.5)	0.007
Unexposed	5	16,882		
Vasculitis				
Exposed	6	5118	4 (1.01–16.4)	0.049
Unexposed	5	16,882		
Alopecia				
Exposed	40	5084	8.3 (4.5–15.9)	<0.0001
Unexposed	16	16,871		
CNS conditions				

[Open in a separate window](#)

¹The Fisher's exact test was utilized

Table 3 evaluates among cases with general health outcomes and controls the frequency of HPV4 vaccine administration in the VAERS database. It was observed that cases with the outcomes of infection (odds ratio = 0.72), conjunctivitis (odds ratio = 0.88), or diarrhea (odds ratio = 1.01) were no more likely than controls to have received HPV4 vaccine.

Table 3

A summary of exposure to HPV4 vaccine exposure among general health outcomes cases and controls

Group examined	Number of cases (%)	Number of controls (%)	Odds ratio (95 % CI)	<i>p</i> value ¹
Infection				
Exposed	7	5117	0.72 (0.27–1.7)	0.57
Unexposed	32	16,855		
Conjunctivitis				
Exposed	4	5120	0.88 (0.29–2.7)	0.99
Unexposed	15	16,872		
Diarrhea				
Exposed	150	4974	1.01 (0.83–1.22)	0.92
Unexposed	489	16,398		

¹The Fisher's exact test was utilized

Table 4 examines the seriousness and timing of the SAAEs that were significantly associated with HPV4 vaccine administration. It was observed among the SAAEs examined that vasculitis (33 %), gastroenteritis (14.3 %), and systemic lupus erythematosus (12.5 %) were associated with the highest percentages of life-threatening outcomes. It was also observed among the SAAEs examined that CNS conditions (34.6 %), vasculitis (33 %), and arthritis (25 %) were associated with highest percentages of permanent disabilities. Finally, the median onset of symptoms for the SAAEs examined revealed that vasculitis was associated with closest median onset of symptoms following HPV4 vaccination (6 days), and arthritis was associated with the longest median onset of symptoms following HPV4 vaccination (55 days).

Table 4

A summary of SAAEs associated with HPV4 vaccination

Group examined (n)	Life threatening (%) ¹	Permanent disability (%) ¹	Median onset of symptoms ²
Gastroenteritis (7)	1 (14.3)	1 (14.3)	7
Arthritis (24)	1 (4.2)	6 (25)	55
Systemic lupus erythematosus (8)	1 (12.5)	1 (12.5)	19
Vasculitis (6)	2 (33)	2 (33)	6
Alopecia (40)	2 (5)	6 (15)	29.5
CNS conditions (26)	2 (7.7)	9 (34.6)	31

¹Some outcomes may have more than 1 occurrence in any single event report. If data are grouped by any of these items then the number in the may exceed the total number of unique events and the associated percentage of total unique event reports will exceed 100 % in such cases

²Calculated based upon those reports with a specified date of onset of symptoms after vaccination

Discussion

The present epidemiological study of the VAERS database evaluated the potential relationship between HPV4 vaccine administration and the risk for various types of SAAEs. It was observed that the SAAEs of gastroenteritis, arthritis, systemic lupus erythematosus, vasculitis, alopecia, and CNS conditions were associated with HPV4 vaccine administration, whereas the SAAEs of Guillain-Barre syndrome and thrombocytopenia were not associated with HPV4 vaccine administration. In addition, it was observed that the general health outcomes of infection, conjunctivitis, and diarrhea were not associated with HPV4 vaccine administration. The importance of these findings is that the present study provides epidemiological evidence to support an association between HPV4 vaccine administration and specific SAAEs.

The results obtained are consistent with several previous clinical studies. For example, researchers investigated the association between HPV vaccination and autoimmune manifestations compatible with systemic lupus erythematosus or systemic lupus erythematosus-like disease in six women who presented with such symptoms following HPV vaccination [8]. These investigators reported that in their cases, several common features were observed, such as personal or familial susceptibility to autoimmunity or adverse response to a prior dose of the vaccine, both of which may be associated with a higher risk of post-vaccination autoimmunity. Favorable response to immunosuppressant was

observed in all patients, and there was a temporal association between HPV vaccine and the appearance of systemic lupus erythematosus-like conditions. Similarly, other investigators observed a case series of three women that had onset or exacerbation of lupus following HPV immunization [9].

In contrast to the results observed in the present study, Arnheim-Dahlstrom et al. [10] evaluated autoimmune, neurological, and venous thromboembolic adverse events after immunization of adolescent girls with HPV4 in Denmark and Sweden. These investigators examined a cohort of 997,585 girls aged 10–17, among whom 296,826 received a total of 696,420 HPV4 vaccine doses. Unlike the present study that examined adverse event reports to the VAERS database, Arnheim-Dahlstrom et al. examined incident hospital diagnosed autoimmune, neurological, and venous thromboembolic events (53 different outcomes) up to 180 days after each HPV4 vaccine dose, and rate ratios of the outcomes were adjusted for age, country, calendar year, parental country of birth, education, and socioeconomic status, comparing vaccinated and unvaccinated person-time. These investigators observed that the rate ratios for 20 of 23 autoimmune events were not significantly increased. Exposure to HPV4 vaccine was significantly associated with Behcet's syndrome, Raynaud's disease, and type 1 diabetes, but these investigators described that each of these three outcomes fulfilled only one of three predefined signal strengthening criteria. In addition, these investigators observed that the rate ratios for five neurological events were not significantly increased, and there was no association between exposure to HPV4 vaccine and venous thromboembolism. It is interesting to note that despite the number of individuals examined by Arnheim-Dahlstrom et al., their study was significantly underpowered to even examine many types of outcomes, and of those outcomes examined, in many cases, relatively few outcomes were observed in the HPV4-vaccinated group. This may potentially be a consequence of the fact that the source for detecting outcomes in the Arnheim-Dahlstrom et al. study was from hospital records. It seems reasonable to hypothesize that many of the conditions examined by Arnheim-Dahlstrom et al. would not necessarily require hospitalization, and worse still, even if the condition eventually might require hospitalization, the Arnheim-Dahlstrom et al. study examined the diagnosis of the outcome in a hospital within the first 181 days after vaccination. As a result, for many of the outcomes examined by Arnheim-Dahlstrom et al. that overlap that with the outcomes examined in the present study, it was observed that there similar potential trends for outcomes in both studies (i.e., odds ratio for vasculitis in VAERS = 4 vs. adjusted rate ratio in Arnheim-Dahlstrom study = 1.55 or odds for systemic lupus erythematosus in VAERS = 5.3 vs. adjusted rate ratio in Arnheim-Dahlstrom study = 1.35), but none of the outcomes were significantly associated with HPV4 vaccination in the Arnheim-Dahlstrom et al. study.

Also in contrast to the present study findings, Chao et al. [11] undertook an observation safety study of HPV4 in 189,629 women who receive one or more doses of HPV4 vaccine between August 2006 and March 2008 for new diagnoses of autoimmune conditions within 180 days following each dose of HPV vaccine. These investigators identified new-onset autoimmune conditions among HPV recipients by electronic medical records, but then the medical records were reviewed by clinicians to confirm the diagnosis and determine the date of onset (only 31–40 % of the cases were confirmed as new onset). It was observed that there was no cluster of disease onset in relations to vaccination timing, dose sequence, or age was found for any autoimmune condition. None of the incidence rate ratios was significantly elevated except for Hashimoto's disease, but further investigation failed to reveal consistent evidence for a safety signal for autoimmune thyroid conditions. These investigators

concluded that no autoimmune safety signal was found in women vaccine with HPV4. Once again, the Chao et al. [11] study, just like the previously discussed Arnheim-Dahlstrom et al. [10] study, was apparently significantly underpowered to find potential autoimmune conditions associated with HPV vaccination, since more than half of the new-onset autoimmune cases identified from electronic medical records were subsequently eliminated from the study following review by clinicians.

Strengths/limitations

The study design used to evaluate the relationship between exposure and outcome was a significant strength of the present study. The method employed to examine VAERS ensured that the exposures to the various types of vaccines studied occurred prior to the outcomes described in the adverse event reports, since those reporting the adverse outcomes associated the outcomes with the vaccines listed in the adverse event reports.

Another strength of the study was that the VAERS data were collected independently of the study design used in the present study. Among those reporting the adverse event reports examined, it was highly unlikely that any of them could have envisioned methods of analysis used to evaluate the potential relationship between HPV4 vaccine and the adverse events examined.

An additional strength of the present study was the specificity of the types of the SAEs associated with HPV4 vaccine. Namely, despite the fact that a number of different types of potential SAEs were examined for the relationship with HPV4 vaccine administration, it was observed that systemic lupus erythematosus or systemic lupus erythematosus-like or associated events were associated with HPV4 vaccine administration. These types of outcomes are biologically plausibly associated with HPV infection and HPV4 vaccine administration.

In addition, in further support of the phenomena observed in the present study, an examination of the VAERS database for adverse events for laboratory findings consistent with systemic lupus erythematosus or systemic lupus erythematosus-like or associated events revealed reports with rheumatoid factor positive (VAERS code: 10039080) or antinuclear antibody positive (VAERS code: 10060055) or antiphospholipid antibodies positive (VAERS code: 10048678) in comparison to controls were significantly more likely to be exposed to HPV4 vaccine than unexposed (odds ratio = 4.8, 95 % confidence interval = 2.7–8.7, $p < 0.0001$). Also, among the SAEs associated with HPV4 vaccine administration, it was observed, consistent with the biological plausible onset window for SAEs following vaccination, that the median onset of symptoms ranged between 6 and 55 days post-immunization.

However, the results of the present study may have a number of potential limitations. It is possible the results observed may have occurred from unknown biases or cofounders present in the datasets examined. This seems unlikely because a series of general health outcomes were examined, and all were observed to be exposed to HPV4 vaccine at a similar frequency as controls.

An additional potential limitation of the present study of the VAERS database is that VAERS may have shortcomings, such as underreporting, difficulty in determining causal relationship, and a lack of precise denominators. Nevertheless, as previously described by investigators from the CDC, almost all of these types of shortcomings would apply equally to VAERS reports after vaccines administered to

similar populations [12]. The case-control method employed in the present study ensured that all of the adverse event reports examined in VAERS were administered to similar populations (i.e., age and gender), and as a result, examining the relative exposure to HPV4 vaccine among the cases and controls identified from the adverse event reports examined in VAERS should provide accurate relative qualitative and quantitative relationships between differing vaccine exposures and adverse outcomes. Additionally, investigators previously employed a similar case-control study design to the one used in the present study to successfully evaluate the potential relationship between vaccine administration and SAAEs [13].

Another potential limitation of the present study is that the results observed may be the result of statistical chance. However, such a possibility would be unlikely given the limited number of statistical tests performed, the highly significant results observed (most p values observed were <0.01), and the consistency in the direction and magnitude of the results observed.

Still, other potential limitations of the present study include the possibilities that some of the individuals in VAERS may have had more subtle adverse events that were not brought to the attention of their healthcare providers, healthcare providers may have misdiagnosed some individuals, or some vaccine exposures may not have been appropriately classified. These limitations, while possibly present in the data examined in the current study, should not have significantly impacted the results observed because it is unclear how differential application would have occurred based upon different exposures among cases and controls. Moreover, misclassification occurring in the data examined would tend to bias any results observed toward the null hypothesis, since such effects would result in individuals being placed in the wrong exposure and/or outcome categories examined, and result in decreased statistical power to determine true potential exposure-outcome relationships.

In addition, another potential limitation of the present study is that other sources of exposure among cases and controls were not evaluated. It is possible that the findings may be the result of other components of the vaccines studied which, in isolation or synergistically, interacted with the HPV4 vaccine examined.

Finally, the current study suffers from the potential limitation that analyses were not conducted to further explore the cumulative dosing effects from HPV4 vaccine administration or to compare HPV vaccine administration in comparison to unvaccinated populations. In future studies, it would be worthwhile to further explore these precise-timing and cumulative-doses phenomena. In addition, it would be valuable to evaluate other adverse events, as well as other covariates such as race, prior medical history, etc., that may further affect the magnitude of the adverse effects found.

Conclusion

In conclusion, the present study provides epidemiological evidence supporting a significant relationship between HPV4 vaccine administration and SAAEs. The results are consistent with a number of previous case-series of SAAEs observed following HPV4 vaccine administration, and are also consistent with the known biological plausibility of vaccine administration to induce SAAEs in some vaccine recipients. In light of the findings of the present study, we recommend that additional

studies be conducted to further evaluate the potential biological mechanisms involved in HPV4 vaccine-associated SAAEs in animal model systems, and to examine the potential epidemiological relationship between HPV4 vaccine-associated SAAEs in other databases and populations.

Acknowledgments

This study was financially supported by the non-profit 501(c)3 Institute of Chronic Illnesses, Inc. by a grant from the Dwoskin Family Foundation.

Conflict of interest

The authors declare they have no conflicts of interest.

References

1. Stanely M, Lowy DR, Frazer I. Prophylactic vaccines: underlying mechanisms. *Vaccine*. 2006;24:S106–S113. doi: 10.1016/j.vaccine.2006.05.110. [[PubMed](#)] [[CrossRef](#)]
2. Markowitz LE, Dunne EF, Saraiyam M, Lawson HW, Chesson H, Unger ER. Quadrivalent human papillomavirus vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP) *MMWR Recomm Rep*. 2007;56:1–24. [[PubMed](#)]
3. Molina V, Shoenfeld Y. Infection, vaccines and other environmental triggers of autoimmunity. *Autoimmunity*. 2005;38:235–245. doi: 10.1080/08916930500050277. [[PubMed](#)] [[CrossRef](#)]
4. Shoenfeld Y, Aron-Maor A. Vaccination and autoimmunity-'vaccinosis': a dangerous liaison? *J Autoimmun*. 2000;14:1–10. doi: 10.1006/jaut.1999.0346. [[PubMed](#)] [[CrossRef](#)]
5. Pellegrino P, Carnovale C, Pozzi M, Antoniazzi S, Perrone V, Salvati D, Gentili M, Brusadelli T, Clementi E, Radice S. On the relationship between human papilloma virus vaccine and autoimmune diseases. *Autoimmun Rev*. 2014;13:736–741. doi: 10.1016/j.autrev.2014.01.054. [[PubMed](#)] [[CrossRef](#)]
6. Singleton JA, Lloyd JC, Mootrey GT, Salive ME, Chen RT. An overview of the vaccine adverse event reporting system (VAERS) as a surveillance system. *VAERS Work Group Vaccine*. 1999;17:2908–2917. [[PubMed](#)]
7. Geier DA, Geier MR. A review of the vaccine adverse event reporting system database. *Expert Opin Pharmacother*. 2004;5:691–698. doi: 10.1517/14656566.5.3.691. [[PubMed](#)] [[CrossRef](#)]
8. Gatto M, Agmon-Levin N, Soriano A, Manna R, Maoz-Segal R, Kivity S, Doria A, Shoenfeld Y. Human papillomavirus vaccine and systemic lupus erythematosus. *Clin Rheumatol*. 2013;32:1301–1307. doi: 10.1007/s10067-013-2266-7. [[PubMed](#)] [[CrossRef](#)]
9. Soldevilla HF, Briones SF, Navarra SV. Systemic lupus erythematosus following HPV immunization or infection? *Lupus*. 2012;21:158–161. doi: 10.1177/0961203311429556. [[PubMed](#)] [[CrossRef](#)]
10. Arnheim-Dahlstrom L, Pasternak B, Svanstrom H, Sparen P, Hviid A. Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*. 2013;347:f5906. doi:

10.1136/bmj.f5906. [[PMC free article](#)] [[PubMed](#)] [[CrossRef](#)]

11. Chao C, Klein NP, Velicer CM, Sy LS, Slezak JM, Takhar H, Ackerson B, Cheetham TC, Hansen J, Deosaransingh K, Emery M, Liaw KL, Jacobsen SJ. Surveillance of autoimmune conditions following routine use of quadrivalent human papillomavirus vaccine. *J Intern Med*. 2012;271:193–203. doi: 10.1111/j.1365-2796.2011.02467.x. [[PubMed](#)] [[CrossRef](#)]

12. Chen RT, Rosenthal S. An errant critique that misses the mark. *Arch Pediatr Adolesc Med*. 1996;150:464–465. doi: 10.1001/archpedi.1996.02170300018004. [[CrossRef](#)]

13. Geier DA, Geier MR. A case-control study of serious autoimmune adverse events following hepatitis B immunization. *Autoimmunity*. 2005;38:295–301. doi: 10.1080/08916930500144484. [[PubMed](#)] [[CrossRef](#)]

J Investig Med High Impact Case Rep. 2014 Oct-Dec; 2(4):

2324709614556129.

Published online 2014 Oct 28. doi: [10.1177/2324709614556129](https://doi.org/10.1177/2324709614556129)

PMCID: PMC4528880

PMID: [26425627](https://pubmed.ncbi.nlm.nih.gov/26425627/)

Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination A Case Series Seen in General Practice

Deirdre Therese Little, MBBS, DRANZCOG, FACRRM¹ and Harvey Rodrick Grenville Ward, Bsc(Med), MBChB, DMCOG, FCOG(SA), MMed (O&G), FRANZCOG²

¹Bellingen District Hospital, Bellingen, New South Wales, Australia

²University of New South Wales, Coffs Harbour, New South Wales, Australia

[✉]Corresponding author.

Deirdre Therese Little, Bellingen District Hospital, Church Street, Bellingen, New South Wales 2454, Australia.

Email: dradford@wirefree.net.au

Copyright © 2014 American Federation for Medical Research

This article is distributed under the terms of the Creative Commons Attribution 3.0 License

(<http://www.creativecommons.org/licenses/by/3.0/>) which permits any use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access page (<http://www.uk.sagepub.com/aboutus/openaccess.htm>).

Abstract

Three young women who developed premature ovarian insufficiency following quadrivalent human papillomavirus (HPV) vaccination presented to a general practitioner in rural New South Wales, Australia. The unrelated girls were aged 16, 16, and 18 years at diagnosis. Each had received HPV vaccinations prior to the onset of ovarian decline. Vaccinations had been administered in different regions of the state of New South Wales and the 3 girls lived in different towns in that state. Each had been prescribed the oral contraceptive pill to treat menstrual cycle abnormalities prior to investigation and diagnosis. Vaccine research does not present an ovary histology report of tested rats but does present a testicular histology report. Enduring ovarian capacity and duration of function following vaccination is unresearched in preclinical studies, clinical and postlicensure studies. Postmarketing surveillance does not accurately represent diagnoses in adverse event notifications and can neither represent unnotified cases nor compare incident statistics with vaccine course administration rates. The potential significance of a case series of adolescents with idiopathic premature ovarian insufficiency following HPV vaccination presenting to a general practice warrants further research. Preservation of reproductive health is a primary concern in the recipient target group. Since this group includes all

prepubertal and pubertal young women, demonstration of ongoing, uncompromised safety for the ovary is urgently required. This matter needs to be resolved for the purposes of population health and public vaccine confidence.

Keywords: premature ovarian failure, amenorrhea, human papillomavirus vaccination, ovarian insufficiency, menopause

Introduction

Premature ovarian insufficiency (POI) has been defined as hypergonadotropic hypogonadism developing before age 40 years due to follicle depletion or dysfunction.¹ Oocyte depletion may be due to low initial numbers or accelerated loss. The function of the ovary may fluctuate in this state before failure, hence the recent preferred usage of the term POI (terminology used in this article will be consistent with references). POI with possible ovarian failure is a devastating diagnosis for a young woman's health and hopes of motherhood. The condition is important to identify and its causes are important to investigate and research for the preservation of future well-being. The physical, psychological, reproductive, and social impact is significant and will be greater when the condition develops in very young women and adolescents. Life expectancy may be reduced because of skeletal and organ effects. This impact will increase where diagnosis is delayed or the condition and its causes inadequately treated. Causation is unknown in 74% to 90% of cases^{2,3} and the background age-specific incidence of idiopathic premature ovarian failure (POF) in early to mid-adolescence is so rare as to be also unknown, with the annual incidence reported as 10/100 000 person-years up to age 30 years.⁴ The development of idiopathic POI and POF in a series of young teenagers after receiving the quadrivalent human papillomavirus (HPV) vaccine therefore has no age-specific background rates for comparison.

Each quadrivalent HPV vaccine is a recombinant protein particulate vaccine, containing 20, 40, 40, 20 µg of the major capsid (L1) protein of HPV types 6, 11, 16, and 18 respectively, 225 µg aluminum hydroxyphosphate sulfate, 9.65 mg sodium chloride, 780 µg; L-histidine, 50 µg polysorbate 80, and 35 µg sodium borate ("Gardasil," "HPV4," "4vHPV"). It is recommended to young women for its protective role against the 2 most common HPV oncogenic types, HPV 16 and HPV 18. This vaccine could potentially prevent 70% of cervical cancer.⁵ Protection against 2 other HPV types (6 and 11) causing genital warts is included in HPV4. Since 30% of cervical cancer may still occur in vaccinated individuals, papanicolaou smears to the seventh decade are still required. Prior to vaccine introduction, the incidence and mortality rate of cervical cancer were steadily declining. These rates more than halved in the decade prior to 2000 in the 20- to 69-year age group in Australia and 578 new cases were diagnosed in 2000.⁶ The incidence was highest in remote areas,⁷ with the risk of death from cervical cancer for an Indigenous woman in Australia 6 times that of a non-Indigenous woman. In 1989, it was estimated that cervical cancer pap screening could potentially prevent 90% of squamous malignancies.⁸ Increasing success of the Australian National Cervical Screening Programme has been moving toward this capacity with prevention of 70% of squamous cell cancers in 1998,⁹ up from 46% in 1989. In 2002, the Australian incidence of cervical cancer was 6.2 per 100 000 women⁸ and the mortality rate 1.7 per 100 000 women. In 2011 in Australia, there were 229 deaths from cancer of the cervix.¹⁰ Five-year relative survival is 72.1%.¹¹

A consideration of vaccine benefit versus vaccine risk requires high-quality safety evidence. This case series is therefore presented for its possible significance to young women's health and fecundity. The limited capacity of existing HPV4 research to attest to ovarian safety together with factors that impede vaccine adverse event reporting could affect the quality of information supplied to informed consent. This second case series of adolescent POI/POF increases evidence suggesting that the hypothesis of an association between HPV vaccine and premature ovarian demise needs to be tested.

Background

Early symptoms and signs of POI vary and a delay in presentation and diagnosis of POI is common. It has been observed that 92% of women with idiopathic POF describe an altered menstrual cycle as their initial symptom.¹² A total of 58% have described amenorrhea lasting 3 months or longer as the presenting symptom and 29% have described oligomenorrhea as the presenting symptom. Polymenorrhea, infertility, metrorrhagia, and vasomotor symptoms were less common presentations. In all, 25% of karyotypically normal women with noniatrogenic POF took more than 5 years from onset of a menstrual cycle abnormality for the diagnosis to be established. The median duration to diagnosis was 2 years. Overall, 57% of women with POF required 3 or more clinician visits prior to laboratory testing and 61% of women reported seeing 3 or more clinicians prior to diagnosis. Noninvestigation of new menstrual pattern abnormalities in young women may be due to a low perception of importance by the patient or low perceived importance by the physician. It has been observed that 39% of women developing amenorrhea consult a doctor.¹³ Similarly, clinicians appreciate that some 4% of reproductive-aged women may miss 3 periods each year.^{14,15}

Since the incidence of POF increases with age, we need finer gradations of incidence for very young teens at 13 and 14 years of age in whom this condition following HPV4 has been reported.^{16,17} The unknown prevalence of idiopathic premature ovarian failure in the early to mid-teenage HPV4 vaccine target group renders adverse event analysis methods such as "rapid cycle" vaccine event analysis inapplicable.¹⁸

Premature ovarian insufficiency has serious health implications. A Swedish study of 22 000 postmenopausal women suggests those entering menopause aged 40 to 45 years have a 40% increased risk of cardiac failure than those entering menopause at age 50 to 54 years.¹⁹ For every year delay in the onset of menopause the rate of cardiac failure was lowered 2%. The cardiac implications for teenagers entering menopause have yet to be defined. Altered ovulatory and menstrual patterns also lead to accelerated loss of bone density and increased wrist and hip fractures in later life.²⁰ POF is one of the greatest risk factors for osteoporosis.²¹ Furthermore, lowered bone mineral density begins with diminished ovarian function before the onset of amenorrhea²² and suboptimal bone density in teens is a factor in the development of osteoporosis.²³ Other health implications of POI will differ by cause.

Published case reports have considered a possible link between quadrivalent human papillomavirus vaccine and premature ovarian failure.^{17,24} Declining menstrual function in girls aged 14, 15, and 20 years followed HPV4 vaccination and preceded POF in the previous case series. The formerly

published *BMJ* case report of a 16-year-old with irregular menses gradually progressing to oligomenorrhea, amenorrhea, and POF after HPV4 was the first such case presenting to this practitioner and is therefore summarized as “Case 1” below.

This case series presents 3 young women who consulted a primary care general practice in rural New South Wales, Australia. Two experienced a duration of cycle disruption progressing to amenorrhea and 1 had an unknown prodrome to amenorrhea due to oral contraceptive pill (OCP) usage. These symptoms followed HPV4 vaccination. The girls are not known to be related and reside 40 to 500 km apart (1 patient was holidaying). Vaccination batches that were identified were dissimilar and administered in locations 3, 500, and 570 km from this attending practitioner.

Case 1

This case has previously been published in the *BMJ Case Reports*.²⁴ It was the initial presenting case diagnosed in this series. Therapeutic Goods Administration of Australia adverse event report reference number is 285383.

Menarche at age 13 years in 2007 was followed by light periods, which became heavier and regularized over the next 12 months. HPV4 was administered in February, May, and August of 2008 (Department of Health New South Wales, 2011). Cycles became irregular early in 2009 and become scant and infrequent in 2010. Menstruation ceased in January 2011 and hot flushes commenced. There was no past history of significant illness or surgery. She was a nonsmoker, took no medications, and had no history of injury. Body mass index was 22.6 kg/m². There was no family history of premature menopause. At her initial consultation for oligomenorrhea becoming amenorrhea, she was prescribed the OCP without investigation. She was not sexually active.

She declined the OCP and consulted a second clinician. Investigations revealed that follicle-stimulating hormone was 108 U/L (menopausal range 20-140 U/L); luteinizing hormone was 31 U/L (menopausal range 10-65 U/L); estradiol was low at 63 pmol/L (normal follicular range >110 pmol/L, menopausal range = 40-200 pmol/L). Progesterone was 1.1 nmol/L (menopausal range <2.2 nmol/L). Anti-Müllerian hormone was <1.0. There were no antiovarian antibodies or antiadrenal antibodies detected. Thyroid peroxidase antibodies were 2 IU/mL and thyroglobulin antibodies were 44 IU/mL (levels up to 100 IU/mL can occur in normal subjects). A pelvic ultrasound was reported normal. Full blood count, renal, liver and thyroid function, and prolactin were normal. Premature ovarian failure was diagnosed at age 16 years. Some irregular anovulatory pattern bleeds occurred before commencement of hormone replacement therapy.

Karyotype was 46XX. Galactosemia testing was negative. Fragile X testing was normal.

This girl was counseled about the need for bone strength preservation. Her bone mineral density testing suggested femoral neck to be in the low range for age, height, and weight at 0.766 g/cm² and lumbar spine bone mineral density to be normal for height and weight but lower than the expected range for age at 0.903 g/cm². She is considering ovarian tissue cryopreservation.

Case 2

An 18-year-old young woman presented with 6 months amenorrhea. Menarche had occurred at age 11 years. She suffered from mild cerebral palsy (possibly due to low birth weight of 1.88 kg at 38 weeks' gestation), mild asthma, Asperger's syndrome, anxiety, and epileptic events from age 14 to 15 years, considered secondary to cerebral palsy. She had a ruptured appendix at age 12 years. There was no other significant past history; no drug usage; she did not smoke or drink alcohol, and had not become sexually active. Sertraline was used for treatment of anxiety from 2009 to 2010 followed by fluoxetine. There was a family history of osteoarthritis and osteopenia and of pancreatic cancer; no family history of premature menopause. The OCP was commenced at age 12 years. The attending gynecologist recorded "although her periods were reasonably normal, she was put on the pill (20 µg ethinyloestradiol and 100 µg levonorgestrol) the next year because coping with her periods made her anxiety and depression symptoms worse." Her first HPV4 vaccination was administered at age 12 years and 9 months; the second vaccination near her 13th birthday, and the third vaccination at age 13 years and 5 months. The first HPV4 vaccination was given concomitantly with hepatitis B vaccination in the other arm. OCP usage continued for 2 years to age 14 years. It was briefly ceased at age 14 and this was followed by 3 months amenorrhea. OCP was then resumed without further investigation. At age 18 years, the OCP was again ceased and amenorrhea again ensued.

Follicle-stimulating hormone 1 month later was elevated at 44.5 IU/L (menopausal range is 25-130 IU/L). Luteinizing hormone was 29.2 IU/L (basal range 2.0-12, midcycle peak range 8.0-90, postmenopausal range 5.0-62 IU/L). Estradiol was 157 pmol/L. She continued amenorrheic and presented again for investigation 6 months later. At this time, follicle-stimulating hormone remained elevated at 34 IU/L. Luteinizing hormone was elevated at 46 IU/L. Estradiol (Oest2) was 413 pmol/L and progesterone 2 nmol/L. Anti-Müllerian hormone was 1.5 pmol/L (14.0-30.0 pmol/L normal; levels <14 pmol/L suggest diminished ovulatory reserve) tested by Beckman Coulter Gen II ELISA assay. Anti-Müllerian hormone repeated 6 months later was <1 pmol/L and estradiol was <37 pmol/L. At this time and at age 18 years POI was diagnosed.

Full blood count, iron levels, liver function, blood glucose, and renal function were normal. Thyroid-stimulating hormone was normal 0.4 mIU/L (normal 0.3-3.5 mIU/L) and thyroid antibodies were normal. Prolactin was normal 294 mIU/L. Testosterone 0.9 nmol/L (normal 0.2-1.8 nmol/L); free androgen index 2.6 (normal 0.3-4.0); iron studies were normal. There were no antiadrenal or antiovarian antibodies detected. Morning cortisol was 218 nmol/L (normal range 160-650) nmol/L, ACTH 14 ng/L (normal range 9-51 ng/L), growth factor-1 27 nmol/L (normal range 21-76 nmol/L). Pelvic ultrasound performed at the time when the anti-Müllerian hormone level was 1.5 showed a normal uterus with an endometrial echo of 8.2 mm. Transvaginal ultrasound was declined and the left ovary was not visualized. The right ovary was 3.1 cm³ in size and there was a 9-mm follicle within it. Brief menstrual bleeds then occurred for 4 months before amenorrhea resumed.

Testing for Fragile X revealed 2 normal-sized triplet alleles 23 and 37 cytosine-guanine-guanine n repeats (the normal zone is <44). Testing for galactosemia showed a normal Gal-1-P uridyl transferase-RC at 0.31 U/g hemoglobin (normal range 0.26-0.52 U/g). Records reported a vitamin B₁₂ deficiency at age 16 years, but levels of vitamin B₁₂ were within normal limits at 275 pmol/L (normal range 135-650 pmol/L). Karyotype was established as 46XX.

This young woman elected to undergo right ovary cryopreservation through Monash IVF in the hope that future developments, such as stimulation of ovarian stem cells, may be of later benefit. She was not deemed a suitable candidate for gonadotropin stimulation for oocyte preservation due to the undetectable anti-Müllerian hormone level. The pathologist described the macroscopic appearance of the ovary as “cystic and disrupted.” Microscopic histology of three right ovarian biopsies reported fibrovascular connective tissue with no primordial follicles in the ovarian cortex of sample one. Ovarian sample 2 reported a cystic follicle and a cystic corpus luteum but no primordial follicles within surrounding parenchyma. Ovarian sample 3 reported “fibrofatty connective tissue only. No ovarian parenchyma is identified.” Summary: “Levels through all tissue containing ovarian parenchyma show a single primordial follicle. No other follicular structures are identified.” No samples contained evidence of atypia or malignancy (Sullivan Nicolaides Pathology, Brisbane, Queensland, Australia). Personal communication with the reporting pathologist confirmed no lymphoid or granulomatous inflammation and suggested the ovarian appearance was “consistent with that of a woman in her late forties.”

She has been counseled about bone density preservation and the need for hormone replacement therapy. This case was notified to the Therapeutic Goods Administration (TGA) of Australia in January 2014 (reference number 333136) as diagnosed POI. Its listing as “amenorrhoea” on the TGA database in May 2014 was later altered to POF (July 2014).

Case 3

Menarche had commenced at age 10 years, and was followed by regular menses. The first 2 HPV4 vaccinations were received at age 14 years and the third vaccine after turning 15 years in 2008 (Department of Health New South Wales. School vaccination programme. Vaccinations administered February 18, May 23, and October 24 in 2008). The patient reports “prior to this, my periods were like clockwork.” The period due after the third vaccination dose was 2 weeks late and was the first late period she had experienced. The next period occurred 2 months later. The next and final menstruation occurred 9 months later, approximately 1 year after completion of the third HPV4 vaccination. Hot flushes developed and 10 kg weight gain was noted over the next year. Previously present acne improved. Pelvic ultrasound was unremarkable apart from a 3.7-mm endometrial width and the absence of visible ovarian follicles. She had not become sexually active, had no history of drug or alcohol usage and there was no history of trauma, surgery or of significant past illness. There was no family history of premature menopause. She was allergic to benzoyl peroxide. POF was diagnosed just before her 17th birthday.

At age 15 years, initial testing was undertaken: testosterone was 1.1 nmol/L (normal range <2.6), sex hormone binding globulin 41 nmol/L (normal range 20-118 nmol/L), free androgen index 2.7% (normal range <7.2%). There is no significant further testing until nearly 17 years of age: prolactin 160 mIU/L (normal range 40-570 mIU/L), thyroid-stimulating hormone 1.1 mIU/L (normal range 0.5-4.5 mIU/L), dihydroepiandrosterone (DHEA-S) 3.5 µmol/L (normal range 3.6-9.8 µmol/L), androstenedione 1.8 nmol/L (normal range 1.0-11.5 nmol/L), testosterone <0.7 nmol/L (normal range <3.2 nmol/L), serum hormone binding globulin 32 nmol/L (normal range 30-90 nmol/L), free androgen index <2.2%, luteinizing hormone 32.8 IU/L (midcycle range 17.7-47.5; postmenopausal range >9.3 IU/L), follicle-stimulating hormone 73.8 IU/L (midcycle range 9.6-24.1; postmenopausal >50 IU/L),

estradiol <100 pmol/L (midcycle range 500-1500; postmenopausal <100 pmol/L). Estradiol (radioimmune assay) <10 pmol/L. Repeated hormone levels 7 weeks later revealed luteinizing hormone 42.9 IU/L, follicle-stimulating hormone 61.8 IU/L, and estradiol 18 pmol/L. Antiovarian antibodies were negative <1:10 and antiadrenal antibodies were negative. Anti-Müllerian hormone level was unrecordable. Bone mineral density scan was reported normal at age 17 years and 1 month (z-score 0.9 for lumbar spine and 1.4 for “whole body”).

When reviewed in the Department of Clinical Endocrinology at Westmead Hospital, New South Wales, it was determined that she would not respond to gonadotropin stimulation for oocyte collection for cryopreservation. She has been counseled about the need for bone preservation and is currently on hormone replacement therapy. This case was reported to the Therapeutic Goods Administration of Australia in April 2014. No response was received and the case was renotified to the TGA in June 2014 and to the New South Wales Chief Medical Officer. Reference number and notification response are awaited. Consultation for ovarian cryopreservation has commenced.

Discussion

Consideration of the possible significance of this second case series of idiopathic POI/POF after HPV4 requires review of preclinical and clinical safety studies identified at licensing²⁵ and review of larger postlicensing safety studies. A summarized report of existing HPV4 research in relation to the very young ovary was presented by this author at the 18th World Congress of Controversies in Obstetrics, Gynecology and Infertility in October 2013²⁶ and to the Brighton Collaboration Journal Club (as author response to review of *BMJ* September 2012 Case Report).²⁷

Preclinical Studies

Safety assessment of a new vaccine begins with preclinical studies for toxic effects in rodents. After diagnosis of case 1, and in response to a query from this patient, rodent ovarian histology after HPV4 vaccination testing was sought. No histology report of the vaccine-tested rodent ovary was available under Freedom of Information Request to the Therapeutic Goods Administration of Australia.²⁸ There is no cellular observation available on tested rodents' ovaries beyond a numbering of corpora lutea present on the ovary at caesarian section.²⁹ Five-week-old tested rats conceived only 1 litter before euthanasia.

It is unfortunate that available toxicology studies only provide histology of the male rodent reproductive system after HPV4 vaccine^{30,31} and not of the female rodent reproductive tract or ovaries. Vaccine-tested rat ovary histology reports would have been useful to consult to better understand any possible link between cases of teenage premature ovarian insufficiency and rat vaccine effects.

Published Sprague-Dawley rat testing for HPV4 vaccine fertility safety comprised 2 control groups and 2 vaccine groups.³² Control group 1 was given a formulation of phosphate-buffered saline as placebo (the chemical formulation selected is not stated). Control group 2 consisted of the carrier solution components of Gardasil. It contained “aluminum (0.45 mg per mL), sodium chloride (18.7 mg/mL), sodium borate (70 mg/mL [sic]), L-histidine (1.55 mg/mL), and polysorbate 80 (100 µg/mL).” Vaccine

group 1 consisted of rats only given the vaccine after their first mating and resultant conception. Vaccine group 2 rats received 2 vaccine doses 5 and 2 weeks prior to first mating/conception and at 6 days after conception and on lactation day 7.

Twenty-two rats within each of these 4 groups were assigned to caesarian section, and 22 from each group were assigned to give live birth before postweaning euthanasia. In the caesarian section data,^{32,33} the total number of corpora lutea present in the group of 22 rats not vaccinated before mating, of whom all 22 fell pregnant at mating, was 366. The total number of corpora lutea present in 22 rats who received the first and second vaccinations before mating, of whom 20 fell pregnant at mating, was 326. The ratio of corpora lutea per rat that did fall pregnant was 16.30 (± 2.5 SD) for those receiving 2 vaccinations before mating, and for those not vaccinated prior to mating was 16.63 (± 2.3 SD). While these were only small differences of corpora lutea numbers, it is not known whether administration of the complete 3-dose vaccination course to test fertility may have shown a more significant disparity. The overall fecundity index of rats who received two thirds of the vaccination course prior to mating was 95%, the lowest of the 4 groups and very slightly lower than the fecundity index of 98% in rats who received no vaccination prior to mating. In controls 1 and 2, the fecundity index was 97% and 98%, respectively. In preclinical fertility studies submitted at licensing, no rats were tested with the complete vaccination course, with representative interval administration, prior to mating. The study concludes that vaccine rodent fertility testing conferred “a safety margin of 200-fold by body weight for adolescents.” “Guidance for Industry” research guidelines state “where possible we recommend that you administer the maximum human dose (eg, 1 human dose = 1 rabbit dose) regardless of body weight.”³⁴ The reason for omission of the third vaccination dose prior to measuring the rats’ capacity to conceive is unclear.

The 200-fold safety prediction was derived from the 0.25 kg weight of a rat compared with the “average body weight of an adolescent girl (50 kg).” The HPV4 target girl group is aged from 9 years and administration in Australia is to girls aged 12 and 13 years under the National Immunization Programme. The 50th centile weight of 9-year-olds is 28 kg, of 12-year-olds is 42 kg, and of 13-year-olds is 46 kg.³⁵ Australian age-specific weights therefore also reduce modeled calculations of fertility safety.

Long-term fecundity studies of vaccinated female rodents’ duration of reproductive lifespan, recorded numbers of litters and pup numbers in subsequent litters was also requested under the original freedom of information application but were unavailable.

Clinical Studies

Research consideration of ongoing female fertility was similarly absent from phases II and III clinical safety studies. The capacity of safety studies to assess ovarian function, particularly of the target age group, was reduced by several factors. The phase II and phase III studies identified as safety studies at the time of licensing²⁵ by the Vaccine and Related Biological Products Advisory Committee (VRBPAC) to the Food and Drug Administration are study protocols V501 007,³⁶ 016,³⁷ 018,³⁸ and 013,³⁹ and 015,⁵ respectively. Only protocols 016 and 018 studied safety in the young female vaccine target group. Mean ages in these groups were 12.6 and 11.9 years, respectively. It is not clear what proportion of these were postmenarche.

In protocol 016, 240 girls (aged 10-15 years) were left in the study at 12 months, comprising 47.4% of screened healthy participant younger girls. Immune response data were collected through month 7, and safety data through to month 12. More than 52% were lost from the 12-month safety follow-up instituted as a protocol amendment. Loss of the majority of participants to safety observation significantly compromised this trial as a safety study of younger adolescents forming the vaccine's target group. One girl in this study experienced vaginal hemorrhages meeting Serious Adverse Event Criteria⁴⁰ after second and third vaccinations. These were initially deemed vaccine related, but subsequently considered by gynecological review³⁷ to have been related to a preexisting condition not excluded at general health screening. Protocol 018 fully vaccinated 587 girls. A total of 52.3% of enrolled girls were aged 9 to 12 years. It is not clear what proportions of girls in these target group safety studies could potentially have reported menstrual cycle patterns or aberrations of patterns. Similarly, health interviews with the participants 18 months after the first vaccination may not have been able to determine menstrual abnormalities while cycles are commencing or establishing ovulatory patterns.

Given the masking effects of hormonal contraception on ovarian function it is relevant that contraceptive hormone usage was reported at 58% to 60% of vaccine recipients in safety trials at baseline interview in phase III studies.⁴¹ This rose to 68% to 83% of participants in the 2 substudies of protocol 013.^{42(p143)} In all, 75% to 82% used hormonal contraception within 15 days of any vaccination in trial 007,^{42(p216)} and more than two thirds recorded concomitant hormonal contraception usage within 14 days of any vaccination in protocol 015.^{42(p244)} Phase III studies' participants, mostly 16 years and older, were required to use effective contraception for at least 7 months. A major review of the HPV4 vaccine safety profile reports: "new medical conditions were not considered adverse events if they occurred post month 7, or were not considered by the investigator to be vaccine related."⁴³

The design of safety studies with use of a vaccine report card further restricted the recording and reporting of menstrual dysfunction. The largest safety study, phase III study protocol 015, enrolled older females predominantly aged 16 to 23 years (1 was 15 years old, 46 were older than 23 years) of whom 5916 completed the 3-dose HPV4 vaccination period and 5953 completed placebo dosages.^{42(p58)} A subgroup selected from among these formed the Detailed Safety Cohort. It followed 448 recipients of at least 1 vaccination and 447 control recipients, asking them to record nonserious adverse events (NSAEs) for 2 weeks after each vaccination on a vaccine report card. Serious adverse events (SAEs) in the 2 weeks following each vaccination were also recorded.⁵ Participants not included in the NSAE substudy were solicited only for SAEs occurring within 2 weeks after each vaccination.^{42(p52)} All SAEs that were considered to be potentially related to administration of the vaccine were to be reported throughout the study. However, menstrual cycle disruption, oligomenorrhea, and amenorrhea will not signal as SAEs by definition. SAEs are defined as life-threatening, resulting in death, permanent disability, congenital anomaly, hospitalization, prolongation of hospitalization, or necessitating medical or surgical intervention to prevent one of these outcomes.⁴⁴ The use of a vaccine report card to record other adverse events occurring within 2 weeks of each vaccination has limited ability to detect diminishing menstrual cycles. This is a weakness in the safety design of clinical trials. It would not have detected the menstrual cycle decline evident in the cases of

premature ovarian insufficiency presented in this series. Protocol 018 VRC prompted for additional information such as headaches, rashes, muscle/joint pain, and diarrhea that occurred within 14 days but not menstrual aberration.

When the Center for Biologics Evaluation and Research requested an analysis of autoimmune conditions over the entire safety database, the sponsor noted that “there were subjects with additional new medical conditions that were not reported in the Clinical Study Reports for 011 and 012 [within protocol 013]. These included two subjects with amenorrhea.”^{42(p198)}

Longer term follow-up beyond the vaccination interval was limited to SAEs. Protocol 015 mean follow-up was 3 years from first vaccination for SAEs. The second largest study, protocol 013, fully vaccinated 2582 women^{42(p136)} and vaccine report cards recorded NSAEs for 2 weeks after each injection. Lack of long-term follow-up is identified as a limitation of this study.^{39,42(p136)}

Underrepresentation of the vaccine’s target age group, incomplete and short-term follow-up, definitional limitations, hormone usage, fortnight restrictions of vaccine report card documentation and the decision not to report new medical conditions as adverse events which occurred post month seven from first vaccination compromised safety studies’ observation of ovarian health.

Vaccine Components Used as Safety Study Controls

The choice of placebo affects the validity and quality of scientific information available from placebo-controlled studies. The control in any experiment should lack the factor being tested. The placebo that formed the control selected for phase III safety studies of Gardasil (older girls) was the aluminum adjuvant present in the vaccine solution, amorphous aluminum hydroxyphosphate sulfate. The selection of aluminum as a control in vaccine studies is at variance with the scientific principles of a control. The placebo in the only controlled study of very young girls was the remainder of the vaccine carrier solution: “The placebo used in this study contained identical components to those in the vaccine, with the exception of HPV L1 VLPs and aluminum adjuvant.”³⁸ It contained 50 µg polysorbate 80 (polyoxyethylene sorbitan mono-oleate also known as Tween 80), 35 µg borax, 9.56 mg sodium chloride, and 0.78 mg L-histidine.

Safety studies identified at licensing did not compare HPV4 with normal saline controls. The second placebo contained several substances together with saline. The researchers’ reference to the “carrier solution” placebo conflicts with the licensing review. The Center for Biologics Evaluation and Research states, “Protocol 018 provides saline placebo-controlled safety data for subjects 9 to 15 years. This is of particular interest because the other studies used alum placebo as a safety comparison.”^{42(p330)} Subsequent reviews of safety studies also claim a saline placebo was the comparator of younger girl safety studies and variously refer to this placebo control as “non-aluminum containing (saline) placebo”⁴³ and “saline placebo.”⁴⁵ Gardasil Product Information itself refers to the control as a “saline placebo.”⁴⁶ Published safety studies only compared HPV4 vaccine with its own components. This may be significant since injected substances in both placebo control arms have either a suggested association with autoimmune ovarian damage¹⁷ or known direct ovarian toxicity.⁴⁷

Completed vaccine and placebo courses each administered 675 µg of aluminum to older girl safety study participants; or components including 150 µg polysorbate 80 to all 9- to 15-year-old safety study participants.

When polysorbate 80 (“Tween 80”) was injected into newborn rats, it caused similar ovarian damage to injected diethylstilboestrol. Rat ovary effects occurred at all doses tested over a tenfold range.⁴⁷ Since this study provides a relevant ovary histology report of a substance in HPV4 it bears detailed consideration. 1%, 5%, or 10% solutions of polysorbate 80 at 0.1 mL per rat were injected into rats at 4, 5, 6, and 7 days after birth. The oestrous cycle was examined at weeks 10, 14, and 18 of age. Findings were compared with control rats given no treatment; negative controls given water injections; and a “positive” control group given a formulation of 50 µg diethylstilboestrol. Rats injected with polysorbate 80 had an oestrous cycle ranging from 9 to 14 days, compared with 4.3 days average length throughout the test in untreated controls and 9.4 days in diethylstilboestrol injected rats. Postmortem conducted at 20 weeks of age on “Tween”/polysorbate 80 tested rats reported

1. All Tween-treated groups showed a statistically significant ($P < .001$) decrease in the relative weight of the ovaries in comparison with the untreated control. The relative weight (% of body weight) was slightly lower in the 1% Tween 80–treated groups than in the 10% Tween 80–treated groups.
2. In the group of 6 rats given the lowest dose of Tween 80 “in two rats the uterus was enlarged and had a marked vascular pattern.”
3. The 5 rats given diethylstilboestrol showed “microscopically degenerated follicles in the ovaries with complete absence of corpora lutea. Findings in the ovaries similar to those in the positive control [diethylstilbestrol control] group were also observed in all of the groups given Tween 80.”
4. Abnormal histological findings in the cells lining the uterus were observed in all 17 rats given Tween 80 and resembled the abnormal histology observed in diethylstilboestrol-treated rats, which had high cylindrical epithelial cells and some mitoses. The study concluded, “4-day administration of Tween 80 to female rats during the period crucial for the development and function of reproductive organs accelerates the maturation of these organs.” As well as a prolonged oestrous cycle researchers also noted induction of persistent vaginal oestrous. This was slightly more marked in the 1% solution of Tween 80 than in the 5% or 10% solutions. Statistically significant increased weight of the adrenals ($P \leq .05$) was also noted in the 1% polysorbate injected rats.

No dose response curve was identified. This chemical is present in orally ingested medicines and foods, but did not affect rat reproduction when subject to digestive processes at up to 5% of their oral intake. It did decrease rat reproduction at 20% of their oral intake.⁴⁸ It is not known whether some protection may be conferred by digestive processes to smaller loads of polysorbate 80 that is not present in the parenteral route of administration to young female rats. This research highlights 4 issues. First, the scientific role of control groups and placebo selection. Second, a possible confounding effect of polysorbate 80 used as placebo in younger girls’ HPV4 safety trials. A potential ovarian toxin in both control and vaccine arms could obscure the already limited ability to observe risk differences of adverse menstrual events. Third, the absence of crucial histological reporting of the rodent ovary after

HPV4 vaccination containing 150 µg polysorbate 80. Fourth, whether clinical investigators of vaccine safety considered the potential ovarian effects of this vaccine component when determining a “likelihood” relationship between menstrual aberration and the study vaccine. Safety trial investigators determined the relationship of both Vaccine report card documented adverse events and new medical conditions before month 7 to vaccination, based on criteria of “likely cause,” exposure, time course, and rechallenge. Licensing bodies asserting “no biological plausibility”^{49,50} of ovary effects arising from vaccine constituents accept a null hypothesis at odds with existing research. This may also reflect research investigator considerations of “likelihood.”

Histologically evident toxic ovarian effects of polysorbate 80 evidenced 5 months after serial injections into very young rats have not been compared with the histological effect of the HPV4 vaccine course containing 150-µg dosage. The relevance of polysorbate 80 ovarian damage to the cases presented here is unresearched and unknown and assurances of “no biologically plausible” link between HPV4 vaccine and ovarian effects cannot be given.

The role of the aluminum adjuvant as a safety study placebo also requires consideration. The development of an “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA) has been postulated by some immunologists to be implicated in the development of premature ovarian failure.¹⁷ The 3 young women in the previous published case series of POF following HPV4 had associated symptomatology which fulfilled criteria for this syndrome. These criteria include clinical signs (such as neurological, sleep, or cognitive disturbances, myalgia, arthralgia, fatigue, and fever) with a major feature of prior exposure to external stimuli such as infection, vaccine or vaccine adjuvants, and possible other autoimmune phenomena.⁵¹ Existence of this syndrome is under dispute, but proponents suggest autoimmunity may be induced in this context in genetically predisposed individuals. Antiovarian antibodies were found in the 15-year-old girl diagnosed with POF in that series. A possible autoimmune implication of injected aluminum reinforces the scientific principle that placebos should not contain the factor being tested. Respect owed to this principle is further endorsed by findings that “the structure of the ovary was disrupted” in rats exposed to subchronic ingestion of aluminum chloride.⁵² Other associations with this aluminum salt included reduced levels of alkaline phosphatase, acid phosphates, and ATPase and lowered protein expression of follicle-stimulating hormone receptor and luteinizing hormone receptor. The selection of aluminum as the safety comparator may have confused safety trial outcomes. Its use as a placebo is therefore questionable.

Postlicensing studies

Two large safety studies, sentinel cohort follow-up, reviews of existing research, and vaccine adverse event reporting systems have reported on postmarketing vaccine safety.

The first of the 2 largest post marketing studies sought to evaluate vaccine safety “during the course of routine clinical care” by reviewing presentations at emergency departments and hospitalizations from within a cohort of 189 629 vaccinees.⁵³ This group included 44 000 females who had completed 3 vaccinations. Eleven- to 12-year-olds comprised 4.3% of the total vaccine group. Emergency department visits are not the consultation context for seeking medical management of altered menstrual cycles, oligomenorrhea, or amenorrhea. These conditions rarely require hospitalization. This study had

no capacity to evaluate ongoing ovarian health or safety. Further analysis of these emergency department presentations/hospitalizations to review the risk of 16 autoimmune conditions did not include ovarian dysfunction or failure.

The largest and most recent published cohort study from Denmark and Sweden of 997 585 girls measured incident hospital diagnosed autoimmune, neurological, and thromboembolic events.⁵⁴ Menstrual cycle aberrations indicative of ovarian malfunction were not included and, again, do not usually present to emergency and hospital settings. This study of approximately 1 million girls sheds no light on reproductive function or egg-bearing capacity.

The sentinel study of 577 girls from protocol V501 018 was to provide the first long-term data of vaccinated adolescents. It assessed safety by monitoring for serious adverse experiences and pregnancy outcomes.^{45,55} The Nordic extension of the long-term follow-up of protocol V501 015⁴⁵ addressed the hypothesis that Gardasil will remain effective for 14 years after vaccination. This long-term follow-up study will connect with National Hospital Registers in participating countries and cancer registries searching for adverse events such as deaths, hospitalizations, cancers and other safety outcomes. It has the capacity to search health-related registries to find “safety events of interest,” comparing adverse event rates to those in the age-matched general population. Ovarian function is not recorded in its research focus. Furthermore, data search of ovarian insufficiency if undertaken may be impeded by evidenced delays to diagnosis within 5 years,¹² OCP usage and lack of incidence statistics in an age-matched population.

Postlicensure monitoring is relied on to detect rarer adverse events. The Vaccine Safety Datalink⁵⁶ has reviewed associations between HPV4 vaccination and outcomes prespecified as Guillan-Barre, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, and anaphylaxis. Ovarian dysfunction was not studied and rare events need background incidence rates for comparison. Monitored outcomes were those with relatively acute onset, which could “represent a biologically plausible association with vaccination.” Rapid cycle analysis of vaccine safety datalink information requires comparison between vaccinated and unvaccinated groups.⁵⁷ The Clinical Immunization Safety Assessment Network reviews SAEs reported to the Vaccine Adverse Event Reporting System (VAERS) following immunization and have therefore reported on deaths, venous thromboembolism, neurological, and allergic outcomes.

The VAERS⁵⁸ accessed August 2013 noted 104 cases of amenorrhea following HPV4. Less than 9% had a reported return of menses. Only 1 girl out of 105 amenorrhea notifications had a follicle-stimulating hormone level recorded. This was “elevated at 72” (no units given). No notifications had an anti-Müllerian hormone level reported. A comparison of adverse events following immunization reported to VAERS with adverse events following immunization reported to the World Health Organization “Vigibase” reveals similar proportions of notifications.⁵⁹ As with all passive reporting systems, reliance is placed on voluntary reporting accessing the reporting process. These reports often derive from a population of unknown size. It is not possible, therefore, to determine the incidence of these events or to assess causality. The chief function of adverse event reports and of case reporting is to generate hypotheses for further study.

Considerations

The great quantity of research concerning HPV4 vaccine does not necessarily establish a comprehensive, qualitative safety assurance. The administration of vaccines to all well prepubertal and peripubertal young persons necessitates a consideration of reproductive health that has not been met in the context of ovarian health. Selection of large numbers of participants may not produce the best data if the vaccine target group is underrepresented, or if research for adverse events is focused on hospitalizations and emergency settings rather than routine primary care settings—the context for many disease category presentations. Regardless of vast data, pre- and postlicensing studies have not assessed ovarian safety. Neither vaccine target age group study considered the proportion of girls postmenarche. Research reviews have not always analyzed safety study design quality. An Australian review of this vaccine's safety research spoke of "impressive clinical trial results" conducted before licensing.⁶⁰ However, younger person safety studies comprised 2 phase II studies of which only 1 had a "control" group, with very small numbers of young females receiving all 3 vaccinations. One of these 2 studies had lost more than half to 12 month follow-up even though these 10- to 15-year-olds were to be followed for 1 year after first vaccination for safety related data.³⁷ Only 40.4% of boys studied, 205 in total, completed 12-month safety follow-up in this designated safety study in which one 15-year-old boy died suddenly 27 days after his second vaccination.³⁷ With no clinical findings at autopsy, the investigator determined his death was unrelated to the study vaccine "because of the lack of any plausible or temporal relationship."

Other considerations await research. The relevance of claimed detection of HPV L1 gene DNA sequences in Gardasil vials in separate studies is unknown.^{61,62} A recent report states "preliminary data showed the presence of contaminating HPV L1 DNA in all tested different batches of Gardasil® Vaccine from France. Our observations confirm independently and extend the previous observations by Lee SH." Researchers concluded "the persistence in muscle tissue of residual HPV DNA fragments is uncertain after intramuscular injection and requires further investigation for vaccine safety."

The occurrence of increased adverse vaccine events in girls who had not previously been exposed to the HPV vaccine viral types before vaccination also has unknown relevance. Food and Drug Administration summary of safety trials reported most adverse events occurring in girls naïve to the injected vaccine HPV types prior to vaccination.^{42(p288, p432)} Those who were polymerase chain reaction (PCR) negative and seronegative to all 4 vaccine HPV types at baseline reported the highest incidence of systemic adverse events, the highest proportion of "moderate to severe" systemic adverse events and the highest incidence of headache after Gardasil when compared with groups who evidenced prior HPV type exposure at baseline. The difference in adverse event recording between those naïve to the HPV 6, 11, 16, 18 types and those who had been previously exposed was most marked in the "Detailed Safety Cohort" of protocol 015 (United States).^{42(p93)} In all, 63.8% of previously unexposed (seronegative/PCR negative) vaccine recipients recorded clinical adverse events after any injection. This compared with 51.5% of previously exposed (seropositive or PCR positive) recipients. The disparity within control groups was less marked. The Detailed Safety Cohort analysis records adverse clinical events in 60.4% of HPV naïve recipients of the aluminum control compared with 56.1% of HPV-exposed recipients. In the vaccine cohort, the disparity between the rates of clinical adverse events recorded in those who were naïve to HPV types 6, 11, 16, 18 prior to vaccination and those who were not naïve increased with each successive dose. The greatest difference was observed

after dose 3, when 27.9% of naïve recipients had clinical adverse events recorded, compared with 16.8% of those who evidenced previous exposure to HPV types 6, 11, 16 and 18. Where only one HPV type was present in the tested vaccine, phase II study 005 of HPV 16 L1 VLP, there were no increased clinical adverse events in the sexually naïve. None of the 3 girls in the case series discussed was sexually active. The relevance of this status is not known. Since the preferred target group of the HPV4 vaccination program is virgins, and this group is less represented in safety studies, further clarification is appropriate.

These cases presented to a part-time general practitioner in a 5-doctor general practice. Cases 1 and 2 lived in different towns 40 km apart. Case 3 had been diagnosed elsewhere but her case had not been notified to the TGA. Her presentation, while holidaying, was stimulated by her awareness of case 1 in medical literature and by identification of the township of the author. The third case had passed unnoticed in the context of preceding HPV vaccination. The number of girls in the population who may have a similar unnotified diagnosis is not knowable. The pattern of ovarian demise here is not clear, but a gradual process is apparent. Lack of diagnosis in cases 1 and 2 prompted investigation in preference to further issuing of oral contraceptive prescriptions. OCP prescribing would delay appropriate diagnosis and management as well as notification of a possible adverse event. Therapeutic management was commenced with a more appropriate level of hormone replacement, attention to calcium, vitamin D, exercise, bone mineral density, and subsequent monitoring for autoimmune conditions that may be associated. Psychological health will also be monitored given the physiological and emotional effects of this diagnosis. Depressive symptoms were not found in these patients. Anxiety symptoms have been found in premature ovarian failure and psychosocial stress has scored higher during the year before cessation of menses.⁶³

Diagnosis of idiopathic POI in mid-adolescence raises questions around future childbearing. Because of unrecordable anti-Müllerian hormone levels, 2 of these cases were not considered suitable for oocyte collection and cryopreservation. Recent studies of mouse oogonial stem cells have suggested the possibility of in vitro propagation and of future egg generation in vivo. Ovary tissue cryopreservation is being considered for future assistance in fertility preservation.⁶⁴

Future Research

Further research would consider a delayed onset of ovarian decline as suggested in this case series. The starting point of these girls' anti-Müllerian hormone levels is not known, but the decline in case 2 from 1.5 to <1 in 6 months may reflect the gradual decline that has possibly taken 5 years to complete. Anti-Müllerian hormone levels are a biomarker of ovarian reserve, with 1 study suggesting peak levels at 15.8 years and a decline commencing after age 25 years.⁶⁵ Their measurement may have a role to play in researching and monitoring ovarian demise and toxicity, since anti-Müllerian hormone levels strongly correlate with the existing antral follicle count and are therefore a quantitative measure of ovarian reserve.⁶⁶ Rodent ovarian histology—similar to the manufacturer's rodent testis histology report postvaccination—is also required. The delayed onset evidenced by this case series could also inform belated rodent ovary and fecundity studies to observe rodent ovaries and reproductive capacity at intervals after completed vaccination through their reproductive life span. Rodent fertility studies did not evaluate the standard vaccine course prior to conception, or the cumulative effect over time of 3

serial vaccinations, or the possibility of a delayed effect on reproductive capacity. Further research is needed to determine whether fecundity and fertility indices in rats are affected by the completed dosages administered to young teens as per industry guidelines.

Cohort studies of menstrual patterns in vaccinated and unvaccinated individuals are also required with timed anti-Müllerian hormone sampling. All such research should be wholly independent of commercial interests and manufacturer.

Conclusion

It is not known whether idiopathic POI developing progressively in young teens following HPV4 is related to this vaccination. Case reports do not and cannot establish causation. It is known that safety research before and after licensing has inadequate capacity to determine ovarian safety. Small numbers of young persons represented in research, hormonal usage in older females' studies, vaccine report card limitations, omission of a true placebo, inconsistent rodent toxicity studies, limitations of SAEs recording, subjective investigator decisions of likelihood and failure to record new conditions arising after month 7 as vaccine-related have weakened safety research. Diagnosis of premature ovarian insufficiency and failure is delayed in the general population and notified teenage amenorrhea is similarly underinvestigated in VAERS documentation. This primary care issue reduces the effectiveness of postmarketing surveillance. POF/POI notifications would be further compromised by OCP treatment of uninvestigated amenorrhea and hormonal contraception levels in the general population. Analysis of adverse event reporting is impeded by lack of background age-specific teen incidence figures. Long-term follow-up data after HPV vaccination has not surveyed ovarian function, recorded, measured, or analyzed symptoms or signs of dysfunction. Disparagement of adverse event reporting by licensing bodies' instruction to health providers that "there is no biologically plausible way in which HPV vaccine could cause infertility" lacks science and compromises safety monitoring by undermining "reporting efficiency"⁶⁷ safety signaling and informed consent. Public reassurance that "studies have not found ovarian failure to be associated with HPV vaccination"⁶⁸ in the absence of sound research may be harmful to vaccine confidence. Edward Jenner, considered the father of vaccines, was known to say "let's not speculate, let's do the experiment." Further studies are required to make any claims of ovary complications. Principles of informed consent, population health, and vaccine confidence require careful, rigorous and independent research to establish ovarian safety following HPV vaccination.

Acknowledgments

The authors gratefully acknowledge Helen Wyborn, Dr Don Radford, Michael Driscoll, Sally Toms, Kathleen O'Malley, Harriet Radford, Sandra Kremor, Janice Knopke, and the young woman of case 1 who asked if her condition could be related to GARDASIL.

Footnotes

Declaration of Conflicting Interests: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Baker VL. Primary ovarian insufficiency in the adolescent. *Curr Opin Obstet Gynecol*. 2013;25:375-381. [[PubMed](#)]
2. Nelson LM. Primary ovarian insufficiency. *N Engl J Med*. 2009;360:606-614. [[PMC free article](#)] [[PubMed](#)]
3. Vujovic S. Aetiology of premature ovarian failure. *Menopause Int*. 2009;15:72-75. [[PubMed](#)]
4. Coulam CB, Adamson SC, Annegers JF. Incidence of premature ovarian failure. *Obstet Gynecol*. 1986;67:604-606. [[PubMed](#)]
5. Future II Study Group. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med*. 2007;356:1915-1927. [[PubMed](#)]
6. Cancer in Australia 2000. AIHW Cat. No. CAN 18 (Cancer Series Number 23). Canberra, Australia: AIHW; 2003.
7. Cervical Screening in Australia 2000-2001 and 1999-2000, AIHW Cat. No. 19 (Cancer Series Number 24). Canberra, Australia: AIHW; 2003.
8. National Health and Medical Research Council. Screening to Prevent Cervical Cancer: Guidelines for the Management of Asymptomatic Women With Screen-Detected Abnormalities. Canberra: Australian Government National Health and Medical Research Council; 2005.
9. Mitchell HS. How much cervical cancer is being prevented? *Med J Aust*. 2003;178:298. [[PubMed](#)]
10. Australian Cancer Incidence and Mortality (ACIM) Books. Cervical Cancer for Australia. 2013. <http://www.aihw.gov.au/acim-books/>. Accessed October 6, 2014.
11. Cancer survival and prevalence in Australia: period estimates from 1982 to 2010, AIHW Cat. No. CAN 65 (Cancer Series Number 69). Canberra, Australia: AIHW; 2012.
12. Alzubaidi NH, Chapin HL, Vanderhoof VH. Meeting the needs of young women with secondary amenorrhea and spontaneous premature ovarian failure. *Obstet Gynecol*. 2002;99(5 pt 1):720-725. [[PubMed](#)]
13. Munster K, Helm P, Schmidt L. Secondary amenorrhoea: prevalence and medical contact—a cross-sectional study from a Danish county. *Br J Obstet Gynecol*. 1992;99:430-433. [[PubMed](#)]
14. Bachmann G, Kemmann E. Prevalence of oligomenorrea and amenorrhea in a college population. *Am J Obstet Gynecol*. 1982;144:98-102. [[PubMed](#)]
15. Petterson F, Fries H, Nillius SJ. Epidemiology of secondary amenorrhea. I. Incidence and prevalence rates. *Am J Obstet Gynecol*. 1973;117:80-86. [[PubMed](#)]
16. HPV (GARDASIL) Adverse Event Report #342035. Notified March 18, 2009.

17. Colofrancesco S, Perricone C, Tomljenovic L, Shoenfeld Y. Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants. *Am J Reprod Immunol*. 2013;70:309-316. [[PubMed](#)]
18. Baggs J, Gee G, Lewis E, Fowler G, Benson P. The vaccine safety datalink: a model for monitoring vaccine immunization safety. *Pediatrics*. 2011;127(suppl 1):545-553. [[PubMed](#)]
19. Rahman I, Åkesson A, Wolk A. Relationship between age at natural menopause and risk of heart failure [published online May 12, 2014]. *Menopause*. 10.1097/GME.000000000-0000261.
20. Nicodemus K, Folsom A, Anderson K. Menstrual history and risk of hip fractures in postmenopausal women: the Iowa Women's Health Study. *Am J Epidemiol*. 2001;153:251-255. [[PubMed](#)]
21. Apler MM, Garner PR. Premature ovarian failure: its relationship to autoimmune disease. *Obstet Gynecol*. 1996;66:27-30. [[PubMed](#)]
22. Kalantaridou SN, Davies SR, Nelson LM. Premature ovarian failure. *Endocrinol Metab Clin North Am*. 1998;27:989-1006. [[PubMed](#)]
23. NIH Consensus Development Panel. Osteoporosis prevention, diagnosis and therapy. *JAMA*. 2001;285:785-795. [[PubMed](#)]
24. Little DT, Ward HR. Premature ovarian failure 3 years after menarche in a 16-year-old girl following human papilloma-virus vaccination. *BMJ Case Rep*. 2012. 10.1136/bcr-2012-006879. [[PMC free article](#)] [[PubMed](#)]
25. Background document GARDASIL™ Human Papillomavirus Quadrivalent Vaccine VRBPAC Meeting, May 2006.
26. Little DT. Human papillomavirus vaccine and the ovary: the need for research. Paper presented at: Proceedings of the 18th World Congress on Controversies in Obstetrics, Gynecology and Infertility; October 24-27, 2013; Vienna, Austria.
27. Little DT. Response to the 4th Brighton Collaboration Journal Club. *Vaccine Saf Q*. 2014(2). http://u.b5z.net/i/u/16000121/f/Author_Little_DT_Response_to_4th_Brighton_Collaboration_Journal_Club.pdf. Accessed October 6, 2014.
28. FOI Request 001-1112 in relation to GARDASIL testing and complied with in the public interest Sept 2011. Application not displayed on TGA FOI website listing due to “commercially sensitive nature”. 2011.
29. Extract study no. TT#03-703-0 (CTD Module 4, volumes1-3) Study summary for non-clinical study report “Intramuscular developmental toxicity and immunogenicity study in rats with post-weaning evaluation”. Whitehouse Station, NJ: Merck & Co; 2005.
30. Wise LD, Pauley CJ, Bindhu M, Wolf JJ. Lack of effects on male fertility from a quadrivalent HPV vaccine in Sprague-Dawley rats. *Birth Defects Res B Dev Reprod Toxicol*. 2010;89:376-381. [[PubMed](#)]

31. TGA Australian Public Assessment Report for Human Papillomavirus Quadrivalent Vaccine. February 2011. <http://www.tga.gov.au/pdf/auspar/auspar-gardasil.pdf>. Accessed October 6, 2014.
32. Wise LD, Wolf JJ, Kaplanski CV, Pauley CJ, Ledwith BJ. Lack of effects on fertility and developmental toxicity of a quadrivalent HPV vaccine in Sprague-Dawley rats. *Birth Defects Res B Dev Reprod Toxicol.* 2008;83:561-572. [[PubMed](#)]
33. Intramuscular developmental toxicity and immunogenicity study in rats with postweaning evaluation. Extract Study no. TT#03-703-0 (CTD Module 4, volumes 1-3). Table A-6.
34. US Department of Health and Human Services. *Guidance for Industry: Considerations for Developmental Toxicity Studies for Prevention and Therapeutic Vaccines for Infectious Disease Indications.* Rockville, MD: Center for Biologics Evaluation and Research; 2006.
35. Oates K, Currow K, Hu W. *Child Health: A Practice Manual for General Practice.* Sydney, New South Wales, Australia: MacLennan + Petty; 2001.
36. Villa LL, Costa RL, Petta CA. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16 and 18) L1 virus-like particle vaccine in young women: a randomized double-blind placebo-controlled multicentre phase II efficacy trial. *Lancet Oncol.* 2005;6:271-278. [[PubMed](#)]
37. Block S, Nolan T, Sattler C, et al. Comparison of the immunogenicity and reactogenicity of a quadrivalent human papillomavirus (types 6, 11, 16 and 18) virus-like particle vaccine in male and female adolescents and young adult women. *Pediatrics.* 2006;118:2135-2145. [[PubMed](#)]
38. Reisinger KS, Block SL, Lazcano-Ponce E, et al. Safety and persistent immunogenicity of quadrivalent human papilloma-virus Types 6, 11, 16 and 18 L1 virus-like particle vaccine in preadolescents and adolescents. *Pediatr Infect Dis J.* 2007;26:201-209. [[PubMed](#)]
39. Garland SM, Hernandez-Avila M, Wheeler CM, et al. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. *N Engl J Med.* 2007;356:1928-1943. [[PubMed](#)]
40. Serious Adverse Events as defined by Code of Federal Regulations USA CF600.80 Postmarketing reporting of adverse experiences (hospitalization, life-threatening illness, disability, death, illness requiring surgical/medical intervention).
41. Lu B, Kumar A, Castellsagué X, Giuliano AR. Efficacy and safety of prophylactic vaccines against cervical HPV infection and diseases among women: a systematic review and meta-analysis. *BMC Infect Dis.* 2011;11:13. [[PMC free article](#)] [[PubMed](#)]
42. Miller NB. *Clinical Review of Biologics License Application for Human Papillomavirus 6, 11, 16, 18 L1 Virus Like Particle Vaccine (S. cerevisiae) (STN 125126 Gardasil).* Rockville, MD: Center for Biologics Evaluation and Research Food and Drug Administration; 2006.
43. Block S, Brown D, Chatterjee A, et al. Clinical trial and post licensure safety profile of a prophylactic human papilloma-virus (types 6, 11, 16 and 18) L1 virus-like particle vaccine. *Pediatr Infect Dis J.* 2010;29:95-101. [[PubMed](#)]

44. US Food and Drug Administration. CFR–Code of Federal Regulations Title 21. Sec. 314.80 Postmarketing reporting of adverse drug experiences. <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfrcfr/cfrsearch.cfm?fr=314.80>. Accessed October 6, 2014.
45. Bonanni P, Cohet C, Kjaer SK, et al. A summary of post-licensure surveillance initiatives for GARDASIL/SILGARD. *Vaccine*. 2010;28:4719-4730. [PubMed]
46. Gardasil® (Product information). WPC-V501-I-022011. 2010. GARDASIL PI A130709v11.0.doc.
47. Gajdova M, Jakubovsky J, Valky J. Delayed effects of neonatal exposure to Tween 80 on female reproductive organs in rats. *Food Chem Toxicol*. 1993;31:183-190. [PubMed]
48. Oser BL, Oser M. Nutritional studies on rats of diets containing high levels of partial ester emulsifiers. II. Reproduction and lactation. *J Nutr*. 1956;60:489-505. [PubMed]
49. *Myths and Realities: A Guide for Providers*. TGA Australian Government Department of Health and Ageing; 2013.
50. Therapeutic Goods Administration. No link between gardasil and infertility. *Australian Medicine*. May 17, 2013.
51. Perricone C, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y. Autoimmune/inflam-matory syndrome induced by adjuvants (ASIA) 2013: unveiling the pathogenic, clinical and diagnostic aspects. *J Autoimmunity*. 2013;47:1-16. [PubMed]
52. Fu Y, Jia FB, Wang J, et al. Effects of sub-chronic aluminum chloride exposure on rat ovaries. *Life Sci*. 2014;100:61-66. [PubMed]
53. Klein NP, Hansen J, Chao C, et al. Safety of human papillomavirus vaccine administered routinely to females. *Arch Pediatr Adolesc Med*. 2012;166:1140-1148. [PubMed]
54. Arnheim-Dahlström L, Pasternak B, Svanström H, Sparén P, Hviid A. Autoimmune, neurological and venous thromboembolic events after immunization of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study. *BMJ*. 2013;347:f5906. [PMC free article] [PubMed]
55. Iverson O. Long-term extension study of Gardasil in adolescents; results through month 96. http://www.dagensme-disin.no/Global/Dagens_medicin_norge/Bilder/PDF%20og%20word-dokumenter/018%20extension%20Iversen%20revi-sed%2017May2013.pdf. Accessed October 6, 2014.
56. Gee J, Naleway A, Shui I, et al. Monitoring the safety of quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink. *Vaccine*. 2011;29:8279-8284. [PubMed]
57. Markowitz LE, Hariri S, Unger E, Saraiya M, Datta SD, Dunne EF. Post-licensure monitoring of HPV vaccine in the United States. *Vaccine*. 2010;28:4731-4737. [PubMed]
58. VAERS data. <https://vaers.hhs.gov/data/index>. Accessed August 2013.

59. Labadie J. Postlicensure safety evaluation of human papillomavirus vaccines. *Int J Risk Saf Med*. 2011;23:103-112. [[PubMed](#)]
60. Macartney KK, Chiu C, Georgousakis M, Brotherton J. Safety of human papillomavirus vaccines: a review. *Drug Saf*. 2013;36:393-412. [[PubMed](#)]
61. Pere H, Fayard C, Belec L. Confirmation of the creation of a novel molecule in Gardasil. Hopitaux de Paris, Laboratoire de Virologie, Hopital Europeen Georges Pompidou, Paris, and Faculte de Medecine Paris Descartes (Paris V), Sorbonne Paris Cite, Paris. France.
62. Lee SH. Detection of human papillomavirus (HPV) L1 gene DNA possibly bound to particulate aluminium adjuvant in the HPV vaccine Gardasil. *J Inorg Biochem*. 2012;117:85-92. [[PubMed](#)]
63. de Taraciuk MB, Nolting M, Fernandez G, Colela D, Onetto C, Straminsky V. Psychological assessment of patients with premature ovarian failure. *Gynecol Endocrinol*. 2008;24:44-53. [[PubMed](#)]
64. Donnez J, Dolmans M. Fertility preservation in women. *Nat Rev Endocrinol*. 2013;9:735-749. [[PubMed](#)]
65. Lie Fong S, Visser JA, Welt CK, et al. Serum anti-Müllerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. *J Clin Endocrinol Metab*. 2012;97:4650-4655. [[PMC free article](#)] [[PubMed](#)]
66. Tremellen K, Kolo M. Serum anti-Müllerian hormone is a useful measure of quantitative ovarian reserve but does not predict the chances of live-birth pregnancy. *Aust N Z J Obstet Gynaecol*. 2010;50:568-572. [[PubMed](#)]
67. Varricchio F, Iskander J, Destafano F. Understanding vaccine safety information from the vaccine adverse event reporting system. *Pediatr Infect Dis J*. 2004;23:287-294. [[PubMed](#)]
68. Centers for Disease Control and Prevention. Frequently asked questions about HPV vaccine safety. Atlanta, GA: Centers for Disease Control and Prevention; 2013.

Articles from Journal of Investigative Medicine High Impact Case Reports are provided here courtesy of
SAGE Publications

PubMed

Format: Abstract

Full text links

ELSEVIER
FULL-TEXT ARTICLE

J Inorg Biochem. 2013 Nov;128:237-44. doi: 10.1016/j.jinorgbio.2013.07.022. Epub 2013 Jul 19.

Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes.

Shaw CA¹, Li Y, Tomljenovic L.

Author information

Abstract

Our previous ecological studies of autism spectrum disorder (ASD) has demonstrated a correlation between increasing ASD rates and aluminium (Al) adjuvants in common use in paediatric vaccines in several Western countries. The correlation between ASD rate and Al adjuvant amounts appears to be dose-dependent and satisfies 8 of 9 Hill criteria for causality. We have now sought to provide an animal model to explore potential behavioural phenotypes and central nervous system (CNS) alterations using s.c. injections of Al hydroxide in early postnatal CD-1 mice of both sexes. Injections of a "high" and "low" Al adjuvant levels were designed to correlate to either the U.S. or Scandinavian paediatric vaccine schedules vs. control saline-injected mice. Both male and female mice in the "high Al" group showed significant weight gains following treatment up to sacrifice at 6 months of age. Male mice in the "high Al" group showed significant changes in light-dark box tests and in various measures of behaviour in an open field. Female mice showed significant changes in the light-dark box at both doses, but no significant changes in open field behaviours. These current data implicate Al injected in early postnatal life in some CNS alterations that may be relevant for a better understanding of the aetiology of ASD.

KEYWORDS: Adjuvants; Aluminium; Autism; Neurodevelopmental disorders; Neurotoxicity; Vaccines

PMID: 23932735 DOI: [10.1016/j.jinorgbio.2013.07.022](https://doi.org/10.1016/j.jinorgbio.2013.07.022)

[Indexed for MEDLINE]

Publication type, MeSH terms, Substances

LinkOut - more resources



**EVENTS REPORTED TO VAERS AFTER HPV VACCINES
THROUGH Oct 14, 2018**

Event	Female	Male	Unknown	Totals
<u>Disabled</u>	2662	115	55	2832
<u>Deaths</u>	330	23	86	439
<u>Did Not Recover</u>	11,042	824	208	12,074
<u>Abnormal Smear</u>	660	1	5	666
<u>Cervical Dysplasia</u>	316	1	4	321
<u>Cervical Cancer</u>	142		5	147
<u>Life Threatening</u>	860	85	12	957
<u>Emergency Room</u>	13,653	1569	175	15,397
<u>Hospitalization</u>	5597	316	76	5989
<u>Extended Hospital Stay</u>	271	17	1	289
<u>Serious</u>	8135	441	206	8782
<u>TOTAL REPORTS</u>	42,824	6651	10,704	60,179

The Vaccine Adverse Event Reporting System (VAERS) Results

These are saved results

Saved Jul 9, 2017, 2:07 AM

[More Information](#)

the link that creates
this page

Share to social media:  



This dataset has been updated since this request was saved, which could lead to differences in results.

Still Processing, Click "Cancel Request" to stop...

Vaccine	VAERS ID
HPV (GARDASIL) (1098)	<u>287888-1</u>
HPV (GARDASIL) (1098)	<u>291804-1</u>
HPV (GARDASIL) (1098)	<u>293388-1</u>
HPV (GARDASIL) (1098)	<u>297528-1</u>
HPV (GARDASIL) (1098)	<u>305606-1</u>
HPV (GARDASIL) (1098)	<u>309233-1</u>
HPV (GARDASIL) (1098)	<u>310262-1</u>
HPV (GARDASIL) (1098)	<u>316983-1</u>
HPV (GARDASIL) (1098)	<u>317757-1</u>
HPV (GARDASIL) (1098)	<u>319533-1</u>
HPV (GARDASIL) (1098)	<u>319810-1</u>
HPV (GARDASIL) (1098)	<u>321696-1</u>

HPV (GARDASIL) (1098)	<u>324002-1</u>
HPV (GARDASIL) (1098)	<u>325063-1</u>
HPV (GARDASIL) (1098)	<u>334611-1</u>
HPV (GARDASIL) (1098)	<u>336473-1</u>
HPV (GARDASIL) (1098)	<u>344160-1</u>
HPV (GARDASIL) (1098)	<u>351970-1</u>
HPV (GARDASIL) (1098)	<u>356938-1</u>
HPV (GARDASIL) (1098)	<u>380740-1</u>
HPV (GARDASIL) (1098)	<u>403759-1</u>
HPV (GARDASIL) (1098)	<u>405821-1</u>
HPV (GARDASIL) (1098)	<u>406289-1</u>
HPV (GARDASIL) (1098)	<u>417137-1</u>
HPV (GARDASIL) (1098)	<u>425513-1</u>
HPV (GARDASIL) (1098)	<u>430780-1</u>
HPV (GARDASIL) (1098)	<u>437735-1</u>
HPV (GARDASIL) (1098)	<u>437999-1</u>
HPV (GARDASIL) (1098)	<u>442402-1</u>
HPV (GARDASIL) (1098)	<u>449334-1</u>
HPV (GARDASIL) (1098)	<u>453010-1</u>
HPV (GARDASIL) (1098)	<u>457904-1</u>
HPV (GARDASIL) (1098)	<u>485757-1</u>
HPV (GARDASIL) (1098)	<u>494024-1</u>
HPV (GARDASIL) (1098)	<u>501081-1</u>
HPV (GARDASIL) (1098)	<u>501663-1</u>
HPV (GARDASIL) (1098)	<u>510130-1</u>
HPV (GARDASIL) (1098)	<u>513554-1</u>

HPV (GARDASIL) (1098)	<u>515434-1</u>
HPV (GARDASIL) (1098)	<u>518872-1</u>
HPV (GARDASIL) (1098)	<u>526687-1</u>
HPV (GARDASIL) (1098)	<u>532797-1</u>
HPV (GARDASIL) (1098)	<u>538295-1</u>
HPV (GARDASIL) (1098)	<u>568282-1</u>
HPV (GARDASIL) (1098)	<u>570801-1</u>
HPV (GARDASIL) (1098)	<u>612719-1</u>
HPV (GARDASIL) (1098)	<u>622986-1</u>
HPV (GARDASIL) (1098)	<u>691836-1</u>
HPV (GARDASIL) (1098)	<u>695378-1</u>
HPV (GARDASIL 9) (1170)	<u>611452-1</u>
HPV (GARDASIL 9) (1170)	<u>641317-1</u>
HPV (GARDASIL 9) (1170)	<u>648057-1</u>
HPV (GARDASIL 9) (1170)	<u>669596-1</u>
HPV (NO BRAND NAME) (1102)	<u>655074-1</u>
HPV (NO BRAND NAME) (1102)	<u>655670-1</u>
HPV (NO BRAND NAME) (1102)	<u>691319-1</u>

Note: Submitting a report to VAERS does not mean that healthcare personnel or the vaccine caused or contributed to the adverse event (possible side effect).

Notes:

Caveats: DISCLAIMER: VAERS staff at CDC and the Food and Drug Administration (FDA) follow up on all serious adverse event reports to obtain additional medical, laboratory, and/or autopsy records to help understand the circumstances. However, VAERS public data do not generally change based on the information obtained during the follow-up process. There are limitations to VAERS data. A report to VAERS does not mean that the vaccine caused the adverse event, only that the adverse event occurred sometime after vaccination. Read more about interpreting VAERS data: [More information.](#)

Some items may have more than 1 occurrence in any single event report, such as Symptoms, Vaccine Products, Manufacturers, and Event Categories. If data are grouped by any of these items, then the number in the Events

Reported column may exceed the total number of unique events. If percentages are shown, then the associated percentage of total unique event reports will exceed 100% in such cases. For example, the number of Symptoms mentioned is likely to exceed the number of events reported, because many reports include more than 1 Symptom. When more than 1 Symptom occurs in a single report, then the percentage of Symptoms to unique events is more than 100%. [More information.](#)

Data contains VAERS reports processed as of 11/14/2018. The VAERS data in WONDER are updated monthly, yet the VAERS system receives continuous updates including revisions and new reports for preceding time periods. [More information.](#)

Values of Event Category field vary in their availability over time due to changes in the reporting form. The "Emergency Room/Office Visit" value was available only for events reported using the VAERS-1 form, active 07/01/1990 to 06/29/2017. The "Congenital Anomaly/Birth Defect", "Emergency Room", and "Office Visit" values are available only for events reported using the VAERS 2.0 form, active 06/30/2017 to present. These changes must be considered when evaluating count of events for these categories.

Help: See [The Vaccine Adverse Event Reporting System \(VAERS\) Documentation](#) for more information.

Query Date: Dec 18, 2018 12:13:41 PM

Suggested Citation:

United States Department of Health and Human Services (DHHS), Public Health Service (PHS), Centers for Disease Control (CDC) / Food and Drug Administration (FDA), Vaccine Adverse Event Reporting System (VAERS) 1990 - last month, CDC WONDER On-line Database. Accessed at <http://wonder.cdc.gov/vaers.html> on Dec 18, 2018 12:13:41 PM

Query Criteria:

Title:	
Adverse Event Description:	All
Adverse Events After Prior Vaccinations:	All
Age:	All
Current Illness:	All
Date Died:	Before 1980 to May, 2017
Date of Onset:	Before 1980 to May, 2017
Date Report Completed:	Before 1990 to May, 2017
Date Report Received:	Jul., 1990 to May, 2017
Date Vaccinated:	Before 1980 to May, 2017
Days In Hospital:	All
Event Category:	Death
Grantee:	All
History/Allergies:	All
Lab Data:	All

Medications At Time Of Vaccination:	All
Mfr/Imm Project Number:	All
Onset Interval:	All
Recovered:	All
Report Form Version:	All
Serious:	All
Sex:	All
State / Territory:	The United States/Territories/Unknown
Symptoms:	APPARENT DEATH, BRAIN DEATH, CARDIAC DEATH, CELL DEATH, DEATH, SUDDEN CARDIAC DEATH, SUDDEN DEATH, TERMINAL STATE
Vaccine Administered By:	All
Vaccine Dose:	All
Vaccine Lot:	All
Vaccine Manufacturer:	All
Vaccine Products:	HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE (HPV4), HUMAN PAPILLOMAVIRUS (TYPES 6, 11,16, 18, 31, 33, 45, 52, 58) RECOMBINANT VACCINE (HPV9), HUMAN PAPILLOMAVIRUS VACCINE (HPVX), HUMAN PAPILLOVAVIRUS BIVALENT (HPV2)
Vaccine Purchased By:	All
VAERS ID:	All
Group By:	Vaccine, VAERS ID
Show Totals:	False
Show Zero Values:	False

VAERS Event Details

Details for VAERS ID: 287888-1

Event Information			
Patient Age	22.00	Sex	Female
State / Territory	Unknown	Date Report Completed	2007-08-10
Date Vaccinated	2007-05-21	Date Report Received	2007-08-13
Date of Onset	2007-05-23	Date Died	2007-05-23
Days to onset	2	Grantee	Non-Grantee
Vaccine Administered By	Other	Vaccine Purchased By	Other **
Mfr/Imm Project Number	WAES0708USA00407	Report Form Version	1
Recovered	No	Serious	Yes

* VAERS 2.0 Report Form Only

** VAERS-1 Report Form Only

"Not Applicable" will appear when information is not available on this report form version.

Event Categories	
Death	Yes
Life Threatening	No
Permanent Disability	No
Congenital Anomaly / Birth Defect *	N/A
Hospitalized	No
Days in Hospital	None
Existing Hospitalization Prolonged	No
Emergency Room / Office Visit **	Yes
Emergency Room *	N/A
Office Visit *	N/A

* VAERS 2.0 Report Form Only

** VAERS-1 Report Form Only

"N/A" will appear when information is not available on this report form version.

Vaccine Type	Vaccine	Manufacturer	Lot	Dose	Route	Site
HUMAN PAPILLOMAVIRUS (TYPES 6, 11, 16, 18) RECOMBINANT VACCINE	HPV (GARDASIL)	MERCK & CO. INC.	0389U	UNK	IM	UN

Symptom
AUTOPSY
DEATH

Adverse Event Description
<p>"Information has been received from a nurse practitioner concerning a 22 year old female patient with no pertinent medical history or drug allergies who on 21-MAY-2007, was vaccinated IM with a 0.5ml dose of Gardasil (Lot# 657736/0389U). Concomitant therapy included hormonal contraceptives (unspecified) ("MERCET"). On 23-MAY-2007, the patient died suddenly. The cause of death was unknown. Unspecified medical attention was sought. Laboratory diagnostic studies included an autopsy which showed no findings. No product quality complaint was involved. The reporter stated that Gardasil did not</p>

cause the patient's death. Additional information is not expected. 7/2/08-records received-Adverse effect of drugs.Toxicology survey findings:urine positive for methadone, benzodiazepines, benzoylcegonine (from cocaine), cannabinoids, nicotine, diphenhydramine and naproxen."

Lab Data	Current Illness	Adverse Events After Prior Vaccinations
autopsy - no findings		

Medications At Time Of Vaccination	History/Allergies
hormonal contraceptives	None 7/2/08-records received-HX of heroin and prescription drug abuse.,

Note: Submitting a report to VAERS does not mean that healthcare personnel or the vaccine caused or contributed to the adverse event (possible side effect).

Notes:

Caveats: DISCLAIMER: VAERS staff at CDC and the Food and Drug Administration (FDA) follow up on all serious adverse event reports to obtain additional medical, laboratory, and/or autopsy records to help understand the circumstances. However, VAERS public data do not generally change based on the information obtained during the follow-up process. There are limitations to VAERS data. A report to VAERS does not mean that the vaccine caused the adverse event, only that the adverse event occurred sometime after vaccination. Read more about interpreting VAERS data: [More information.](#)

Data contains VAERS reports processed as of 11/14/2018. The VAERS data in WONDER are updated monthly, yet the VAERS system receives continuous updates including revisions and new reports for preceding time periods. [More information.](#)

Help: See [The Vaccine Adverse Event Reporting System \(VAERS\) Documentation](#) for more information.

Query Date: Dec 18, 2018 12:14:41 PM

Suggested Citation:

United States Department of Health and Human Services (DHHS), Public Health Service (PHS), Centers for Disease Control (CDC) / Food and Drug Administration (FDA), Vaccine Adverse Event Reporting System (VAERS) 1990 - last month, CDC WONDER On-line Database. Accessed at <http://wonder.cdc.gov/vaers.html> on Dec 18, 2018 12:14:41 PM

- WND - <http://www.wnd.com> -

Now Japan pulls Gardasil shots for young girls

Posted By *Bob Unruh* On 10/01/2013 @ 8:49 pm In Education,Front Page,Health,Politics,U.S.,World | [No Comments](#)

Japanese government officials, stunned by nearly 2,000 reports of “adverse effects” of a highly touted cervical cancer vaccine promoted widely in the United States, have decided to withdraw their recommendation for its use in the island nation.

Word comes from Judicial Watch, the Washington-based corruption watchdog that has been monitoring the effects of the drug’s use in the U.S. for years.

“Japanese health officials have recorded nearly 2,000 adverse reactions – hundreds of them serious – in girls who got a dangerous U.S. government-backed cervical cancer vaccine that’s also been linked to thousands of debilitating side effects in this country,” Judicial Watch reported Tuesday.

“The alarming reports have led Japan’s government to take action, suspending recommendation for the controversial vaccine which is billed as a miracle shot that can prevent certain strains of cervical cancer caused by Human Papillomavirus (HPV).”

The organization said the U.S. government has taken the opposite approach amid equally alarming cases of serious side effects.

Not only does the Obama administration continue recommending Gardasil, it spends large sums of taxpayer dollars promoting it and works hard to keep details involving its dangers secret, Judicial Watch said.

Multiple reports uncovered and cited by Judicial Watch discuss the dangers – including death – that the drug presents to children who are given the injections, which cost \$600 per patient.

Other side effects have included seizures, blindness, paralysis, speech problems, pancreatitis and short-term memory loss.

“Incredibly, the Food and Drug Administration (FDA) fast-tracked Gardasil’s approval and the Centers for Disease Control and Prevention (CDC) recommends it for girls starting at age 9,” Judicial Watch confirmed.

The organization started investigating in 2007 and has had to sue for the records in the face of Obama administration stonewalling.

Judicial Watch said that in Japan, the Ministry of Health, Labor and Welfare warned local governments that the HPV vaccine should not be recommended amid safety concerns.

Judicial Watch quoted from a report released just days ago by Japanese cardiologist Dr. Sataro Sato, who said documents from the manufacturer suggested the vaccine is linked to seizures and brain damage.

Sato also addressed the use of another brand of vaccine, called Cervarix.

Following the lead of the U.S., Japanese officials had allocated more than \$187 million for "urgent HPV vaccination programs" for girls between 11 and 14. Government leaders then visited junior high schools to push for the drugs.

"But health officials were taken aback with the high number of side effects reported to Japan's Vaccine Adverse Reactions Review Committee," Judicial Watch said. "Since the government began offering girls HPV shots, 1,968 adverse events were reported, including 358 that were evaluated as serious by a JMLHW committee, Dr. Sato writes. Parents began calling the country's health minister and furnishing videos in which girls who had received the HPV vaccine suffered from walking disturbances, body tics and seizures. In other cases many girls injected with the vaccine fell to the floor, injuring their head or face and some fracturing their jaw or teeth."

A review followed and health officials sent formal notifications to local governments that the vaccine should not be recommended, Judicial Watch said.

WND reported earlier this year when a Judicial Watch investigation found the government had paid almost \$6 million to victims of the shot, which covered only about one-fourth of the claims.

WND also has reported the federal government has recommended the HPV vaccination for girls and boys as young as 11.

A recent video, Judicial Watch said, is part of the Obama administration's "full-throttle effort" to promote the drug. But it doesn't mention side effects such as death.

"The administration has worked hard to keep details involving the dangers of the vaccine secret as the government spends large sums of taxpayer dollars promoting it for girls and young women," the report said.

The organization explained it became interested in Gardasil when the drug was offered as a

treatment for certain strains of cervical cancer caused by HPV. Judicial Watch said it discovered an "atrocious" from the "profitable vaccine manufactured by pharmaceutical giant Merck."

"The reality is that dozens of government records uncovered by Judicial Watch show that Gardasil has been linked to thousands of adverse reactions and debilitating side effects that the government wants to keep secret," the new report said. "They include seizures, blindness, paralysis, speech problems, pancreatitis, short-term memory loss and dozens of deaths."

The new 13-minute video endorsing the three-dose HPV vaccine series is being presented by the Centers for Disease Control and Prevention as part of National Immunization Awareness Month.

"The video, designed to reach 'underserved areas' and 'minority populations,' features young women and healthcare professionals touting the vaccine. It lies about side effects, saying ... there's 'little pain and discomfort' and 'dizziness and stomach aches,'" Judicial Watch said.

The video:



The legal team also said the Obama administration recently spent \$1.2 million to promote Gardasil among low-income and minority girls.

"Notably absent in this latest DVD and all other Gardasil promotional campaigns are the potentially lethal side effects documented in the government's own Vaccine Adverse Event

Reporting System (VAERS). The data is kept by the FDA and CDC as a vaccine safety surveillance program that can be easily accessed by the public yet Judicial Watch had to sue for information related to Gardasil," Judicial Watch said.

WND earlier reported the damage payments of nearly \$6 million covered only some of the 200 claims that have been filed to date.

At the time, Judicial Watch found:

Only 49 of the 200 claims filed have been compensated for injury or death caused from the HPV vaccine. Of the 49 compensated claims, 47 were for injury caused from HPV vaccine; the additional two claims were for death caused due to the vaccine.

Ninety-two (nearly half) of the total 200 claims filed are still pending. Of those pending claims 87 of the claims against HPV vaccine were filed for injury, the remaining five claims were filed for death.

Fifty-nine claims have been dismissed outright by VICP. The alleged victims were not compensated for their claims against the HPV vaccine. Of the claims dismissed, 57 were for injuries, two were for deaths allegedly caused by the HPV vaccine.

The amount awarded to the 49 claims compensated totaled \$5,877,710.87, or approximately \$120,000 per claim.

See coverage of the Obamacare government-shutdown:

Breakthrough? Obama 'willing to negotiate'

Kingston to Senate: Be responsible

Obama sued for fiddling with health takeover

'Fakers': Dems hurl verbal bombs at GOP

Obamacare to Americans: 'Please wait'

Veterans visit 'closed' site in Washington

Troops could lose thousands during shutdown

Black professor: Shutdown due to Obama's skin color

Commentary from Molotov Mitchell: '61% of Americans are right-wing nutjobs?'

Commentary from Troy Newman: 'Now I'm an unwilling Obamacare outlaw'

Article printed from WND: <http://www.wnd.com>

URL to article: <http://www.wnd.com/2013/10/now-japan-pulls-gardasil-shots-for-young-girls/>

© Copyright 1997-2013. All Rights Reserved. WND.com.

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: July 10, 2017

* * * * *

CHASE BOATMON & MAURINA
CUPID, *parents of J.B., deceased,*

Petitioners,

v.

SECRETARY OF HEALTH
AND HUMAN SERVICES,

Respondent.

* * * * *

PUBLISHED DECISION

No. 13-611V

Special Master Gowen

Entitlement Decision; Diphtheria-Tetanus-acellular Pertussis (DTaP) Vaccine; Inactivated Polio Vaccine (IPV); Haemophilus Influenzae (HiB) Vaccine; Pneumococcal Conjugate (PCV) Vaccine; Rotavirus Vaccine; Sudden Infant Death Syndrome (SIDS).

Ronald C. Homer & Joseph M. Pepper, Conway, Homer P.C., Boston, MA, for petitioners.
Lara A. Englund & Ryan M. Pyles, United States Department of Justice, Washington, DC, for respondent.¹

RULING ON ENTITLEMENT²

On August 27, 2013, Chase Boatmon and Maurina Cupid (“petitioners”), as the representatives of the estate of their deceased minor child, J.B., filed a petition under the National Vaccine Injury Compensation Program (“Vaccine Act” or the “Program”),³ 42 U.S.C. § 300aa-10 *et. seq.* (2012). Petitioners allege that as a result of receiving vaccinations for

¹ Mr. Homer is petitioners’ attorney of record, while his colleague Mr. Pepper appeared at the entitlement hearing. Similarly, for respondent, Ms. Englund has always been the attorney of record, but Mr. Pyles appeared at the entitlement hearing.

² Because this decision contains a reasoned explanation for the action in this case, the undersigned intends to post it on the website of the United States Court of Federal Claims, pursuant to the E-Government Act of 2002, *see* 44 U.S.C. § 3501 note (2012). The court’s website is at <http://www.uscfc.uscourts.gov/aggregator/sources/7>. Before the decision is posted on the court’s website, each party has 14 days to file a motion requesting redaction “of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy.” Vaccine Rule 18(b). “An objecting party must provide the court with a proposed redacted version of the decision.” *Id.* If neither party files a motion for redaction within 14 days, the decision will be posted on the court’s website. *Id.*

³ The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3705, codified as amended, 42 U.S.C. §§ 300aa-1 to -34 (2012). All citations in this decision to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

Diphtheria-Tetanus-acellular Pertussis (“DTaP”), inactivated polio (“IPV”), haemophilus influenzae (“HiB”), Pneumococcal Conjugate (“PCV”), and Rotavirus vaccinations on September 2, 2011, J.B. passed away from Sudden Infant Death Syndrome (“SIDS”) on September 3, 2011. *See* Petition (ECF No. 1); Amended Petition (ECF No. 15).

After carefully analyzing and weighing all of the evidence and testimony presented in this case in accordance with the applicable legal standards, the undersigned finds that petitioners have met their legal burden. Petitioners have put forth preponderant evidence that the vaccines J.B. received on September 2, 2011 actually caused or substantially contributed to his death from Sudden Infant Death Syndrome. Furthermore, respondent has failed to put forth preponderant evidence that J.B.’s death was in fact caused by factors unrelated to the vaccines. Accordingly, petitioners are entitled to compensation.

I. BACKGROUND

A. Procedural History

Petitioners filed a petition for compensation pursuant to the Vaccine Act on behalf of their deceased minor son, J.B., on August 27, 2013. Petition (ECF No. 1). They filed an amended petition on February 6, 2014. Amended Petition (ECF No. 15). Petitioners filed the expert report of Dr. Douglas C. Miller, a neuropathologist, along with the medical literature referenced in his report, on May 20, 2014. Exhibit 13, 14 (ECF No. 21).⁴

On September 9, 2014, respondent filed a Rule 4(c) report advising against compensation. Rule 4(c) Report (ECF No. 28). That same day, he filed an expert report and medical literature referenced therein from Dr. Brent Harris, a pathologist. Exhibit A (ECF No. 29). Respondent also filed an expert report and medical literature from Dr. Christine T. McCusker. Exhibit C (ECF Nos. 30-32). Petitioners filed a supplemental report from Dr. Miller on November 10, 2014. Exhibit 16 (ECF No. 35). Extensive and detailed medical literature was submitted in support of all of the expert reports.⁵

At numerous stages of this case, the undersigned encouraged the parties to pursue the possibility of an informal resolution and/or to consider mediation. *See, e.g.*, Order filed December 9, 2014 (ECF No. 37). The parties ultimately did not settle the case. An entitlement hearing was held on Thursday, August 6, and Friday, August 7, 2015, in Washington, D.C. Dr. Miller testified on behalf of petitioners, and Dr. Harris and Dr. McCusker testified for respondent. The case was well tried and involved detailed expert testimony from both sides. *See*

⁴ On October 14, 2014, petitioners refiled the medical literature cited in Dr. Miller’s report, highlighting the specific portions being relied upon to support causation. Petitioners’ Notice of Refiling Documents (ECF No. 34).

⁵ I have read and digested all of the literature submitted in this case and will reference numerous but not all articles in the course of this opinion. However, all articles have been considered in coming to a conclusion in this case. More recent articles, particularly those by the same authors or groups, are referenced more frequently because they incorporate, build upon, and update the earlier literature. Petitioners and Dr. Miller filed Exhibits 13-A through 13-V and Exhibits 14 through 21. Respondent and Dr. Harris filed Exhibits A-1 through A-6. Respondent and Dr. McCusker submitted Exhibits C-1 through C-20 and Exhibits D through G.

Transcript filed on September 9, 2015 (ECF Nos. 50, 52). Petitioners filed their post-hearing brief on December 7, 2015. (ECF No. 61). Respondent filed his post-hearing brief on March 7, 2016. (ECF No. 63). Petitioners filed their reply to respondent's post-hearing brief on March 28, 2016. (ECF No. 64). This matter is now ripe for adjudication.

B. Standards for Adjudication

The Vaccine Act established the Program to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" *Rooks v. Sec'y of Health & Human Servs.*, 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

There are two avenues to compensation under the Program. The first is to demonstrate a "Table injury," that is, a specified injury within a specified period of time following administration of a vaccine listed on the Vaccine Injury Table. § 300aa-14(a). A Table injury creates a presumption of causation, which is only defeated if respondent shows that the injury was caused by a factor or factors unrelated to the vaccine. In the present case, petitioners allege that J.B. died suddenly of a cause that remained unexplained after a site investigation and autopsy, often referred to as SIDS, shortly after receiving various vaccines listed on the Table. The Table does not list SIDS occurring in any period of time after any vaccine.

Therefore, petitioners must take the second avenue towards compensation: they must establish an "off-Table injury," meaning that the vaccine(s) were the cause in fact of the vaccinee's injuries. In *Althen*, the Federal Circuit established a three-prong test: petitioners must establish (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a proximate temporal relationship between vaccination and injury. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The legal standard is by a preponderance of the evidence." §300aa-13(a)(1)(a). This does not require "conclusive scientific evidence" or "certainty." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 (Fed. Cir. 2010). Instead, the standard has been interpreted to mean that a fact is more likely than not. *Id.* at 1322 n.2. The Federal Circuit has observed that this preponderance standard enables "the finding of causation in a field bereft of complete and direct proof of how the vaccines affect the human body." *Althen*, 418 F.3d at 1280. Petitioners must establish each *Althen* prong by the preponderance of the evidence. *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 132 (2011), *aff. per curiam*, 463 Fed. Appx. 932 (Fed. Cir. 2012).

Each *Althen* prong may be satisfied by medical records or a medical opinion. *Althen*, 418 F.3d at 1279; *see also Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006) (noting that the same piece of evidence can support several *Althen* prongs). Petitioners are not required to provide "objective confirmation" by way of "medical

documentation.” *Id.* at 1278. Such a requirement would “contravene the plain language of the statute.” *Id.* at 1281.

In determining whether a petitioner is entitled to compensation, a special master must consider the entire record and is not bound by any particular piece of evidence. § 13(b)(1) (stating that a special master is not bound by any “diagnosis, conclusion, judgment, test result, report, or summary” contained in the record). Thus, a special master must weigh and evaluate opposing expert opinions, medical and scientific evidence, and the evidentiary record in deciding whether petitioners have met their burden of proof.

Epidemiological studies, or the lack thereof, are not dispositive of the causation in fact determination. *Grant v. Sec’y of Health & Human Servs.*, 956 F.2d 1144, 1149 (Fed. Cir. 1992). Indeed, petitioners are not required to present medical literature or epidemiological evidence to establish any *Althen* prong. *Andreu v. Sec’y of Health & Human Servs.*, 569 F.3d 1367, 1380 (Fed. Cir. 2009). However, the special master can consider [epidemiological evidence] in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury.... Medical literature and epidemiological evidence must be viewed... not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act’s preponderant evidence standard.” *Andreu*, 569 F.3d at 1380.

Under the second *Althen* prong, petitioners need to show that the vaccine(s) was “not only a but-for cause of the injury but also a substantial factor in bringing about the injury.” *Shyface v. Sec’y of Health & Human Servs.*, 165 F.3d 1344, 1352-53 (Fed. Cir. 1999). They do not need to show that the vaccine(s) was the “sole” or even the “predominant” cause. *Id.* at 1352. For example, in *Shyface*, the Federal Circuit affirmed that petitioners were entitled to compensation, based on their expert’s testimony that the vaccine together with a bacterial infection caused the child’s high fever and death (although the expert could not testify that the vaccine was the “sole” or “predominant” cause. 165 F.3d at 1353.

Showing a logical sequence of cause and effect between the vaccine(s) and the injury will tend to show that the injury was not caused by an alternative cause. However, a petitioner is not required to eliminate all possible alternative causes of the injury. *See Walter v. Sec’y of Health & Human Servs.*, 485 F.3d 1146, 1150 (Fed. Cir. 2007) (“the Vaccine Act does not require the petitioner to bear the burden of eliminating alternative causes where the other evidence on causation is sufficient to establish a *prima facie* case”). This standard permits the use of “circumstantial evidence” and accomplishes Congress’s goal that “close calls regarding causation are resolved in favor of injured claimants.” *Althen*, 165 F.3d at 1280.

Once a petitioner fulfills the *Althen* test, the burden of persuasion shifts to respondent to show that the alleged injury was caused by a factor unrelated to the vaccination. *Knudsen*, 35 F.3d 543 at 548; § 13(a)(1)(B). Respondent has the burden of demonstrating that “a factor unrelated to the vaccination is the more likely or principal cause of the injury alleged. Such a showing establishes that the factor unrelated, not the vaccination, was ‘principally responsible’ for the injury.” *Deribeaux v. Sec’y of Health & Human Servs.*, 717 F.3d 1363, 1369 (Fed. Cir. 2013). Section 13(a)(2) specifies that factors unrelated “[do]not include any idiopathic, unexplained, unknown, hypothetical, or undocumented causal factor, injury, illness, or

condition.” Close calls regarding causation must be resolved in favor of the petitioner. *Althen*, 418 F.3d at 1280; *Knudsen*, 35 F.3d at 551 (“If the evidence (on alternative cause) is seen in equipoise, then the government has failed in its burden of persuasion and compensation must be awarded.

C. Summary of Relevant Facts

J.B. was born on April 7, 2011, when his mother became pre-eclamptic and underwent a Caesarean section. Exhibit 1 at 10. J.B. was born 4 weeks prematurely at 36 weeks gestation. Exhibit 2 at 3. The mother’s medical records report no history of tobacco, alcohol, or illicit drugs. Exhibit 1 at 3. At birth, J.B. was noted to be “well appearing, non-dysmorphic[,] alert and in no acute distress.” Exhibit 2 at 9. His Apgar scores⁶ were 8 at 1 minute and 9 at 5 minutes. Exhibit 2 at 9. J.B. and his mother are both noted to be African-American. Exhibit 2 at 3, 25.

On April 14, 2011, one week after birth, J.B. received his first Hep B vaccination. Exhibit 2 at 82.⁷ At his two-week well baby visit on April 21, 2011, J.B. was “well appearing, alert . . . a healthy appearing 2 [week] old with normal growth and development.” *Id.* at 79-81. On June 7, 2011, J.B. – exhibiting a cough and a runny nose – was brought to the emergency room. *Id.* at 73. He underwent a chest x-ray that revealed “no radiographic evidence of acute cardiopulmonary disease.” *Id.*

J.B.’s subsequent well-baby visits were scheduled to account for the fact of his being born 4 weeks prematurely. On July 22, 2011, more than three months after J.B.’s birth, he had a two-month well baby visit with his pediatrician, Laura Wright, M.D. Exhibit 3 at 8-10. Dr. Wright’s evaluation was thorough and well documented. *Id.* J.B. had no feeding difficulties, slept best at night, slept in his own room, and slept on his back. *Id.* at 8. He was noted to be a “well child, almost 4 months but behind on [vaccinations]” with “normal growth and development.” *Id.* at 10. J.B. received DTaP, IPV, PCV, rotavirus, and Hep B vaccinations at this visit. *Id.* at 2, 8.

On September 2, 2011, almost five months after J.B.’s birth, he had his four-month well baby visit with Dr. Wright. Exhibit 3 at 5-7. He was nearly five months post-delivery, although his gestational age was about four months given his early delivery. J.B. was sleeping up to seven hours at a time, on his back, in a crib in his own room. *Id.* at 5. He was described as “healthy appearing and cooperative . . . well-nourished and well developed.” *Id.* His chest and lungs were normal with no adventitious⁸ sounds. *Id.* at 6.

⁶ Apgar score is defined as “a numerical expression of the condition of a newborn infant, usually determined at 60 seconds after birth, being the sum of points gained on assessment of the heart rate, respiratory effort, muscle tone, reflex irritability, and color.” *Dorland’s Illustrated Medical Dictionary* (32d ed. 2012) (“*Dorland’s*”) at 1682.

⁷ Petitioners’ expert, Dr. Miller, stated that normally an infant receives the first Hep B vaccination a day after delivery or just before going home. Exhibit 13 at 3. Dr. Miller characterized J.B. receiving the first Hep B vaccination one week after delivery as “a little unusual [but...] likely inconsequential.” *Id.*

⁸ Adventitious is defined as “accidental or acquired; not natural or hereditary.” *Dorland’s* at 34.

J.B.'s heart rate was regular with normal heart sounds and no pericardial friction rubs. *Id.* His reflexes were all 2/2 and his red reflex was normal. *Id.* His weight was 16 pounds, 8 ounces. *Id.* at 5. For infants of his age, his weight was stable at the 50th percentile, his height was up at the 50th percentile, and his head circumference was at the 75th percentile. *Id.* Nasal mucosa was normal, turbinates⁹ were normal, and nares¹⁰ were patent. Oropharynx was normal. *Id.* at 6. He was recorded as not having a fever, nasal congestion, or cough and history of wheezing. *Id.* at 5. He met numerous 4-month developmental milestones, including "head up 45 degrees, head up 90 degrees, sits – head steady." *Id.* During this visit, J.B. received DTaP, IPV, PCV, rotavirus, and Hep B vaccinations. *Id.* at 6; Exhibit 4 at 1. Dr. Wright completed her records from this visit on September 2, 2011, at 10:45 a.m., suggesting that the appointment had concluded by that time. Exhibit 3 at 7.

J.B.'s father attested that during the well-baby visit, J.B. was "smiling and cooing like normal." Exhibit 11 at 1. However, later that day after J.B. received the vaccinations, he "was not laughing or cooing like he normally did[,] he was not moving as much[, and] he seemed quiet and withdrawn." *Id.* That night, J.B. had a fever and he did not sleep well. *Id.*¹¹

J.B.'s mother and father stated that on September 3, 2011, at 4:00 a.m., they gave J.B. Advil,¹² after which he went to bed in a supine position (on his back). Exhibit 8 at 2. When J.B. woke up a few hours later, he was distant, very quiet, and would not eat. Exhibit 11 at 2. He began running a fever again and was given another dose of Advil at approximately 8:00 a.m. *Id.*;

⁹ Turbinate is defined as "any of the nasal conchae.*" *Dorland's* at 1991.

¹⁰ Nares is defined as "the external orifices of the nose; [also known as] nostrils." *Dorland's* at 1232.

¹¹ The following factual summary draws from:

- Exhibit 5 – Suffolk, Virginia Department of Fire & Rescue records of responding to the home on September 2, 2011.
- Exhibit 7 – Suffolk, Virginia Police Department records. This includes notes from the police's response to the home on September 3, 2011, and the police department's formal report on their response and a handwritten statement from J.B.'s mother, both completed on September 8, 2011.
- Exhibit 8 – Office of the Chief Medical Examiner, Tidewater District, Norfolk, Virginia, Records. This exhibit contains a summary of a child death reenactment with a doll, performed with J.B.'s parents in their home on September 8, 2011. Exhibit 8 at 3. The autopsy report was completed on November 2, 2011. Exhibit 8 at 1-2; 4-9.
- Exhibit 9 – Suffolk, Virginia Police Department records – photos of a bottle of Advil, taken on September 8, 2011; J.B. following the autopsy, undated; and the crib, bedroom, and exterior of the home, taken on September 3, 2011.

J.B.'s mother and father were not present to testify at the entitlement hearing.

¹² A bottle of children's Advil was taken into evidence. Exhibit 7 at 47. *But see* Exhibit 6 at 2, 5 ("aspirin"); Exhibit 8 at 2 ("infant Tylenol"); Exhibit 8 at 4-6 ("over-the-counter acetaminophen"). To the extent that it makes any difference it would seem most likely that it was the Advil that was given and the other notations were made subsequently without that same attention to this detail that the site investigation utilized.

Exhibit 7 at 11. J.B.'s mother said that J.B. sat up and played with her nephews during the morning. Exhibit 7 at 16.

In the early afternoon, J.B. became fussy and his father put him down for a nap in his bedroom, on the second floor of the house. Exhibit 7 at 3, 16; Exhibit 8 at 2. His father attested that he placed J.B. supine with his head to the right. Exhibit 7 at 5; Exhibit 8 at 3. J.B. seems to have had a pacifier in his mouth. Exhibit 7 at 16. He was placed in the middle of his crib, with a blanket across his midsection. Exhibit 8 at 3. The crib also contained a "little crib pillow – very flat," but no clutter or toys. Exhibit 7 at 5; Exhibit 8 at 3. J.B.'s mother attested that the air conditioning was always set at 76 degrees Fahrenheit. Exhibit 7 at 4. She indicated that J.B. slept on his back and that he could roll over on his own, lift his head, and pull or push himself up. Exhibit 7 at 5.

After putting J.B. down for his nap, his father left the home to get lunch. Exhibit 11 at 2. His mother remained in the home, but "heard [J.B.] fussing in crib" while she was cleaning and on the phone. Exhibit 7 at 16. After some period of time, J.B.'s mother went upstairs and put the pacifier in J.B.'s mouth. *Id.* (noting that J.B. "tend[ed] to cry when he spit the pacifier out"). When she returned, she found J.B. on his right side, with his head turned slightly, and unresponsive. Exhibit 7 at 17; Exhibit 8 at 2-3. She called J.B.'s father and said that J.B. was not breathing. Exhibit 7 at 17; Exhibit 11 at 2. The father told her to call 911 and he headed home. Exhibit 11 at 2.

J.B.'s mother said that "approximately 50 minutes passed" between his father placing J.B. down for a nap and when she found J.B. unresponsive. Exhibit 8 at 2. There was a "10-minute window" between when his mother checked on J.B. and replaced his pacifier, and when she returned to find him unresponsive. Exhibit 5 at 2. She informed the police that his nose and mouth were not covered. Pet. Ex 7 p 5.

J.B.'s mother called 911 at 2:39 p.m. Exhibit 7 at 35. She then attempted CPR. Exhibit 5 at 2; Exhibit 7 at 17. It appears that she removed him from the crib and placed him on his back on the floor. Exhibit 7 at 9-10. Officer Anderson was the first to arrive, at 2:42 p.m. – just 3 minutes and 21 seconds after the call. Exhibit 7 at 7, 9, 11, 35. Upon entering the home and going upstairs, the officer found J.B. lying on the bedroom floor, perpendicular to his crib. *Id.* at 9. J.B. was face up, with his eyes closed, and unresponsive. *Id.* He was still warm, but had no pulse or breath. *Id.* J.B.'s mother was kneeling over him. *Id.* The officer performed chest compressions until EMS arrived. *Id.*

The first responders left with J.B. at 3:02 p.m. and arrived at the emergency department of Harborview Medical Center at 3:08 p.m. Exhibit 7 at 36. J.B. was given oxygen under pressure during transport, but PEA (pulseless electrical activity) was noted on the monitor. Exhibit 5 at 1-2. Efforts at resuscitation were unsuccessful and J.B. was pronounced dead at the hospital, on September 3, 2011, at 4:01 p.m. Exhibit 7 at 10.

On September 5, 2011, a medical examiner, Dr. Jeffrey Gofton, completed an autopsy report for J.B. Exhibit 8 at 4-6. The medical examiner noted that the scene reenactment indicated that J.B. was placed to sleep on his back and was later found on his right side. *Id.* at 6. Scene photographs indicated a crib with soft blankets and a flat soft pillow, but no clutter or toys in the bed. *Id.* It was further noted that J.B. had no known medical problems, with regular infant care and immunizations. *Id.* He had a well-baby check-up on the day prior to his death, during which he received multiple vaccinations. *Id.* He had reportedly been fussy and had an intermittent temperature that seemed to be controlled with Tylenol. *Id.* J.B. was reportedly placed to sleep on his back and later found on his right side. *Id.* The medical examiner stated that J.B.'s lungs exhibited congestion and pulmonary edema.¹³ *Id.* However, J.B. had no traumatic injury, congenital abnormalities, or viruses such as influenza. *Id.* Both a cerebral spinal fluid culture and a nasopharyngeal swab for viruses were negative. *Id.* J.B.'s brain weighed 876 grams (normal is 620 plus or minus 71 grams). *Id.* There was no evidence of epidural, subdural, or subarachnoid hemorrhage. *Id.* Serial sectioning showed normal configuration and infantile myelination of the cerebrum. *Id.* The brainstem was normally formed with no focal lesions. *Id.* at 5. Extensive drug testing was performed and was negative. *Id.* at 6. The medical examiner, based on the "absence of findings and the reported sleeping position in a child with no anatomic or microscopic significant findings," stated that "the cause of death was SIDS and the manner was "natural." *Id.* The parties agree that the characterization of J.B.'s cause of death as SIDS is appropriate. Joint Prehearing Submission at 2.

The parties' experts in neuropathology – Dr. Miller for petitioners and Dr. Harris for respondent – reviewed 21 slides from J.B.'s autopsy, including two of J.B.'s brain. Exhibit 13 at 4-5; Exhibit A at 5. The first brain slide is a cross-section of pons at the level of the locus coeruleus (the upper pons), and the second slide is of two cingulate gyri with a portion of the adjacent corpus callosum. Exhibit 13 at 5. These brain sections demonstrated no abnormalities. *Id.* However, the medical examiner did not make slides from other parts of the brain, such as the medulla or hippocampus. *Id.* Furthermore, he did not take any photographs of the internal examination. *Id.* The parties' experts agreed that the medical examiner did not collect all of the data necessary to definitively analyze whether J.B. fit the Triple Risk Model of SIDS, introduced in the following section. Tr. 42-43 (testimony of Dr. Miller); Tr. 334 (testimony of Dr. Harris). The experts agreed that they would section considerably more of the brain in a possible SIDS autopsy than the two frontal lobes and one area of the pons that were sectioned in this case. Dr. Harris indicated that usually a SIDS autopsy should include samples of at least ten areas, including the medulla and hippocampus, which can help to show hypoxic ischemic changes as well as epilepsy related changes. Tr. 334. Both experts agreed, however, that in many SIDS cases, brains are not examined with the precision that they would recommend or that Dr. Kinney's group at Harvard did in their studies (introduced in the following section). Tr. 346.

¹³ Dr. Miller and Dr. Harris agreed that congestion in the brain and lungs and other organs is a very common and non-specific finding at autopsy from which they would not draw any conclusion. Tr. 103 (Miller); Tr. 332-33 (Harris).

II. SUMMARY OF THE EVIDENCE

A. Medical Literature

The parties submitted voluminous literature to explain what is understood about sudden infant death syndrome (“SIDS”), the potential role of inflammatory cytokines generated by vaccines in acting as a necessary trigger, and the epidemiology of SIDS. Both parties submitted various studies from Hannah C. Kinney, M.D., a neuropathologist at Harvard, and others on her team which leads the research and current understanding of SIDS. The later articles tend to build upon and incorporate the earlier articles. Studies by other authors on SIDS and related subjects served to supplement and generally confirm that by Kinney et al.

A review of the literature is critical to the determination of whether petitioners have satisfied the *Althen* prongs (a reliable theory of how vaccines *can* cause death from SIDS, that the vaccines did in J.B.’s particular case, and that there was a medically acceptable temporal relationship between the vaccinations and J.B.’s death). This review is also necessary to determine whether respondent has sufficiently rebutted petitioners’ theory by demonstrating that J.B.’s death was caused by factors unrelated to the vaccine.

SIDS is defined as “the sudden death of an infant under one year of age which remains unexplained after a thorough case investigation, including performance of a complete autopsy, death scene investigation, and review of the clinical history.”¹⁴ “Epidemiological studies link SIDS with sleep periods, leading to the premise that SIDS occurs during sleep or transitions between sleep and waking.” *Id.*

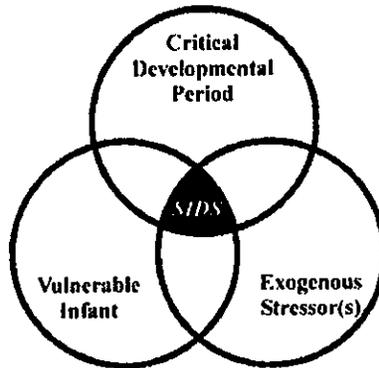
SIDS is the leading cause of infant mortality in the United States, with an incidence of 0.53 per 1,000 infants.¹⁵ Research has revealed that infants put to sleep in the prone position, i.e., with their heads facing downward, are twice as likely to experience SIDS. *Id.* Other risk factors for SIDS related to the “sleeping environment” have been recognized, including “[being] found face-down, head covered, sleeping on an adult mattress, couch or playpen, soft bedding, [and] bed-sharing.” *Id.*

In 1994, Dr. Hannah C. Kinney, Dr. James Filiano, and their colleagues synthesized many neuropathological studies into their proposed Triple Risk Model.¹⁶ This model posits that SIDS occurs when: (1) an infant in a critical development period; (2) possessing an underlying vulnerability; (3) encounters an exogenous stressor. *Id.* The following Venn diagram has been used to illustrate the Triple Risk Model:

¹⁴ Filiano, J.J. & H.C. Kinney, *Arcuate Nucleus Hypoplasia in the Sudden Infant Death Syndrome*, 51 J. Neuropathol. Exp. Neurol. 394 (1992), Exhibit 13-A at 394.

¹⁵ Trachtenberg F.L., E.A. Haas, H.C. Kinney, C. Stanley & H.F. Krous, *Risk Factor Changes for Sudden Infant Death Syndrome After Initiation of Back-to-Sleep Campaign*, 129 Pediatrics 630 (2012), Exhibit C-11 at 631.

¹⁶ Filiano, J.J. & H.C. Kinney, *A Perspective on Neuropathologic Findings in Victims of the Sudden Infant Death Syndrome*, 65 Biol. Neonate 194 (1994), Exhibit 13-B at 195 [also filed as Exhibit A-2].



Id. at 3, Figure 1. This model emphasizes the intersection of multiple factors in the pathogenesis of SIDS. According to this model, SIDS occurs only when components of all three factors are present simultaneously, which explains why all infants who are placed prone to sleep or who bed share do not die of SIDS.¹⁷

1. First Risk Factor: Critical Development Period

The first factor in the Triple Risk Model of SIDS is the critical development period, which Kinney et al. initially defined as the first year of life.¹⁸ However, their more recent literature tends to define it as the first six months of life.¹⁹ The peak incidence of SIDS deaths has historically occurred between two and four months of age. A study by Trachtenberg, Kinney, and others published in 2012 found slightly more younger and older infants succumbing to SIDS than had been seen in earlier studies. In the groups studied, the percentage of SIDS babies who were five months or more rose from 11.8% in the pre-Back-to-Sleep²⁰ era, to 17.6% in the 1996-2008 post-Back-to-Sleep era.²¹ Kinney and Thach wrote, “Given the wide array of homeostatic functions modulated by the medullary 5-hydroxytryptamine system, sudden death may result from a convergence of defects in protective response to homeostatic stressors during sleep that are modulated by 5-hydroxytryptamine, probably in conjunction with related neurotransmitters.”²²

¹⁷ Kinney, H.C. et al., *The Brainstem and Serotonin in the Sudden Infant Death Syndrome*, 4 *Annu. Rev. Pathol. Mech. Dis.* 517 (2009), Exhibit 13-H at 521.

¹⁸ Filiano & Kinney (1992), Exhibit 13-A at 394.

¹⁹ See, e.g., Kinney et al. (2009), Exhibit 13-H at 521.

²⁰ The “Back to Sleep” campaign refers to a major public health effort to encourage parents to place their infants on their backs to sleep, particularly during the first year of life as a means of reducing the incidence of SIDS.

²¹ Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 634.

²² Kinney, H.C. & B. Thach, *The Sudden Infant Death Syndrome*, 361 *New England J. of Med.* 795 (2009), Exhibit A-4 at 6.

2. Second Risk Factor: Vulnerable Infant

After Kinney et al. formulated the Triple Risk Model, the initial research was focused on determining why particular infants were “vulnerable”, possibly because of environmental or genetic factors. Exhibit 13-H at 5. Intrinsic risk factors include “male gender, African-American race, poverty, adverse prenatal factors such as maternal smoking or alcohol use during pregnancy, and genetic polymorphisms.” *Id.* It was also hypothesized as early as 1987 that most likely SIDS was related to a brainstem abnormality in the neuroregulation of cardiorespiratory control.²³ These intrinsic factors when combined with the vulnerable developmental period of the infant and a critical exogenous factor resulted in sudden infant death. As research progressed over the following decades, the above intrinsic risk factors remained but a significant emphasis was placed on the brainstem hypothesis, based upon the research of Dr. Kinney and others. In 2009, Dr. Kinney explained: “To date the most robust evidence for a neurochemical abnormality comes from research on the medullary 5-HT system,²⁴ in that approximately 50-70% of infants with SIDS appear to have abnormalities in this system. The medullary 5-HT system, which is considered critical for the modulation and integration of diverse homeostatic functions, is involved in ventilation and gasping, thermoregulation, autonomic control, response to carbon dioxide and oxygen, arousal from sleep, and hypoxia-induced plasticity.²⁵

The 5-HT system refers to the serotonin system. “The caudal serotonergic (5-HT) system is a critical component of a medullary “homeostatic network” that regulates protective response to metabolic stressors such as hypoxia, hypercapnia and hyperthermia.”²⁶ “Homeostasis refers to the ability of an organism to maintain a constant internal environment, thereby allowing survival over a wide range of external environmental conditions. It becomes self-sufficient at the moment of birth as the fetus takes the first breath in the extra-uterine world and begins to adjust instantaneously and independently to the myriad of changing metabolic demands. ... Receptor systems that sense deviations in any internal milieu (e.g., oxygen and carbon dioxide, glucose, and temperature levels) have been defined as well as the effector systems that are the final common pathway in mediating adjustments. Major focus has been placed upon the brain as the ‘control center’ which sets the range at which a particular parameter namely CO₂ is maintained, and determines the protective response to deviations from this range namely hypercarbia.”^{27,28}

²³ Kinney et al. (2009), Exhibit 13-H at 519.

²⁴ 5-HT (5-hydroxytryptamine), also called serotonin, is defined as “a monoamine vasoconstrictor, synthesized in the intestinal chromaffin cells or in central or peripheral neurons and found in high concentrations in many body tissues, including the intestinal mucosa, pineal body, and central nervous system.” *Dorland's* at 1699.

²⁵ Kinney & Thach (2009), Exhibit A-4 at 6.

²⁶ Kinney, H.C. et al., *The Serotonergic Anatomy of the Developing Human Medulla Oblongata: Implications for Pediatric Disorders of Homeostasis*, 41 *J. Chem. Neuroanat.* 12 (2011), Exhibit 13-F at 182.

²⁷ Hypercarbia, also called hypercapnia, is defined as “excess of carbon dioxide in the blood.” *Dorland's* at 887.

²⁸ Kinney et al. (2009), Exhibit 13-F at 183.

The serotonergic system, primarily concentrated in the medulla oblongata, which is called the caudal 5-HT system or the medullary 5-HT system, is now recognized as a key component of the brain's control system of homeostasis. *Id.* Dr. Kinney proposed that deficits in the caudal 5-HT system will lead to imbalances in respiratory, cardiovascular, and/or metabolic regulation – including in response to stress – in the pediatric age range, particularly in the first days and months following birth. *Id.* As noted by the Kinney group in a 2011 article on the serotonergic anatomy, “extensive experimental data implicate the caudal 5-HT system in homeostasis and respiratory and autonomic regulation, including upper airway control, respiration (including via modulation of the pre-Botzinger complex, the putative central rhythm generator of respiration), autoresuscitation, central chemoreceptor responses to hypercapnia and hypoxia, cardiovascular control, pain, motor function, and thermoregulation.” *Id.* The article also notes that the medullary 5-HT system “interfaces with the cytokine system which is critical to homeostasis in its mediation of ‘protective sickness’ behaviors and cellular defenses against tissue damage.” *Id.*

Dr. Kinney's team's research on the brainstem focused on a collection of neurons in the ventral medullary surface known as the arcuate nucleus “based upon cytological and positional homologies between the respiratory chemosensitive fields on the ventral medullary surface in cats. Structural underdevelopment of the arcuate nucleus was subsequently observed in SIDS cases.”²⁹ As the research advanced, it was recognized that the “arcuate anomaly was similar to that reported in infants with clinical insensitivity to CO₂ and sleep related sudden death.” *Id.* By 2009, Dr. Kinney reported, “*Serotonergic neurons at the medullary ventral surface and in the midline (raphe) are now known to be preferentially chemosensitive to CO₂* and although they are not the only central chemosensitive neurons they appear to play a critical potentially modulatory role...A small but important population of 5-HT neurons is embedded within the human arcuate nucleus suggesting that the putative dysfunction in chemosensitivity related to the arcuate anomaly specifically involved these embedded 5-HT neurons.” *Id.* (emphasis added).

“Serotonergic neurons are well-suited to a role as central respiratory chemo-receptors, as they are closely associated with the basilar artery and its largest branches near the ventral surface of the medulla namely they are in a position to directly monitor arterial PCO₂... 5-HT neurons respond intrinsically to increased PCO₂³⁰ with large increases in firing rate; this response is due to a decrease in intracellular pH induced by hypercapnia. On average these neurons increase their firing rate threefold in response to a decrease in pH of 7.4 to 7.2. Chemosensitivity increases during postnatal development, with a blunted response to pH before postnatal date 12 in rats. Physiological delay in chemosensitivity is potentially relevant to SIDS because it indicates that 5-HT neurons may be immature during the critical developmental period, throughout which all infants are susceptible to hypercapnia.”³¹ Harper and Kinney state the data now suggest that SIDS is associated with a brainstem (medullary) 5-HT deficiency rather than 5-

²⁹ Kinney et al. (2009), Exhibit 13-H at 522. Kinney defines chemosensitivity as “the ventilator response to a change in carbon dioxide/pH as sensed by tissue chemoreceptors, which are composed of neurons and/or astrocytes.” *Id.*

³⁰ PCO₂ is defined as “the partial pressure of carbon dioxide.” *Dorland's* at 2120.

³¹ Kinney et al. (2009), Exhibit 13-H at 530.

HT overproduction.³² Of note, the medullary 5-HT profile differed between infants dying of SIDS and those dying with known chronic oxygenation disorders, suggesting that chronic hypoxia does not necessarily play a major role in the pathogenesis of the impairments in the 5-HT tissue markers. *Id.*

Harper & Kinney explained that the insufficient function of the 5-HT system, which is necessary for breathing, leaves an infant vulnerable to a variety of crisis situations. These include external airway obstruction, upper airway obstruction resulting from loss of tone in the upper airway musculature in association with diaphragmatic movements, or importantly of central apnea, which has occupied a central focus of attention. These are also proposed mechanisms underlying the fatal event in SIDS. This failure can result from several components of the breathing process, including impaired sensory transduction or integration of either carbon dioxide or oxygen, or non-recruitment of gasping mechanisms, the final restorative mechanism to low oxygen. In SIDS, a principal concern is the “loss of the wakefulness drive to breathe.” *Id.* at 5. The waking state activates processes which maintain breathing, while during sleep those influences are suppressed or not recruited. Thus, impaired central chemosensitivity to excess carbon dioxide or inadequate oxygen contributed to by defects in the medullary serotonin system, in addition to the normal reduction of the function of the 5-HT system during sleep, may play a central role in SIDS, which occurs primarily during sleep. *Id.* at 4-5.

Despite the emphasis on brainstem abnormality or underdevelopment, the other intrinsic risk factors are thought to continue to play an important role in the multi-factorial analysis of SIDS causation. Some of these factors may be related to the medullary 5-HT deficits described above. Several intrinsic risk factors are apparent in J.B.’s case. First, prematurity is defined as less than 37 weeks at birth³³ and J.B. was born at 36 weeks. Male gender, as boys exceed girls in SIDS deaths by a two-to-one ratio, and African-American race have also been called intrinsic risk factors because they are over-represented among SIDS victims.³⁴ Importantly, maternal smoking and alcohol consumption during pregnancy are considered important risk factors but are not relevant in this case, as J.B.’s mother did not smoke or drink during or after her pregnancy.

Dr. Kinney has hypothesized that males may predominate among SIDS deaths because males tend to be less responsive to the accumulation of carbon dioxide, and in the situation with a defective medullary 5-HT system may be particularly impaired from responding to excess carbon dioxide during sleep. *Id.* The predominance of males in the occurrence of SIDS appears to be potentially related to the reduction of 5-HT binding in the medullary raphe compared to females dying of SIDS, as well as the report that plasma levels of testosterone, but not estradiol, are significantly higher in both male and female SIDS infants compared to age-matched controls. Several studies in knockout mice and piglets also “underscore gender differences in brainstem-mediated 5-HT function, with females’ brains apparently relying less on 5-HT neurons in chemoreception and adapting more readily to the loss of 5-HT function. *Id.*

³² Harper, R.M. & H.C. Kinney, *Potential Mechanisms of Failure in the Sudden Infant Death Syndrome*, 6 *Curr. Pediatr. Rev.* 39 (2010), Exhibit C-12 at 7.

³³ Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 631.

³⁴ Kinney et al. (2009), Exhibit 13-H at 532.

The role of African-American race in SIDS is less defined, other than statistically. Most authors speculate that the statistical predominance of African-American children may represent lower socioeconomic status resulting in inadequate medical care. If that be the case however, J.B.'s race should not be an increased risk factor as he was receiving regular medical care with comprehensive and well-documented well baby visits occurring in July and September. His first set of vaccinations was somewhat late, but the second dose, those received on September 2, 2011, brought him up to date. His growth and functional milestones appeared to be normal. It is also reported that 75% of white infants are placed to sleep in the supine position, while only 53% of black infants are, and that there is greater incidence of bed sharing among black infants than in other groups.³⁵ J.B. was placed on his back and was in his own crib.

3. Third Risk Factor: Exogenous Stressor(s)

The third and last factor is referred to as exogenous stressor[s] present at the time of death.³⁶ These stressors identified in the literature include “prone sleep position, face-down position, covered face in the supine position, soft bedding, bed sharing, over-bundling, elevated room temperature, and minor infection at the time of death.”³⁷ Virtually every SIDS case includes one or more exogenous stressors, implying that they act as “triggers” for SIDS.³⁸ Studies also show that often multiple risk factors are present in a given SIDS case. Trachtenberg et al. found that “at least 2 extrinsic risk factors” were present in a majority of 568 cases reviewed. *Id.* at 632.

Dr. Kinney has hypothesized that exogenous stressors “lead to asphyxia, hypoxia, hypercapnia, or thermal imbalance requiring intact brainstem defense systems to protect against lethal consequences.”³⁹ Non-vulnerable infants are generally able to recover from these conditions, but vulnerable infants are less able to recover and succumb to SIDS. *Id.* at 521.

As a result of their research, Dr. Kinney and her team proposed the Triple Risk Model to explain the occurrence of SIDS. Dr. Kinney’s group then proposed the “Back to Sleep Campaign” in the early 1990s in which they recommended that babies always be put to sleep on their backs (supine) on a firm mattress, without pillows, blankets, toys, bumpers or other items that could potentially obstruct breathing. The prone or face-down sleeping position was considered to make an infant particularly vulnerable because an infant in the first six months of life with one or more intrinsic defects may re-breathe excess carbon dioxide and lack the corrective arousal mechanisms during sleep that would prevent a fatal outcome. Generally, the accumulation of excess carbon dioxide in the body causes signaling to breathe, thereby exhaling

³⁵ Moon R.Y. et al., American Academy of Pediatrics – Task Force on Sudden Infant Death Syndrome, *SIDS and Other Sleep Related Infant Deaths: Expansion of Recommendations for a Safe Infant Sleeping Environment*, 128 *Pediatrics* 1030 (2011), available at <http://pediatrics.aappublications.org/content/128/5/1030.long>.

³⁶ Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 631.

³⁷ Kinney et al. (2009), Exhibit 13-H at 521.

³⁸ Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 633.

³⁹ Kinney et al. (2009), Exhibit 13-H at 520.

carbon dioxide and inhaling room air containing oxygen. During sleep it is thought that excess carbon dioxide normally causes a person to turn the head toward fresh air and become aroused from sleep. When those mechanisms fail, the gasp reflex is triggered, which brings in oxygen and resets the rhythm of breathing. In SIDS, the dominant theory is that all of these mechanisms fail, leading to death.

The Back to Sleep Campaign has succeeded remarkably in reducing the number of SIDS deaths in the United States by approximately 50%.⁴⁰ In the U.S., the rate was reduced from more than 1 per 1,000 infants to 0.53 per 1,000, the current rate where it has plateaued. *Id.* However, SIDS remains the leading cause of post neo-natal infant death in the United States, raising some of the questions at issue in this case. *Id.* The emphasis has continued to be on the cardiorespiratory failure explanation of SIDS. Research has indicated that prone sleeping position increases the risk twofold or more. *Id.* They concluded that those not found prone sleeping were subject to alternative SIDS risk factors. *Id.* at 635.

The Trachtenberg article concluded that virtually all SIDS infants have at least one risk factor, and the majority have at least one intrinsic risk factor and two extrinsic factors. *Id.* The article also notes that the American Academy of Pediatrics risk reduction guidelines also include recommendations against side-sleeping and bed-sharing, and suggest a separate but proximate sleeping environment and pacifier use. *Id.* at 636. The data from the Trachtenberg study found a decline in prone position sleeping from 84% in the pre-Back-to-Sleep era to 48.5% in the post-era, but it also found that in the post-era 17.3% of SIDS infants were found on their sides while 22.6% were initially placed on their sides. *Id.* at 634, Table 2. Interestingly, 29% of the SIDS babies in that study were found supine while 41.7% were placed on their backs, suggesting that SIDS is not exclusively caused by prone sleeping. *Id.* at 632.

The Trachtenberg and Kinney articles emphasize the belief in the medical community that SIDS is multifactorial. As Trachtenberg noted, they were only able to evaluate which SIDS risk factors are most common, not which factors raise the odds of SIDS most significantly. *Id.* at 635. The authors suggest that the number of risks is probably underestimated and that “the majority of SIDS infants were subject to at least two extrinsic risk factors, suggesting that SIDS occurs from the simultaneous occurrence of multiple factors, rarely just one.” *Id.* Additionally, Dr. Kinney has noted that under the Triple Risk Model, only infants with an underlying brainstem disease process die of SIDS, which explains why all infants who are placed prone to sleep or who bed share do not die of SIDS.⁴¹ She states that SIDS essentially represents the occurrence of “the biologic version of the perfect storm in which the chance combination of multiple events is far more powerful than each individual event alone.” *Id.* at 539. She suggests a possible scenario in which a child with the underlying brainstem deficit, during the critical developmental period, is exposed to excess carbon dioxide while he is sleeping. This may be based upon his sleeping position or he may have an issue with the laryngeal chemoreflex stimulated by reflux of gastric contents *or may have a mild infection with fever* causing the laryngeal chemoreflex induced apnea to be inordinately prolonged by mild hyperthermia” *Id.*

⁴⁰ Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 631.

⁴¹ Kinney et al. (2009), Exhibit 13-H at 521.

(emphasis added). In this scenario, “if the infant’s ventilator response to the progressive hypoxia and hypercapnia during the apnea is depressed, and if the hypoxic gasping and/or arousal mechanism is abnormal, oxygen lack from uninterrupted apnea results. Ultimately, death occurs *within minutes to hours.*” *Id.* (emphasis added).

Respondent filed the article by Trachtenberg et al., which emphasized that they could find no positive correlations between risk factors or risk clusters but it appeared that any combination of risks together increased the odds of SIDS. The fact that most infants have at least two extrinsic risk factors suggests that SIDS occurs as a result of the occurrence of multiple factors and rarely just one.⁴² The Kashiwagi article⁴³ filed by petitioners suggests that vaccines provoke an inflammatory cytokine response similar to that provoked by a mild infection. Petitioners theorize that these cytokines travel to the brainstem and further suppress the function of the already impaired medullary 5-HT system in a subset of SIDS infants.

a. Cytokines, Mild Infection and Vaccines

Relevant to this case, in a 2009 article in the New England Journal of Medicine, Kinney and Thach stated, “A causal role for mild infection in sudden infant death is suggested by reports that in approximately half of SIDS cases, the infants have a seemingly trivial infection around the time of death, as well as mild tracheobronchial inflammation, altered serum immunoglobulin or cytokine levels and the presence of microbial isolates at autopsy. In infants who die unexpectedly of infection, the given organism may precipitate a lethal cytokine cascade or toxic response.”⁴⁴ The question arises as to whether the cytokine response stimulated by vaccination can have the same effect as a mild or trivial infection in a baby who presumably has a defect in the medullary 5-HT system.

The role of cytokines stimulated by either mild infection or by vaccination is central to petitioners’ theory in this case. Approximately 50% of SIDS babies have been found in multiple studies to have had mild or even “trivial” infections, primarily of the upper respiratory tract at the time of death. In this case, J.B. was documented the prior day as being healthy with patent nares, normal turbinates, and clear chest, but during the 28 hours after the vaccine he was reported to have a fever, which is generated by cytokine signaling. He also was distant, quiet, and would not eat, according to his parents. The case raises the issue of whether inflammatory cytokines stimulated by the innate response to the vaccines triggered the fever and his fussiness, and ultimately suppressed his 5HT system sufficiently so that he could not process the carbon dioxide in his system. The question of whether inflammatory cytokines stimulated by the innate response to the vaccine could have been the trigger that led to his death was central to the testimony and much of the literature submitted by the parties particularly in light of the clear medical evaluation on the day of the vaccination and a fever within hours afterward.

⁴² Trachtenberg, Kinney, et al. (2012), Exhibit C-11 at 7.

⁴³ Kashiwagi Y et al., *Production of Inflammatory Cytokines in Response to Diphtheria-Pertussis-Tetanus (DPT), Haemophilus Influenzae Type B (Hib) and 7-Valent Pneumococcal (PC7) Vaccines*, 10 Hum. Vacc. Immunother. 677 (2014), Exhibit 17.

⁴⁴ Kinney & Thach (2009), Exhibit A-4 at 2.

As Dr. Kinney and her colleagues explained in 2011: “Cytokines orchestrate immune responses to microbial invasion and other insults and coordinate these responses with those of other physiological systems, including the autonomic nervous system, in the protection of the organism against tissue injury. They also mediate sickness behavior, including fever, anorexia, excessive sleepiness, blunted arousal, deep rest respiration, and lowered heart rate, which is thought to protect the organism during systemic illness by dampening excessive metabolic demands and thereby speeding repair and recovery - a form of homeostasis.”⁴⁵ “Cytokines determine this sickness behavior by binding to endogenous cytokine receptors on neuronal populations in the hypothalamus and/or brainstem that mediate respiration, autonomic function, satiety, sleep, and arousal.” *Id.* at 190. The cytokines which act within the brain in response to tissue injury are produced by astrocytes, and endothelial cells, microglia, *and/or peripheral immune cells* which enter the brain in response to binaural signals of tissue damage.” *Id.* (emphasis added). During infection, peripherally produced IL-6 may cross the blood brain barrier and bind to IL-6 receptors on 5 HT neurons that mediate homeostasis in response to the infectious stressor and potentially mediate sickness behavior. *Id.* at 191. The role of pro-inflammatory cytokines in the pathology of SIDS is thought by multiple authors to be a potentially critical factor in tipping the molecular balance in the underdeveloped brainstem leading to death in infants in the vulnerable time period. IL-1 β , IL-2, and IL-6 are pro-inflammatory cytokines that have been studied in connection with SIDS leading to theories about their potentially neuro-modulatory role in SIDS babies.

Kadhim et al. described a distinct cytokine profile in a SIDS brain in a study comparing SIDS brains with non-SIDS brains. The non-SIDS brains were from infants who died of known causes, including AIDS, cirrhosis of the liver, mononucleosis, purulent meningitis, and congenital heart disease with post-operative acidosis-shock. He found an over-expression of interleukin 1 β in arcuate and dorsal vagal nuclei in all SIDS victims. In arcuate nuclei, high levels of interleukin 1 β were detected in 17/17 SIDS brains vs. only 1 of 6 non-SIDS brains.⁴⁶ In dorsal vagal nuclei, interleukin 1 β was also detected in high levels in 17 of 17 SIDS brains vs. only 2 of 7 non-SIDS brains. *Id.* Kadhim found a “region-specific pattern of cytokine expression in [the arcuate and dorsal vagal nuclei] of SIDS brains compared to non-SIDS brains.” *Id.* at 1259. Kadhim theorized: “cytokines could exert neuromodulatory effects. Infectious inflammatory conditions and injury to the brain could up regulate pro inflammatory cytokines and produce functional alteration ... Cytokine/neurotransmitter interactions could therefore modify vital CNS functions.” *Id.* Kadhim et al. further concluded that IL-1 causes prolonged apnea and depresses respiration, and that the brain appears to be less effective than the peripheral nervous system in inducing IL-1 antagonists to control IL-1 action.

⁴⁵ Kinney et al. (2011), Exhibit 13-F at 189.

⁴⁶ Kadhim, H. et al., *Distinct Cytokine Profile in SIDS Brain: A Common Denominator in a Multifactorial Syndrome?*, 61 *Neurol.* 1256 (2003), Exhibit 13-L at 1256.

In a second study from 2010, Kadhim focused on the expression of IL-2 in 28 autopsied infants who died at less than one year of age.⁴⁷ He described IL-2 as major immune-related cytokine that was originally thought to be a T-lymphocyte growth factor but is now recognized to have a wider spectrum of functions, targets and sources. *Id.* The study compared 18 SIDS brains to those of infants who died of diverse severe pathological conditions including infectious, hemodynamic, metabolic or other serious genetic conditions. In the severely ill children (non-SIDS), they found that IL-2 was preferentially expressed in specific neuronal centers within the brainstem (SNT-solitary nucleus tractus and TSNT-spinal trigeminal nucleus/tractus) in 10 of 10 cases of the fatally sick (non-SIDS) children and in the arcuate and dorsal vagal nuclei in 8 of 10. “Examination of the brainstem in the SIDS group showed a topographically similar profile with an equally intense immune reactivity within the very same neuronal circuits; precisely the strongly expressed cytokine labeling of IL-2 in SNTT and/or TSNT was observed in 17 out of 18 cases that constituted the 2nd study group (SIDS). IL-2 was also notable in the arcuate nucleus and dorsal vagus nucleus in 17 cases. These brainstem neuronal centers are known to be intricately implicated in autonomic control of vital homeostatic functions namely cardiorespiratory control mechanisms.”⁴⁸ The authors concluded that it was not surprising to see the intense IL-2 expression in the infants who were severely ill before they died, but the SIDS victims are generally free from apparent potentially fatal conditions. “The SIDS victims often have preceding mild infectious/inflammatory conditions (like coryza⁴⁹/mild upper respiratory infections, soft stools mild gastroenteritis, *postvaccinal fever*, etc.). Such trivial infections were found to induce a hypertuned immune/inflammatory response including high levels of immune inflammatory cytokines.” *Id.* at 122. (emphasis added). Kadhim reviewed the Triple Risk Model, placing his study findings with regard to inflammatory cytokines in that framework; “Such mild infectious inflammatory conditions (extrinsic environmental stressors), if contracted in a vulnerable infant (intrinsic factors including prematurity and gene polymorphisms) during a critical developmental period whereby brainstem command centers undergo rapid maturation could provoke exaggerated immune responses with over expression of cytokines. We believe that this hypertuned immune response is behind the high IL-2 immune-reactivity we detected in situ in the brainstem of these victims.” *Id.* at 125. Kadhim also noted that while pro-inflammatory cytokines have immune function, it is noteworthy here that cytokines have *neuro-modulatory effects* whereby they can modify neurotransmission. *Id.*

The role of mild infection was further discussed in an article by Rognum et al.⁵⁰ The Rognum group compared three groups of deceased infants. The group of 25 SIDS cases was selected from those subjects in whom no explanation for death was found. A second group died from known infectious causes and the third control group died primarily from violent causes

⁴⁷ Kadhim, H. et al., *Interleukin-2 as a Neuromodulator Possibly Implicated in the Physiopathology of Sudden Infant Death Syndrome*, 480 *Neurosci. Lett.* 122 (2010), Exhibit 13-O at 123.

⁴⁸ Kadhim et al. (2010), Exhibit 13-O at 124.

⁴⁹ Coryza, also known as acute rhinitis, is defined as an “inflammation of the mucous membranes of the nose.” *Dorland’s* at 423, 1639.

⁵⁰ Rognum, I.J., R.L. Haynes, A. Vege, M. Yang, T.O. Rognum & H.C. Kinney, *Interleukin-6 and the Serotonergic System of the Medulla Oblongata in the Sudden Infant Death Syndrome*, 118 *Acta Neuropathol.* 519 (2009), Exhibit 13-N at 519-30.

such as drowning, suffocation or strangulation. *Id.* at 522. The IL-6 levels were significantly higher in SIDS subjects than in controls. The IL-6 levels in SIDS infants with minor infection were comparable to those infants who succumbed to severe infection. *Id.* at 520.

Rognum et al. wrote: “We previously showed that IL-6 is elevated in the cerebrospinal fluid of SIDS infants and that this elevation may be induced by a peripheral immune reaction. Approximately one half of the SIDS cases we have studied show signs of a mild infection, but IL-6 levels are comparable to those of infants succumbing to severe infection, suggesting an overreaction to the slight infection.” *Id.*

According to Rognum: “In addition to its pro-inflammatory properties, IL-6 exerts effects outside the immune system. Non-immune cells including neurons can produce and secrete IL-6 and express its receptor. Of critical relevance to the premise that cytokines interact with central neurons to affect their function, IL-6 is shown to be important in neuronal development in the modulation of neuronal signaling.” *Id.* “A major site of 5-HT cell bodies in the human infant brainstem is in the arcuate nucleus, the putative site for central carbon dioxide (CO₂) sensitivity in humans and animal models. In this regard the synergistic effect of prone sleeping and infection on SIDS risks may be a set up for CO₂ accumulation, as both rebreathing in the face down prone position and increased metabolism due to infection may increase CO₂ levels. Death may be triggered if CO₂ sensing regions in the brainstem, such as the arcuate nucleus, are compromised and cannot mount an arousal response to protect the infant from the dangerous situation. The arcuate nucleus is of particular interest in the study due to the previous finding by others of high neuronal IL-1 β immunoreactivity at this site in SIDS cases compared to controls.” *Id.*

Rognum et al. did identify one particular confounder to this theory in that they found that the mean IL-6R (receptor) intensity grade in the arcuate nucleus was significantly higher in the SIDS group than in the control group but the gp130 transducer was significantly higher in the infection group but less so in SIDS relative to the controls. While Rognum et al. acknowledged difficulty in grading the immunosensitivity of IL-6R and gp130 in this study due to its small size as a major limitation in the study, the result led the authors to hypothesize that the increased expression of IL-6R in the arcuate nucleus may be a compensatory mechanism as defective arcuate neurons may require excessive IL-6 stimulation in order to respond to altered carbon dioxide levels and there may be an inability in the SIDS babies to upregulate gp130 to mount an effective response.⁵¹ *Id.* at 528. Nevertheless, the study concluded that abnormal IL-6R expression was found in the arcuate nucleus of SIDS babies 44% of whom had mild infections prior to death and thereby “provides evidence for aberrant interactions in SIDS infants between IL-6 and the arcuate nucleus, a key medullary 5-HT related region involved in protective responses to hypercapnia, potentially induced by the combined effect of prone position and mild infection.” *Id.* at 529.

⁵¹ Dr. Miller explained that gp130 is a second messenger in the cell that takes the message that the receptor has bound something and does something with it to take (tell) the cell to do something else. This is a very common mechanism in membrane signaling, that there's a second messenger system that then tells the cell to do something. Tr. p 32.

Rognum et al. concluded: “The key finding in this study is abnormal IL-6R expression in the arcuate nucleus in the SIDS cases, 44% of whom had signs of mild infection immediately prior to death. *Id.* at 528. Rognum further noted that the arcuate nucleus contains 5-HT and glutamatergic neurons that have been shown in animals to be critical to chemosensitivity. It is also the site for several neurotransmitter abnormalities in SIDS, including in 5-HT, muscarinic and kainite receptor binding. It is well documented that CO₂ levels are elevated during severe neonatal infection and, interestingly, even mild upper respiratory infection may increase CO₂ levels in infants over 3 months of age. Animal studies indicate that the *CO₂ elevation can be attributed to a hyper metabolic state induced by proinflammatory cytokines.*” *Id.* at 527-28 (emphasis added).

Kashiwagi studied the production of cytokines after vaccination in 61 vaccine recipients with fever and 18 without fever within 24 hours of vaccination. Blood samples were taken within 48 hours of vaccination in both groups. He reviewed the role of the innate immune system in responding to vaccination noting that the activation of the innate immune system including the enhanced production of inflammatory cytokines is indispensable for immunogenicity and these cytokines may be related to the occurrence of adverse events.⁵² This group found that cytokine production began about 6 hours after the stimulation by a single or combination of vaccines and *increased for 24 hours, showing the same level afterward.* *Id.* at 679. They found that higher levels of IL-1 β , IL-6, G-CSF⁵³ and TNF- α were produced with the concurrent stimulation by multiple vaccines than with the single vaccine in PBMC cultures (peripheral blood mononuclear cells - obtained from young infants in this study). *Id.* at 679. Higher levels of IL-6, IL-10, IL 12, G-CSF, IFN γ and TNF α in both the febrile and non-febrile groups were found after vaccination and G-CSF was significantly higher in the febrile group. *Id.* at 680. He noted that innate immune systems are not fully functional at the time of birth. Kashiwagi’s group found that TLR (Toll-Like Receptors) stimulated the production of pro-inflammatory cytokines (specifically IL- β , IL-6, and IL-8) which was markedly higher in neonates than in adults. He also found that higher levels of IL-1 β were produced in PBMC cultures stimulated with PCV7 than with DPT or Hib. Hib induced higher levels of IL-6 and TNF- α . IL-1 β increased in PBMCs stimulated concurrently with Hib/PCV7 and DPT/Hib/PCV7 with similar patterns of TNF- α and G-CSF. However, when blood was drawn 48 hours post-vaccination, IL-1 β was not found. *Id.* Dr. Miller theorized that IL-1 β rises rapidly and then disappears by 48 hours whereas the other inflammatory cytokines have a longer half-life. Tr. 47

Kashiwagi noted: “All effective vaccines induce the production of cytokines or chemokines, which modulate immunogenicity and are also involved in inducing adverse events, such as systemic febrile illness and immunotoxicity. In this standpoint, IL-6, IL-10, IL-12, G-CSF, IFN- γ , and TNF- α were detected in both febrile and non-febrile groups after vaccination in comparison with those in normal subjects.” *Id.* at 683. Inflammatory cytokine profiles after vaccination were similar to the outpatient group infected with the influenza virus. *Id.*

⁵² Kashiwagi, et al. (2014), Exhibit 17 at 678.

⁵³ G-CSF is granulocyte colony stimulating factor *Dorlands* at 767- It is now classified as another cytokine. Tr. 47.

Vege and Rognum reviewed the literature and their own work and noted that “in 1995 they found that half of the SIDS victims had elevated levels of interleukin-6 (IL-6) in their cerebrospinal fluid (csf). The concentrations of IL-6 in SIDS infants were comparable to those we found in infants dying from infectious diseases like meningitis and septicaemia.” They concluded that there were two groups of SIDS infants—one with IL-6 levels similar to infants dying of severe infections and another having low levels similar to those dying violent deaths. They hypothesized that one group of SIDS deaths may be attributable to sleep position and another to an uncontrolled inflammatory response to infection, predominantly occurring at night when cortisol levels, another mechanism for controlling inflammatory responses, are low.⁵⁴

Others have studied cytokine expression in animals. Brambilla demonstrated in animal studies that Interleukin 1 (IL-1) inhibited firing of excitatory or wakefulness producing neurons in the dorsal raphe nucleus and enhanced activity of GABAergic or inhibitory neurons and, as such, induces enhancement of NREM sleep.⁵⁵

Respondent submitted an article by Siljehav, Hofstetter et al. which sheds additional light on the possible mechanism involved with apnea in infants occurring in response to infection. These authors wrote: “Our data suggest that PGE2⁵⁶ induced by IL-1 β as well as hypoxia selectively modulates respiration-related neurons in the rostral ventrolateral medulla, including the preBotzinger Complex via EP3R. Other neuromodulators, including PGE1, have been shown to inhibit preBotC neurons and slow respiration-related rhythm and preBotC lesions may disrupt anoxic gasping and evoke central apneas and ataxic breathing. Moreover, these respiration-related neurons were recently shown to be critical for adequate response to hypoxia, maintaining brainstem homeostasis with gasping and autoresuscitation and thus restoring oxygen levels. PGE2-induced depression of this vital brainstem neuronal network, e.g., during an infectious response, could result in gasping and autoresuscitation failure and ultimately death.”⁵⁷ The model of the IL-1 β induced respiratory depression and autoresuscitation failure via a PGE2-mediated pathway was described. “During a systemic immune response, the proinflammatory cytokine IL-1 β is released into the peripheral blood stream. It binds to its receptor (IL-1R) located on endothelial cells of the blood brain barrier. Activation of IL-1R induces the synthesis of PGH2 from arachidonic acid via COX-2 and the synthesis of PGE2 from PGH2 via the rate limiting enzyme mPGES-1. PGE2 is released into the brain parenchyma and binds to the EP3R located in respiratory control regions of the brainstem, e.g., nucleus tractus solitarius and rostral ventrolateral medulla. This results in depression of central respiration-related neurons and

⁵⁴ Vege, A & T. Rognum, *Sudden Infant Death Syndrome, Infection, and Inflammatory Responses*, 42 FEMS Immunol. Med. Microbiol. 3 (2004), Exhibit 13-Q at 5 and 8.

⁵⁵ Brambilla, D. et al., *Interleukin-1 Inhibits Firing of Serotonergic Neurons in the Dorsal Raphe Nucleus and Enhances GABAergic Inhibitory Post-Synaptic Potentials*, 26 Eur. J. Neurosci. 1862 (2007), Exhibit 13-M at 1862.

⁵⁶ PGE2 is a symbol for a prostaglandin. *Dorland's* at 1529. Prostaglandins are “any of a group of components derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway; they are potent mediators of numerous different physiologic processes.” *Dorland's* at 1528.

⁵⁷ Siljehav, V. et al., *mPGES-1 and Prostaglandin E2: Vital Role in Inflammation, Hypoxic Response, and Survival*, 72 *Pediat. Res.* 460 (2012), Exhibit C-9 at 9897.

breathing, which may fatally decrease the ability to gasp and autoresuscitation during hypoxic events." *Id.* at 9898.

Stoltenberg⁵⁸ experimented on piglets and concluded IL-1 stimulates the release of beta endorphin and indicated that his group had shown that the level of beta-endorphin in cerebral spinal fluid correlates strongly with the duration of apnea. Furthermore IL-1 β stimulates GABA transmission and hence increases the inhibitory postsynaptic function by opening of chloride defective channels, and this will reduce the activity in the central respiratory neurons and may produce hypoxia. He concluded that intravenous and intrathecal injections of interleukin 1 β in piglets' prolonged apnea and modified autoresuscitation. Such a mechanism may play a role in depressing respiration in some infants dying of sudden infant death syndrome. *Id.* at 427.

In a study looking at the role of vaccination in producing apnea, bradycardia and oxygen desaturations in pre-term infants who received first DPT (whether whole cell or acellular pertussis, inactivated polio and Haemophilus influenza B), Lee found elevations in apnea, bradycardia and desaturations defined as cessation of respiration for 20 seconds, with a heart rate less than 100 and oxygen saturation less than 85%. Almost half had adverse cardiorespiratory events in the 72 hours post-vaccination which was statistically significantly higher than the control group which did not receive a vaccination in the prior 72 hours.⁵⁹

Schulzke also studied apnea and bradycardia in pre-term infants, not on oxygen or respiratory support but in the NICU when they received pentavalent or hexavalent vaccines. Rate of increased apnea and bradycardia (defined the same as by Lee) was 13% in otherwise stable infants. Infants received ventilatory support and recovered. Events occurred between 8 and 24 hours after vaccination with onset of fever between 6 and 24 hours post immunization.⁶⁰

B. SIDS Epidemiology

Although epidemiology is not required to demonstrate entitlement to compensation in the Vaccine Program, the parties submitted multiple articles, primarily from European studies, which looked at the question of the possible relationship between vaccination and the incidence of SIDS, as well as several articles that reported on cases. Articles by Venneman⁶¹, Jonville Bera, Traversa, VonKries, Goldman, and Kuhnert studied the question of vaccine causation in SIDS by various methodologies all of which described their own limitations. Others by Ottaviani and

⁵⁸ Stoltenberg, L. et al., *Changes in Apnea and Autoresuscitation in Piglets After Intravenous and Intrathecal Interleukin-1 β Injection*, 22 J. Perinat. Med. 421 (1994), Exhibit 13-J.

⁵⁹ Lee et al., *Frequency of apnea, bradycardia, and desaturations following first diphtheria-pertussis inactivated polio-Haemophilus influenzae type B immunization in hospitalized preterm infants*, BMC Pediatrics (2006), Exhibit 20 at 3-4.

⁶⁰ Schulzke, *Apnea and bradycardia in preterm infants following immunization with pentavalent or hexavalent vaccines*, European Journal of Pediatrics (2005), Exhibit 21 at 432-35.

⁶¹ Vennemann M.M. et al., *Sudden Infant Death Syndrome: No Increased Risk After Immunization*, 25 Vaccine 336 (2007), Exhibit C-17.

Zinka discussed individual cases of unexplained deaths occurring in close temporal proximity to receipt of vaccinations.

Goldman looked at VAERS data from 1990 to 2010 for hospitalizations and deaths after vaccinations and found a statistically significant positive correlation between mortality and receipt of five to eight vaccines compared to one to four.⁶² (J.B. received 7 counting DTaP as three as the study did). Traversa conducted a large study using data from the Italian health system where vaccines are offered for free and the belief is that 95% of children are vaccinated. The study found a statistically significant relative risk for death in the first seven days after vaccination for the first hexavalent vaccine (six vaccines) but not after subsequent doses.⁶³

Kuhnert did a review of studies from Germany, England, and New Zealand and critiqued the case control methodology through the use of the self-controlled case series method (SCCS). It concluded that the re-analysis using the latter method showed that the risk of SIDS was neither increased or decreased in SIDS cases or controls during the early post-vaccination periods but did “provide more detailed insights into the methodological pitfalls of such analyses using conventional case control methods.”⁶⁴ Dr. McCusker testified that the Kuhnert study looked at three different studies and applied 39 statistical tests to them. She read the study as concluding that despite the application of multiple statistical post hoc tests, they still did not see anything. Tr. 236.

Other papers submitted in evidence included Zinka⁶⁵ reporting on six deaths in Germany within 48 hours of receipt of hexavalent vaccines. Kries⁶⁶ reported on a slight elevation in day one in the first year of life after one particular hexavalent vaccine but a significant increase in deaths in the second year of life after receipt of that vaccine. Ottaviani⁶⁷ did a detailed case study of one young child who died three hours after receipt of a hexavalent vaccine at 3 months of age. He did a detailed autopsy identifying bilateral hypoplasia of the arcuate nucleus. He concluded that this death could be consistent with the Triple Risk Model or be one of the SIDS

⁶² Goldman, G.S. and N.Z. Miller, *Relative Trends in Hospitalizations and Mortality Among Infants by the Number of Vaccine Doses and Age, based on the Vaccine Adverse Event Reporting System (VAERS): 1990-2010*, 31 Hum. Exp. Toxicol. 1012 (2012), Exhibit 19 at 1016, Table 4.

⁶³ Traversa, G. et al., *Sudden Unexpected Deaths and Vaccinations During the First Two Years of Life in Italy: A Case Study*, 6 PLoS One 1 (2011), Exhibit 13-U at 4.

⁶⁴ Kuhnert R. et al., *Reanalyses of Case Control Studies Examining the Temporal Association Between Sudden Infant Death and Vaccination*, 30 Vaccine 2349 (2012), Exhibit C-20 at 2355.

⁶⁵ Zinka, B. et al., *Unexplained Cases of Sudden Infant Death Syndrome Shortly After Hexavalent Vaccination*, 24 Vaccines 5779 (2006), Exhibit 13-S.

⁶⁶ Kries, R. et al., *Sudden and Unexpected Deaths After the Administration of Hexavalent Vaccines (Diphtheria, Tetanus, Pertussis, Poliomyelitis, Hepatitis B, Haemophilus Influenza Type B): Is There a Signal?*, 164 Eur. J. Pediatr. 61 (2005), Exhibit 13-R.

⁶⁷ Ottoviani, G. et al., *Sudden Infant Death Syndrome (SIDS) Shortly After Hexavalent Vaccination: Another Pathology in Suspected SIDS?*, 448 Virchows Arch. 100 (2006), Exhibit 13-T at 4.

“grey zone” cases in which it is difficult to establish if the pathological findings were sufficient to cause death.

Each of the studies contained considerable acknowledgment of its own methodological deficiencies that may have affected the results. In different papers, these included inclusion without autopsies, small samples, comparing SIDS victims to living children rather than vaccinated SIDS to unvaccinated SIDS, as well as having no control group or having potential underreporting as in VAERS. The Kuhnert paper which analyzed three other case control studies including Venneman, said, “The small number of cases is a problem with the three case control studies, particularly in view of the short time periods under investigation. This problem is illustrated by the very broad confidence intervals of estimates that are only related to the events of the first few days.”⁶⁸

Dr. Miller criticized several of the studies for failing to use cases that were verified by autopsy, that the Vennemann study compared a new hexavalent vaccine to older vaccines rather than asking the question as to whether vaccines regardless of new or old could be associated with SIDS, and used data based on the number of vaccines sold rather than administered. Tr. 70-74. He noted that the IOM concluded that the evidence that it reviewed was insufficient to accept or reject causation. Tr. 387. In his report, Dr. Miller explained why it is difficult to do reliable epidemiological studies of SIDS. He said, “[I]f the risk for SIDS is present only in those infants who are already vulnerable because of a pre-existing brainstem abnormality, then no retrospective (or prospective) epidemiological study not grounded in a thorough neuropathological examination of all of the supposed SIDS cases would be likely to identify that putative causal relationship.” Exhibit 13 at 5. He observed that J.B. would be one of those not counted as he did not have a complete neuropathological autopsy. *Id.* at 6.

Dr. McCusker criticized some studies as case reports or having no control group. She looked to Kuhnert which incorporated Vennemann to argue that there was no significant finding that SIDS occurred more often than chance. Tr. 228.

The Vaccine Program does not require epidemiological evidence and the studies presented contained multiple methodological flaws, and did not tend to shed much light on the question at issue, that is, whether the death of the child in this case was caused or triggered by the vaccinations received the day before. Thus the studies were read and considered and credited to show that vaccines are generally safe, but were specifically unpersuasive as to whether they are on rare occasions the exogenous factor resulting in the perfect storm in a child with a defective arcuate nucleus or other 5HT structure during the vulnerable period of life. They were also unpersuasive to reject causation as they frequently showed some temporal correlation to the receipt of vaccines even if those correlations were not found to be statistically significant.

⁶⁸ Kuhnert et al. (2012), Exhibit C-20 at 2355.

C. Expert Opinions

1. Petitioners' Expert Douglas C. Miller

Dr. Douglas C. Miller earned his bachelor's degree from Williams College and his medical degree from the University of Miami School of Medicine in 1978.⁶⁹ He received a Ph.D. in Physiology and Biophysics from the University of Miami in 1980. *Id.* Dr. Miller was a resident at Massachusetts General Hospital from 1980-1984, focusing in the areas of anatomic pathology and neuropathology. *Id.* He currently serves as a clinical professor of pathology and anatomical sciences, as well as the program director of pathology residency, at the University of Missouri School of Medicine. *Id.* at 3. He also serves as an associate medical examiner for Boone, Callaway, and Greene Counties in Missouri. *Id.*; Tr. 10. Dr. Miller has been a full-time faculty member at the medical schools at Robert Wood Johnson in New Jersey, New York University, and the University of Missouri. He has published over 150 articles in medical journals and is the author of a textbook on neuropathology.

i. *Althen* Prong One: Medical Theory

Dr. Miller, consistent with the dominant literature in the field, proposed the Triple Risk Model of SIDS as the framework for his theory of causation.⁷⁰ Tr. 19. As explained above, this model first provides that SIDS can occur only when an infant is in a critical developmental period (the first year of life). Tr. 20. Second, SIDS can occur only to an infant who is inherently vulnerable in some way. *Id.* Third, the infant must encounter an exogenous stressor. *Id.*

Dr. Miller explained the normal physiological process for handling carbon dioxide and stimulating breathing. He said if the carbon dioxide levels rise above a normal threshold to an abnormal threshold, a normal brainstem's response – in this age group – is mediated by the arcuate nuclei alone. The excess carbon dioxide stimulates other neuronal systems to alert the cervical spinal cord motor neurons to tell the diaphragm and other muscles of respiration to contract, at the same time signaling up through other mechanisms in the basal forebrain, underneath the lower part of the frontal lobes, to wake up. In general, there is arousal and there is deeper breathing to blow off the carbon dioxide, and if it is position-related, the infant would also move so that homeostasis is restored. Tr. 29. He explained that this process is dependent on serotonin, an excitatory neurotransmitter, which stimulates the cells to which it signals to fire more rapidly to increase breathing or arousal. Tr. 28. That is in contrast to GABA, which is inhibitory and balances the excitatory effect of serotonin. *Id.*

Dr. Miller explained that the majority opinion in the medical community is based principally but not exclusively on work done by Dr. Hannah C. Kinney, in a series of papers that stretch back more than 25 or 30 years and has been verified by other people. She has shown that “the medulla, the lowest part of the brainstem, in infants who have died of SIDS and have been autopsied and have had the appropriate examinations is defective. In particular, it has a defect in

⁶⁹ Curriculum Vitae of Dr. Douglas C. Miller, Exhibit 14 at 1.

⁷⁰ Kinney, H.C. et al., *Medullary Serotonergic Network Deficiency in the Sudden Infant Death Syndrome: Review of a 15-Year Study of a Single Dataset*, 60 J. Neuropathol. Exp. Neurol. 228 (2001), Exhibit 13-C.

a set of nuclei [or] groups of neurons, which use, as a neuro-transmitter a molecule called serotonin ... which is also known as 5-hydroxytryptophan and which is abbreviated as 5-HT.” Tr. 19. He further explained that Dr. Kinney and others have shown various deficits in infants, but the ones who die of SIDS have in common deficits in either the number of 5-HT neurons or in receptors for serotonin on those neurons or various other associated abnormalities. All of these suggest that the infants who die of SIDS usually die in their sleep and usually after an episode of apnea – that is, the cessation of breathing with elevated carbon dioxide in the blood to which they fail to respond normally. They fail to respond because the 5-HT system is the system which, in that age group, allows for arousal and increased breathing to respond to that kind of a danger. Since they fail to respond, they do not wake up, they do not breathe, and they die. Tr. 20.

Dr. Miller theorized, consistently with the research of Dr. Kinney and others, that many SIDS infants have “abnormalities of the medullary serotonergic synaptic systems governing respiration and arousal from apnea.” *Id.* at 6. He said that “we have data that at least 70 percent of infants who ultimately die of SIDS have a defective 5-HT system which is way over half and thus statistically likely that [J.B.] was one of those.” Tr. 62. Dr. Miller said, “It’s really a neurochemical question. These molecules (cytokines) are provoked by an immune response, an innate immune response, originally in the periphery, but their effect in terms of SIDS is a neurochemical effect, affecting synaptic transmission and neuronal activity of the 5-HT system and maybe the GABA system in the medulla, and that’s a neurochemical synaptic effect.” Tr. 61. He stressed that the role of the cytokines in SIDS was in their capacity to modify normal neurologic function rather than being purely immune in nature. He assumed that J.B. was an immunologically normal child, who when given a vaccination would have had an appropriate immune response, including the production of cytokines such as the ones identified by Kashiwagi et al. Therefore, he would expect the level of cytokines to be transiently increased after vaccination. Tr. 62. “These cytokines would have been circulating in his body after vaccination and we have direct evidence that there was some cytokine-central nervous system interaction in that he had fever. Then there is a logical chain of events that says cytokines depressed the 5-HT system in a defective medulla leading to SIDS during sleep.” Tr. 62-63.

Dr. Miller stated that research is still identifying all of the exogenous stressors for SIDS. Tr. 44. He opined that one very well-recognized exogenous stressor for SIDS is mild infection. Tr. 45. Some of the estimates indicate that 40 - 50% of SIDS victims have had a very recent or current mild upper respiratory infection (URI) at the time of death. Tr. 45. He said that it is explicit in the literature from Dr. Kinney’s laboratory and others that what happens with mild infections is that the response to the infection involves the production of certain cytokines and that those cytokines can act on the central nervous system. He presented a theory: that a mild upper respiratory infection can act as a neurochemical stressor by prompting the upregulation of cytokines, which he theorizes are detrimental in two ways. He said that an infection could cause fever, an extrinsic risk factor, and can cause elevated IL-1 β levels, which would further depress a defective medullary 5-HT system. The system would then be incapable of responding to excess carbon dioxide, resulting in death. Tr. 46.

Dr. Miller cited several studies, including ones discussed above by Rognum, Kashiwagi, Kadhim, Brambilla, Stoltenberg, and Froen, that addressed the issue of cytokine stimulation and the function of cytokines entering the central nervous system. From these studies, Dr. Miller concluded that either mild URIs or vaccinations upregulate the production of cytokines, and these inflammatory cytokines, can “shut down” a structurally vulnerable 5-HT system and completely prevent it from restoring an infant’s normal breathing. Tr. 35. In other words, the cytokines and the structural defect in the serotonin system acting in concert during a vulnerable period have the cumulative effect of causing SIDS by making the baby incapable of responding to excess carbon dioxide.

Dr. Miller noted that Kashiwagi found similar cytokine profiles in the recently-vaccinated population and those suffering from influenza, and further that the cytokine profiles were similar in post-vaccination babies whether they had a fever or not. Tr. 49. He explained that cells that are injured by infection initially produce an innate immune response. The cells of the innate immune system release cytokines which signal further activation of the adaptive immune system to respond to the foreign antigen. He said that there is a wide range of things that the cytokines produce, but the initial production is certainly peripheral where there is infection. Tr. 50. He testified that there is a whole lot of evidence that cytokines, produced peripherally, interact with the central nervous system and the easiest one to understand is the way fever is produced. He explained that fever is mediated by the central nervous system and specifically by the hypothalamus in the brain. The hypothalamus sets our body temperatures. It causes us to shiver if we are in the cold and need to warm up, or to sweat when we are overheated. Tr. 50-51. He further explained that if the fever was generated in response to an infection outside of the brain, such as in the case of a URI, there would be no inflammation in the brain as the brain is not infected, but there is still an interaction with the hypothalamus in the brain caused by cytokine signaling that causes fever in response to an infection outside of the brain. Tr. 51-52. Dr. Miller stated that he was not aware of any literature describing URI as a *mechanical* exogenous stressor and that in his professional experience conducting autopsies, he had never seen a URI “obstruction of the airway” that would be sufficient on its own to cause death. Tr. 46.

Dr. Miller stated that vaccinations can be an extrinsic risk factor in SIDS, as they prompt the upregulation of cytokines that, among other things, produce fever. Tr. 62-63. He testified that, based on the literature, there is a scientifically-plausible mechanism for vaccinations acting as the extrinsic risk factor in SIDS in much the same way as a mild infection. He explained that when you get a vaccination or a whole group of them at once, as J.B. did, it evokes a response which includes the production of cytokines, and that among those cytokines are IL-6, TNF α , and IL-1 β . The physiological studies have shown that these can raise body temperature by producing fever, which is a risk factor, and they can inhibit the activity of 5-HT neurons in the medulla causing prolonged apneas and interference with autoresuscitation. Tr. 54, 62-63. When the vaccines are administered in the presence of the defects in the medulla, during the critical developmental period, they are likely to have a similar effect as mild infection that may cause a failure of the medullary response system and ultimately a death. Tr. 54.

Dr. Miller stated that mild upper respiratory tract infection is widely recognized to be an exogenous stressor under the Triple Risk Model. However, he acknowledged that there is not wide recognition, or a generally accepted theory, that vaccinations are an exogenous stressor. He stated that the Institute of Medicine concluded “the evidence is insufficient to say that there is an effect or there isn’t an effect.” Tr. 55. The Kinney research team has not studied the relationship between vaccination and SIDS. Tr. 60. Dr. Miller pointed to “multiple reports of similar cases of SIDS following various neonatal or infant vaccinations, mostly stressing the close temporal relationships between vaccination, increased cytokine production, and death from apparent SIDS as seen with this case.”⁷¹ He said that these individual cases and small case series show a “suspicious association between the timing of vaccination and the timing of SIDS deaths.” Tr. at 55.

Summarizing his theory and review of the literature, Dr. Miller testified that the papers cited, including Kadhim, Kashiwagi, Rognum, Stoltenberg, and Froen, “verify the importance of the 5-HT system and its interactions with the GABA system in the medulla in terms of response to apnea or other respiratory-related insults.” Tr. 34. Second, “they showed that there’s an altered cytokine profile in SIDS cases versus non-SIDS cases, dying of other things, like drowning or trauma.” *Id.* Third is the specific information on IL-1 β , in that it inhibits the 5-HT system. *Id.* Therefore, in the context of SIDS, this suggests that if there is an elevated level of IL-1 β to which the 5-HT neurons are exposed in an infant who already has too little 5-HT activity because of a defective brainstem, this additional cytokine effect would shut down the system such that it would not respond to other external stressors such as prone sleeping, nicotine, infection or fever. Tr. 34-35.

Dr. Miller addressed this analysis in terms of the cytokine reaction generated by vaccines. He said that we know that when a child gets a vaccine or a whole group of vaccines all at once, as occurred in this case, it evokes a response which includes the production of cytokines; that among those cytokines are IL-6, TNF α , and IL-1 β . Those levels go up in the blood. We know that IL-1 β can inhibit the activity of the 5-HT neurons in the medulla. If you take an infant who has a defective medulla with a defective 5-HT system already, you put in a stress situation with elevated carbon dioxide or low oxygen, and there is a vaccination which further shuts down the 5-HT system, and you can get a complete failure of response and therefore a death. He concluded that the mechanism is plausible. Tr. 54.

ii. *Althen* Prong Two: Logical Sequence of Cause and Effect

Dr. Miller then applied his theory to J.B.’s specific case. As an initial matter, he agreed with the decision to classify J.B.’s death as SIDS. Exhibit 13 at 1. Under the Triple Risk Model, Dr. Miller opined that J.B. was in the critical developmental period. Tr. 44. Statistically, he was inherently vulnerable. Dr. Miller opined that Kinney et al. have found that a significant proportion – up to 70% – of SIDS infants have abnormalities in the arcuate nuclei and other sections of the medulla. Exhibit 13 at 3. Dr. Miller said that there is also a Japanese study in

⁷¹ Vege & Rognum (2004), Exhibit 13-Q; Kries et al. (2005), Exhibit 13-R; Zinka et al. (2006), Exhibit 13-S; Ottoviani et al. (2006), Exhibit 13-T; Traversa et al. (2011), Exhibit 13-U; Institute of Medicine, *Adverse Effects of Pertussis and Rubella Vaccines* (1991), Exhibit 13-V.

which that number went as high as 90 percent. Tr. 38. He testified that it is statistically most likely that J.B. also had this medullary 5-HT defect based on the Kinney data and other studies, even though it was not confirmed because the medical examiner did not sample that section of the brain. Exhibit 13 at 4-6; Tr. 37-38. Dr. McCusker agreed that “according to the Triple Risk theory, the brain problem must exist [in J.B.’s case].” Tr. 206.

A great many autopsies of SIDS infants outside of the research context do not section all of the necessary areas of the brain or view them histopathologically, which is typical of medical examiner autopsies. Tr. 16. Respondent’s expert pathologist, Dr. Harris, acknowledged that based on Dr. Kinney’s research, the majority of SIDS babies and up to 70% in some of her studies had an abnormality of the 5-HT system. Tr. 346. However, “[d]etection of these abnormalities requires special immune-histochemical research techniques not generally available for a ‘routine’ autopsy.” *Id.* Dr. Miller testified that even in some autopsies where no structural abnormality was found in Dr. Kinney’s research, when the full histochemistry was performed, there were still receptor binding deficits, such as in the IL-6 and gp130 studies. Tr. 41-42. Unfortunately, the types of tools she used including autoradiography and immunohistochemistry are not generally available for autopsies. Tr. 42-43.

Dr. Miller discussed the logical sequence of cause and effect between vaccines administered on September 2, and J.B.’s death on September 3. He opined that the vaccines acted as a critical external stressor in this case. He noted that J.B. was a “healthy infant... developing normally.” Exhibit 13 at 4. He was “immunologically normal.” Tr. 62. Therefore, after receiving vaccinations, his body mounted an innate immune response including the production of cytokines. Exhibit 13 at 6; Exhibit 16 at 1; Tr. 63. Those cytokines circulated in J.B.’s body, specifically into the central nervous system. Exhibit 13 at 6; Tr. 63. These peripheral cytokines interacted with the hypothalamus to provoke fever the night after the vaccinations, and the following day (before J.B.’s death). Exhibit 13 at 6; Exhibit 16 at 1; Tr. 62-64. “Those cytokines then acted in the brainstem which was already deficient in serotonergic drive for respiratory effort, leading to an apneic episode from which he did not recover, i.e., SIDS.” Exhibit 13 at 6; *see also* Tr. 62 (the cytokines “depress[ed the] 5-HT system in a defective medulla, leading to SIDS during sleep”).

He opined that there was “no other demonstrable inciting event” for J.B.’s death. Exhibit 13 at 1. There was no evidence of the fever being related to anything other than J.B.’s vaccinations. Tr. 66. The autopsy did not identify any other infectious processes. Tr. 66.⁷²

Dr. Miller was asked whether the pillow in J.B.’s crib increased the risk of SIDS. Tr. 87. Dr. Miller was not sure whether J.B.’s head was on the pillow. *Id.* He said, “If the pillow was by his feet, I don’t think it’s a risk factor.” *Id.* A review of the investigation files indicates that there was no evidence as to whether or not his head was on the pillow. The only relevant evidence was that it was “a little crib pillow-very flat” and that his mother told the police that his nose or mouth were not covered when she found him about ten minutes after replacing his pacifier. Exhibit 7 at 5.

⁷² Dr. Miller noted that there was bacterial growth and food particles in J.B.’s lungs and epithelial cells in the upper airways. He opined that this was not evidence of a separate infectious process. He agreed with the medical examiner that these were terminal or resuscitative events. Tr. 17-18; 66; 352-53.

On cross-examination, Dr. Miller stated that J.B. was placed on his back but was found on his side, which demonstrates that he was able to “move around.” Tr. 92. However, J.B. did not pass away until “something else intervened.” Tr. 85. Based on his theory and the temporal association, Dr. Miller opined that the vaccines were the intervening factor that caused J.B.’s death. Tr. 85; Exhibit 7 at 5. He said that he looks at SIDS cases individually and that it was his diagnosis that the vaccines contributed substantially to the death of J.B. in this case. Tr. 106-08.

iii. *Althen* Prong Three: Timing

With regard to timing, Dr. Miller stated several reports “have noted an elevated risk for SIDS within the first 48 hours following immunization, although this is not statistically significant.” Exhibit 13 at 5. He stated that J.B. died within this 48-hour “window of elevated risk” following vaccination. *Id.*

Dr. Miller also stated that the available evidence is that foreign antigens, like those contained in vaccinations, activate the production of cytokines “within hours” and that production “peaks within 2 to at most 4 days.” Exhibit 16 at 1. Thus, a vulnerable infant who receives vaccinations is most likely to suffer a fatal event if one is to occur “within the first 48 hours to at most 4 days.” *Id.* Dr. Miller opined that J.B.’s death was “well within this vulnerable period.” *Id.*

2. Respondent’s Expert Dr. Christine McCusker

Dr. Christine McCusker earned a Masters in Molecular Virology in 1988, followed by an M.D. in 1993, at McMaster University, in Hamilton, Ontario. Exhibit D at 1. Her residency training was in pediatrics, at Montreal Children’s Hospital, McGill University, from 1993-1996. *Id.* at 2. She was then a clinical fellow in allergy and immunology at McGill University from 1996-1999. *Id.* Dr. McCusker is board certified in pediatrics. *Id.* She is currently the division director of pediatric allergy, immunology, and dermatology at the Montreal Children’s Hospital at McGill University Health Center and is the director of the Clinical Immunology Lab. Tr. 122. She has a wet lab that studies developmental immunology, which has peer-reviewed funding. *Id.* She also runs a clinical research program that uses databases to follow patients with primary immunodeficiency. *Id.* In addition, she sees pediatric patients at McGill Children’s emergency room and at several allergy, immunology, and general pediatrics clinics. Tr. 124. Dr. McCusker also teaches medical students in the areas of immunology, dermatology, and malignant hematology. *Id.*

i. *Althen* Prong One: Response to Petitioners’ Medical Theory

Like petitioners’ expert Dr. Miller, Dr. McCusker accepted Dr. Kinney’s formulation of the Triple Risk Model. Dr. McCusker agreed with Dr. Miller on the critical development period, and that an infant may be “vulnerable” because of a brain defect, premature birth, male gender, and/ or African American race. Dr. McCusker disagreed with Dr. Miller’s opinion that upper respiratory infection, and by extension, vaccines, act as *neurochemical* exogenous stressors within the Triple Risk Model.

Dr. McCusker spent considerable time explaining why upper respiratory infection and other exogenous stressors, such as “being placed or found in a prone/ side-sleep position, found face down, head covered, sleeping on an adult mattress, couch, or playpen, soft bedding, bed-sharing, and signs of upper respiratory tract infection,” are *mechanical*. Specifically, each one impedes an infant’s ability to exhale carbon dioxide and inhale fresh oxygen, thereby increasing the risk of SIDS. Tr. 127-28.⁷³

She opined that the prone sleep position is more widely recognized as an exogenous stressor for SIDS, but that the side-sleep position poses just as much risk. Tr. 131. She stated that breathing depends on “drop[ping] the diaphragm down and creat[ing] a negative airspace, [in which] the air comes rushing in.” Tr. 130. An infant’s body is not fully developed, so it uses “more than just the diaphragm” and “a lot of abdominal muscle to breathe.” *Id.* An infant lying supine with the head back breathes most easily. *Id.* In contrast, an infant in either the prone or side-sleep position has more difficulty dropping the diaphragm and exhaling carbon dioxide. *Id.* Dr. McCusker also opined that the side-sleep position compresses “at least half your rib cage.” Tr. 132. She stated that an infant’s rib cage is “soft” and “very pliable.” Therefore, it does not take much to influence the infant’s ability to exchange air. *Id.* She also noted that an infant’s breath is much more shallow and rapid than an adult’s, and therefore the diffusion of exhaled carbon dioxide is less than in adults and rebreathing is more likely. *Id.* Theoretically, this means that an infant is at greater risk of re-inhaling expelled carbon dioxide. *Id.* Dr. McCusker acknowledged that the Back to Sleep Campaign previously advised parents to avoid all risk factors for SIDS, and that early research emphasized avoiding prone sleeping. *Id.* at 132-33. However, she said more recent studies looking “a little bit more closely” indicate that “prone and side-sleeping have equal risk.” Tr. 134. She also stated that an infant learns to roll from the supine position to the side or prone position, but “usually not until somewhere between four and six months.” Tr. 134-35. She did acknowledge, however, that the American Academy of Pediatrics does say that once a child is able to roll from his back to his side or to prone, then the parent should not disturb them. They should just have nothing else in the crib that could obstruct breathing. Tr. 135.

She also stated that gastroesophageal reflux is an exogenous stressor. Tr. 137. Specifically, an infant’s airway and esophagus are linked at the back of the throat. *Id.* An infant may regurgitate and inhale at the same time, and therefore stop breathing momentarily. *Id.* at 138. If the infant neither swallows nor expels the food, his breathing will become obstructed and he will not recover. *Id.*

Dr. McCusker stated that bundling is an exogenous stressor and suggested several possible reasons why. *Id.* at 135. First, she opined that bundling decreases an infant’s arousal, which helps the infant go back to sleep, but may increase the incidence of SIDS. *Id.* at 136. Second, a bundled infant may be less able to roll out of the prone or side-sleeping position. *Id.* Third, bundling may be an exogenous risk factor by leading to hyperthermia. *Id.* It should be noted that there is no evidence of bundling in this case, as J.B.’s father said he placed him on his back with a blanket across the midsection, but there was no indication that he was wrapped or bundled.

⁷³ Trachtenberg, Kinney, et al. (2012), Exhibit C-11.

Dr. Miller stated that hyperthermia was a term encompassing both high ambient temperature and fever. But Dr. McCusker disagreed. She testified that hyperthermia was high ambient temperature, and *hyperpyrexia* was fever. She stated that older literature listed both hyperthermia and hyperpyrexia as exogenous risk factors for SIDS. Tr. at 201, 287. However, she opined that newer literature, such as an article by Trachtenberg, lists hyperthermia as a risk factor for SIDS, but not fever. Tr. at 201, 287, 290. She agreed with this distinction. She reasoned that an infant experiencing hyperthermia tries to cool himself down. Tr. 289. To do so, the infant takes short, shallow breaths, which increase CO₂ levels, which trigger the pathway to SIDS. Tr. 288, 295. She cited an article by Harper and Kinney, which provides that “vasodilation associated with overheating makes compensation for low blood pressure more difficult.”⁷⁴ Dr. McCusker opined that fever is *not* a risk factor for SIDS. Specifically, she said in fever the body fasciculates or shivers – it makes small muscle movements that create friction, which generates heat inside the body. *Id.* at 184. The body cannot make these movements during deep REM sleep. Therefore, it stays in NREM sleep. *Id.* at 184-85. She opined that an infant generating or maintaining a fever, who does not descend into REM sleep, is less susceptible to SIDS. *Id.* at 202. It should be noted that nowhere in the submitted literature was an explicit distinction made between hyperthermia and hyperpyrexia, including in Trachtenberg or the Harper & Kinney article. Dr. McCusker is correct that in a 1992 article by Dr. Kinney, she mentioned “infection, fever and hyperthermia” as exogenous stressors.⁷⁵ Later articles generally reference hyperthermia and overheating. However, in a 2009 article, Dr. Kinney described a SIDS scenario in which in part she describes “an infant may be slightly febrile due to an otherwise trivial upper respiratory tract infection (3) as a consequence, the apnea component of the LCR is inordinately prolonged by mild hyperthermia,”⁷⁶ This reference would appear to suggest that the term hyperthermia may be more broadly inclusive.

Unlike Dr. Miller, Dr. McCusker characterized mild upper respiratory infection as a purely mechanical extrinsic risk factor for SIDS. Tr. at 127-28. She opined that an infant is accustomed to breathing through the nose, which enables uninterrupted bottle or breast-feeding. *Id.* at 138-39. When the nose is congested, she said, the infant still exerts significant effort to breathe through the nose, which elevates carbon dioxide. *Id.* at 139. If and when the infant finally resorts to breathing through the mouth, that is less effective and also increases the risk of respiratory distress. *Id.* at 140-43.

Dr. McCusker then spoke about cytokines. She asserted that cytokines serve a variety of positive functions in the healthy human brain. *Id.* at 145-58.⁷⁷ Researchers initially theorized that cytokines found in the brain, including IL-6, IL-1 β , and tumor necrosis factor-alpha (TNF-alpha), had traveled there through the cerebrospinal fluid, to respond to inflammation in the brain. *Id.* at 151-52. However, research beginning in the late 1990s indicates that the brain itself

⁷⁴ Harper & Kinney (2010), Exhibit C-12 at 3.

⁷⁵ Filiano & Kinney (1992), Exhibit 13-A at 401.

⁷⁶ Kinney et al. (2009), Exhibit 13-H at 539.

⁷⁷ Besedovsky, H.O. and A. del Ray, *Central and Peripheral Cytokines Mediate Immune-Brain Connectivity*, 36 *Neurochem Res.* 1 (2011), Exhibit C-3.

produces cytokines. *Id.* at 152. Dr. McCusker cited articles reporting that inflammatory cytokines such as IL-6 and IL-1 β regulate pain sensitivity, memory consolidation, stress, fever, and sleep. *Id.* at 152-56.⁷⁸ Ron-Harel wrote, “Pro-inflammatory cytokines are abundantly expressed in healthy brain and are involved in the regulation of many physiological functions such as pain sensitivity, memory consolidation and neural plasticity. Elevation in brain cytokine levels is considered part of the adaptive response to external stimuli. Exposure to acute psychological stressors by induction of adrenalin, noradrenalin and dopamine induces an increase in brain proinflammatory cytokines which modulate the neuroendocrine and behavioral response to the stressor. *Id.* at 3. She also cited an article by Moidunny et al. suggesting that cytokines including IL-6 may play a neuroprotective role in the brain after stroke or head trauma. *Id.* at 157.⁷⁹ Moidunny was studying the role of IL-6 in reducing glutamate excitotoxicity in stroke and head trauma with the goal of further research to identify additional pharmacological protection with IL-6 from glutamate neurotoxicity in these patients. Moidunny does not discuss SIDS or the role of peripheral cytokines in this article.

Dr. McCusker also cited to an article by Chen Miller, which discusses the role of Tryptophan Hydroxylase 2 which is a rate limiting enzyme in 5-HT biosynthesis. The article discusses advances in understanding Tryptophan Hydroxylase TPH and TPH2 which are critical for the initiation of the synthesis of 5-HT (serotonin) which modulates the stress response by interacting with the hormonal hypothalamic pituitary adrenal axis and neuronal sympathetic nervous system. The TPH2 mRNA expression is abundant in the raphe nuclei or regions containing raphe nuclei such as the pons and medulla, while it is detectable in a number of other regions including the cortex, hypothalamus, thalamus, hippocampus, amygdala and cerebellum. TPH2 gene expression is sensitive to stressful events including hemorrhage and hypoxia and involves neuronal and hormonal mechanisms. The article hypothesizes about the role of TPH2 and serotonin in response to stimulating events such as hypotensive hemorrhage, hypoxia and adverse events experienced in early life or as an adult, and a possible role in such conditions as PTSD but it was not clear how this paper directly addresses the issue of respiratory depression in SIDS.⁸⁰

Dr. McCusker argued that the various animal studies cited by Dr. Miller were not relevant to cytokines’ effect in infant brains *in vivo*. *Id.* at 162-87. First, she stated that the Brambilla article,⁸¹ which showed that IL-1 β depressed serotonin in rats’ brain tissue, was not

⁷⁸ Ron-Harel, N. et al., *Brain Homeostasis is Maintained by “Danger” Signals Stimulating a Supportive Immune Response Within the Brain’s Borders*, *Brain Behav. Immun.* (2011), Exhibit C-1; Su, Y. et al., *Predator Exposure-Induced Cerebral Interleukins are Modulated Heterogeneously in Behavioral Asymmetry*, *135 Immunol. Let.* 158 (2011), Exhibit C-4; Kinney et al. (2011), Exhibit 13-F.

⁷⁹ Moidunny, S. et al., *Interleukin-6-Type Cytokines in Neuroprotection and Neuromodulation: Oncostatin M, but not Leukemia Inhibitory Factor, Requires Neuronal Adenosine A1 Receptor Function*, *114 J. Neurochem.* 1667 (2010), Exhibit C-2.

⁸⁰ Chen, G.L. & G.M. Miller, *Advances in Tryptophan Hydroxylase-2 Gene Expression Regulation: New Insights into Serotonin-Stress Interaction and Clinical Implications*, *159B Am. J. Med. Genet. B. Neuropsychiatr. Genet.* 152 (2012), Exhibit C-15.

⁸¹ Brambilla, D. et al., *Interleukin-1 Inhibits Firing of Serotonergic Neurons in the Dorsal Raphe Nucleus and Enhances GABAergic Inhibitory Post-Synaptic Potentials*, *26 Eur. J. Neurosci.* 1862 (2007), Exhibit 13-M.

relevant to sleeping infants. *Id.* at 185. Specifically, the Brambilla study submerged rats' brain tissue in "super-physiologic doses" of IL-1 β for an extended period of time; and kept it isolated in petri dishes, which would not reflect what happens to a vulnerable infant in a "crisis situation." *Id.* at 186-87.

Similarly, Dr. McCusker opined that the Stoltenberg and Froen articles,⁸² which reported that very young piglets did not recover from apnea as quickly when they received super-physiological doses of cytokines, had limited significance. *Id.* at 162-63. The articles reported this effect only in piglets younger than fifteen days old; in a previous study, cytokines did not have any effect on older piglets. *Id.* at 163. Dr. McCusker opined that pigs' and infants' respiratory systems develop at similar paces; therefore, piglets younger than fifteen days old could be compared only to infants under one month old. *Id.* at 164. Furthermore, she argued that Froen induced extremely high cytokine levels that would not occur naturally in infants. *Id.* at 171. On rebuttal, Dr. Miller responded to this criticism, by saying that pigs' brains are very different from human brains. Pigs are born with much more myelin than adult brains; they are much more mature than our brains. The piglets are walking and do things early in piglet life that humans take up to a year or more to do. Thus, this model is not an irrelevant model for a 4-month-old in terms of brain development. He noted correctly that what Stoltenberg and Froen were looking at was *brain physiology* or pathophysiology. They were not looking at respiratory development in terms of pulmonary or bronchial development or vascular or cardiac development. They were looking at the responsive neurons in the brain. Tr. 358.

Dr. McCusker also argued that studies of cytokine levels in human brains were only observational, and did not support Dr. Miller's theory. She stated that the Rognum article⁸³ found similar IL-6 levels in SIDS infants *with* and *without* minor infections. She argued that if infection upregulates cytokine levels, the data between these two groups should be different. *Id.* at 173-74.

Dr. McCusker opined that cytokines play a protective role. Specifically, they maintain homeostasis in the body. She stated that cytokines carry messages (e.g., that an infant's breathing is disrupted) to receptor cells, which contain gp130 molecules, which are supposed to respond to those messages (e.g., by prompting the infant to arouse or gasp). *Id.* at 174-77. Dr. McCusker noted that the Rognum article reported that SIDS brains showed increased binding of IL-6 to neurons in the arcuate nucleus, but no corresponding increase in expression of gp130 (a "signal transducer" for the 5-HT system).⁸⁴ She said that if the lack of a corresponding increase in gp130 is physiologically important, which "is a big if," it would imply that the increased IL-6 would not be doing anything. Tr. 175

⁸² Stoltenberg et al. (1994), Exhibit 13-J; Froen, J.F. et al., *Adverse Effects of Nicotine and Interleukin-1 β on Autoreuscitation After Apnea in Piglets: Implications for Sudden Infant Death Syndrome*, Pediatrics (April 2000), Exhibit 13-K.

⁸³ Rognum, Kinney et al. (2009), Exhibit 13-N; Kadhim et al. (2010), Exhibit 13-O.

⁸⁴ Rognum, Kinney et al. (2009), Exhibit 13-N.

As Dr. Miller mentioned, Rognum suggested that IL-6 may have “aberrant interactions” with the arcuate nucleus, leading to SIDS. However, Rognum also suggested another theory: that the “increased expression of the IL-6R in the arcuate nucleus *may be a compensatory mechanism* as defective arcuate neurons may require excessive IL-6 stimulation in order to respond to altered CO2 levels.” *Id.* at 528 (emphasis added). Kinney cited this theory, writing: “The expression of IL-6 is elevated in the arcuate nucleus in SIDS infants, which may reflect a compensatory mechanism whereby defective arcuate 5-HT neurons require excessive cytokine stimulation to respond to infection-induced hypercapnia.”⁸⁵ Dr. McCusker adopted and elaborated on this theory suggesting that IL-6 mounts a protective response. Tr. 157. She cited an article by Moidunny, which states that some IL-6 cytokines have “neuroprotective properties” and that IL-6 requires gp130 receptor subunits to be activated for signaling.⁸⁶ When a stressor – such as inadequate oxygen or hypoxia – occurs, the cytokines bind to the 5-HT system, which expresses gp130 molecules to prompt a response – such as prompting the body to turn over or gasp. Tr. 155-56, 161, 175-77, 241. Dr. McCusker opined that these responses can be “quite rapid, within hours or days.” Tr. 180-81. Based on these findings, Dr. McCusker suggested that SIDS infants have potentially protective IL-6 molecules in the brain, but in SIDS infants they fail to prompt the upregulation of gp130 molecules. Thus the IL-6 is ineffective. Tr. 176

Dr. McCusker stated that neither the Kinney team nor the AAP lists vaccinations as a risk factor for SIDS. *Id.* at 144. Dr. Miller testified to a conversation that he had with Dr. Kinney who told him that she did not want to study vaccines because she did not want to testify and did not want to be involved in vaccine controversies. Tr. 60. Dr. McCusker acknowledged that medical literature has reported a temporal association between vaccination and infant death in certain cases. Specifically, the Ottaviani study reported that a three-month-old white female infant received a hexavalent vaccine, lost consciousness one hour later, did not recover upon resuscitation, and passed away a few hours later.⁸⁷ Dr. McCusker highlighted that Ottaviani suggested the case might fall into a “SIDS ‘gray zone’” because it was “difficult to establish whether the pathological findings [were] sufficiently severe to have caused the death.” *Id.* Dr. McCusker noted that Ottaviani published another study of five infants displaying those same pathological abnormalities; however, that study did not mention vaccinations.⁸⁸ Therefore, she suggested that the vaccination in the first Ottaviani case was temporally associated with, but did not cause, that infant’s death despite the fact that the author stated that in this case the sudden death in a child with arcuate hypoplasia could have been triggered by the hexavalent vaccine or could have been a gray zone case where it is difficult to determine if the pathological findings were sufficient to cause the death. Tr. at 103. It should be noted that the gray zone study focused on the neuropathology and histopathology of five specific SIDS victims to identify the possible brainstem abnormalities. The victims were chosen for study with no reference to vaccines or other specific causal pattern. The case report involving the child who died three

⁸⁵ Kinney et al. (2011), Exhibit 13-F at 195.

⁸⁶ Moidunny et al. (2010), Exhibit C-2 at 1668.

⁸⁷ Ottaviani et al. (2006), Exhibit 13-T at 101-02.

⁸⁸ Ottaviani G. et al., *Sudden Infant Death Syndrome “Gray Zone” Disclosed Only by a Study of the Brainstem on Serial Sections*, 33 J. Perinat. Med. 165 (2005), Exhibit C-16 at 6.

hours after receipt of the hexavalent vaccine was published subsequently to the gray zone study and mentions it as the group's prior work. It does hypothesize that the death could have been triggered by the vaccination or fall into the gray zone category.⁸⁹

Dr. McCusker's comments in her report about the literature submitted by petitioners caused some concern, in that they could be read as misleading. Exhibit C at 7-8. Dr. McCusker stated that in the study by Rognum et al., "although [in SIDS infants] there was increased intensity staining for IL-6R, it was not different from those dying of infectious causes." Exhibit C at 7 (discussing Exhibit 13-N). However, Dr. McCusker did not note that at most the SIDS infants had mild infections, which would not be expected to cause elevated cytokines in the brain, while the other group had severe infections which *would* be expected to cause elevated cytokines in the brain and that "the mean IL-6R intensity grade in the arcuate nucleus was significantly higher in the SIDS group than in the control group."⁹⁰ [the control group died of "primarily violent causes."] *Id.* at 521.

Of greater concern was Dr. McCusker's characterization of the article by Kadhim et al. Exhibit C at 7-8 (discussing Exhibit 13-O). She stated: Kadhim et al. "examined IL-2 levels in SIDS versus non-SIDS brains and showed no difference in expression in IL-2 and they hypothesize that IL-2, like the cytokines IL-1 β , TNF α , and IL-6, may be expressed in normally functioning brains of infants." Exhibit C at 7-8. Kadhim et al. actually stated; "SIDS victims often have preceding mild infectious/ inflammatory conditions (like coryza/ mild upper respiratory infections, soft stools/ mild gastroenteritis, post-vaccinal fever, etc.)"⁹¹ They compared the brains of SIDS infants to those of infants who died of *severe* infectious/ inflammatory conditions. *Id.* at 123. They found that IL-2 levels were unexpectedly comparable in the two groups. *Id.* Kadhim said, "the comparable (equally intense) expression of IL-2 in SIDS infants was rather unexpected as SIDS victims have no obvious or detectable serious health conditions before death and that autopsies show no obvious cause for their demise. (as per definition). However, this high expression in SIDS would corroborate the tenet that SIDS victims experience hyperimmune reactions with 'exaggerated cytokine response to the often reported preceding mild/trivial infectious/inflammatory conditions. Upregulated cytokines exert serious effects on many biological systems including the turnover, release, and transmission of neurotransmitters; cytokines therefore act as neuro-modulators that could modify neural, neuroimmune, and neuroendocrine functions, and can modify synaptic transmissions." *Id.* at 125. The authors further concluded, "Thus various biological stressors such as infectious inflammatory, ischemic or anoxic, and hyperimmune conditions, and metabolic disorders induce IL-2 which is preferentially expressed in vital brainstem neuronal centers. IL-2 and other subsequently triggered cytokines in downstream immune inflammatory mediators interact with neurotransmitters and/or their receptors and modify their function. The resulting neuronal molecular disequilibrium tips the delicate molecular balance causing dysfunction in those vital

⁸⁹ Ottoviani et al. (2006), Exhibit 13-T at 103.

⁹⁰ Rognum, Kinney et al. (2009), Exhibit 13-N at 521.

⁹¹ Kadhim et al. (2010), Exhibit 13-O at 122.

brainstem centers in producing disturbed homeostasis with potentially drastic effects on target organs systems and eventual death.” *Id.*

Dr. McCusker reviewed the epidemiological papers submitted and noted that an article by Kuhnert found a *decreased* incidence of SIDS in days 1-3 after vaccination, then *increased* incidences of SIDS in days 4-7, 8-14, and 15-21. Tr. 229-35.⁹² Furthermore, she stated that other studies did not find *any* temporal association between vaccination and SIDS. First, an article by Jonville-Bera et al. did not find a heightened risk of SIDS in French infants vaccinated at three months old.⁹³ Second, Toro et al. found that the incidence of SIDS in two-month-old children in Hungary decreased when that country instituted vaccinations at that age. *Id.* at 7.⁹⁴ Third, Vennemann et al. did not find an increased risk of SIDS with vaccination.⁹⁵ In Dr. McCusker’s opinion, “large studies, designed to unmask rare events, have shown no link between vaccination and SIDS and have at least in some studies demonstrated a vaccine protective effect for SIDS.” Exhibit C at 7.

At trial, Dr. McCusker added that the Kries study cited by petitioners did not support their case. Specifically, SIDS is defined as a syndrome that only affects children “under one year of age.”⁹⁶ However, Kries et al. did not find an association between vaccination and death in children under one year old. They found an increased incidence of SIDS only in children vaccinated during the *second* year of life. *Id.* Therefore, she said this study does not support petitioners’ theory about vaccination and SIDS. Tr. at 257.

ii. *Althen* Prong Two: Response to Petitioners’ Opinion of a Logical Sequence of Cause and Effect

Dr. McCusker stated that there was “no evidence” that vaccinations contributed to J.B.’s death from SIDS on September 3, 2011. Exhibit C at 8; Tr. 126. She did not dispute that J.B. was in the critical development period. She agreed that “according to the triple-risk theory, the brain problem must exist” for an infant to succumb to SIDS. Tr. 206.

She agreed that vaccines “increase cytokine circulation.” Tr. 195. She also stated that Kashiwagi et al. showed that 24-48 hours after vaccination, a child will have elevated cytokines, whether or not he has a fever. Tr. 199. “Cytokine elevation in this model is independent of fever.” *Id.* Dr. McCusker stated that J.B. had a fever, and because he was generally healthy and had no signs of upper respiratory infection, the fever could be attributed only to his vaccinations. Tr. 204-05. The fever was “an indication that [J.B.] was responding... to the vaccine.” Tr. 238.

⁹² Kuhnert et al. (2012), Exhibit C-20.

⁹³ Jonville-Bera A., et al., *Sudden Unexpected Death in Infants Under 3 Months of Age and Vaccination Status – A Case Control Study*, 51 Br. J. Clin. Pharmacol. 271 (2001), Exhibit C-18.

⁹⁴ Toro K. et al., *Change in Immunization Schedule and Sudden Infant Death Syndrome in Hungary*, 42 FEMS Immunol. and Med. Microbiol. 119 (2004), Exhibit C-19.

⁹⁵ Vennemann et al. (2007), Exhibit C-17.

⁹⁶ Kries et al. (2005), Exhibit 13-R at 1.

She stated that J.B. had a fever on September 3, 2011, but after he was given Advil that morning at approximately 8:00 a.m., his fever resolved. Exhibit C at 4; Tr. 204-05, 237. She also stated that a non-steroidal would last for eight hours. Tr. 192. She stated that “if IL-1 β mediated respiratory depression [occurred] in the case of J.B., the Advil he was given would have acted to counter this effect, suggesting that this mechanism was not involved in his death from SIDS.” Exhibit C at 5, 8.

Her theory was that J.B. “was put down for his nap, he rolled over, he started rebreathing, and he died of a sudden infant death due to hypercapnia... independent of any cytokines.” Tr. 206. She opined that there were several recognized exogenous stressors in J.B.’s case: formula feeding, side sleeping, soft bedding, and a pillow under his head. Exhibit C at 5; *also* Tr. 128-29. In her report, Dr. McCusker stated that J.B. “was found on his side with his face down on a pillow.” Exhibit C at 4 (citing Exhibit 7 at 6). (The sixth page of this exhibit is a confirmation of faxing the record.) However, the preceding page is a handwritten scene investigation form. It states that J.B.’s crib had a “little crib pillow.” Exhibit 7 at 5. J.B. was found “on side with head downward.” *Id.* The form also indicates that neither J.B.’s nose nor his mouth was covered. *Id.*

At the hearing, Dr. McCusker first testified that J.B.’s “face was downward according to the reports.” Tr. 128. On cross-examination, she could not identify where in the record it said that his face was down on a pillow. Tr. 265. She thought “he was found with his head down. There was a pillow in the bed, which is clear from the photos. So, it would be easy to hypothesize that he was at least found face down in the general vicinity of a pillow, and one would wonder what the pillow was doing in the bed if it wasn’t for under his head.” Tr. 266. She noted that the photos of the crib showed a pillow on one end of the bed and diapers and wipes on the other end. Tr. 266 (discussing Exhibit 9 at 8-9). She opined that J.B.’s head would have been on the end of the bed where the pillow was. Tr. 266-67. Dr. McCusker acknowledged, however, that she did not know whether J.B. was actually found with his head on the pillow. Tr. 267. She also agreed that J.B.’s crib was taken down shortly after his death, after which law enforcement and J.B.’s parents participated in a death scene reenactment. Tr. 267-68. That reenactment does not mention the pillow or any other elements that were in the crib. Tr. 268.

The undersigned asked Dr. McCusker about the “mechanical effect” of the sleep position she assumed that J.B. was found in. Tr. 269. Dr. McCusker stated that side-sleeping, a pillow under the head, “the lack of tight bed sheets,” and the “disarray” in the crib all together present “the same risk factors as prone” sleeping. Tr. 269-72. The undersigned commented that these facts were not completely clear from the record. Tr. 272.

iii. *Althen* Prong Three: Response to Petitioners’ Timing Argument

Dr. McCusker stated that she understood Dr. Miller’s testimony to be that “the upregulation of the serotonin through the TPH2 and 1433 system... would not be an instantaneous event and that it would take time and presumably more than 24 hours’ time.” Tr. 180. She stated that “the production of increasing cortisol that occurs following a stimulus and

upregulation through IL-6 is actually quite rapid, within hours, not days.” Tr. 181.⁹⁷ But she also stated that Kashiwagi et al. showed that a child will have elevated cytokine levels in the blood 24-48 hours after vaccination. Tr. 198.

3. Respondent’s Expert Dr. Brent Harris

Dr. Brent A. Harris earned a Masters in Biology from Hahnemann University in 1988. Exhibit A at 1. He then earned a M.D. and a Ph.D. in Pharmacology from Georgetown University in 1995. *Id.* He then obtained post-doctoral training at Stanford Medical School, where he was a resident in Anatomic Pathology from 1995-1999, chief resident from 1997-1998, and a neuropathology fellow from 1997-1999. *Id.* Dr. Harris is board certified in anatomic pathology and neuropathology and is a Fellow of the College of American Pathologists. *Id.* He is currently an Attending Pathologist, Associate Professor in Neurology and Pathology, and Director of Neuropathology at Georgetown University Medical Center. *Id.* He also serves as a Neuropathology Consultant for the Chief Medical Examiner, the National Institutes of Health, Howard University Hospital, the Washington, DC Veterans Administration Hospital, and the American International Pathology Laboratory. *Id.*

i. *Althen* Prong One: Response to Petitioners’ Theory

Dr. Harris agreed with the other experts that the Triple Risk Model is a generally accepted and reliable model of SIDS. Tr. 345. He could not say whether all extrinsic risk factors are mechanical or whether some of them may be neurochemical. *Id.* at 346. However, he testified that he would want to see conclusive proof before he would list vaccines as a risk factor in a medical report that he wrote. Tr. 348. He was aware of studies finding that vaccinations induce the production of cytokines in the brain, but not of any studies finding that those cytokines have a detrimental effect. Exhibit A at 6.

ii. *Althen* Prong Two: Response to Petitioners’ Opinion of a Logical Sequence of Cause and Effect

Dr. Harris agreed with the characterization of J.B.’s death as SIDS and that under the Triple Risk Model, J.B. was in the critical development period. Exhibit A at 6. It cannot be confirmed whether J.B. had a brain defect rendering him “vulnerable” because the autopsy did not sample that section of the brain. Exhibit A at 6.

Dr. Harris opined that if vaccinations are found to be an exogenous stressor, they “certainly cannot be proven in J.B.’s death.” Exhibit A at 6. He stated that there were “no pathologic findings in the brain or other organs in this case that indicate a vaccine-related death.” Exhibit A at 7; *see also* Tr. 328. J.B.’s brain was found to have metabolic glia, which are not fully understood. Exhibit A at 6-7. Dr. Harris also opined: Induction of cytokines after

⁹⁷ This may not be an accurate characterization of Dr. Miller’s opinion. A review of the transcript did not find a clear statement from Dr. Miller about the timing of cytokine production. But in his expert report, Dr. Miller actually opined that cytokine production would *begin* “within hours” and would *peak* “within 2 to at most 4 days.” *See* section above (citing Exhibit 16 at 1).

vaccination is a recognized physiological response involved in the immune process. The primary immune surveillance cells in the brain are microglia. These cells when activated by circulating molecules or direct invasion in the brain by organisms change their morphology and produce a host of cytokines in response. Over-activation of these cells in J.B.'s brain is a non-specific finding that could be related to the prior day's vaccination and/ or infection." Exhibit A at 6. Dr. Harris testified that the "circulating molecules" that activate microglia can be either lipopolysaccharides from bacteria or "circulating cytokines," although this is not completely understood. Tr. 342.

iii. *Althen* Prong Three: Response to Petitioners' Timing Argument

Dr. Harris agreed with Dr. McCusker's opinion that cytokine signaling "doesn't happen immediately but happens over a period of time." Tr. 343. He did not otherwise address the timing for the cytokine response or whether it fit the case of J.B.

III. ANALYSIS

A. Summary of the Arguments

The parties agree that the sole issue to be resolved is "whether the vaccines that J.B. received on September 2, 2011 caused or substantially contributed to his death." Joint Prehearing Submission at 2. Pursuant to *Althen*, petitioners must show by a preponderance of the evidence a reasonable theory as to how the vaccine could cause the harm at issue, a logical but not scientifically certain explanation of how it did, and show the timing was appropriate given the theory of causation. The Federal Circuit has observed that this preponderance standard enables "the finding of causation in a field bereft of complete and direct proof of how the vaccines affect the human body." *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1280 (Fed. Cir. 2005). The standard permits the use of "circumstantial evidence" and accomplishes Congress's goal that "close calls regarding causation are resolved in favor of injured claimants." *Id.* (citing *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed. Cir. 1994) ("to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program")).

To address the issue in the case, several questions must be addressed. The specific questions for decision are whether inflammatory cytokines generated by a mild infection are likely the critical exogenous stressor in many cases of SIDS when mild infection is also present. The second question is whether the same cytokines are stimulated by the innate immune response to vaccines and whether they are likely to be the exogenous stressor in some SIDS cases, particularly, as in this case, when the child was thoroughly examined by a physician the day before he died and found to be completely healthy, and there was no evidence of viral infection by nasal swab at autopsy.

Petitioners' theory is essentially that a high percentage of SIDS infants, almost 50% in most studies, have no history of a serious illness in the days and weeks prior to death, but have a mild infection or fever at the time of death. In most instances, the mild infection was an upper

respiratory infection, although one author listed post-vaccinal fever among the conditions.⁹⁸ In this case, J.B., a nearly five-month-old African American boy, who had been born at 36 weeks, died of unknown causes while napping in the early afternoon one day after receiving his scheduled four-month vaccines. He had a well-documented physical examination the prior day, performed by an M.D. pediatrician who had performed a similar examination about five weeks prior. J.B. was documented to be healthy, with no signs or symptoms of illness. He had patent nasal passages and clear lungs, and he was progressing well in terms of growth and milestones. His pediatrician noted that he was able to raise his head, hold it steady and roll over. In the 28-hour period following vaccination, at 4 a.m. and again at 8 a.m., his mother noticed that he had a mild fever and gave him children's Advil. He seemed to be fine and playing normally during the morning, but was fussy and started running a fever again in the early afternoon. Exhibit 8 at 2. His father then put him in his crib for a nap. He was put in the crib on his back, with a blanket over his midsection. He was using a pacifier. There was a small, flat, crib pillow in the bed. The air conditioning in the house was set at 76 degrees. His mother checked on him and replaced his pacifier during his nap. She came back about ten minutes later, noticed that he had rolled onto his side with his head tilted slightly downward, and he was not breathing. There is no evidence that his breathing passages were in any way obstructed or that his face was down in the bed or pillow when his mother found him. She called 911. Police and emergency medical personnel responded within minutes. J.B. was transported to the hospital when he could not be revived on scene. He was pronounced dead at the hospital.

Under the first leg of the Triple Risk Model, petitioners theorize that J.B. likely had a defective or under-developed serotonin system in the arcuate nucleus or other medullary area, which unfortunately was not examined or sectioned at autopsy. He was clearly within the vulnerable risk period for SIDS in that he was between four and five months old and, given his pre-maturity, only about four months based on dates of conception. He had several intrinsic risk factors in that he was born at 36 weeks, he was male and he was African American, all of which groups are overrepresented among SIDS deaths – blacks more than whites and Hispanics, boys more than girls, and preterm babies more than term babies. As noted above, at birth, J.B. had Apgar scores of 8 at one minute and 9 at five minutes. He had grown to 16 pounds and was well within the average ranges for height, weight and head circumference. He appeared to be meeting expected milestones as documented by his pediatrician. He was receiving good medical care and did not appear to be affected by issues associated with poverty, which is often speculated to account for the overrepresentation of African American babies in the SIDS statistics. He was a boy and it has been suggested, as noted above, that boys are more dependent than girls on an effective serotonin system for sensing the accumulation of carbon dioxide and responding appropriately to clear it.

Also, J.B. was put to bed on his back. At J.B.'s two last appointments, Dr. Wright noted that he slept on his back. The available evidence indicates that he rolled onto his side but was not prone. His mother described in the police reenactment that he had turned to his right side and his head was turned slightly downward. Nothing in the notes of the reenactment indicated that the baby's mouth or nose were in or close to the bedding, and in her police interview his mother noted that his nose and mouth were not covered. His father indicated that he had a fever when he was put down for his nap.

⁹⁸ Kadhim et al. (2010), Exhibit 13-O at 122.

Thus, petitioners theorize that he did have a fever during the night, early morning and before his nap. Dr. Miller testified that the fever documents the effect of inflammatory cytokines, likely IL-1 and/or IL-6 signaling from the periphery to the hypothalamus to cause the fever. They also theorize that the fever elevates body temperature, which is another risk factor for SIDS. According to petitioners' theory, because J.B. had no evidence of illness or infection prior to vaccination, it is therefore highly likely that the fever was generated by the vaccines, which likely caused a cascade of cytokines to cross the blood brain barrier and further suppress the function of the already underdeveloped medullary serotonin system during sleep. This caused his death to occur within about 28 hours of the administration of the four-month vaccines.

Respondent disagrees, saying that J.B. was premature, an African American boy, and was side sleeping, all of which are risk factors for SIDS. Citing the principle of Occam's Razor, he argues that it is unnecessary to consider anything beside these known risk factors and that the proximate timing to the administration of the vaccines can be explained by coincidence given that the peak time period of the occurrence of SIDS deaths coincides with the timing of the two month and four month vaccine administration schedules. He further argues that there has not been epidemiology to substantiate a causal relationship between vaccines and SIDS. Dr. McCusker argued that the role of mild infection in relation to SIDS deaths is one of obstructing airways rather than one of chemosensitivity, and she discussed her experience of suctioning the noses of infants brought into the emergency room with upper respiratory infections.

Dr. Miller and Dr. Harris agreed that an ideal autopsy would have sectioned the ventral medulla and that that was not done in this case. They also agreed that the type of histological examination that was done by Dr. Kinney and others would be unlikely to be done in a standard autopsy. Tr. 339. They agreed that there is not definitive proof of defective medullary structures.

B. *Althen Prong One*

After extensive review of the literature in the field of SIDS causation and listening to the testimony of the experts in this case, I think it is clear that the Triple Risk Model is broadly accepted as the general structure for understanding SIDS, even if the lack of comprehensive autopsies do not allow the medical profession to say that SIDS always has a deficient medullary serotonin system, as demonstrated in up to 75% of the cases examined by Dr. Kinney and her group.⁹⁹ She has said that "the most compelling hypothesis is that SIDS is related to a brainstem abnormality in the neuroregulation of cardiorespiratory control."¹⁰⁰ She further observed, "according to the Triple Risk Model, *only* infants with an underlying brainstem disease process die of SIDS, which explains why all infants who are placed prone to sleep or who bed share do not die of SIDS. They do not have the underlying vulnerability." *Id.* at 521. Dr. Miller opined that it is likely that J.B. had this defect based on the data from these studies. Tr. 37. Dr. McCusker agreed, "according to the triple-risk theory that the brain problem must exist." Tr. 206. The "brain problem" described in the triple-risk literature is that in the respiratory control center in the medulla. As such, it is reasonable to conclude that the petitioners have shown by a

⁹⁹ Kinney & Thach (2009), Exhibit A-4 at 6.

¹⁰⁰ Kinney et al. (2009), Exhibit 13-H at 519.

preponderance of the evidence that an infant who has died of unknown causes, and in whom autopsy has ruled out other causes, had the inherent brainstem vulnerability. I do conclude that J.B. did.

There is also no disagreement that the Back to Sleep Campaign convincingly demonstrated the danger of prone sleeping. By persuading parents to place babies on their backs to sleep during the vulnerable risk period, the campaign brought about an approximate 50% reduction in the rate of SIDS. Side-sleeping has also been recognized as having an elevated relative risk for SIDS, but the reason for this is not entirely clear. Dr. McCusker stated at some length her understanding of the mechanics of breathing in an infant. Essentially, she explained that the diaphragm drops down creating negative pressure within the lung relative to the atmosphere, at which point air rushes in. She suggested that the stomach muscles which the baby uses to help drop the diaphragm are compressed, as are the soft ribs in infants who are prone or side-sleeping, which reduces the gas exchange. Tr. 129-32. Dr. Miller disagreed with her explanation of respiratory physiology in that he did not find persuasive the notion that side-sleeping in a four-month-old is going to inhibit the ability to have inspiratory motion in the diaphragm, which creates the negative pressure in the lungs. Rather, he said the literature in SIDS has emphasized the pocket of air and re-inhaled carbon dioxide. Tr. 354.

The policy statement by the American Academy of Pediatrics, which was repeatedly referenced by Dr. McCusker but not marked as an exhibit, says that the risk of side-sleeping is similar in magnitude to prone sleeping (2.0 vs. 2.6).¹⁰¹ The statement appears to focus on the risk of turning if the infant is placed on his side. “The risk of SIDS is exceptionally high for infants who are placed on their sides and found on their stomach. The side sleep position is inherently unstable, and the probability of an infant rolling to the prone position from the side sleep position is significantly greater than rolling prone from the back.” *Id.* at 7. Interestingly, the same report addresses the issue of children who are able to roll over, which it notes generally occurs at 4-to-6 months of age, and that as they age it is more likely that they will roll. The Academy recommends, “If the infant can roll from supine to prone and from prone to supine, the infant can then be allowed to remain in the sleep position that he or she assumes.” *Id.* at 8.

In this case, J.B. was placed supine and he rolled to his side, but not prone. It would appear from this policy statement that the greatest concern with side sleeping is when the infant is placed on its side and can easily roll to the prone position. The fact that the Academy recommends allowing the baby to remain in the position to which he rolls after being placed supine suggests that it is likely that a baby who can roll probably also has developed the ability to raise and turn his head.

All of the experts in this case appeared to agree that at least the predominant thinking in medicine as to the cause of SIDS is explained by the Triple Risk Model. Although as Dr. Harris testified we do not know with certainty that the medullary serotonergic network deficiency is always present because a great many autopsies, such as the one in this case, are not adequate to

¹⁰¹ Moon R.Y. et al., American Academy of Pediatrics – Task Force on Sudden Infant Death Syndrome, *SIDS and Other Sleep Related Infant Deaths: Expansion of Recommendations for a Safe Infant Sleeping Environment*, 128 Pediatrics 1030 (2011), available at <http://pediatrics.aappublications.org/content/128/5/1030.long>.

document that deficiency, it was also recognized that as Dr. Kinney stated in a 2009 paper, “only infants with an underlying brainstem disease process die of SIDS.”¹⁰² Dr. McCusker agreed that according to the triple risk theory the brain problem must exist. Tr. 206. There has also not been significant debate about the statistical relevance of the other intrinsic risk factors. The success of the Back to Sleep Campaign in educating the public about the danger of prone sleeping has been remarkable in reducing SIDS deaths by half. But the other half still occur. The question remains as to what extrinsic risk factors come to play at that “fatal intersection of vulnerability, critical period and stressor.”¹⁰³ The literature strongly suggests that SIDS is likely to be multifactorial. Some cases are likely to be caused by continued prone sleeping, but others are likely caused by other factors. Mild infections, often described as “trivial” infections, appear to be a factor as they have been reported to be present in nearly 50% of SIDS deaths, raising the question of what it is about mild, otherwise non-life threatening infections that appear to interact with the impaired medullary serotonin system during the vulnerable period to cause the “perfect storm” that results in an unexplained death of a child?

Dr. Miller, relying on multiple pieces of research described in the SIDS literature, opined that it is likely that the cytokine signaling triggered in the immune system by mild infection interacts with the underdeveloped 5-HT system in the brainstem, during sleep when the excitatory function of serotonin is reduced, to further suppress the function of the brainstem to cause a cardio-respiratory crisis. The further issue raised is whether, in the absence of a mild infection, can the multiple vaccines administered together – in this case the day before – trigger the same cytokines as does a mild infection with the same fatal result? Dr. Miller concluded that they do.

Petitioners refer to the significant number of SIDS deaths that document the co-occurrence of mild or trivial infections which appear to stimulate a cytokine response similar to that generated by severe infections with adverse or repressive effects on the 5-HT system for chemosensitive response to hypercarbia, leading to failure to arouse and failure to initiate a gasping reflex and ultimately death. Petitioners are not the first to suggest this theory. Dr. Kinney has written, “A causal role for mild infection in sudden infant death is suggested by reports that in approximately half of SIDS cases, the infants have a seemingly trivial infection around the time of death, as well as mild tracheobronchial inflammation and altered serum immunoglobulin or cytokine levels and the presence of microbial isolates at autopsy. In infants who die unexpectedly of infection, the given organism may precipitate a *lethal cytokine cascade or toxic response*.”¹⁰⁴ Another article by her group explained the likely mechanism: “During infection, peripherally produced IL-6 may cross the blood brain barrier and bind to IL-6 receptors on 5-HT neurons that mediate homeostasis in response to the infectious stressor and potentially mediate sickness behavior. ... We found ubiquitous expression of IL-6 receptors and gp130 neurons in all regions in the infant medulla, including those effector nuclei critical to respiratory and autonomic control, and those that contain 5-HT source neurons. Serotonergic

¹⁰² Kinney et al. (2009), Exhibit 13-H at 521.

¹⁰³ Filiano & Kinney (1994), Exhibit 13-B at 197 [also filed as Exhibit A-2].

¹⁰⁴ Kinney & Thach (2009), Exhibit A-4 at 2 (emphasis added).

neurons in the caudal 5-HT system, including in the raphe obscurus and arcuate nucleus, express IL-6Rs on somata and processes, indicating the site of IL-6/5 HT interaction.”¹⁰⁵

Various authors have identified the presence of IL-1 β , IL-6, and IL-2, which are all pro-inflammatory cytokines, in elevated levels in the infant medulla in SIDS. Stoltenberg studied the effects of injection of IL-1 β in piglets, and theorizes that in addition to cytokines being transported to the brain by retrograde axonal transport, his findings suggested an equally important alternative route in the immune-stimulation of the brain, inducing hypoxia and sudden infant death. He said that it has been shown that IL-1 β is internalized by blood brain barrier endothelial cells, which implies that this cytokine passes through the blood brain barrier at the endothelial rather than the ependymal or blood cerebrospinal fluid part of the brain barrier. He found in his experiments with piglets that IL-1 stimulates the release of β -endorphin and the level of β -endorphin in CSF correlates strongly with the duration of apnea. Further, he found that “IL-1 β stimulates GABA-transmission and hence increases the inhibitory postsynaptic function by opening of chloride-delective channels, and this will reduce the activity in the central respiratory neurons and may produce hypoxia.”¹⁰⁶ Dr. McCusker referred to an article by Besedovsky for the proposition that cytokines are produced in the brain, suggesting that cytokines active in the brain necessarily originate in the brain. However, on review of the article, Besedovsky also noted that some cytokines such as IL-1 and IL-6 are produced both peripherally and within the brain.¹⁰⁷ He postulated that tripartite synapses possess the cellular and molecular components to function as a “relay system” capable of receiving and integrating peripheral immune signals with central neural signals. *Id.* at 5.

One of the best understood functions of cytokines in the case of infection and vaccination is the triggering of fever. When this occurs, cytokines from the periphery at the site of the infection travel to the brain, in particular to the hypothalamus, which then causes fever. As J.B. had a fever in the day following vaccination after having a completely clear medical examination the day before, Dr. McCusker agreed with Dr. Miller that in order for fever to have occurred there had to be a hypothalamic signal, which is mediated by endogenous pyrogens, i.e. IL-6 or TNF α . Tr. 286. The literature also recognizes IL-1 and others which are known pyrogens as well. She also agreed that in the absence of an infection, the only thing we can attribute the fever to is the vaccine. Tr. 205.

After identifying a plausible mechanism for the means of activation of cytokines in the medullary brainstem from a peripheral source, the next key question is why does mild or trivial infection appear to occur in conjunction with SIDS? It is not the infection itself which causes death, as by its mild nature it is not life threatening. Whether the infection is mild or severe, it triggers the innate immune response, which in turn triggers the release of cytokines. As Dr. McCusker explained, cytokines are small molecules that are released by different cell types originally described in immune cells. They are viewed primarily as communication molecules,

¹⁰⁵ Kinney et al. (2011), Exhibit 13-F at 191.

¹⁰⁶ Stoltenberg et al. (1994), Exhibit 13-J at 427.

¹⁰⁷ Besedovsky, H.O. and A. del Ray, *Central and Peripheral Cytokines Mediate Immune-Brain Connectivity*, 36 *Neurochem Res.* 1 (2011), Exhibit C-3 at 1.

because they are released by one cell and bind to another through a series of signaling steps. Tr. 145. Dr. Miller explained that cytokines are messenger molecules that have a lot of different effects which were first identified as products of the innate immune system, but are seen elsewhere as well, including the brain. IL-6 binds with 5-HT and IL-1 has been shown in animals to inhibit 5-HT firing. Tr. 30. There was no disagreement between the experts or in the literature that cytokines are released by the innate immune response to infection, whether it be mild or severe.

The Siljehav-Hofstetter article filed by respondent provides an additional theoretical basis for the role of cytokines in SIDS. The authors found that IL-1 β stimulates a prostaglandin (PGE2) with receptors in the rostral ventrolateral medulla. They explained that once stimulated by IL-1 β , PGE2 induced depression of this vital brainstem neuronal network, e.g., during an infectious response, that could result in gasping and autoresuscitation failure and ultimately death.”¹⁰⁸

Dr. Miller found further support in the work of Kadhim, who found overexpression of IL-1 β in the arcuate nuclei in 17 of 17 SIDS brains studied, but only in 1 of 6 non-SIDS brains.¹⁰⁹ Kadhim noted that cytokines could exert neuromodulatory effects in the ascending reticular activating system, which is involved in the arousal reflex. He noted that IL-1 causes prolonged apneas and depresses respiration and the brain appears to be less effective than the periphery in inducing IL-1 antagonist to terminate IL-1 β actions. He hypothesized that the particular pattern of neuronal cytokine he detected might therefore overturn a subtle equilibrium in a molecular chain involving vital brain centers, causing SIDS. *Id.* at 1259.

In a second study involving SIDS brains, Kadhim’s group noted that SIDS victims often have preceding mild infections and that cytokines have neuromodulatory effects whereby they can modify neurotransmission. In this study, they compared the brainstems of SIDS victims to those of infants who died of diverse severe pathological conditions, mainly infectious, hemodynamic, metabolic, severe congenital, or other serious conditions. They found that IL-2, another inflammatory cytokine, was preferentially expressed in specific neuronal centers within the brainstem. In this study, they found equally intense immune reactivity within the arcuate and dorsal vagal nuclei in fatally sick infants, as with SIDS victims who had no obvious or detectable serious health condition before death. They hypothesized that a hyperimmune response to mild infection in the SIDS babies may result in a molecular disequilibrium which tips the delicate molecular balance, causing dysfunction in those vital brainstem centers and producing disturbed homeostasis with potentially drastic effects on target organs/systems and eventual death.¹¹⁰

¹⁰⁸ Siljehav (2012), Exhibit C-9 at 9897.

¹⁰⁹ Kadhim et al. (2003), Exhibit 13-L at 1256.

¹¹⁰ Kadhim et al. (2010), Exhibit 13-O at 122-26.

Brambilla also provided some support for this theory by demonstrating in animals that IL-1 inhibited firing of neurons that promoted wakefulness in the dorsal raphe nucleus and enhanced activity of GABAergic neurons which are inhibitory and induce enhancement of NREM sleep.¹¹¹

Rognum further compared brains of SIDS victims to those of babies who died of severe infections and to another group who died from drowning, suffocation, strangulation, or other violent causes. They found that the SIDS babies had higher cytokines in the medullary brainstem than did those who died of violent causes but their levels were not as high as those that died of infectious causes. In a small section of their study, the Rognum group found elevations of IL-6R in the arcuate nucleus in the SIDS and infection groups relative to the controls. However, they found that the gp130, which is necessary for IL-6 to function, did not rise as high above the controls as did the infection group, although it was higher than in those dying violent deaths. This caused them to speculate that the IL-6R might be reactive to an excess carbon dioxide crisis rather than its cause. Thus significant evidence has been produced to show that cytokines are abundantly present in the medullary brainstem of SIDS infants relative to those dying of other causes which strongly suggests a hyperimmune response to mild infection in these children well out of proportion to the mild or trivial infection that they had. The presence of these cytokines also appears likely to suppress the 5-HT response to the accumulate of carbon dioxide in the body and the ultimate failure of the respiratory response system.

The next important question is whether the vaccines can play the same cytokine generating role as mild infection in a child who does not have an infection. If, as his father described, the child developed symptoms such as a fever, crankiness and not being himself, signs of cytokine activation, and had no evidence of infection, could one or more of the seven vaccines he received the day before have generated a cytokine cascade that caused him to be unable to respond to elevated carbon dioxide in his system, whether it was produced by rebreathing or metabolically? Dr. Miller's thesis was that the main role for mild inflammation as a risk factor for SIDS is thought to be in elevating cytokines. He said that is explicit in multiple articles that have been submitted. Then, if vaccines produce the same cytokine responses as very mild upper respiratory infections, which is what is demonstrated by Kashiwagi, it would seem logical to impute both having the same effect on the central nervous system. Tr. 370.

Indeed, Kashiwagi conducted testing with multiple vaccines and studied the cytokine response. He found that there was a more significant response in children who received three or four vaccines at one time than in those who received fewer, and he found that higher IL-1 β production was noted in young infants, but decreased at around 2 years or older.¹¹²

He also examined the cytokine profiles in 61 serum samples obtained from recipients who exhibited febrile illness within 24 hours of being vaccinated and 18 serum samples from recipients without febrile illness. The samples were taken within 48 hours of vaccination in both groups. These were compared to each other and to cytokine profiles of ten normal subjects

¹¹¹ Kinney et al. (2009), Exhibit 13-H.

¹¹² Kashiwagi et al. (2014), Exhibit 17 at 680.

without vaccination. “Higher levels of IL-6, IL-10, IL-12, G-CSF,¹¹³ and IFN- α were detected in both the febrile and non-febrile vaccination subjects in comparison with those in normal subjects.” *Id.* at 680.

The Lee and Schulzke studies of multiple vaccine administration to premature infants, referenced above, found an elevation in the rate of apnea, bradycardia, and, in the Lee study, oxygen desaturations (Schulzke did not look at desaturations). Both authors hypothesized that the adverse events may be related to the immune response to the vaccines, particularly as Lee found there was no difference in the rate of adverse events between whole cell pertussis and acellular pertussis.¹¹⁴ Schulzke noted that the adverse events occurred within 6 to 24 hours of vaccination.¹¹⁵ While not studying SIDS, these studies focused on premature infants in a controlled environment – a hospital – where the mechanism that is hypothesized to occur in SIDS could be rapidly recognized, addressed, and treated. It seems quite likely that the same sequence occurring post-administration of multiple vaccines may be what occurs in the uncontrolled environment of the home when the child and often the parents are sleeping, or at least not in the same room with the child when the combination of events leading to the fatal sequence occurs.

Dr. Miller’s theory, consistent with many of the articles in the literature, is that SIDS is multifactorial. Multiple factors come together at the fatal moment that causes the perfect storm leading to death. He theorizes that the cytokines triggered by the vaccines in the initial innate immune response to the vaccines travel to their receptors in the arcuate nucleus and suppress the serotonin function in a child whose functionality in that area is already impaired by an underdeveloped or defective 5-HT system while he is asleep, which further reduces 5-HT function. The input of the cytokines stimulated by the vaccines causes the lack of response to elevation of carbon dioxide that converts a recoverable event to a fatal one. Whether the vaccine generated cytokines cause additional metabolic activity generating fever and additional production of carbon dioxide, or whether they caused the neurons in the brainstem to be unable to respond to rebreathed or accumulated carbon dioxide, it is probable that they played an important role in causing the death of this infant.

Dr. McCusker disagreed. She argued that the presence of the various intrinsic risk factors together with a flat pillow in the bed and side-sleeping to which the child turned after being placed supine was sufficient to explain the death. She argued that the role of mild infection was that it caused obstruction in the nasal passages in infants who are “obligate nose breathers” (Tr. 138) and mucous in the nose would obstruct the breathing of the child sufficient to cause death. She referred to infants she sees in the emergency room with upper respiratory tract infections who need to be suctioned which then brings down their carbon dioxide level. Tr. 139-40. Dr. Miller disagreed. He stated that he had never seen a SIDS autopsy where the death was

¹¹³ G-CSF is an abbreviation for granulocyte colony stimulating factor. It is another cytokine which mobilizes and recruits neutrophils to the site of inflammation from the marginal pool. Kashiwagi et al. (2014), Exhibit 17 at 693.

¹¹⁴ Lee, J. et al., *Frequency of Apnea, Bradycardia, and Desaturations Following First Diphtheria-Tetanus-Pertussis-Inactivated Polio-Haemophilus Influenzae Type B Immunization in Hospitalized Preterm Infants*, 6 *BMC Pediatr.* 20 (2006), Exhibit 20.

¹¹⁵ Schulzke (2005), Exhibit 21 at 3.

attributed to nasal passage obstruction by mucous and that he had never seen any literature to support that concept. Tr. 355.

The literature certainly suggests that Dr. McCusker's interpretation of the role of mild infection was too limited in that she ignored the entire concept of brainstem chemosensitivity in response to carbon dioxide accumulation. Dr. Kinney wrote, "Serotonergic neurons at the medullary ventral surface and in the midline (raphe) are now known to be preferentially chemosensitive to CO₂ and although they are not the only central chemosensitive neurons they appear to play a critical potentially modulatory role. ... A small but important population of 5 HTE neurons is embedded within the human arcuate nucleus suggesting that the putative dysfunction in chemosensitivity related to the arcuate anomaly specifically involved these embedded 5 HT neurons."¹¹⁶ In an article in the *New England Journal of Medicine*, Kinney wrote, "the arousal from sleep that is triggered by abnormal levels of carbon dioxide and oxygen is essential for the initiation of protective airway responses. ... Arousal involves a progressive activation of specific subcortical to cortical brain structures and consists of ascending and descending components that mediate cortical and subcortical arousal respectively."¹¹⁷ The importance of the chemosensitive role in the stimulation of breathing, arousal, and ultimately gasping in response to the accumulation of excess carbon dioxide appears critical to all of the triple risk hypotheses. A stuffy nose does not explain the inability of the neurons in the arcuate nucleus to modulate breathing rhythm and respond to excess carbon dioxide by initiating breathing, particularly when there was no evidence of mucous congestion in the nose the day before at the medical exam, in the report of the parents, or at the autopsy. The role of cytokines stimulated by vaccines administered approximately 28 hours before seems much more likely to play a critical role, similar to that of mild infection in causing the ultimate convergence of the multiple factors leading to death. The inhibition of the 5-HT response, beyond its initially impaired level with which the child had lived to that date, seems more likely to be caused by the cytokine response to the multiple vaccines than to a stuffy nose or the side-sleeping position to which he had turned, particularly when there was no evidence of nasal congestion or of the breathing passages being obstructed. Exhibit 7 at 5. In fact the evidence was to the contrary.

Dr. McCusker, citing to the Imeri article¹¹⁸ on sleep in general, also testified that fever would tend to push the child out of REM sleep and into NREM, which she argued would make him more arousable. A review of the Imeri article, which discusses the immune system and sleep in general, and not specifically in infants, does indeed discuss the role of fever and the generation of shivering in NREM sleep and that during the course of most infections there is an increase in the amount of time spent in NREM sleep and a decrease in the amount of REM sleep. *Id.* However, it also discusses the role of IL-1 and the generation of GABAergic inhibitory cytokines. *Id.* at 205. Imeri also acknowledged the role of peripherally generated cytokines in the regulation of sleep. Imeri concluded that at present we know little about these mechanisms

¹¹⁶ Kinney et al. (2009), Exhibit 13-H at 522.

¹¹⁷ Kinney & Thach (2009), Exhibit A-4 at 5.

¹¹⁸ Imeri L. & M.R. Opp, *How (and Why) the Immune System Makes Us Sleep*, 10 *Nat. Rev. Neurosci.* 199 (2009), Exhibit C-6 at 201.

by which cytokines inhibit REM sleep and argued that it is important because REM sleep is disrupted in many pathologies that involve altered cytokine concentrations. *Id.*

Dr. Miller hypothesized two roles for fever – overheating and travel of cytokines to the brain in the mechanism of SIDS. Dr. McCusker agreed with cytokine signaling as relevant to the production of fever but disagreed that fever was the equivalent of hyperthermia in the SIDS literature. On the witness stand she drew a sharp distinction between environmental hyperthermia and overheating secondary to fever, which she called hyperpyrexia. The literature was unclear on this point. But the significant importance of fever to this case was in demonstrating the travel of peripheral cytokines stimulated by the vaccines across the blood brain barrier to the hypothalamus. Fever is the most obvious manifestation of the signaling of cytokines from the peripheral location of the vaccinations to the brain. The SIDS literature suggests that production of inflammatory cytokines IL-6, IL-10, IL-12, and IFN γ in response to DPT, Hib, and PCV7 were detected in both febrile and non-febrile groups, with febrile illness appearing 12-16 hours post vaccination.¹¹⁹ NREM sleep is also implicated in SIDS. A distinctive feature of 5-HT neurons is that they exhibit differential firing rates according to the level of arousal, with increased firing during waking, decreased firing during NREM, and almost complete absence of firing during REM. Given the relationship of the firing of raphe 5-HT neurons to arousal, the medullary 5-HT system is postulated to modulate and integrate homeostatic function according to the level of arousal.¹²⁰ Thus, particularly in the deeper levels of NREM sleep, the 5-HT system is also functioning at lower levels, potentially contributing to the multi-factorial causal picture.

After review of all of the above, I have concluded that petitioners have presented a reasonable and reliable theory of vaccine causation involving the role of inflammatory cytokines acting as an extrinsic stressor in a baby with a brainstem deficit during the vulnerable time period. It is particularly important to note that the literature indicates that SIDS is likely caused by a multi-factorial process. Dr. Kinney wrote in the *New England Journal of Medicine* in 2009, “Current evidence suggests that SIDS involves a convergence of stressors that probably results in the asphyxia of a vulnerable infant who has defective cardiorespiratory or arousal defense systems during a critical developmental period when immature defense mechanisms are not fully integrated. Thus our current understanding of the pathogenesis of SIDS reflects the simultaneous juxtaposition of multiple events that, when taken individually, are far less powerful than the result of their chance combination.”¹²¹ In another 2009 article she wrote; “We now conceptualize SIDS as the biologic version of the perfect storm, in which the simultaneous and chance combination of multiple events is far more powerful than any individual event alone.”¹²²

¹¹⁹ Kashiwagi et al. (2014), Exhibit 17 at 680.

¹²⁰ Kinney, H.C., *Brainstem Mechanisms Underlying the Sudden Infant Death Syndrome: Evidence from Human Pathologic Studies*, 51 *Dev. Psychobiol.* 223 (2009), Exhibit 13-E at 226.

¹²¹ Kinney & Thach (2009), Exhibit A-4 at 7.

¹²² Kinney et al. (2009), Exhibit 13-H at 539.

I have concluded that the petitioners have demonstrated by a preponderance of the evidence that the vaccines can and likely did play a critical role in this child's death by stimulating the production of inflammatory cytokines that suppressed the respiratory response system and caused the vulnerable infant to be unable to respond in the normal way to the accumulation of carbon dioxide in his system. Accordingly, petitioners have satisfied the requirement of *Althen* Prong One by presenting a reasonable explanation of how the vaccine could cause or substantially contribute to the child's death.

C. *Althen* Prong Two

Althen Prong Two requires the demonstration of a logical cause and effect as to how the vaccine caused the harm, in this case the sudden unexplained death of J.B. Under *Althen* Prong Two, petitioners must prove that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278).

Dr. Miller testified that it was his diagnosis that J.B. died of SIDS and that the vaccines were a substantial contributing factor to his death. Tr. 126. Having accepted the theory of a causal role of vaccine stimulated cytokines as an exogenous factor converging with the first two prongs of the Triple Risk Model, the question of logical cause and effect requires a review of the likely mechanism and comparing it to the operative facts of the case. Kashiwagi in particular found that cytokines began to be produced 6 hours after stimulation and increased until 24 hours, showing the same level thereafter. Higher levels of IL-1B, IL-6, G-CSF, and TNF α were produced in that study by the concurrent stimulation of three vaccines than by one alone.¹²³ J.B. received seven vaccines at his 4 to 5 month well baby visit with his pediatrician on September 2, 2011. He was carefully examined and documented to be in entirely good health the day before. Overnight, he developed a mild fever, consistent with cytokine signaling from the vaccination site to the brain. In the early afternoon of September 3, he died during his nap.

Dr. Miller discussed the logical sequence of cause and effect explaining how he believed the vaccines acted as an exogenous stressor which caused J.B. to succumb to SIDS. He noted that J.B. was a "healthy infant... developing normally." Exhibit 13 at 4. He was "immunologically normal." Tr. 61. Therefore, after receiving vaccinations, his body mounted an innate immune response including the production of cytokines. Exhibit 13 at 6; Exhibit 16 at 1; Tr. 62. Those cytokines circulated in J.B.'s body, going to the central nervous system. Exhibit 13 at 6; Tr. 62. These peripheral cytokines interacted with the hypothalamus to provoke fever the night after the vaccinations and during the following day (before J.B.'s death). Exhibit 13 at 6; Exhibit 16 at 1; Tr. 62-64. "Those cytokines then acted in the brainstem which was already deficient in serotonergic drive for respiratory effort, leading to an apneic episode from which he did not recover, i.e., SIDS." Exhibit 13 at 6; *see also* Tr. 62 (the cytokines "depress[ed] the] 5-HT system in a defective medulla, leading to SIDS during sleep").

¹²³ Exhibit 17 at 679.

He opined that there was “no other demonstrable inciting event” for J.B.’s death. Exhibit 13 at 1. There was no evidence of the fever being related to anything other than J.B.’s vaccinations. Tr. 66. The autopsy did not identify any other infectious processes. Tr. 66.¹²⁴

On cross-examination, Dr. Miller stated that J.B. was placed on his back but was found on his side, which demonstrates that he was able to “move around.” Tr. 92. However, J.B. did not pass away until “something else intervened.” Tr. 85. Based on his theory and the temporal association, Dr. Miller opined that the vaccines were the intervening factor that caused J.B.’s death. Tr. 85.

An innate immune response to either mild infection or to a vaccine is likely to be fast and begins the process of immune attack of a foreign antigen. Part of that response is the triggering of cytokines to signal further response in the immune system. The triggering of the innate immune system by vaccination is necessary and fundamental to producing the adaptive response and immune memory which vaccines are designed to produce. After review and consideration of all of the testimony and the literature submitted, I have concluded that Dr. Miller has presented a reasonable and persuasive theory that the cytokine cascade triggered by the innate response to the vaccine antigens is similar to the cytokine response to a mild infection, and that the inflammatory cytokines had an immune modulatory effect on J.B.’s impaired medullary 5-HT system causing a prolonged apneic event resulting in his death. As such, the progression from vaccination to an unexplained death within approximately 28 hours is logical.

This logical progression is also consistent with reports of at least mildly elevated SIDS deaths in some studies such as Traversa, which found a 2.0 relationship in the first 7 days.¹²⁵ Goldman reported a statistically significant increase in deaths when 5 to 8 vaccines were administered simultaneously as opposed to 1 to 4.¹²⁶ Ottaviani¹²⁷ and Zinka¹²⁸ reported on SIDS deaths within 48 hours of receiving vaccinations. Other studies, such as Kuhnert¹²⁹, found neither a protective effect nor elevated risk, but Kuhnert noted that the small number of cases is a problem with the three case control studies he reviewed, particularly in view of the short time periods under investigation. According to Kuhnert, this problem was illustrated by the very broad confidence intervals of estimates that were related to the first few days. *Id.* at 2355.

¹²⁴ Dr. Miller noted that there were bacterial growth and food particles in J.B.’s lungs and epithelial cells in the upper airways. He opined that this was not evidence of a separate infectious process. He agreed with the medical examiner that these were terminal or resuscitative sequelae. Tr. 17-18; 66; 352-53.

¹²⁵ Traversa et al. (2011), Exhibit 13-U at 8.

¹²⁶ Goldman & Miller (2012), Exhibit 19 at 1016.

¹²⁷ Ottaviani et al. (2006), Exhibit 13-T.

¹²⁸ Zinka et al. (2006), Exhibit 13-S.

¹²⁹ Kuhnert et al. (2012), Exhibit C-20.

The statistical prevalence of boys, African Americans and premature babies among the victims of SIDS also seems to be clear and causes their inclusion as intrinsic risk factors. I think it is reasonable to question in this case whether the influence of prematurity would still be a likely factor, given that he had nearly reached the age of five months and appeared to be developing very well. It is also reasonable to question whether the statistical prevalence of African Americans should be a significant factor, as it is often speculated that this may be a function of socioeconomic status and poor medical care. This child appeared to have been living in a two-parent household, with attentive parents, was well-nourished, and was receiving good medical care. The role of his male gender may well have been important, as Dr. Kinney has reported a greater reduction in 5-HT-1A in the medullary raphe in males compared to females dying of SIDS.¹³⁰

Given that Dr. Miller's thesis and that of much of the literature for the Triple Risk Model is that SIDS results from the convergence of multiple factors, it seems likely that his male gender may well have been a contributing intrinsic factor that may have amplified the effect of the cytokine response to the vaccines on the day that he died. But, his gender, his race, and his prematurity – all intrinsic factors – do not explain his death without the interaction with a critical extrinsic factor, which I have concluded was likely the cytokines triggered by the vaccines which depressed his 5-HT system sufficiently that he did not respond when carbon dioxide became elevated in his system.

The evidence for J.B.'s death occurring as a result of his having turned to his side without a causal input from another significant extrinsic factor such as the vaccine stimulated cytokines suppressing his response system is weak in this case. As noted above, the Academy of Pediatrics recommends leaving a child in the assumed position when he has rolled from his back presumably because it is also likely that he can push up and lift his head by the time he can roll. This capability was documented in J.B.'s case by his pediatrician. Although there was a flat pillow and a light blanket in the bed, J.B.'s mother told the police investigators that his head was not covered and that his head was turned downward only slightly. The scene investigation noted her report that J.B.'s mouth and nose were not covered. Exhibit 7 at 5. It was described that he had been put to sleep in the middle of the bed. Thus, there is no evidence in this case that the baby's breathing passages were obstructed or that he was breathing into an air pocket. The possibility of rebreathing carbon dioxide in that position cannot be ruled out, but seems less likely based upon this evidence derived from the extensive interviews and the site re-enactment performed by the responding police. Thus, even if the side- sleeping position did cause some rebreathing of carbon dioxide, I have concluded from the evidence that it is most likely that the cytokines stimulated by the vaccines caused suppression of the already impaired medullary serotonin system with the consequent failure to chemically sense elevated carbon dioxide, which caused the ultimate failure to arouse and to breathe normally thus substantially contributing to the death of J.B.

The emphasis of the Triple Risk Model on prone sleeping has had a powerful impact in reducing SIDS deaths by approximately 50%. But there remains a significant number of SIDS deaths each year, some of which are likely related to continued prone-sleeping and some to side-sleeping. But the co-occurrence of mild infection in the statistics in nearly 50% of cases raises a

¹³⁰ Kinney et al. (2009), Exhibit 13-H at 532.

significant issue about the operative extrinsic risk factor or factors in the remaining cases, including many that are found supine. In this case, an apparently perfectly healthy child was found dead a day after vaccination, having had a mild fever in the interim without evidence of infection. He was not prone sleeping but had turned to his side, with no evidence that his breathing passages were in any way impaired. Significant literature introduced demonstrates that the triggering of inflammatory cytokines in response to vaccines is similar to that raised in response to mild infection. J.B.'s post-vaccinal fever provided confirmation of responsive cytokine activity. The cause and effect between the vaccines, the cytokines triggered by the vaccines, and their co-occurrence with other intrinsic and/or extrinsic risk factors in the presence of a defective or underdeveloped brainstem seems likely to have produced the perfect storm that resulted in J.B.'s death. Thus, I am persuaded that petitioners have proved prong two.

D. *Althen* Prong Three

Under *Althen* prong three, petitioners must provide “preponderant proof that the onset of symptoms occurred within a timeframe for which, given the understanding of the disorder’s etiology, it is medically acceptable to infer causation-in-fact.” *De Bazan*, 539 F.3d at 1352. The acceptable temporal association will vary according to the particular medical theory advanced in the case. See *Pafford*, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., *Veryzer v. Sec’y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that “a temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting the vaccine and injury”).

Dr. Miller stated that the available evidence is that foreign antigens, like those contained in vaccinations, activate the production of cytokines “within hours” and that production “peaks within 2 to at most 4 days.” Exhibit 16 at 1. Thus, a vulnerable infant who receives vaccinations is most likely to suffer a fatal event if one is to occur “within the first 48 hours to at most 4 days.” Exhibit 13 at 5. Dr. Miller opined that J.B.’s death was “well within this vulnerable period.” *Id.*

In this case, the timing of the innate immune response to the multiple scheduled vaccinations that J.B. received on September 2, to his death the following afternoon appears entirely appropriate for an innate immune response in the vulnerable risk period for SIDS. It is also consistent with reports of at least mildly elevated SIDS deaths in some studies and reports of deaths that occur within the first several days after the vaccination. In this case, one day post-vaccination is appropriate timing, in that inflammatory cytokines stimulated during the innate immune response to the vaccine antigens are likely to be active in close proximity to the stimulating event. As Dr. Miller stated, an adverse event that can be caused by the inflammatory cytokine response to vaccine antigens would be likely to occur within a few days of the vaccination. The cytokine response has been shown by Kashiwagi¹³¹ to occur within 6 to 24 hours of the vaccination, and the very essence of the innate immune response is one that occurs rapidly after the invasion by a foreign antigen. As noted above, that rapid innate immune response is necessary to initiate the ultimate adaptive immune response necessary to achieve the

¹³¹ Kashiwagi et al. (2014), Exhibit 17 at 679.

design purpose of vaccination. The close temporal relationship of the child's death to the receipt of seven vaccines is reasonable and consistent with the theory of neuro-modulation in the arcuate nucleus by the cytokine response to the vaccines. Accordingly, I am persuaded that prong three of *Althen* has been satisfied.

IV. CONCLUSION

In this case, I have concluded that petitioners have presented sufficient evidence and testimony to entitle them to compensation in the Vaccine Program. I have not concluded that vaccines present a substantial risk of SIDS. In fact, the evidence is to the contrary. The vast majority of vaccine recipients do not succumb to SIDS. Under the multi-factorial analysis of the Triple Risk Model, it is theorized that the ultimate fatal event may occur when multiple factors converge during this vulnerable period to cause death when one stressor acting alone may not have. As Dr. Kinney wrote, "Current evidence suggests that SIDS involves a convergence of stressors that probably results in the asphyxia of a vulnerable infant who has defective cardiorespiratory or arousal defense systems during a critical developmental period when immature defense mechanisms are not fully integrated. The convergence of these factors appears to be far more powerful than any one taken individually."¹³² Thus, even if J.B. were rebreathing some carbon dioxide on this occasion, it was likely the combination with the cytokines that caused depression of the 5-HT system that caused his death by blunting the normal chemosensitive response to excess carbon dioxide. The multi-factorial analysis, including vaccines as an extrinsic risk factor, meets the *Shyface* standard that the vaccine need not be the sole or even predominant factor but must be a "but for cause" and a substantial factor in causing the death. *Shyface*, 165 F.3d at 1352. In this case, I have concluded, after review of the evidence, that it is more likely than not that the vaccines played a substantial causal role in the death of J.B. without the effect of which he would not have died. The role of inflammatory cytokines as neuro-modulators in the infant medulla has been well described and is likely the reason for a significant number of SIDS deaths occurring in conjunction with mild infection. I have concluded that it is more likely than not that the vaccine-stimulated cytokines had the same effect in this vulnerable infant during sleep.

Accordingly, petitioners are entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/ Thomas L. Gowen
Thomas L. Gowen
Special Master

¹³² Kinney et al. (2009), Exhibit 13-H at 539.



IL-4 mediates the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination that involves the down-regulation of the IL-4 receptor in the hippocampus

Xiao Wang¹, Junhua Yang¹, Zhiwei Xing, Hongyang Zhang, Yaru Wen, Fangfang Qi, Zejie Zuo, Jie Xu, Zhibin Yao*

Department of Anatomy and Neurobiology, Zhongshan School of Medicine, Sun Yat-sen University, PR China

Guangdong Province Key Laboratory of Brain Function and Disease, Zhongshan School of Medicine, Sun Yat-sen University, PR China

ARTICLE INFO

Keywords:

Neonatal period
Hepatitis B vaccine
Interleukin (IL)-4
Cytokine
Hippocampus

ABSTRACT

We have previously verified that neonatal hepatitis B vaccination induced hippocampal neuroinflammation and behavior impairments in mice. However, the exact mechanism of these effects remain unclear. In this study, we observed that neonatal hepatitis B vaccination induced an anti-inflammatory cytokine response lasting for 4–5 weeks in both the serum and the hippocampus, primarily indicated by elevated IL-4 levels. Three weeks after the vaccination schedule, however, hepatitis B vaccine (HBV)-mice showed delayed hippocampal neuroinflammation. In periphery, IL-4 is the major cytokine induced by this vaccine. Correlation analyses showed a positive relationship in the IL-4 levels between serum and hippocampus in HBV-mice. Thus, we investigated whether neonatal over-exposure to systemic IL-4 influences brain and behavior. We observed that mice injected intraperitoneally with recombinant mouse IL-4 (mIL-4) during early life had similar neuroinflammation and cognition impairment similar to those induced by neonatal hepatitis B vaccination. Next, the mechanism underlying the effects of IL-4 on brain in mice was explored using a series of experiments. In brief, these experiments showed that IL-4 mediates the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination, which involves the permeability of neonatal blood–brain barrier and the down-regulation of IL-4 receptor. This finding suggests that clinical events concerning neonatal IL-4 over-exposure, including neonatal hepatitis B vaccination and allergic asthma in human infants, may have adverse implications for brain development and cognition.

1. Introduction

Hepatitis B vaccination, recommended for newborns to prevent hepatitis B virus infection and associated liver diseases globally [1], is administered to infants and children. This period is critical for brain development, and immune activation during the critical period can significantly alter brain development programming [2–4], which results in a long-lasting impact on the brain development and behavior [5]. Several studies have reported that early postnatal immune activation increased anxiety or vulnerability to later life cognition impairment in animal models [6–8].

Therefore, neonatal hepatitis B vaccination, which induces strong immune activation during the critical period of brain development, may be a risk factor for certain disorders of neuropsychological development. In fact, there has been a controversy about whether neonatal

hepatitis B vaccination is associated with the occurrence of autism, multiple sclerosis and myelitis, with some reports argue for [9–11] and other reports argue against [12] this potential association. Moreover, the routine childhood vaccines have been worried by some parents to be associated with adverse neurological outcomes, specifically autism spectrum disorder [13]. Furthermore, our recent study revealed that neonatal hepatitis B vaccination led to impairments in mood- and cognition-related behaviors, neurogenesis and hippocampal long-term potentiation in mice [14].

We have given an initial explanation that the neonatal hepatitis B vaccination induced neurobehavioral impairments through a T helper (Th)-2 bias of systemic cytokines. However, the exact mechanism or pathway by which the systemic Th-2 bias influences the central nervous system (CNS) is still not clear. In our previous study, the peripheral Th-2 bias induced by HBV was assessed by the ratio value of IFN- γ /IL-4 in

* Corresponding author at: #74, Zhongshan No. 2 Road, Guangzhou 510080, PR China.

E-mail address: yao.zb@163.com (Z. Yao).

¹ These authors contributed equally to the work and should be regarded as co-first authors.

serum [14]. However, it was the alteration of the IL-4 level that contributed to the Th-2 bias without any significant alteration in the serum IFN- γ level [14]. Other studies concerning the immune responses to this HBsAg/alum vaccine, which was used by our previous work, also demonstrated that IL-4 is the major cytokine induced by this vaccine [15,16]. Hence, IL-4 may play a key role in the HBV-induced neuro-behavioral influences.

There is a homeostasis between anti-inflammation and proinflammation in mice with normal development involving a series of anti-inflammatory and proinflammatory cytokines. Many of these anti-inflammatory and proinflammatory cytokines have important roles in neural development and function [17]. Any factor that disturbs this homeostasis may cause brain developmental and functional abnormalities [17]. IL-4 itself is a powerful anti-inflammatory cytokine that induces the anti-inflammatory response and inhibits the production of proinflammatory cytokines [18]. Thus, high levels of IL-4 exposure during the critical stages of brain development are likely to break the physiological anti-inflammatory/proinflammatory profile of the brain, altering brain developmental programming.

Our current study investigated the potential role of IL-4 induced by neonatal hepatitis B vaccination in affecting brain development and cognition and its possible mechanism.

2. Materials and methods

2.1. Animals and breeding

Litters of newborn C57BL/6 mice were purchased from the Laboratory Animal Center of Sun Yat-sen University (Guangzhou, China). They were housed in a specific pathogen-free conditions under 12-h light:12-h dark conditions with food and water available *ad libitum*. Male neonatal mice were used. This study was approved by the Institutional Animal Ethics Committee of Sun Yat-sen University.

2.2. Immunization procedures

Experiments in this study utilized one of the following two injection approaches: hepatitis B vaccine immunization and recombinant mouse IL-4 (mIL-4) injection. In the hepatitis B vaccine immunization approach, mice were immunized with HBV (yeast-derived, Kangtai Biological Pharmaceutical Company, China) in a three-dose series [19] or a same volume of PBS. The immunization procedure of HBV started on postnatal day 0 (P0) and was followed by two identical doses of HBV on P7 and P21 as the booster inoculations. The dosage (1 μ g HBsAg/50 μ l per pup) of HBV was used according to our previous research [14]. In the mIL-4 injection approach, mice were injected intraperitoneally with mIL-4 (PepruTech, once every other day; 25 ng/kg in 50 μ l PBS from P0 to P20 and 50 ng/kg in 50 μ l PBS once every other day from P22 to P34) or a same volume of PBS. The period and dosage for the mIL-4 injection were determined to imitate the period and amplitude of serum IL-4 elevation induced by hepatitis B vaccination. All mice were weaned on P21.

2.3. Cytokine analysis

A mouse cytokine/chemokine magnetic bead panel (MCYTO-MAG-70K-06; Millipore, Billerica, MA, USA) was used to evaluate the levels of interferon (IFN)- γ , tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-4, IL-6 and IL-10 in the serum and hippocampus, according to the manufacturer's instructions. The mice were anaesthetized deeply and the blood was collected immediately. Then the mice were transcardially perfused with 0.9% NaCl and hippocampi were collected. The serum samples were diluted 1:2 in assay buffer. Hippocampal homogenates were also assayed to evaluate the levels of mouse and rat IL-4 using the enzyme-linked immunosorbent assay kits as indicated by the manufacturer (Cusabio Biotech Co. Ltd., Wuhan, China). The

hippocampi were homogenized in PBS at pH 7.4 supplemented with 1% BSA, 0.1% Triton X-100, and protease inhibitor cocktail (Sigma), according to the manufacturer's instructions (Milliplex MAP kit, Millipore). A BCA protein assay kit (Beyotime, Shanghai, China) was used to adjust the total protein concentration of each sample to 4.5 mg/ml. Then, the prepared serum and hippocampal samples were used strictly according to the manufacturer's protocols for the multiplex assays. The assays were run in triplicate. The data were collected on a Bio-Plex-200 system (Bio-Rad, Hercules, CA, USA) and analyzed using professional software (Bio-Plex Manager).

2.4. Morris water maze (MWM)

Another cohort of mice were subjected to the MWM task at 4, 8 and 12 weeks of age to evaluate the spatial learning and memory of the mice. A pool 100 cm in diameter and 60 cm in height was filled with water made opaque with non-toxic white dye at (22 \pm 1) $^{\circ}$ C. The pool was divided into four equal imaginary quadrants and a white stationary circular platform 9 cm in diameter was below the water surface 1 cm. Each mouse was subjected to 4 trials per day and was given a maximum of 60 s to find the hidden platform for 5 consecutive days. Then, on the 6th day, each mouse was exposed to a probe trial with the platform removed and was allowed to swim for 60 s. The time spent in finding the platform and the distance traveled by each mouse to find the platform was recorded with a MT-200 Morris image motion system (Chengdu Technology & Market Corp., China).

2.5. Evans Blue injection

Evans Blue staining was applied to assess the permeability of the blood-brain barrier (BBB) as described previously [20] with minor modifications. In brief, the mice were injected intraperitoneally with a 2% solution of Evans Blue dye (Sigma-Aldrich, St. Louis, MO, USA) in 0.9% NaCl at a dose of 8 ml/kg on P0 or P14. Four hours later, all the mice were deeply anaesthetized and transcardially perfused with cold 0.9% NaCl until the outflow was clear. To assess Evans Blue leakage, their brain tissues were homogenized in 99% dimethylformamide and incubated for 48 h at 50 $^{\circ}$ C. After centrifuging at 12,000g for 30 min at 4 $^{\circ}$ C, the supernatant was collected to measure the absorbance of the samples at 620 nm using a microplate reader.

2.6. Immunofluorescence staining and cell quantification

Another cohort of mice were subjected to the morphological test. The mice were anaesthetized deeply and transcardially perfused with 0.9% NaCl, which was followed by 4% paraformaldehyde (PFA). The brains were removed and immediately post-fixed in 4% PFA overnight at 4 $^{\circ}$ C. Then, the brains were gradient dehydrated with 10%, 20% and 30% sucrose for 24 h each at 4 $^{\circ}$ C. Free-floating, serial coronal sections (40 μ m) were obtained using a Leica SM2000R freezing microtome (Leica Microsystems, Richmond Hill, Ontario, Canada) and stored at 4 $^{\circ}$ C prior to immunostaining.

Free-floating sections were washed in PBS three times and then blocked in PBS containing 1% bovine serum albumin (BSA) and 0.25% Triton X-100 (Sigma-Aldrich, St. Louis, MO, USA) for 1 h at 37 $^{\circ}$ C. The slices were then incubated in the primary antibodies, including rabbit anti-Iba-1 (1:1000; Wako Chemicals), rat anti-CD68 (1:200; Bio-Rad) and rat anti-MHC-2 (1:100; IQ Products) at 37 $^{\circ}$ C for 2 h, followed by overnight incubation at 4 $^{\circ}$ C. The primary antibodies were diluted in PBS containing 1% BSA and 0.25% Triton X-100. The next day, the specimens were washed three times and then were incubated with secondary antibodies, including Alexa Fluor 555-conjugated goat anti-rabbit and Alexa Fluor 488-conjugated donkey anti-rat for 2 h at 37 $^{\circ}$ C. Both secondary antibodies (Invitrogen) were diluted to 1:400. A Zeiss LSM780 confocal laser-scanning microscope was used to capture the representative confocal micrographs of the labeled cells.

Quantitative analyses of the Iba-1⁺ cells in the hippocampus of each mouse were done on a Stereo Investigator stereological system (MicroBrightField, Williston, USA). Measurements were made in an equidistant series of six coronal sections. To avoid oversampling, actual section thickness was measured, and the appropriate guard zones at the top and the bottom of the section were defined. The 40× objective of a Nikon microscope was used for all of the stereological analyses.

2.7. Real-time quantitative polymerase chain reaction (qRT-PCR)

Another cohort of mice were subjected to the qRT-PCR analyses. The qRT-PCR analyses were performed as previously described [14]. In brief, TRIzol reagent (Sangon Biotech, Shanghai, China) was used to extract the total RNA first. Then, a GoScript™ cDNA Reverse Transcription Kit (Promega, Madison, USA) was applied to convert the mRNAs (2 µg) into cDNAs. Fluorescence-based real-time quantitative PCR was used to assay the expression of several interested mRNAs. For each sample, the quantitative PCR reactions were conducted in triplicate using the TransStart Tip Green qPCR SuperMix (TransGen Biotech, Beijing, China). According to its stability, β-actin was selected to be the reference gene in the hippocampus. The amplification cycles were set as 94 °C for 5 s and 60 °C for 30 s. A melting curve was constructed to evaluate the specificity of the reaction. A Bio-Rad IQ5 Real-Time PCR System with the comparative Ct method was used to determine and analyze all the qRT-PCR reactions. The primers used in this study were as follows:

IL-1β, Forward 5'-TGTCTTTCCCGTGACCTTC and Reverse 5'-CTAATGGGAACGTACACACC;
 IL-6, Forward 5'-TCTGGGAAATCGGGAAATGAG and Reverse 5'-TCTCTGAAGGACTCTGGCTTTGTC;
 Ym1, Forward 5'-GGCATACTTTATCCTGAG and Reverse 5'-CCACTGAAGTCATCCATGTC;
 ARG, Forward 5'-AGCCAATGAAGAGCTGGCTGGT and Reverse 5'-AACTGCCAGACTGTGGTCTCCA; and
 β-actin, Forward 5'-GGTACCACCATGTACCCAGG and Reverse 5'-ACATCTGCTGGAAGGTGGAC.

2.8. Western blot analysis

Another cohort of mice were subjected to the Western blot analyses. The protein levels of phospho-p65, p65, phospho-Stat6, Stat6 and IL-4R in the hippocampus of the mice were examined by Western blotting analyses. After being anaesthetized and perfused with PBS, the hippocampus of the mice were separated from the brains and then were homogenized in ice-cold RIPA buffer (Beyotime, Shanghai, China). The homogenate was centrifuged at 9000g for 15 min at 4 °C, and the supernatant was isolated for Western blot assay. The protein concentration was quantified using a BCA protein assay kit (Beyotime, Shanghai, China). Tissue homogenates (containing 50 µg total protein) were separated on 10% or 8% SDS-PAGE gels and were then transferred onto presoaked PVDF membranes (Millipore). The blots were then blocked in 5% no-fat milk in TBST (20 mM Tris-HCl pH 7.5, 150 mM NaCl and 0.05% Tween-20) for 2 h at RT. The following primary antibodies were used: rabbit anti-phospho-p65 (Ser536) (bioworld, 1:1000), rabbit anti-p65 (bioworld, 1:1000), rabbit anti-phospho-Stat6 (Thr645) (bioworld, 1:1000), rabbit anti-Stat6 (CST, 1:1000) and rabbit anti-IL-4R (bioworld, 1:1000) overnight at 4 °C. HRP-conjugated secondary goat anti-rabbit antibodies (Fdbio science, Hangzhou, China) were used at 1:10,000. All blots were visualized using electrogenerated chemiluminescence (ECL) (Amersham Biosciences). Quantification was performed using the ImageJ software and normalized using β-actin.

2.9. IL-4 neutralization

Another new experiments were conducted, aiming to investigate

whether IL-4 neutralization would block the effects on brain and behavior induced by neonatal hepatitis B vaccination. In this experiment, four groups of mice were prepared, namely CON-mice, HBV-mice, HBV + IgG1-mice and HBV + anti-IL-4-mice. The procedure of IL-4 neutralization was performed as previously described with minor modifications [21].

An IL-4-neutralizing antibody (11B11, BD Pharmingen) or isotype control antibody, IgG1 (BD Pharmingen) at 10 µg/g body weight was co-administered intraperitoneally with HBV on P0, P7 and P21. In addition, the administration of IL-4-neutralizing antibody or isotype control antibody was repeated intraperitoneally at 10 µg/g body weight on P1, P2, P8, P9, P10, P11, P22, P23, P24, P25. Mice in the CON group and HBV group received injection of PBS of a corresponding schedule. These injections (HBV, IL-4-neutralizing antibody, isotype control antibody or PBS) described above were actually performed in mice that were sacrificed for tests at ages larger than P25 and these injections were ceased when the mice were sacrificed at ages before P25 as shown in Figs. 9 and S6.

2.10. Statistical analyses

The data were statistically analyzed using the SPSS 23.0 statistical software for Windows (Chicago, IL, USA). The data are expressed as the mean ± standard error of the mean. The data in Fig. 5A-F, Fig. 6E, Fig. 10A-C and Fig. S3 were analyzed using two-way RM-ANOVA followed by the Bonferroni post hoc test. The data in Fig. 3 were analyzed using Pearson's correlation coefficient. The data in Figs. 7J-K, 9, 10D-E and S6 were analyzed using one-way ANOVA. Except the data in Fig. 3M and Fig. 6C and D, all the other data were analyzed using Student's *t*-test or Welch's *t*-test. *p* < 0.05 was considered to indicate a statistically significant difference.

3. Results

3.1. Neonatal hepatitis B vaccination induced an instant anti-inflammatory cytokine response and a subsequent proinflammatory cytokine response in the hippocampus

We first observed the influences of neonatal hepatitis B vaccination on the levels of several major anti- and proinflammatory cytokines in the hippocampus from the neonatal period to adulthood. To be specific, we examined the levels of IL-4, IL-10, IFN-γ, IL-1β, IL-6 and TNF-α on P7, P14, P21, P28, P35, P42, P49, P56, P63 and P70 in the hippocampus of HBV- and CON-mice.

From P7 to P21, there were approximately 2.7–3.3-fold increases in the IL-4 concentrations in HBV-mice than CON-mice (Student's *t*-test; P7, *p* < 0.001; P14, *p* < 0.001; P21, *p* < 0.001; *n* = 6; Fig. 1A). On P28, there was only an increase of 1.6-fold compared to CON-mice (Student's *t*-test; *p* < 0.05; *n* = 6; Fig. 1A). However, no significant differences in the IL-4 concentrations were found between two groups from P35 to P70 (Fig. 1A).

From P7 to P21, both IL-1β and IL-6 showed opposite trends in the levels to IL-4 in HBV-mice, with significant decreases than the controls (Student's *t*-test; IL-1β: P7, *p* < 0.05; P14, *p* < 0.05; P21, *p* < 0.05; IL-6: P7, *p* < 0.05; P14, *p* < 0.05; P21, *p* < 0.05; *n* = 6; Fig. 1B and C). Interestingly, the levels of IL-1β and IL-6 in HBV-mice had no significant alterations on P28 and P35 but showed a period of rebounding increases from P42 to P56 or P63 (Student's *t*-test; IL-1β: P42, *p* < 0.05; P49, *p* < 0.05; P56, *p* < 0.05; IL-6: P42, *p* < 0.01; P49, *p* < 0.01; P56, *p* < 0.05; P63, *p* < 0.05; *n* = 6; Fig. 1B and C). TNF-α showed similar alterations to IL-1β and IL-6 from P28 but no significant alterations before this age (Student's *t*-test; P42, *p* < 0.05; P49, *p* < 0.05; P56, *p* < 0.05; *n* = 6; Fig. 1D).

There was a slight decrease (HBV: 35.46 ± 1.51 vs. CON: 42.15 ± 2.32; Student's *t*-test; *p* < 0.05) in the IFN-γ level only on P42 with no significant alterations at all the other ages (Fig. S1A) in HBV-

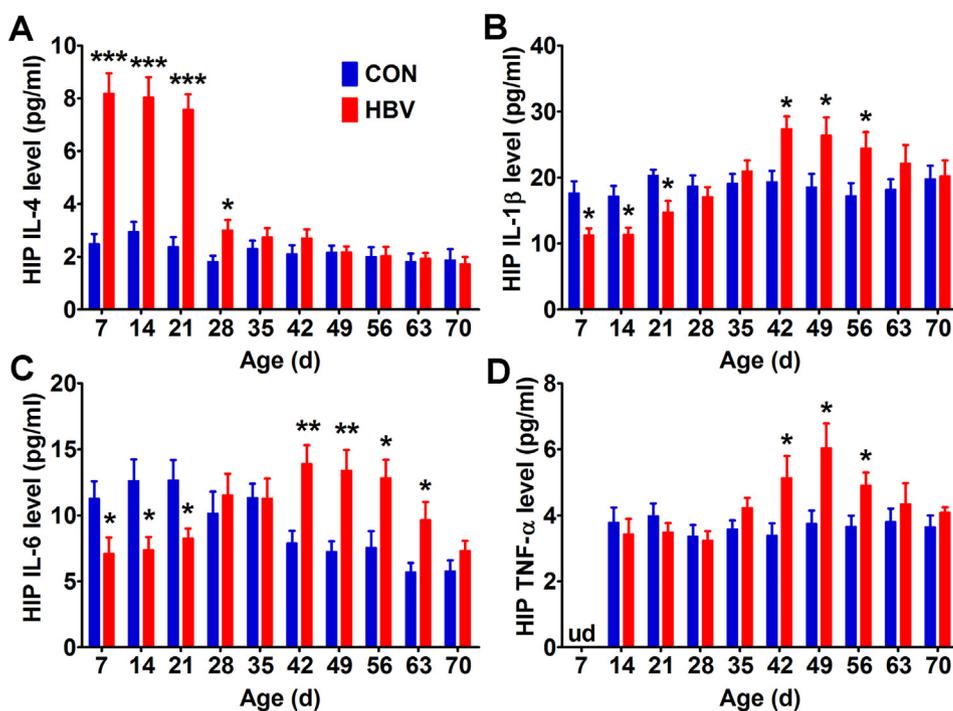


Fig. 1. Neonatal hepatitis B vaccination induced an instant anti-inflammatory cytokine response and a subsequent proinflammatory cytokine response in the hippocampus. (A–D) The bars represent the average levels of IL-4 (A), IL-1 β (B), IL-6 (C) and TNF- α (D) in the hippocampus. The data represent the means \pm SEM. * p < 0.05; ** p < 0.01; *** p < 0.001; n = 6/group; Student's t -test. HIP: hippocampus; ud: undetectable.

mice than CON-mice. At all ages, no significant alterations were found in the IL-10 levels between groups (Fig. S1C).

These findings suggest that the neonatal hepatitis B vaccination induced an anti-inflammatory cytokine response before P21 and a subsequent proinflammatory cytokine response that lasted from P42 to P63 in the hippocampus.

3.2. Neonatal hepatitis B vaccination elevated IL-4 levels and reduced the proinflammatory cytokine levels in serum

Having observed the effects of neonatal hepatitis B vaccination on the levels of IL-4, IL-1 β , IL-6 and TNF- α in the hippocampus, we next examined the levels of these cytokines in the serum at same age points. The IL-4 concentrations in HBV-mice were significantly higher in serum than control mice from P7 to P35 (Welch's t -test; P7, p < 0.001; Student's t -test; P14, p < 0.001; P21, p < 0.001; P28, p < 0.05; P35, p < 0.05; n = 6; Fig. 2A) but showed no significant alterations from P42 to P70 (Fig. 2A).

The level of IL-1 β in HBV-mice showed mild decreases in serum compared to CON-mice on P14 and P21 with no significant alterations at the other ages (Student's t -test; P14, p < 0.01; P21, p < 0.05; n = 6; Fig. 2B). The level of IL-6 in HBV-mice showed mild decreases in serum compared to CON-mice on P14, P21 and P28 with no significant alterations at other ages (Student's t -test; P14, p < 0.05; P21, p < 0.01; P28, p < 0.05; n = 6; Fig. 2C). The level of TNF- α in HBV-mice showed mild decreases in the serum than CON-mice on P14 with no significant alterations at other ages (Student's t -test; p < 0.01; n = 6; Fig. 2D). There were no significant alterations in the levels of IFN- γ (Fig. S1B) and IL-10 (Fig. S1D) in HBV-mice at all ages in contrast to CON-mice.

In summary, it is suggested that the decreased levels of proinflammatory cytokines might reflect the consequence of the elevation of the systemic IL-4 concentration.

3.3. The serum IL-4 levels positively correlated to the levels of the hippocampal IL-4 at the individual level

The findings above showed that IL-4, IL-1 β , IL-6 and TNF- α were altered significantly both in the serum and in the hippocampus in HBV-mice at all or some of the age points before P28. To explore the

relationship of the alterations in the cytokines in the hippocampus to that in the periphery, correlation analyses at the individual level were then performed between the hippocampal level and the serum level of each of the four cytokines tested on P7, P14, P21 and P28. Our results showed that the serum IL-4 levels positively correlated to the levels of the hippocampal IL-4 at all four time points (Pearson's correlation coefficient; P7, r = 0.925, p < 0.01; P14, r = 0.877, p < 0.05; P21, r = 0.907, p < 0.05; P28, r = 0.866, p < 0.05; n = 6; Fig. 3A–D). There was no significant correlation for IL-1 β , IL-6 and TNF- α between serum and hippocampal levels (Fig. 3E–P).

3.4. Neonatal mIL-4 over-exposure imitated the HBV-induced instant anti-inflammatory cytokine response and the subsequent proinflammatory cytokine response in the hippocampus

IL-4 is the only cytokine that has a correlation between its levels in serum and the hippocampus (Fig. 3A–D). Moreover, IL-4 was the cytokine that had the greatest amplitude of change in both the hippocampus and serum in HBV-mice (Figs. 1 and 2). Therefore, we hypothesized that IL-4 might be the mediator by which neonatal hepatitis B vaccination induced the neuroinflammation found above (Figs. 1 and 2) and the behavior impairments reported previously [14]. To verify this hypothesis, mice were administered mIL-4 and were tested for their hippocampal cytokine levels. Mice that were subjected to testing before P28 were injected intraperitoneally with mIL-4 once every other day from P0 until they were sacrificed, and the mice that were subjected to assays after P35 were injected intraperitoneally with mIL-4 once every other day from P0 to P34. The dosage of 25 ng/kg body weight was used for injections from P0 to P20, and 50 ng/kg was used from P22 to P34. The whole time span (P0 to P34) and dosages selected for the mIL-4 injection were determined by imitating the period and extent of serum IL-4 elevation induced by hepatitis B vaccination.

Generally, neonatal mIL-4 over-exposure imitated the HBV-induced instant anti-inflammatory cytokine response and the subsequent proinflammatory cytokine response in the hippocampus. From P7 to P28, the IL-4 concentrations were significantly higher in the hippocampus (Student's t -test; P7, p < 0.001; P14, p < 0.001; P21, p < 0.001; P28, p < 0.05; n = 6; Fig. 4A) of mIL-4-mice compared to that of CON-mice. From P35 to P70, IL-4 returned to normal levels in

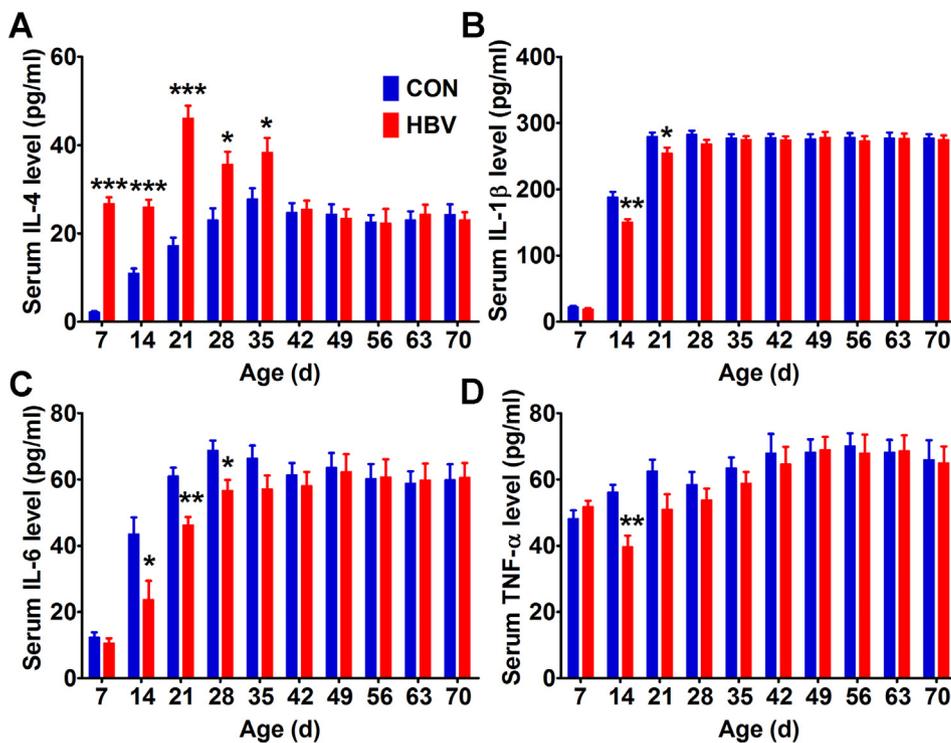


Fig. 2. The neonatal hepatitis B vaccination elevated the IL-4 level and reduced the proinflammatory cytokine levels in the serum. (A–D) The bars represent the average levels of IL-4 (A), IL-1β (B), IL-6 (C) and TNF-α (D) in the serum. The data represent the means ± SEM. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; $n = 6$ /group; Student's t -test or Welch's t -test.

the hippocampus (Fig. 4A).

From P7 to P28, both IL-1β and IL-6 in mIL-4-mice showed an opposite trend in the levels compared to IL-4, with significant decreases than that of the controls (Student's t -test; IL-1β: P7, $p < 0.01$; P14, $p < 0.05$; P21, $p < 0.05$; P28, $p < 0.05$; IL-6: P7, $p < 0.01$; P14, $p < 0.05$; P21, $p < 0.05$; P28, $p < 0.05$; $n = 6$; Fig. 4B and C). The levels of IL-1β and IL-6 showed no significant alterations on P35 but had a period of rebounding increases from P42 to P63 (Student's t -test; IL-1β: P42, $p < 0.01$; P49, $p < 0.05$; P56, $p < 0.05$; P63, $p < 0.05$; IL-6: P42, $p < 0.01$; P49, $p < 0.05$; P56, $p < 0.05$; P63, $p < 0.05$; $n = 6$; Fig. 4B and C). The TNF-α level showed a trend in similar to the IL-1β and IL-6 levels mIL-4-mice from P14 to P70, but only two significant differences were found on P21 and P42 (Student's t -test; P21, $p < 0.05$; P42, $p < 0.05$; $n = 6$; Fig. 4D). At all ages, no significant alterations were found for the IFN-γ (Fig. S2A) and IL-10 (Fig. S2B) levels between groups.

These results showed that neonatal mIL-4 over-exposure induced an instant anti-inflammatory cytokine response and a subsequent proinflammatory cytokine response in the hippocampus of mice, similar to the neonatal hepatitis B vaccination.

3.5. Neonatal mIL-4 over-exposure imitated the HBV-induced impairments in spatial learning and memory in mice at 8-weeks-old

To observe whether neonatal mIL-4 over-exposure could imitate the HBV-induced transient spatial cognition impairment, three new sets of mice were administered with mIL-4 or PBS from P0 and were subjected to MWM tasks at 4, 8 or 12 weeks of age. The time points for testing were determined according to a previous report [14]. In the current study, we also observed the effects of neonatal hepatitis B vaccination on the MWM performances of mice at 8 weeks of age to show the similarity of the results from the mIL-4-mice and the HBV-mice in the same figure without duplicate publication of the data from HBV-mice in our previous work [14].

The results showed that in the acquisition phase, HBV-mice and mIL-4-mice showed a longer average escape latency (RM-ANOVA; HBV: groups × time: $F_{4, 112} = 1.665$, $p > 0.05$; groups: $F_{1, 28} = 10.225$, $p < 0.01$; time: $F_{4, 112} = 16.899$, $p < 0.001$; $n = 15$; mIL-4:

groups × time: $F_{4, 112} = 2.663$, $p < 0.05$; groups: $F_{1, 28} = 18.461$, $p < 0.001$; time: $F_{4, 112} = 41.144$, $p < 0.001$; $n = 15$; Fig. 5A and D) than the control groups at 8 weeks of age. A longer average swimming path in both HBV-mice and mIL-4-mice (RM-ANOVA; HBV: groups × time: $F_{4, 112} = 1.548$, $p > 0.05$; groups: $F_{1, 28} = 9.418$, $p < 0.01$; time: $F_{4, 112} = 15.921$, $p < 0.001$; $n = 15$; mIL-4: groups × time: $F_{4, 112} = 2.649$, $p < 0.05$; groups: $F_{1, 28} = 17.642$, $p < 0.001$; time: $F_{4, 112} = 37.885$, $p < 0.001$; $n = 15$; Fig. 5B and E) than the control groups were also seen at 8 weeks of age. Neither HBV-mice nor mIL-4-mice had significant differences in velocity compared to the controls (Fig. 5C and F). In the probe phase, both HBV-mice and mIL-4-mice had less platform area crossings (Student's t -test; HBV: $p < 0.05$; $n = 15$; mIL-4: $p < 0.05$; $n = 15$; Fig. 5G and I) and spent less time in the target quadrant (Student's t -test; HBV: $p < 0.05$; $n = 15$; mIL-4: $p < 0.05$; $n = 15$; Fig. 5H and J) than the controls at 8 weeks of age. At 4 or 12 weeks, there were no significant different performances in the MWM tasks between mIL-4-mice and the control (Fig. S3). All these results were similar to the effects induced by neonatal hepatitis B vaccination, as reported previously [14].

These results indicated that neonatal mIL-4 over-exposure imitated the HBV-induced impairments in spatial learning and memory in mice.

3.6 Neonatal hepatitis B vaccination induced neuroinflammation, both through the penetration of IL-4 across the BBB into the brain before P14 and through the prolonged penetration period by neonatal IL-4 over-exposure

Then, we tried to explore the pathway by which IL-4 in the periphery affected the brain. The hippocampal IL-4 levels positively correlated to the levels of the serum IL-4 levels in HBV-mice (Fig. 3A–D). Moreover, the BBB is immature in the neonatal period [22,23]. Hence, we hypothesized that IL-4 permeating into the brain across the neonatal BBB mediated the influences of hepatitis B vaccination on the proinflammatory cytokine levels in the hippocampus.

Mice were injected intraperitoneally with Evans Blue on P0 or P14 to assess the integrity of the neonatal BBB. We observed the obvious presence of Evans Blue in the brain parenchyma, especially in the hippocampus on P0 (Student's t -test; prefrontal cortex (PFC): $p < 0.05$; hippocampus (HIP): $p < 0.001$; $n = 6$; Figs. 6A and B and S4). There

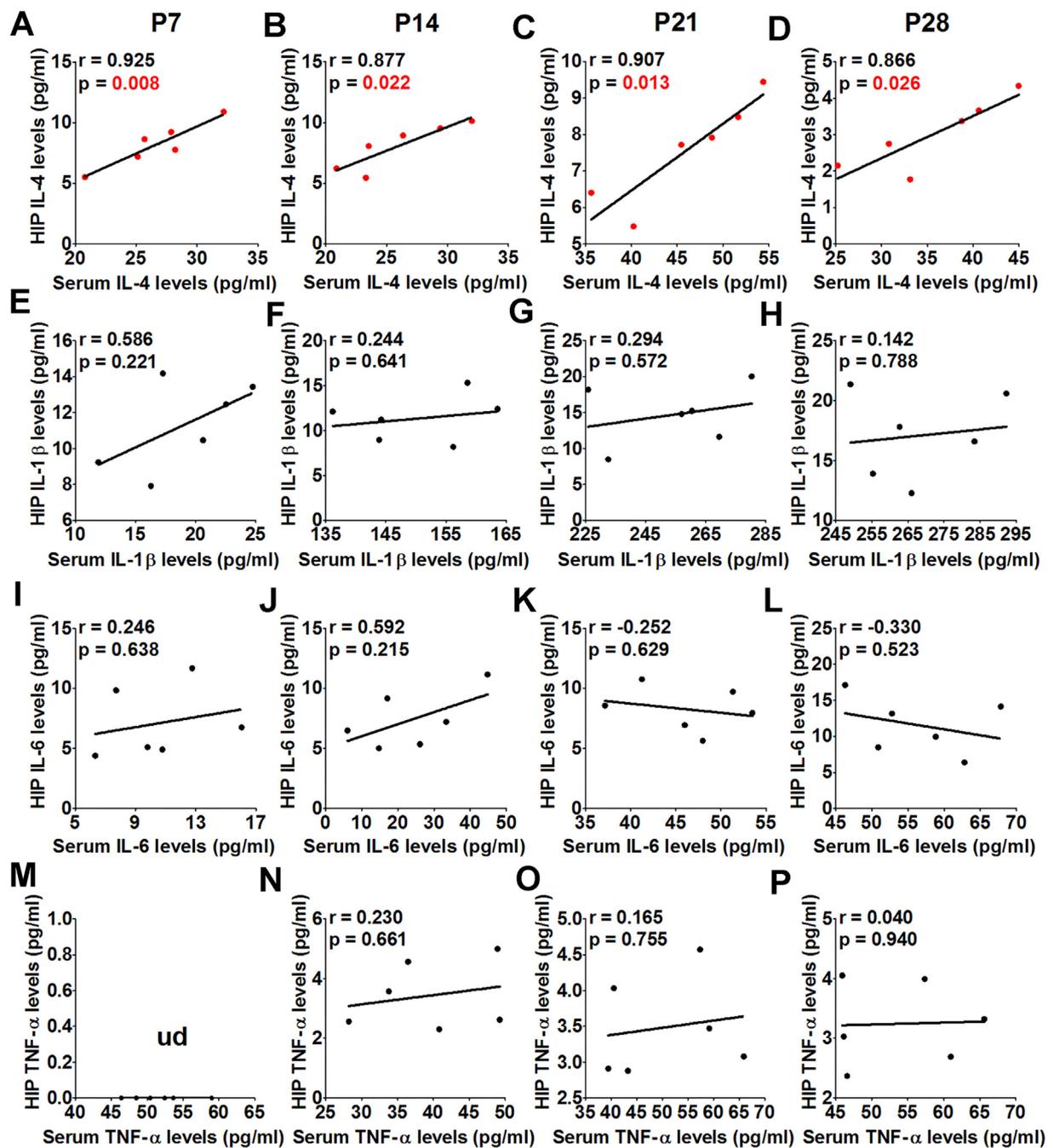


Fig. 3. The positive correlation of the serum IL-4 level with the hippocampal IL-4 level in HBV-mice. (A–D) Correlation analyses between the serum IL-4 level and the hippocampal levels of IL-4. (E–H) Correlation analyses between the serum IL-1 β level and the hippocampal levels of IL-1 β . (I–L) Correlation analyses between the serum IL-6 level and the hippocampal levels of IL-6. (M–P) Correlation analyses between the serum TNF- α level and the hippocampal levels of TNF- α . $n = 6$ /group; Pearson's correlation analysis. HIP: hippocampus; ud: undetectable.

was no Evans Blue dye leakage in the brain on P14 (Fig. 6B). This finding confirmed that the BBB is permeable in the neonatal period.

We next examined whether IL-4 can infiltrate into the brain during the neonatal period. Mice were injected intraperitoneally with 100 ng/kg of recombinant rat IL-4 (rIL-4) on P0, P3, P7 or P14. A rat IL-4 ELISA kit was used to test the level of rIL-4 in the hippocampus of mice 4 h later. There was the presence of rIL-4 in the hippocampus on P0, P3 and P7, but this trend decreased with age (Fig. 6C). On P14, the last time point, there was no longer detectable rIL-4 in the hippocampus (Fig. 6C). These results indicate that IL-4 can cross the BBB into the brain before P14 in mice because mice produce only mouse IL-4 but not rIL-4.

The results in Fig. 6B and C showed that the BBB was mature and no longer permeable on P14. However, the findings that the levels of IL-4 in the hippocampus of HBV-mice (Fig. 1A) and mL4-mice (Fig. 4A) were still higher than control groups until P28 suggested that neonatal exposure to a high level of IL-4 might prolong the penetration period for IL-4. To verify this deduction, we conducted another experiment. Thirty-six mice were divided into two groups. One group was administered intraperitoneally with rIL-4 once every other day from P0 (P0-group), and the other group was administered from P14 (P14-group). At each of the three selected age points, P14, P21 and P28, twelve mice, 6 mice from the P0-group and 6 mice from the P14-group, were assayed for the level of rIL-4 in the hippocampus using an ELISA

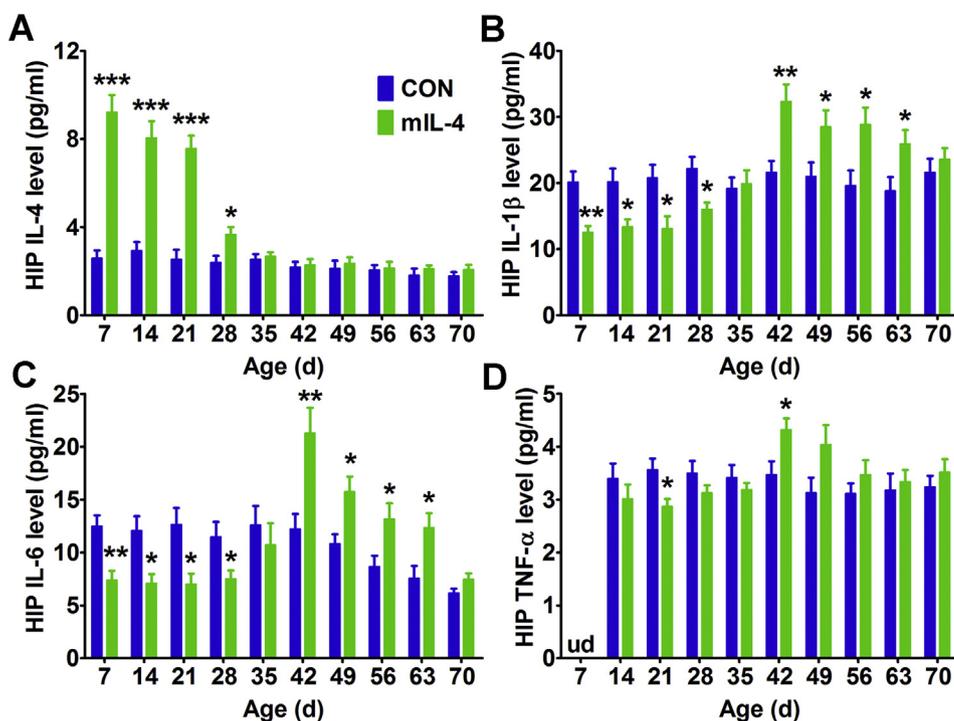


Fig. 4. Neonatal mIL-4 over-exposure imitated the HBV-induced instant anti-inflammation and subsequent proinflammation in the hippocampus. (A-D) The bars represent the average levels of IL-4 (A), IL-1β (B), IL-6 (C) and TNF-α (D) in the hippocampus. The data represent the means ± SEM. **p* < 0.05; ***p* < 0.01; ****p* < 0.001; *n* = 6/group; Student's *t*-test. HIP: hippocampus; ud: undetectable.

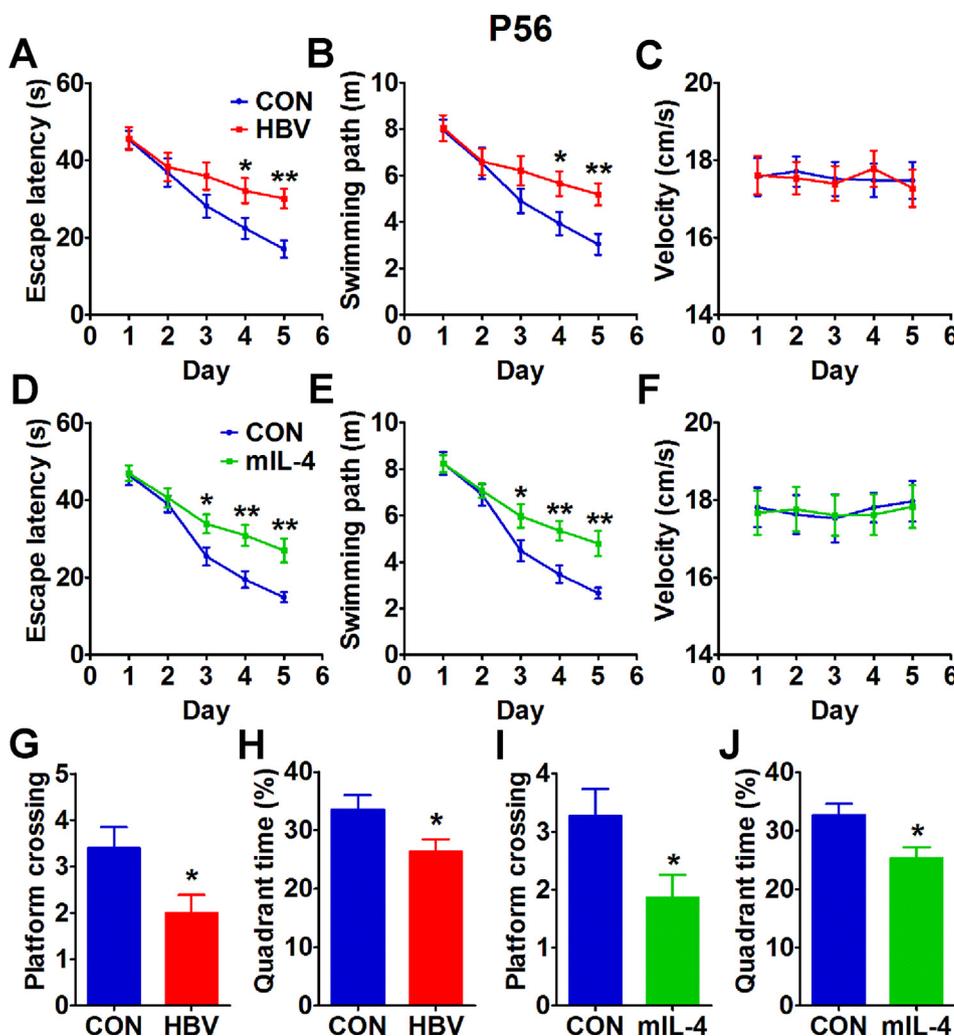


Fig. 5. Neonatal mIL-4 over-exposure imitated the HBV-induced spatial cognition impairment in the MWM task at 8 weeks of age. (A-B, D-E) The average escape latency (A, D) and average swimming path to reach the platform (B, E) of the HBV-mice (A, B) and mIL-4-mice (D, E) were longer than controls (Two-way RM-ANOVA followed by the Bonferroni post hoc test; **p* < 0.05, ***p* < 0.01: significant post hoc differences). (C, F) The data showed the average swimming velocity of the HBV-mice (C) and mIL-4-mice (F) at 8 weeks of age. (G, I) The data showed the average numbers of platform area crossings in the HBV-mice (G) and mIL-4-mice (I) (Student's *t*-test; **p* < 0.05: significant differences). (H, J) The data indicate the average time proportion spent in the target quadrant by the HBV-mice (H) and mIL-4-mice (J). The data represent the mean ± SEM of 15 animals per group.

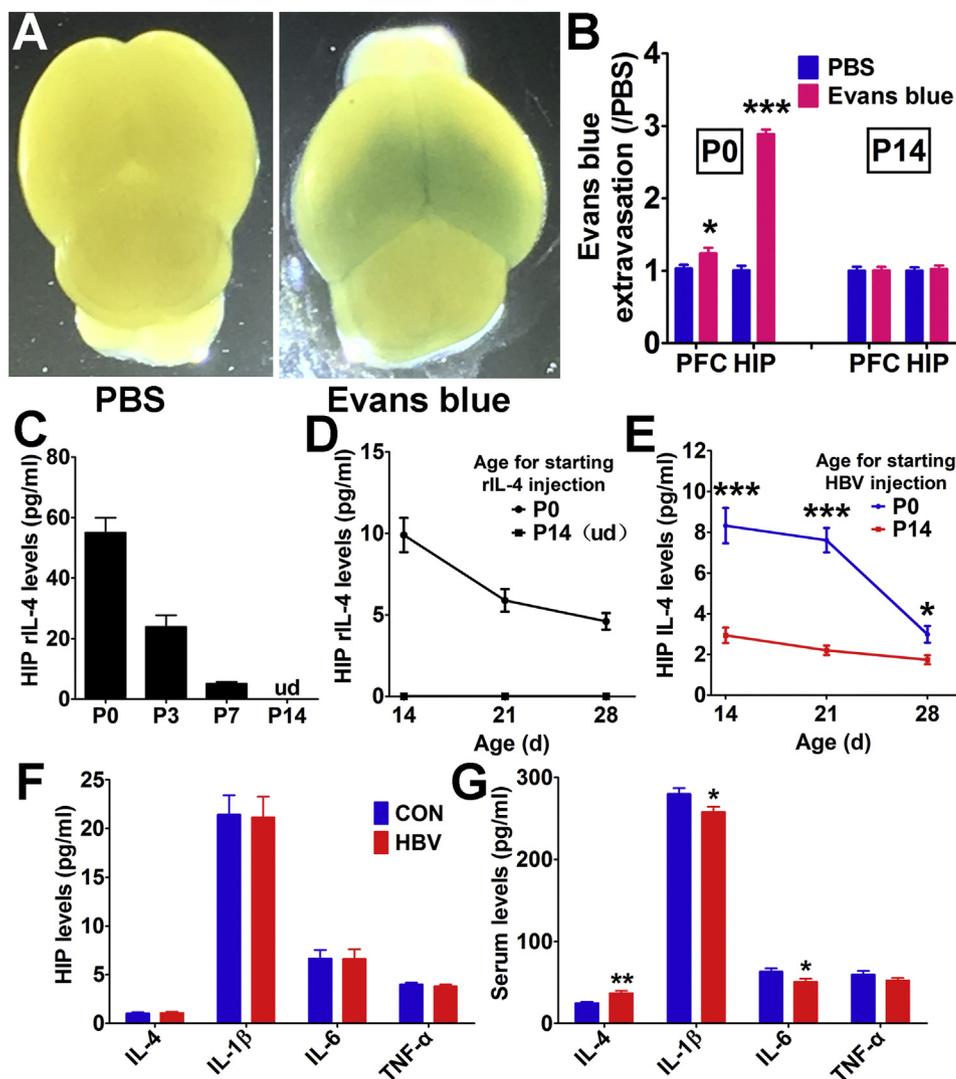


Fig. 6. Neonatal hepatitis B vaccination induced neuroinflammation, both through the penetration of IL-4 across the BBB into the brain before P14 and through the prolonged penetration of neonatal IL-4 over-exposure. (A) Visual inspection of the brains from PBS- and Evans Blue-administered mice, showing that neonatal mice had an immature and permeable BBB. (B) Evans Blue extravasation in the brain in both groups. PFC: prefrontal cortex; HIP: hippocampus. (C) The permeability of the BBB for rIL-4 before P14. ud: undetectable. (D) Exposure to high levels of rIL-4 before P14 increased the permeability of the BBB for rIL-4 infiltrating into the brain in the later life of mice. (E) Neonatal hepatitis B vaccination initiated before P14 increased the permeability of the BBB for IL-4 infiltrating into the brain in later life. The data represent the levels of mIL-4-mice compared to the controls. (F) Hepatitis B vaccination started on P14 had no significant influences on the cytokine levels in the hippocampus. (G) Hepatitis B vaccination started on P14 altered the levels of IL-4, IL-1 β and IL-6 in the serum. The data represent the means \pm SEM. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; $n = 6$ /group; Student's *t*-test.

kit. The kit indicated the presence of rIL-4 in the hippocampus of the P0-group until P28, whereas there was no detectable rIL-4 in the hippocampus of the P14-group (Fig. 6D) at any age point. These results indicated that over-exposure to IL-4 during the neonatal period could prolong the penetration of IL-4 into the hippocampus, suggesting that HBV injection starting after P14 might not influence the brain any more.

To verify this possibility, another set of mice was divided into two groups (18 per group). One group was intraperitoneally administered HBV from P0 (P0-group), and the other group was administered from P14 (P14-group). At each of the three selected age points, P14, P21 and P28, twelve mice, 6 mice from the P0-group and 6 mice from the P14-group, were assayed for the level of IL-4 in the hippocampus using an ELISA kit. There was the mere basal level of IL-4 in the hippocampus of the P14-group on P14, P21 and P28 (Fig. 6E). As expected, there was a significantly higher level of IL-4 in the hippocampus of the P0-group than the P14-group at any of the three age points (RM-ANOVA; groups \times time: $F_{2, 20} = 9.736$, $p < 0.01$; groups: $F_{1, 10} = 139.92$, $p < 0.001$; time: $F_{2, 20} = 20.047$, $p < 0.001$; $n = 6$; Fig. 6E). These results indicated that the peripheral IL-4 induced by hepatitis B vaccination starting after P14 did not penetrate into the hippocampus.

Next, the cytokine levels in the hippocampus and serum were examined in mice that received hepatitis B vaccination or PBS on P14, P21, and P35. The tests were done 4 h after the last injection. There were no significant alterations in the hippocampal levels of any of these cytokines between two groups (Fig. 6F), although there were slight

differences in the serum levels of IL-4, IL-1 β and IL-6 between the two groups (Student's *t*-test; IL-4: $p < 0.01$; IL-1 β : $p < 0.05$; IL-6: $p < 0.05$; $n = 6$; Fig. 6G). These results indicated that hepatitis B vaccination starting after P14 induced no neuroinflammation in the hippocampus.

3.7. Neonatal mIL-4 over-exposure imitated HBV-induced microglia M1 polarization

Our previous study demonstrated that neonatal hepatitis B vaccination induced microglia M1 polarization in the hippocampus [14]. Therefore, we examined whether mere neonatal IL-4 over-exposure could imitate such a microglial response on P42. Mice were given HBV or mIL-4 as described above, and the CON-mice matched to them received PBS in the corresponding approaches. Immunofluorescence was used to detect the expression levels of microglial CD68, a classical marker of proinflammatory microglial activation [24]. The results showed a significant increase in CD68 expression in both HBV-mice and mIL-4-mice (one-way ANOVA; HBV- vs. CON-mice: $p < 0.001$; mIL-4- vs. CON-mice: $p < 0.001$; $n = 6$; Fig. 7A–J) compared with CON-mice. This result indicated more activated microglia and neuroinflammation. Moreover, MHC-2, another classical marker of proinflammatory microglial activation (M1 activation) [25], was also assessed in our present study. The results showed that both HBV-mice and mIL-4-mice had a few microglia (Iba-1 $^{+}$) expressing MHC-2 (Fig. S5). In addition, there were no significant differences between groups in terms of the numbers

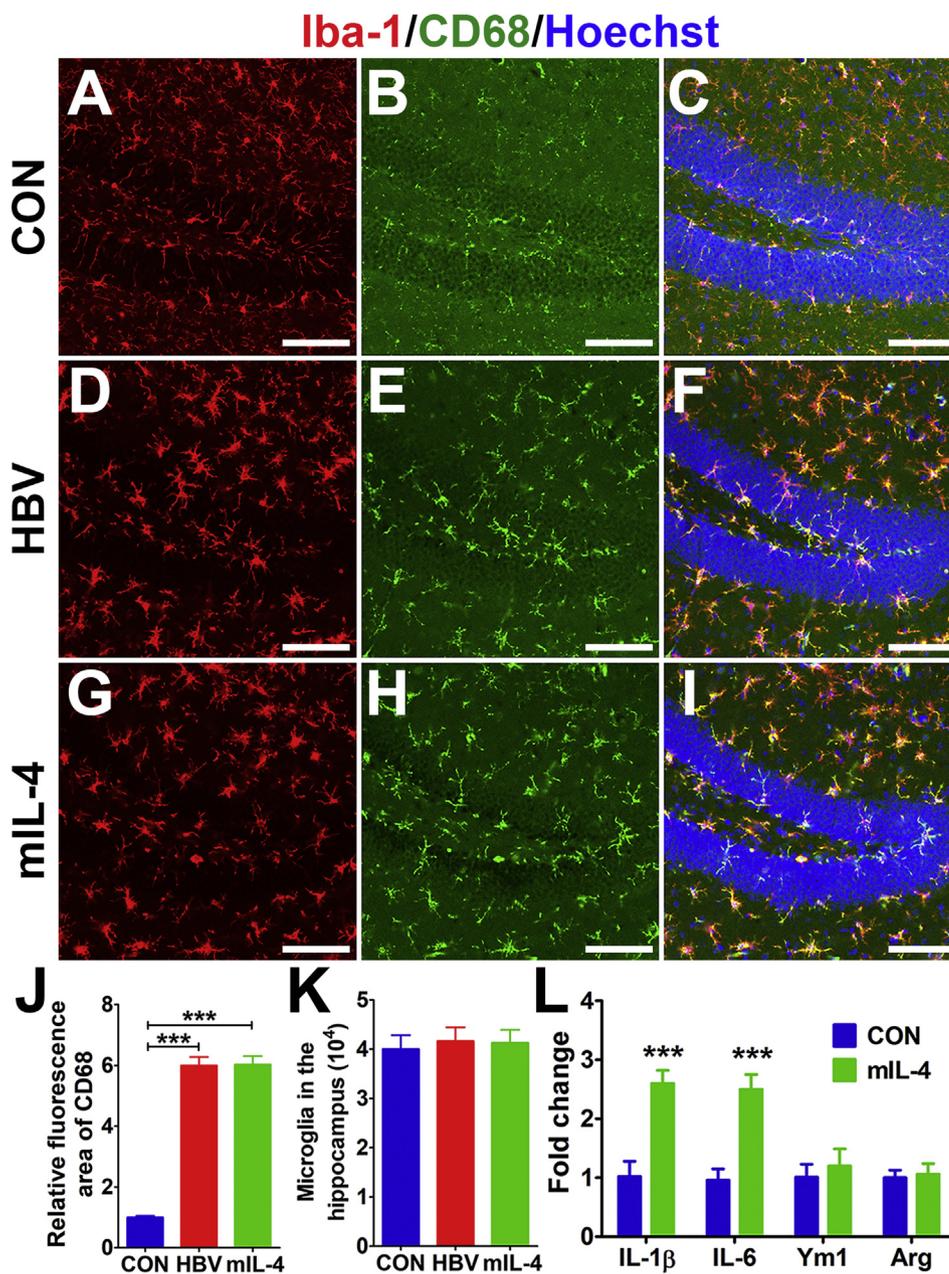


Fig. 7. Neonatal mIL-4 over-exposure imitated the HBV-induced microglia M1 polarization (CD68⁺) without altering their numbers in the hippocampus. (A–I) Representative confocal micrographs of the M1-activated microglia (Iba-1⁺/CD68⁺) in CON- (A–C), HBV- (D–F) and mIL-4-mice (G–I) on P42. Scale bar, 100 μ m. (J) The data represent the relative fluorescence area of CD68 in the hippocampus in all groups of mice. (K) The data represent the average numbers of microglia in the hippocampus in all groups of mice. (L) The data represent the relative mRNA expression of the M1- and M2-type genes in the hippocampus of mIL-4-mice compared to the controls. The data in (J) were analyzed using one-way ANOVA followed by the Dunnett's T3 post hoc test; the data in (K) were analyzed using one-way ANOVA followed by the Bonferroni post hoc test and the data in (L) were analyzed using Student's *t*-test. The data represent the means \pm SEM. *** *p* < 0.001; *n* = 6/group.

of microglia (Fig. 7K), consistent with our previous report [14].

Another two groups of mice received mIL-4 or PBS and were subjected to qRT-PCR for assays of the mRNA levels of IL-1 β and IL-6, representative of M1-type genes, as well as the mRNA levels of Ym1 and Arg, representative of M2-type genes [26,27]. The results showed that the mIL-4-mice had significantly increased mRNA levels of IL-1 β (Student's *t*-test; *p* < 0.001; *n* = 6) and IL-6 (Student's *t*-test; *p* < 0.001; *n* = 6) in the hippocampus compared to the controls (Fig. 7L). However, the mRNA levels of Ym1 and Arg had no significant differences between both groups (Fig. 7L). The results showed that neonatal mIL-4 over-exposure induced microglia M1 polarization. All these findings indicated that neonatal mIL-4 over-exposure imitated the HBV-induced microglia M1 polarization without altering their numbers in the hippocampus. Given the sufficient morphological evidence that neonatal mIL-4 over-exposure imitated the effects of neonatal hepatitis B vaccination on the microglial activation type, qRT-PCR tests were not repeated for HBV-mice as in mIL-4-mice.

3.8. Neonatal mIL-4 over-exposure promoted NF- κ B activation after causing a short inhibition in the hippocampus

The NF- κ B signaling pathway plays a key role in initiating the expression of proinflammatory cytokines, including IL-1 β , IL-6 and TNF- α [28,29]. This transactivation is mainly dependent on the activation of p65 (relA), one of the NF- κ B family members [30]. Therefore, we tested the levels of activation of NF- κ B p65. Western blot analyses revealed that the activation of p65 in the hippocampus, which was represented by the ratio of the phospho-p65 level to the total p65 level, decreased significantly (Student's *t*-test; *p* < 0.01; *n* = 4; Fig. 8A and C) in mIL-4-mice compared with CON mice on P21, when the mIL-4-mice had an anti-inflammatory status in the hippocampus (e.g., higher IL-4 level and lower IL-6 levels as shown in Fig. 4). Contrarily, NF- κ B p65 activation was significantly increased (Student's *t*-test; *p* < 0.001; *n* = 4; Fig. 8B and D) in mIL-4-mice compared to the controls on P42, when the mIL-4-mice showed a proinflammatory status in the hippocampus (Fig. 4). These data indicate that neonatal mIL-4 over-exposure induced an instant anti-inflammatory cytokine response and the subsequent

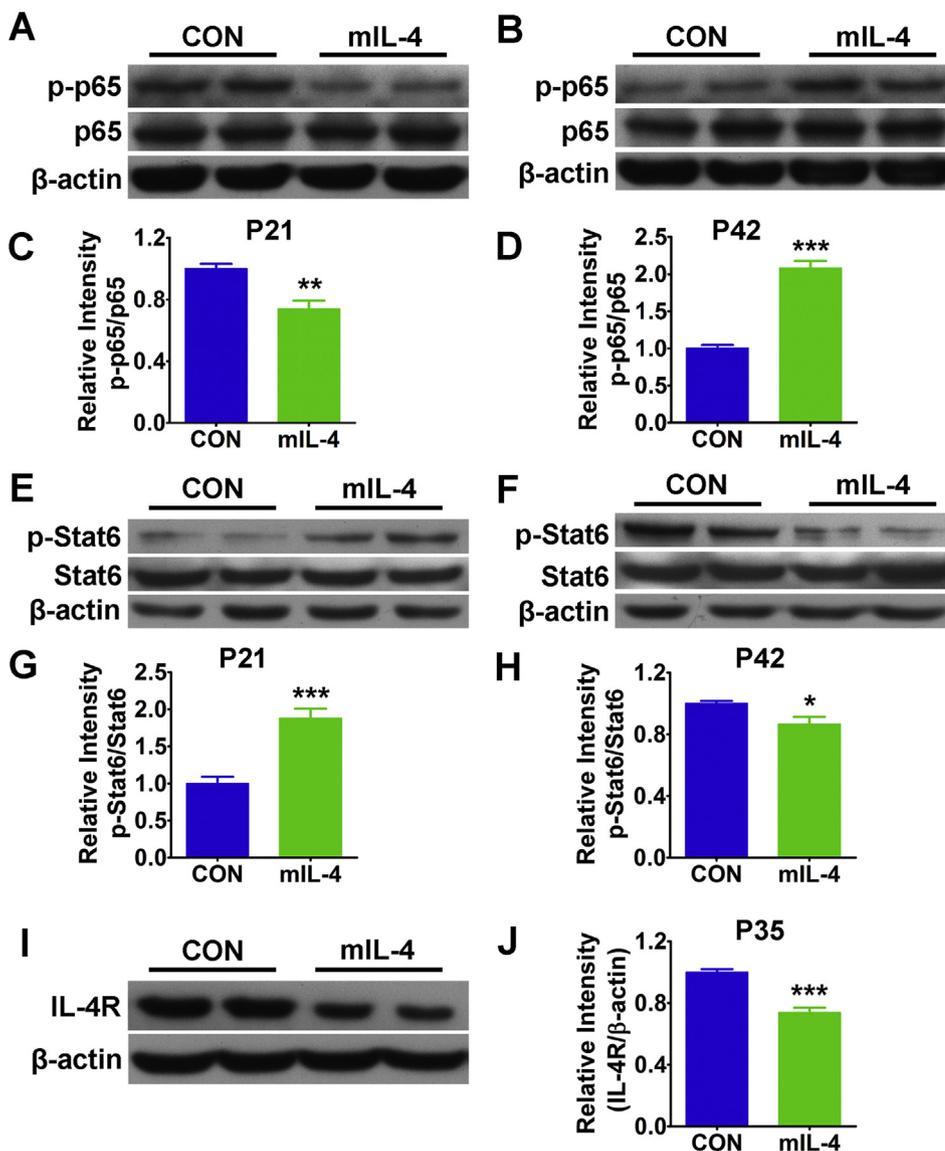


Fig. 8. The effects of mIL-4 administration on the NF- κ B and Stat6 signaling pathways and IL-4R expression. Western blot analysis was used for the expression of p65, p-p65, Stat6, p-Stat6 and IL-4R. (A–D) Representative results for the Western blot analysis of p-p65 and p65 on P21 (A, C) and P42 (B, D). The relative quantification of p-p65 and p65 in each group of mice was normalized using the level of β -actin and presented as the ratio between p-p65 and p65. (E–H) Representative results of the Western blot analysis of p-Stat6 and Stat6 on P21 (E, G) and P42 (F, H). The relative quantification of p-Stat6 and Stat6 in each group of mice was normalized using the level of β -actin and presented as the ratio between p-Stat6 and Stat6. (I–J) Representative results of the Western blot analysis of IL-4R on P35. The data in (C), (D), (G), (H) and (J) represent the means \pm SEM. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; $n = 4$ /group; Student's t -test.

proinflammatory cytokine response in the hippocampus.

3.9. Neonatal mIL-4 over-exposure induced an increase and a subsequent decrease in Stat6 activation in the hippocampus

Stat6, a member of the signal transducer family and a transcriptional activator [31], is an essential component in mediating many biological functions of IL-4 [32–34], and IL-4 can antagonize NF- κ B activation in a Stat6-dependent manner [35]. The Stat6 transcription factor blocks NF- κ B transactivation by inhibiting the interaction of NF- κ B with DNA. Thus, the Stat6 signaling pathway may have an important role in the IL-4-induced alteration of cytokines in the brain. The activation levels of Stat6 were detected using Western blotting on P21 and P42, when the mIL-4-mice had an anti-inflammatory and proinflammatory status in the hippocampus, respectively (Fig. 4). Compared with the controls, the Stat6 activation in the hippocampus, represented by the ratio of phospho-Stat6 level to the total Stat6 level, was increased significantly in mIL-4 mice on P21 (Student's t -test; $p < 0.001$; $n = 4$; Fig. 8E and G) but decreased significantly on P42 (Student's t -test; $p < 0.05$; $n = 4$; Fig. 8F and H).

3.10. Neonatal mIL-4 over-exposure induced the transient down-regulation of the IL-4 receptor

Stat6 acts as an immediate downstream signal transducer of IL-4 receptor activation [32–34]. Therefore, the alterations in Stat6 activation might result from the alteration of the function of IL-4R. Furthermore, receptor down-regulation often occurs when it is exposed to high levels of ligand [36]. Thus, we hypothesized that the down-regulation of IL-4R might be induced by the administration of exogenous mIL-4. The levels of IL-4R were detected using Western blotting on P35 in mIL-4-mice. Postnatal day 35 was chosen as the age for this analysis because it was the age when the elevated IL-4 levels in the hippocampus induced by either neonatal HBV or IL-4 injection restored to normal levels (Fig. 1A; Fig. 4A). As expected, the levels of IL-4R in the hippocampus decreased significantly in mIL-4 mice than controls (Student's t -test; $p < 0.001$; $n = 4$; Fig. 8I and J).

In addition, this down-regulation of IL-4R could not be observed in mIL-4-mice on P70 when neuroinflammation induced by HBV or IL-4 injection completely restored (Fig. 1; Fig. 4) (data not shown). These results demonstrated that neonatal mIL-4 over-exposure induced the transient down-regulation of the IL-4 receptor. This phenomenon explain the restoration of the hippocampal levels of proinflammatory cytokines as well as the spatial cognition impairments.

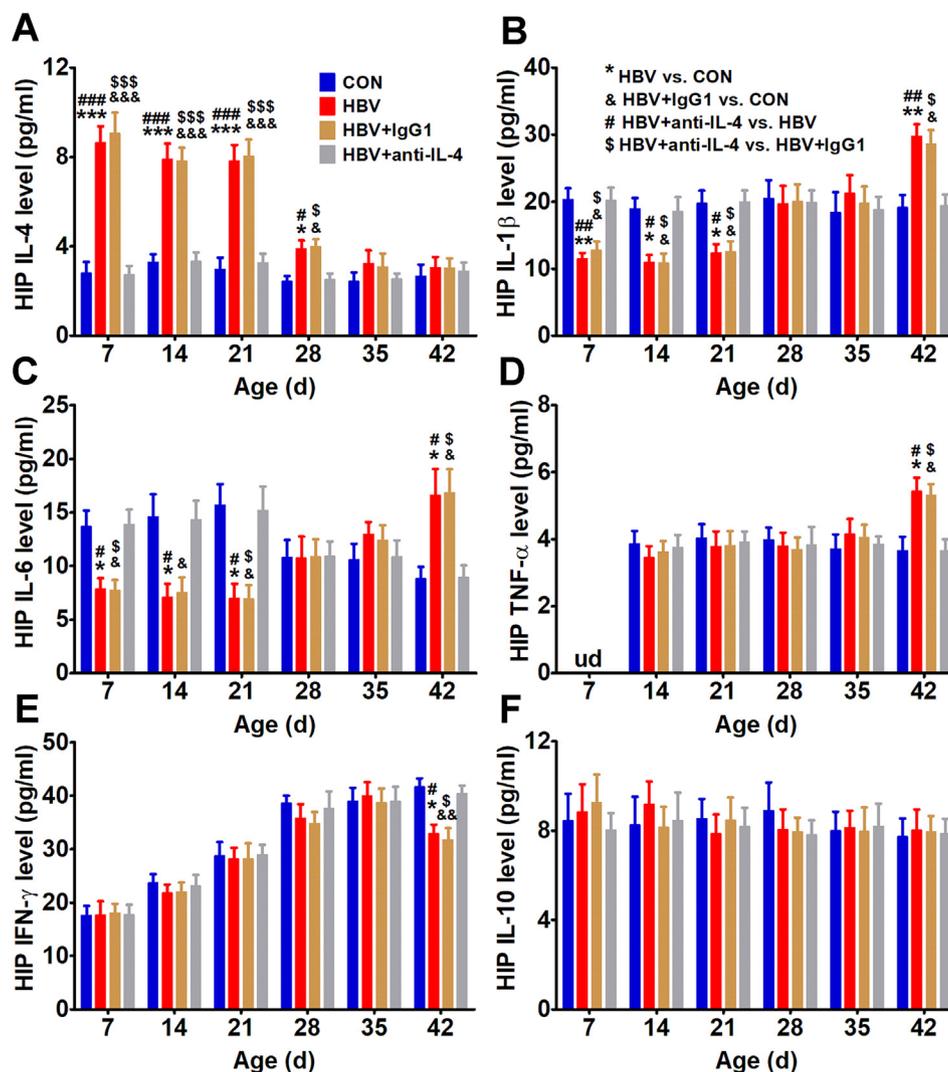


Fig. 9. Neutralization of IL-4 blocks the change of cytokines expression in the hippocampus induced by neonatal hepatitis B vaccination. (A-F) The bars represent the average levels of IL-4 (A), IL-1 β (B), IL-6 (C), TNF- α (D), IFN- γ (E) and IL-10 (F) in the hippocampus. The data represent the means \pm SEM. * p < 0.05; ** p < 0.01; *** p < 0.001; § p < 0.05; §§ p < 0.01; §§§ p < 0.001; # p < 0.05; ## p < 0.01; ### p < 0.001; \$ p < 0.05; \$\$\$ p < 0.001. The data were analyzed using one-way ANOVA followed by the Bonferroni post hoc test. n = 6/group. HIP: hippocampus; ud: undetectable.

3.11. Neutralization of IL-4 blocks the change of cytokines expression in the hippocampus and impairments in spatial learning and memory at 8-weeks-old induced by neonatal hepatitis B vaccination

To confirm the role of IL-4 in mediating the influences of neonatal hepatitis B vaccination on hippocampal cytokines expression and spatial cognition, we performed another experiment using anti-IL-4 neutralizing mAb and an isotype IgG1. We first found that administration of anti-IL-4 neutralizing mAb blocked the over-production of IL-4 in systemic blood at all detection age points (one-way ANOVA; HBV + anti-IL-4-mice vs. CON-mice: p > 0.05; n = 6; Fig. S6) but administration of the isotype IgG1 failed to block the HBV-induced peripheral IL-4 over-expression (one-way ANOVA; HBV + IgG1-mice vs. CON-mice: p < 0.05; HBV + IgG1 -mice vs. HBV-mice: p > 0.05; n = 6; Fig. S6).

Then, we found that neutralization of IL-4 blocked the HBV-induced alterations both in hippocampal cytokines expression (one-way ANOVA; HBV + anti-IL-4-mice vs. CON-mice: p > 0.05; n = 6; Fig. 9) and in the performance in the MWM tasks at 8-weeks-old in mice (RM-ANOVA; HBV + anti-IL-4-mice vs. CON-mice: p > 0.05; n = 12; Fig. 10), while administration of the isotype IgG1 showed no significant effects on blocking those HBV-induced alterations (Figs. 9 and 10).

4. Discussion

Our previous work showed neonatal hepatitis B vaccination led to spatial cognition impairment transiently at 8-weeks-old in mice, as well as a proinflammation profile of cytokine expression in the hippocampus [14]. IL-4 was the major cytokine in periphery induced by the HBV we used [15,16]. IL-4 itself is a powerful anti-inflammatory cytokine that induces the anti-inflammatory response and inhibits the production of proinflammatory cytokines [18]. This seems contrary to the hippocampal proinflammatory cytokine response found in mice that were immunized with HBV neonatally. Therefore, the present study was carried out to investigate the possible reason. We first found that HBV induced an anti-inflammation in the periphery, indicated by elevated IL-4 level and decreased levels of proinflammatory cytokines. Moreover, IL-4 had the largest amplitude and longest lasting alteration induced by HBV among these cytokines tested. After observing the positive correlation in the level of IL-4 in the periphery and that in the hippocampus, a series of experiments were carried out to examine the effects of neonatal IL-4 over-expression on the brain. Eventually, the present study provides direct evidence by means of neutralization of IL-4, supporting that IL-4 mediates a delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination that involves the

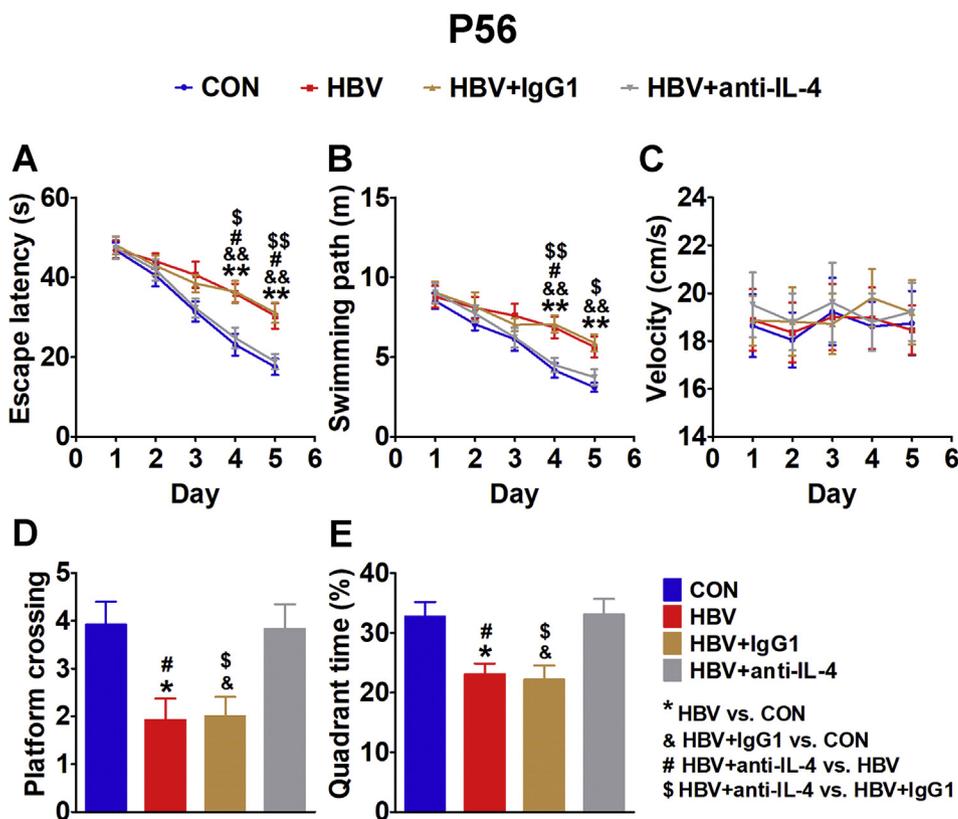


Fig. 10. Neutralization of IL-4 blocks the impairments in spatial learning and memory at 8-weeks-old induced by neonatal hepatitis B vaccination in mice. (A) The average escape latency of mice to reach the platform. (B) The average swimming path of mice to reach the platform. (C) The data showed the average swimming velocity of mice at 8 weeks of age. (D) The data showed the average numbers of platform area crossings by the mice. (E) The data indicate the average time proportion spent in the target quadrant by the mice. The data represent the means \pm SEM. * $p < 0.05$, ** $p < 0.01$; & $p < 0.05$; && $p < 0.01$; # $p < 0.05$; \$\$ $p < 0.05$; \$\$\$ $p < 0.01$. The data in A-C were analyzed using two-way RM-ANOVA followed by the Bonferroni post hoc test and the data in D and E were analyzed using one-way ANOVA followed by the Bonferroni post hoc test; $n = 12$ /group.

down-regulation of the IL-4 receptor in the hippocampus.

Notably, the behavioral impairment appeared in 8-week-old mice (Fig. 5), just during the age span (P42–P63) when the mice showed the delayed hippocampal neuroinflammation in HBV-mice as well as mIL-4-mice (Figs. 1 and 4). This phenomenon suggests that the latency for the emerging behavioral impairments in the HBV-mice and mIL-4-mice can be explained by the instant anti-inflammation caused by IL-4 (Figs. 1 and 4). The same phenomenon also suggests that the restoration of the behavioral impairments at 12 weeks of age in the HBV-mice and mIL-4-mice can be explained by the restoration of the proinflammatory response in the hippocampus from P70 (Figs. 1 and 4).

As stated in the Introduction section, early postnatal time is a critical period of brain development, when immune activation during this period could exert a long-lasting impact on brain development and behavior [2–5]. However, the exact mechanism of the critical period for immune activation affecting the brain is not fully understood yet. Here, we found not only the permeability of the neonatal BBB for IL-4 before P14 but also the prolonged permeability of the BBB for IL-4 by neonatal mIL-4 over-exposure. The present findings suggest that both the permeability of the neonatal BBB for cytokines and its regulation may provide some reasonable explanation for the nature of this critical period, although it needs further investigation to increase clarity on how the prolonging of BBB permeability happens.

The results in 3.8, 3.9 and 3.10 suggested that neonatal mIL-4 over-exposure induced the down-regulation of the IL-4 receptor in the hippocampus, which then led to a decrease in Stat6 activation and eventually resulted in a higher NF- κ B activation level. These serial events concerning the IL-4R/Stat6 and NF- κ B signaling pathways may account for the influences of the neonatal hepatitis B vaccination on the brain.

In our previous study [14], aluminum hydroxide adjuvant contained in the HBV had been verified to induce no significant alterations in the cytokine expression both in the periphery and in the brain and in the behavioral performances. These findings suggested that the immune responses by HBV is triggered by the whole vaccine (HbsAg + aluminum hydroxide adjuvant), but not by aluminum hydroxide adjuvant

alone. Therefore, the effects of aluminum hydroxide adjuvant alone were not observed in our present study.

Given the reports that various neonatal immune stimuli have influences on the brain development and behavior [2,6,37], it is possible that over-exposure to other cytokines would also have a significant impact on long-term function. Addressing this issue would be significant. We will conduct further studies with different cytokines to that neonatal over-exposure often happens, such as IFN- γ and IL-6. However, the present study was designed to explore the mechanism by which neonatal HBV injection affected brain and behavior. Although vaccine may increase the levels of several cytokines in addition to IL-4, IL-4 was the only cytokine that has a significant correlation between its levels in the serum and its levels in the hippocampus (Fig. 3A–D) and was the cytokine with the greatest amplitude of increase both in the hippocampus and in the serum in HBV-mice (Figs. 1A and 2A). What's more, anti-IL-4 neutralizing mAb blocked both hippocampal cytokine expression alterations and behavior impairments induced by HBV. Accordingly, IL-4 is very likely to have a key role in mediating the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination.

An interesting question is which population of cells in the hippocampus are involved in the altered signaling process mentioned above, and addressing this question will contribute to the better understanding of the IL-4-induced neurobehavioral impairments at the cellular level. We are currently working on this issue. However, we will address it in the future because the scientific hypothesis in the present work that IL-4 can mediate the neurobehavioral impairments caused by neonatal hepatitis B vaccination has already been supported by both indirect and direct data provided by the current study.

5. Conclusions

Our current research demonstrates that IL-4 mediates the delayed neurobehavioral impairments induced by neonatal hepatitis B vaccination, which involves the permeability of the neonatal BBB and the

down-regulation of the IL-4 receptor. This conclusion was made according to these major results: 1) neonatal hepatitis B vaccination induced delayed hippocampal neuroinflammation and spatial cognition impairment after an instant anti-inflammatory cytokine response in the hippocampus; 2) neonatal IL-4 over-exposure imitated all the HBV-induced neurobehavioral effects; 3) peripheral IL-4 is able to penetrate into the hippocampus during the neonatal period; and 4) the permeability of the BBB in neonatal mice might explain the penetration of peripheral IL-4 into the brain and 5) the decreased levels of IL-4R in the hippocampus by neonatal IL-4 over-exposure.

These findings suggest that clinical events involving neonatal IL-4 over-exposure, including neonatal hepatitis B vaccination and asthma in human infants, may have adverse effects on neurobehavioral development.

6. Conflict of interest statement

The authors declare that there are no conflicts of interest.

7. Funding

The work was supported by the National Natural Science Foundation of China (No. 31,371,130 and 31600836), the Special Foundation of Education Department of Guangdong Province, the Medical Scientific Research Foundation of Guangdong Province, China (2013-159) and the Foundation of Medical Science and Technology Research of Guangdong Province (A2016273).

Acknowledgments

We thank Dr. Juntao Zou (SYSU), Dr. Kaihua Guo (SYSU), Ms. Qunfang Yuan (SYSU), Dr. Yingying Wu (SYSU), Dr. Yunjie Yang (SYSU) and Dr. Zitian He (SYSU) for their valuable discussions and help with this investigation.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.cyto.2018.04.037>.

References

- C.f.D. Control, Prevention, Global routine vaccination coverage—2012, *MMWR. Morbidity and mortality weekly report* 62(43) (2013) 858.
- S.D. Bilbo, J.M. Schwarz, Early-life programming of later-life brain and behavior: a critical role for the immune system, *Front. Behavioral Neurosci.* 3 (2009) 14.
- S.D. Bilbo, J.M. Schwarz, The immune system and developmental programming of brain and behavior, *Front. Neuroendocrinol.* 33 (3) (2012) 267–286.
- Y. Xia, F. Qi, J. Zou, J. Yang, Z. Yao, Influenza vaccination during early pregnancy contributes to neurogenesis and behavioral function in offspring, *Brain Behav. Immun.* 42 (2014) 212–221.
- S.S. French, E.M. Chester, G.E. Demas, Maternal immune activation affects litter success, size and neuroendocrine responses related to behavior in adult offspring, *Physiol. Behav.* 119 (2013) 175–184.
- S.D. Bilbo, L.H. Levkoff, J.H. Mahoney, L.R. Watkins, J.W. Rudy, S.F. Maier, Neonatal infection induces memory impairments following an immune challenge in adulthood, *Behav. Neurosci.* 119 (1) (2005) 293.
- S.J. Spencer, J.G. Heida, Q.J. Pittman, Early life immune challenge—effects on behavioural indices of adult rat fear and anxiety, *Behav. Brain Res.* 164 (2) (2005) 231–238.
- F.R. Walker, J. March, D.M. Hodgson, Endotoxin exposure in early life alters the development of anxiety-like behaviour in the Fischer 344 rat, *Behav. Brain Res.* 154 (1) (2004) 63–69.
- C.M. Gallagher, M.S. Goodman, Hepatitis B vaccination of male neonates and autism diagnosis, *NHIS 1997–2002, J. Toxicol. Environ. Health, Part A* 73 (24) (2010) 1665–1677.
- M.A. Hernán, S.S. Jick, M.J. Olek, H. Jick, Recombinant hepatitis B vaccine and the risk of multiple sclerosis A prospective study, *Neurology* 63 (5) (2004) 838–842.
- J.P. Stubgen, Immune-mediated myelitis following hepatitis B vaccination, *Autoimmun. Reviews* 12 (2) (2012) 144–149.
- C. Institute of Medicine Immunization Safety Review, The National Academies Collection: Reports funded by National Institutes of Health, Immunization Safety Review: Vaccines and Autism, National Academies Press (US) National Academy of Sciences, Washington (DC), 2004.
- G.L. Freed S.J. Clark A.T. Butchart D.C. Singer M.M. Davis Parental vaccine safety concerns in 2009 *Pediatrics* 125 4 2010 654 9.
- J. Yang, F. Qi, Y. Yang, Q. Yuan, J. Zou, K. Guo, Z. Yao, Neonatal hepatitis B vaccination impaired the behavior and neurogenesis of mice transiently in early adulthood, *Psychoneuroendocrinology* 73 (2016) 166–176.
- S.H. Moon, E.C. Shin, Y.W. Noh, Y.T. Lim, Evaluation of hyaluronic acid-based combination adjuvant containing monophosphoryl lipid A and aluminum salt for hepatitis B vaccine, *Vaccine* 33 (38) (2015) 4762–4769.
- R.D. Weeratna, C.L. Brazolot Millan, M.J. McCluskie, H.L. Davis, CpG ODN can redirect the Th bias of established Th2 immune responses in adult and young mice, *FEMS Immunol. Med. Microbiol.* 32 (1) (2001) 65–71.
- R. Yirmiya, I. Goshen, Immune modulation of learning, memory, neural plasticity and neurogenesis, *Brain Behav. Immun.* 25 (2) (2011) 181–213.
- A.J. Schuerwegh, E.J. Dombrecht, W.J. Stevens, J.F. Van Offel, C.H. Bridts, L.S. De Clerck, Influence of pro-inflammatory (IL-1 alpha, IL-6, TNF-alpha, IFN-gamma) and anti-inflammatory (IL-4) cytokines on chondrocyte function, *Osteoarthritis Cartilage* 11 (9) (2003) 681–687.
- E.E. Mast, M.J. Alter, H.S. Margolis, Strategies to prevent and control hepatitis B and C virus infections: a global perspective, *Vaccine* 17 (13–14) (1999) 1730–1733.
- F. Yang, L. Zhou, D. Wang, Z. Wang, Q.Y. Huang, Minocycline ameliorates hypoxia-induced blood-brain barrier damage by inhibition of HIF-1alpha through SIRT3/PHD-2 degradation pathway, *Neuroscience* 304 (2015) 250–259.
- Y.-W. Tang, B.S. Graham, Anti-IL-4 treatment at immunization modulates cytokine expression, reduces illness, and increases cytotoxic T lymphocyte activity in mice challenged with respiratory syncytial virus, *J. Clin. Invest.* 94 (5) (1994) 1953–1958.
- K.D. Foust, E. Nurre, C.L. Montgomery, A. Hernandez, C.M. Chan, B.K. Kaspar, Intravascular AAV9 preferentially targets neonatal neurons and adult astrocytes, *Nat. Biotechnol.* 27 (1) (2009) 59–65.
- N.R. Saunders, Ontogeny of the blood-brain barrier, *Exper. Eye Res.* 25 (1977) 523–550.
- N.N. Burke, D.M. Kerr, O. Moriarty, D.P. Finn, M. Roche, Minocycline modulates neuropathic pain behaviour and cortical M1–M2 microglial gene expression in a rat model of depression, *Brain Behav. Immun.* 42 (2014) 147–156.
- Y. Shi, V. Chanana, J.J. Watters, P. Ferrazzano, D. Sun, Role of sodium/hydrogen exchanger isoform 1 in microglial activation and proinflammatory responses in ischemic brains, *J. Neurochem.* 119 (1) (2011) 124–135.
- M. Olah, K. Biber, J. Vinet, H.W. Boddeke, Microglia phenotype diversity, *CNS & Neurol. Disorders Drug Targets* 10 (1) (2011) 108–118.
- C.Y. Xia, S. Zhang, Y. Gao, Z.Z. Wang, N.H. Chen, Selective modulation of microglia polarization to M2 phenotype for stroke treatment, *Int. Immunopharmacology* 25 (2) (2015) 377–382.
- M. Karin, M. Delhase, The IκB kinase (IKK) and NF-κB: key elements of proinflammatory signalling, *Elsevier, Seminars in immunology*, 2000, pp. 85–98.
- M. Karin, Y. Ben-Neriah, Phosphorylation meets ubiquitination: the control of NF-κB activity, *Annual Rev. Immunol.* 18 (2000) 621–663.
- D.Q. Xie, G.Y. Sun, X.G. Zhang, H. Gan, Osthole preconditioning protects rats against renal ischemia-reperfusion injury, *Transplant. Proc.* 47 (6) (2015) 1620–1626.
- L.A. Doyle, M. Vivero, C.D. Fletcher, F. Mertens, J.L. Hornick, Nuclear expression of STAT6 distinguishes solitary fibrous tumor from histologic mimics, *Modern Pathol. : an official journal of the United States and Canadian Academy of Pathology, Inc.* 27 (3) (2014) 390–395.
- C.K. Oh, G.P. Geba, N. Molino, Investigational therapeutics targeting the IL-4/IL-13/STAT-6 pathway for the treatment of asthma, *Eur. Respirat. Rev. : an official journal of the European Respiratory Society* 19 (115) (2010) 46–54.
- S. Chapoval, P. Dasgupta, N.J. Dorsey, A.D. Keegan, Regulation of the T helper cell type 2 (Th2)/T regulatory cell (Treg) balance by IL-4 and STAT6, *J. Leukocyte Biol.* 87 (6) (2010) 1011–1018.
- E. Forbes, N. van Panhuys, B. Min, G. Le Gros, Differential requirements for IL-4/STAT6 signalling in CD4 T-cell fate determination and Th2-immune effector responses, *Immunol. Cell Biol.* 88 (3) (2010) 240–243.
- Y. Abu-Amer, IL-4 abrogates osteoclastogenesis through STAT6-dependent inhibition of NF-κB, *J. Clin. Invest.* 107 (11) (2001) 1375–1385.
- M.M. Chi, A.L. Schlein, K.H. Moley, High insulin-like growth factor 1 (IGF-1) and insulin concentrations trigger apoptosis in the mouse blastocyst via down-regulation of the IGF-1 receptor, *Endocrinology* 141 (12) (2000) 4784–4792.
- C.S. Custodio, B.S.F. Mello, A. Filho, C.N. de Carvalho Lima, R.C. Cordeiro, F. Miyajima, G.Z. Reus, S.M.M. Vasconcelos, T. Barichello, J. Quevedo, A.C. de Oliveira, D.F. de Lucena, D.S. Macedo, Neonatal immune challenge with lipopolysaccharide triggers long-lasting sex- and age-related behavioral and immune/neurotrophic alterations in mice: relevance to autism spectrum disorders, *Molecul. Neurobiol.* (2017).

VACCINE SAFETY

Introduction to Vaccine Safety Science & Policy in the United States



Published: October 2, 2017 (Version 1.0)

Address for correspondence: whitepaper@icandecide.org

This white paper provides an introduction to vaccine safety science and policy in the United States.

Section “I” discusses how Congress granted pharmaceutical companies immunity from liability for vaccine injuries and transferred all responsibility for vaccine safety to the United States Department of Health & Human Services (HHS) and its agencies, including the Food & Drug Administration (FDA), the Centers for Disease Control (CDC) and the National Institutes of Health (NIH).

Section “II” discusses how most pediatric vaccines were licensed based on inadequate clinical trials, including follow-up periods too brief to capture adverse outcomes, and illegitimate placebos (e.g., other vaccines).

Section “III” discusses the CDC’s deficient post-licensure vaccine safety surveillance.

Section “IV” discusses the conflicts of interest at HHS regarding vaccine safety, including the issues resulting from placing HHS in charge of vaccine safety and the conflicting duty of promoting and defending vaccines against any claim of injury.

Until a frank conversation is possible regarding vaccine safety, children susceptible to vaccine injury will not be protected from such injury. Nor will children injured by vaccines be able to access the services they need. We can do better in protecting and serving children who are susceptible or succumb to serious injuries from vaccination.

The first step in avoiding vaccine injuries and helping those already harmed is understanding the state of vaccine safety science and policy in America. This paper provides this understanding and highlights areas in need of improvement.

I. Who is responsible for vaccine safety?

Unlike nearly every other company in America, pharmaceutical companies have almost no liability for injuries caused by their vaccine products. How did this happen? As

explained by the Institute of Medicine (IOM)¹, by 1986, the “litigation costs associated with claims of damage from vaccines had forced several companies to end their vaccine

¹ In 2016, the IOM formally changed its name to the National Academies of Sciences, Engineering, and Medicine.

research and development programs as well as to stop producing already licensed vaccines.”² Instead of letting market forces compel vaccine makers to create safer vaccines, Congress granted pharmaceutical companies financial immunity from injuries caused by vaccines recommended by the CDC.³ Congress did so by passing the National Childhood Vaccine Injury Act (the **1986 Act**).⁴

By granting immunity from actual or potential liability from injuries caused by vaccines, Congress eliminated the market forces that are generally relied upon to assure the safety of all other products. As the 1986 Act expressly provides: “No person may bring a civil action ... against a vaccine administrator or manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death.”⁵

The 1986 Act even shields vaccine makers from liability where it is clear and unmistakable that the vaccine in question could have been designed safer.⁶ As recently explained in a U.S. Supreme Court opinion:

[N]o one—neither the FDA nor any other federal agency, nor state and federal juries—ensures that vaccine manufacturers adequately take account of scientific and technological advancements. This concern is especially acute with respect to vaccines that have already been

*released and marketed to the public. Manufacturers ... will often have little or no incentive to improve the designs of vaccines that are already generating significant profit margins.*⁷

Recognizing that the 1986 Act eliminated the incentive for vaccine makers to assure the safety of their vaccine products, the 1986 Act explicitly places this responsibility in the hands of the United States Department of Health & Human Services (**HHS**).⁸

As provided in the 1986 Act, HHS is responsible for “research ... to prevent adverse reactions to vaccines,” “develop[ing] the techniques needed to produce safe ... vaccines,” “safety ... testing of vaccines,” “monitoring ... adverse effects of vaccines,” and “shall make or assure improvements in ... the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, ... and research on vaccines in order to reduce the risks of adverse reactions to vaccines.”⁹

Since passage of the 1986 Act, the number of required pediatric vaccines has grown rapidly. In 1983, the CDC’s childhood vaccine schedule included 11 injections of 4 vaccines.¹⁰ As of 2017, the CDC’s childhood vaccine schedule includes 56 injections of 30 different vaccines.¹¹

² <https://www.nap.edu/read/2138/chapter/2#2>

³ 42 U.S.C. § 300aa-1 et seq.

⁴ Ibid.

⁵ 42 U.S.C. § 300aa-11

⁶ *Bruesewitz v. Wyeth LLC*, 562 U.S. 223 (2011)

⁷ Ibid.

⁸ 42 U.S.C. § 300aa-2; 42 U.S.C. § 300aa-27

⁹ Ibid.

¹⁰ https://www.cdc.gov/vaccines/schedules/images/schedule_1983s.jpg

¹¹ https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adol_escent.html (note that the influenza vaccine is different every year)

CDC Childhood Immunization Schedule ¹²		
1986	2017	
DTP (2 months)	Influenza (pregnancy)	Influenza (18 months)
Polio (2 months)	TDaP (pregnancy)	Influenza (2 years)
DTP (4 months)	Hepatitis B (one day)	Influenza (3 years)
Polio (4 months)	Hepatitis B (one month)	Influenza (4 years)
DTP (6 months)	DTaP (2 months)	DTaP (4 years)
MMR (15 months)	Polio (2 months)	Polio (4 years)
DTP (18 months)	Hib (2 months)	MMR (4 years)
Polio (18 months)	PCV (2 months)	Varicella (4 years)
DTP (4 years)	Rotavirus (2 months)	Influenza (5 years)
Polio (4 years)	DTaP (4 months)	Influenza (6 years)
Tetanus (14 years)	Polio (4 months)	Influenza (7 years)
	Hib (4 months)	Influenza (8 years)
	PCV (4 months)	Influenza (9 years)
	Rotavirus (4 months)	Influenza (10 years)
	DTaP (6 months)	HPV (11 years)
	Polio (6 months)	Men (11 years)
	Hepatitis B (6 months)	TDaP (11 years)
	Hib (6 months)	Influenza (11 years)
	PCV (6 months)	HPV (11 ½ years)
	Rotavirus (6 months)	Influenza (12 years)
	Influenza (6 months)	HPV (12 years)
	MMR (12 months)	Influenza (13 years)
	Varicella (12 months)	Influenza (14 years)
	Hib (12 months)	Influenza (15 years)
	Hepatitis A (12 months)	Men (16 years)
	PCV (12 months)	Influenza (16 years)
	DTaP (15 months)	Influenza (17 years)
	Hepatitis A (18 months)	Influenza (18 years)

It is only when the CDC adds a vaccine to its recommended vaccine schedule that the manufacturer is granted immunity from

liability for vaccine injuries. And due to a federal funding scheme, CDC recommended vaccines are then made compulsory to American children under state laws and subsidized by the Federal government for children unable to afford the vaccine.¹³

The end result is that under the 1986 Act, every pediatric vaccine recommended by the CDC creates for its manufacturer a liability-free captive market of 78 million children with guaranteed payment. This incentive structure is unequal in the marketplace and eliminates the normal market forces driving product safety. Hence the 1986 Act transferred essentially all responsibility for vaccine safety from the pharmaceutical companies to HHS.

II. Pre-Licensure Vaccine Safety Review

HHS, through the FDA, licenses all vaccines used by the American public.

All non-vaccine drugs licensed by the FDA undergo long-term multi-year double-blind safety studies during which the rate of adverse reactions in the group receiving the drug under review is compared to the rate of adverse reactions in a group receiving an inert placebo, such as a sugar pill or saline injection.

For example: Enbrel’s pre-licensure trials followed subjects up to 80 months and

controls received a saline injection.¹⁴ Lipitor’s pre-licensure trials lasted a median of 4.8 years and controls received a sugar pill.¹⁵ Botox’s pre-licensure trials lasted a median of 51 weeks and controls received a saline injection.¹⁶ And even with these long-term studies, drugs are still often recalled.

While most drugs, like the ones above, are given to sick adults, pediatric vaccines are typically given universally to babies and toddlers. And while pharmaceutical companies remain liable for injuries caused by their

¹² The rapid growth of CDC’s vaccine schedule is expected to accelerate since there were 271 new vaccines under development in 2013 and far more currently under development. <http://www.phrma.org/press-release/medicines-in-development-vaccines> (listing 2,300 trials in search for “vaccines” between 2013 and 2017)

¹³ See Section IV below.

¹⁴ https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103795s5503lbl.pdf

¹⁵ https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020702s0561lbl.pdf

¹⁶ https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103000s5302lbl.pdf

non-vaccine drugs, as discussed above, they have no liability for injuries caused by their vaccines. One would therefore expect that pre-licensure safety testing for vaccines would be more rigorous than that conducted for drugs.

Unfortunately, unlike all non-vaccine drugs licensed by the FDA, vaccines are *not* required to undergo long-term double-blind inert-placebo controlled trials to assess safety. In fact, not a single one of the clinical trials for vaccines given to babies and toddlers had a control group receiving an inert placebo. Further, most pediatric vaccines currently on the market have been approved based on studies with inadequate follow-up periods of only a few days or weeks.

For example, there are two Hepatitis B vaccines licensed for one day old babies in the United States – one manufactured by Merck and the other by GlaxoSmithKline. Merck's Hepatitis B vaccine was licensed by the FDA after trials which solicited adverse reactions for *only five days* after vaccination.¹⁷ Similarly, GlaxoSmithKline's Hepatitis B vaccine was licensed by the FDA after trials which solicited adverse reactions for *only four days* after vaccination.¹⁸

Follow-up periods of 4 or 5 days are not nearly long enough to detect possible adverse effects such as autoimmune or neurological disorders, seizures, or death. Worse is that since neither of these clinical trials used a control group, it was impossible to scientifically determine if any adverse

reaction in the limited four or five day safety review period was even caused by the Hepatitis B vaccine being evaluated.

Similarly, the HiB vaccines manufactured by Merck and GlaxoSmithKline were licensed by the FDA based on trials in which adverse reactions were monitored for only three days and four days, respectively, after vaccination.¹⁹ The only stand-alone polio vaccine in the United States was licensed after a mere 48-hour follow-up period.²⁰

Even more amazing is that unlike every drug licensed by the FDA, the control groups in these vaccine trials did not receive an inert placebo.²¹ Rather, the control group was given one or more previously licensed vaccines as the "placebo."²² This means each new vaccine need only be roughly as safe as one (or in some cases numerous) previously licensed vaccines. Such flawed and unscientific study designs cannot establish the actual safety profile of any vaccine. The real adverse event rate for a vaccine can only be determined by comparing subjects receiving the vaccine with those receiving an inert placebo. Yet, this study design, required for every drug, is never required before or after licensing a vaccine.

It is unacceptable that the FDA licensing process for vaccines fails to assess the safety profile of each vaccine. It is also unacceptable that the FDA does not require the use of inert placebo controls to assure the integrity of even the minimal safety review conducted. As HHS's own paid experts, the

¹⁷ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110114.pdf>

¹⁸ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224503.pdf>

¹⁹ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM253652.pdf>

<https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM179530.pdf>

²⁰ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM133479.pdf>

²¹ Ibid. (prior two footnotes)

²² Ibid.

IOM, explains: “Because [vaccine] trials are primarily ... for determination of efficacy,

conclusions about vaccine safety derived from these trials are limited.”²³

III. Post-Licensure Surveillance of Vaccine Safety & the Known and Unknown Risks of Vaccination

HHS also fails to conduct proper post-licensure monitoring and studies of vaccine safety.

1. CDC Blocks Automation of Vaccine Adverse Events Reporting

The paucity of pre-licensure safety reviews for vaccines (see discussion above) leaves the assessment of adverse reactions to the post-licensing period when they are being administered to children in the “real world.”

In order to capture adverse events that may arise from vaccination in the “real world,” the 1986 Act established the Vaccine Adverse Events Reporting System (VAERS) operated by HHS and co-sponsored by the CDC and FDA.²⁴ VAERS is a passive, not mandatory, reporting system.²⁵ Anyone, including health care providers, on a voluntary basis, may report adverse vaccine reactions to VAERS.²⁶ HHS compiles these adverse reaction reports in VAERS and the CDC uses VAERS as a “safety signal detection and hypothesis generating system” to identify potential injuries caused by vaccines.²⁷

In 2016, VAERS received 59,117 reports of adverse reactions following vaccination including 432 deaths, 1,091 permanent disabilities, 4,132 hospitalizations, and 10,284 emergency room visits.²⁸

A problem with VAERS is that it is a passive reporting system, relying on voluntary, rather than mandatory, reporting.²⁹ As such, numerous reviews of VAERS have found that only a tiny fraction of vaccine adverse events are reported. For example, an HHS-funded review of vaccine adverse events over a three-year period by Harvard Medical School involving 715,000 patients found that “fewer than 1% of vaccine adverse events are reported.”³⁰ A U.S. House Report similarly stated: “Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events.”³¹

Assuming VAERS captures 1 percent of adverse events (which is more than is estimated), then the number of adverse events reported to VAERS in 2016 would reflect for that year 5,911,700 adverse events, 43,200 deaths, 109,100 permanent disabilities, 413,200 hospitalizations, and 1,028,400 emergency

²³ <https://www.nap.edu/read/13563/chapter/4>

²⁴ <https://wonder.cdc.gov/vaers.html>

²⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

²⁶ Ibid.

²⁷ Ibid.

²⁸ <https://wonder.cdc.gov/vaers.html>

²⁹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

³⁰ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

³¹ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

room visits. If accurate, these figures are very troubling.

Of course, these figures are merely estimates. It would be far better if adverse events reports were automatically created and submitted to VAERS to avoid the issue of underreporting. Automated reporting would provide invaluable information that could clarify which vaccines might cause which harms and to whom, potentially allowing us to avoid these injuries and deaths.

The idea of automating adverse event reporting to VAERS is not new or even difficult to achieve.³² The Agency for Healthcare Research and Quality, an agency within HHS, sought to do exactly that in 2007 when it provided an approximately \$1 million grant to automate VAERS reporting at Harvard Pilgrim Health Care.³³ The result was the successful automation of adverse event reports at Harvard Pilgrim:

*Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions ... were identified.*³⁴

These results should have been startling to HHS since they show that over only a three-year period, there were 35,570 reportable reactions in just 376,452 vaccine recipients. Given HHS's statutory mandate to assure safer vaccines, it should have rushed forward with automating VAERS reporting. However, this is not what happened.

³² <https://healthit.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system>

³³ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

³⁴ Ibid.

After automating adverse event reports at Harvard Pilgrim, the developers of this system asked the CDC to take the final step of linking VAERS with the Harvard Pilgrim system so that these reports could be automatically transmitted into VAERS. Instead, the CDC refused to cooperate. As the Harvard grant recipients explained:

*Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.*³⁵

After three years and spending \$1 million of taxpayers' money, the CDC refused to even communicate with the HHS' Harvard Medical School grant recipients.

While HHS generally strongly supports automating public health surveillance systems, when it comes to vaccine safety, the CDC has only supported projects that would limit VAERS to passive surveillance.³⁶ Automation would improve safety and address many of the long-standing issues and limitations raised by CDC regarding VAERS.³⁷

Capturing "fewer than 1% of vaccine adverse events" thirty years after the passage of the 1986 Act is unacceptable – and potentially deadly.

³⁵ Ibid.

³⁶ [http://www.ajpmonline.org/article/S0749-3797\(12\)00249-8/pdf](http://www.ajpmonline.org/article/S0749-3797(12)00249-8/pdf); <https://www.ncbi.nlm.nih.gov/pubmed/26209838>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

³⁷ Ibid.

2. CDC Ignores IOM's Calls to Identify Injuries Caused by Vaccines

The IOM was formed in 1863 by congressional charter, to “provide expert advice on some of the most pressing challenges facing the nation and the world.”³⁸ The IOM further claims its “members are among the world's most distinguished scientists, engineers, physicians, and researchers; more than 300 members are Nobel laureates.”³⁹

Under the 1986 Act, the IOM was charged with issuing reports on injuries from vaccination. In 1991, the IOM examined 22 commonly reported serious injuries following the DTP vaccine.⁴⁰ The IOM concluded the scientific literature supported a causal relationship between the DTP vaccine and 6 of these injuries: acute encephalopathy, chronic arthritis, acute arthritis, shock and unusual shock-like state, anaphylaxis, and protracted inconsolable crying.⁴¹

While this picture was troubling enough, equally concerning was that the IOM found that the scientific literature was insufficient to conclude whether or not the DTP vaccine can cause 12 other serious injuries commonly reported from this vaccine:

Aseptic meningitis (serious inflammation of the brain); Chronic neurologic damage; Learning disabilities and attention-deficit disorder; Hemolytic anemia; Juvenile diabetes; Guillain-Barre syndrome;

*Erythema multiforme; Autism; Peripheral mononeuropathy (nerve damage); Radiculoneuritis and other neuropathies; Thrombocytopenia; Thrombocytopenic purpura*⁴²

These commonly reported serious injuries *could* be caused by this vaccine – the IOM just couldn't determine one way or another due to a lack of science.

The IOM lamented that it “encountered many gaps and limitations in knowledge bearing directly and indirectly on the safety of vaccines.”⁴³ The IOM also remarked on the poor design of the few vaccine studies that had been conducted, stating these “studies are too small or have inadequate length of follow-up to have a reasonable chance of detecting true adverse reactions.”⁴⁴ Moreover, the IOM reported that “existing surveillance systems of vaccine injury have limited capacity to provide persuasive evidence of causation.”⁴⁵

The IOM thus cautioned in its 1991 report that: “If research capacity and accomplishment in this field are not improved, future reviews of vaccine safety will be similarly handicapped.”⁴⁶

As charged under the 1986 Act, the IOM issued another report in 1994 entitled *Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causation*.⁴⁷ This second IOM Report examined the scientific literature for evidence that could either prove or disprove a causal link between 54

³⁸ <http://www.national-academies.org/about/whoweare/index.html>

³⁹ Ibid.

⁴⁰ <https://www.nap.edu/read/1815/chapter/2#7>

⁴¹ Ibid.

⁴² Ibid.

⁴³ <https://www.nap.edu/read/1815/chapter/2#8>

⁴⁴ <https://www.nap.edu/read/1815/chapter/9>

⁴⁵ Ibid.

⁴⁶ Ibid.

⁴⁷ <https://www.nap.edu/read/2138/chapter/1>

commonly reported serious injuries and vaccination for diphtheria, tetanus, measles, mumps, polio, hepatitis B, and Hib.⁴⁸

For this Report, the IOM located sufficient science to support a causal connection between these vaccines and 12 injuries, including death, anaphylaxis, thrombocytopenia, and Guillain-Barre syndrome.⁴⁹

Again, as with the IOM Report from 1991, for “the majority of vaccine-adverse event pairs the evidence was considered inadequate to accept or reject causality.”⁵⁰ The problem that basic scientific studies had not been done continued to persist. The IOM could not determine whether there was a causal connection between vaccination and 38 of the most common serious injuries parents reported their children experienced following these vaccines, including:

*Demyelinating diseases of the central nervous system, Sterility, Arthritis, Neuropathy, Residual seizure disorder, Transverse myelitis, Sensorineural deafness, Optic neuritis, Aseptic meningitis, Insulin-dependent diabetes mellitus, SIDS*⁵¹

This means that of the 54 vaccine-injury pairs studied, there was sufficient science to find a causal relationship of harm for 12, and to reject a relationship for 4.⁵² But for the remaining 38, there was insufficient science to reach any conclusion.⁵³

As in 1991, this IOM Report from 1994 again stated: “The lack of adequate data regarding many of the adverse events under study was of major concern to the committee. Presentations at public meeting indicated that many parents and physicians share this concern.”⁵⁴

Another acute concern raised by the IOM in 1994 was the potential risks posed by combining vaccines. The IOM noted that this subject simply had not been studied: “The committee was able to identify little information pertaining to the risk of serious adverse events following administration of multiple vaccines simultaneously. This is an issue of increasing concern as more vaccines and vaccine combinations are developed for routine use.”⁵⁵

In 2011, HHS paid the IOM to conduct another assessment regarding vaccine safety.⁵⁶ This Report, entitled *Adverse Effects of Vaccines: Evidence and Causality*, was the culmination of the largest review by the IOM regarding vaccine safety since the IOM’s reports from 1991 and 1994.⁵⁷

This third IOM Report reviewed the 158 most common vaccine injuries claimed to have occurred from vaccination for varicella, hepatitis B, tetanus, measles, mumps, and/or rubella.⁵⁸ The IOM located science which “convincingly supports a causal relationship” for 14 of these serious injuries, including pneumonia, meningitis, hepatitis, MIBE (deadly brain inflammation a year after vaccination), febrile seizures, and

⁴⁸ <https://www.nap.edu/read/2138/chapter/2#12>

⁴⁹ <https://www.nap.edu/read/2138/chapter/2#12>

⁵⁰ <https://www.nap.edu/read/2138/chapter/1#vi>

⁵¹ <https://www.nap.edu/read/2138/chapter/2#12>

⁵² Ibid.

⁵³ Ibid.

⁵⁴ <https://www.nap.edu/read/2138/chapter/12>

⁵⁵ <https://www.nap.edu/read/2138/chapter/12#307>

⁵⁶ <https://www.nap.edu/read/13164/chapter/2#2>

⁵⁷ Ibid.

⁵⁸ Ibid.

anaphylaxis.⁵⁹ The review found sufficient evidence to support “acceptance of a causal relationship” for 4 additional serious injuries.⁶⁰

The IOM, however, found the scientific literature was insufficient to conclude whether or not those vaccines caused 135 other serious injuries commonly reported after their administration, including:

Encephalitis (brain inflammation), Encephalopathy (gradual degeneration of brain function, including memory, cognitive ability, concentration, lethargy, and eventually consciousness), Infantile Spasms, Afebrile Seizures, Seizures, Cerebellar Ataxia (inflammation of and/or damage to the cerebellum), Ataxia (the loss of full control of bodily movements), Acute Disseminated Encephalomyelitis (brief but widespread attack of inflammation in the brain and spinal cord that damages myelin – the protective covering of nerve fibers), Transverse Myelitis (neurological disorder caused by inflammation across both sides of one level, or segment, of the spinal cord that typically results in permanent impairments), Optic Neuritis (inflammation of the optic nerve and symptoms are usually unilateral, with eye pain and partial or complete vision loss), Neuromyelitis Optica (body’s immune system over time repeatedly mistakenly attacks healthy cells and proteins in the body, most often those in the spinal cord and eyes resulting in permanent disability), Multiple Sclerosis, Guillain-Barre Syndrome (body’s immune system attacks part of the peripheral nervous system), Chronic Inflammatory

Demyelinating Polyneuropathy (auto-immune inflammatory disorder of the peripheral nervous system resulting in loss of nerve axons), Brachial Neuritis (auto-immune reaction against nerve fibers of the brachial plexus), Amyotrophic Lateral Sclerosis (rapidly progressive, invariably fatal neurological disease that attacks the nerve cells responsible for controlling voluntary muscles), Small Fiber Neuropathy (damage to the small unmyelinated peripheral nerve fibers), Chronic Urticaria (chronic hives), Erythema Nodosum (skin inflammation in the fatty layer of skin), Systemic Lupus Erythematosus (autoimmune disease in which the body’s immune system mistakenly attacks healthy tissue), Polyarteritis Nodosa (inflammation resulting in injury to organ systems), Psoriatic Arthritis, Reactive Arthritis, Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Arthralgia (joint pain), Autoimmune Hepatitis, Stroke, Chronic Headache, Fibromyalgia, Sudden Infant Death Syndrome, Hearing Loss, Thrombocytopenia, Immune Thrombocytopenic Purpura⁶¹

Thus, out of the 158 most common serious injuries reported to have been caused by the vaccines under review, the evidence “convincingly supports a causal relationship” for 14, “favors acceptance of a causal relationship” for 4, and “favors rejection of a causal relationship” for only 5 of them.⁶² For the remaining 135 vaccine-injury pairs, over 86 percent of those reviewed, the IOM found

⁵⁹ <https://www.nap.edu/read/13164/chapter/2#3>

⁶⁰ Ibid.

⁶¹ Ibid.

⁶² Ibid.

that the science simply had not been performed.⁶³

3. CDC Ignores IOM's Calls to Identify Children Susceptible to Vaccine Injury

Compounding the lack of adequate science to simply ascertain whether the most commonly reported serious adverse reactions following vaccination are caused by vaccines, the IOM Reports discussed above have consistently acknowledged there is individual susceptibility to serious vaccine injuries.

The IOM has also acknowledged that research on such susceptibility must be done on an individual basis, considering a child's personal genome, behaviors, microbiome, intercurrent illness, and present and past environmental exposure.⁶⁴ Unfortunately, HHS has not conducted this research.

In 1994, the IOM, building on concerns raised in its 1991 Report, stated: "The committee was able to identify little information pertaining to why some individuals react adversely to vaccines when most do not."⁶⁵ The IOM urged that "research should be encouraged to elucidate the factors that put certain people at risk."⁶⁶

Yet, seventeen years later, in 2011, the IOM acknowledged this research had still not been done:

Both epidemiologic and mechanistic research suggest that most individuals who experience an adverse reaction to vaccines

have a preexisting susceptibility. These predispositions can exist for a number of reasons—genetic variants (in human or microbiome DNA), environmental exposures, behaviors, intervening illness, or developmental stage, to name just a few—all of which can interact as suggested graphically in Figure 3-1.

Some of these adverse reactions are specific to the particular vaccine, while others may not be. Some of these predispositions may be detectable prior to the administration of vaccine. ... [M]uch work remains to be done to elucidate and to develop strategies to document the immunologic mechanisms that lead to adverse effects in individual patients.

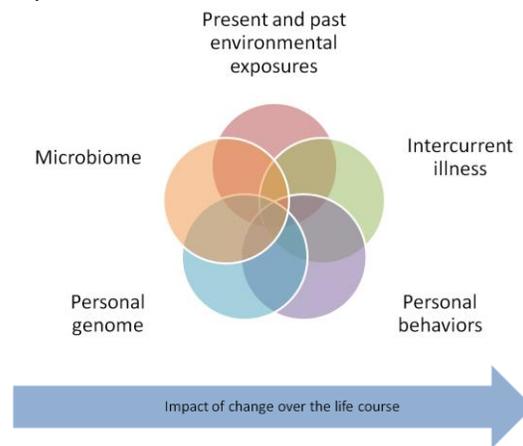


FIGURE 3-1 Present and past environmental exposures.⁶⁷

In 2013, HHS commissioned the IOM to review the safety of the entire vaccine schedule.⁶⁸ The IOM again explained that while "most children who experience an adverse reaction to immunization have preexisting susceptibility," the IOM:

⁶³ Ibid.

⁶⁴ <https://www.nap.edu/read/13164/chapter/5#82>

⁶⁵ <https://www.nap.edu/read/2138/chapter/12#307>. See also <https://www.nap.edu/read/1815/chapter/9>

⁶⁶ Ibid.

⁶⁷ <https://www.nap.edu/read/13164/chapter/5#82>

⁶⁸ <https://www.nap.edu/read/13563/chapter/1>

*found that evidence assessing outcomes in sub populations of children who may be potentially susceptible to adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures and outcomes.*⁶⁹

HHS had failed to even define the terminology for the study of susceptible subpopulations; hence IOM admonished HHS to “develop a framework that clarifies and standardizes definitions of ... populations that are potentially susceptible to adverse events.”⁷⁰ While every vaccine brand is the same, it is plain that every child is different.

The IOM correctly points out in 2011 that given the “widespread use of vaccines” and “state mandates requiring vaccination of children ... it is essential that safety concerns receive assiduous attention.”⁷¹ This is the same call for diligent attention that the IOM made in 1991 and 1994. Unfortunately, all of these calls for action have gone unheeded. The critical scientific inquiry to identify individuals susceptible to serious vaccine injury has simply never commenced.

Since the IOM’s first call for this science in 1991, HHS has spent tens of billions promoting and purchasing vaccines, and

vaccine makers have accumulated hundreds of billions in vaccine revenue.⁷² Yet, during this time, no material funds have been allocated to identify susceptible subpopulations, let alone what injuries are caused by vaccines.⁷³

4. CDC Views Vaccine Safety as a Public Relations Issue

The CDC, unfortunately, has treated vaccine safety as a public relations issue rather than a public health imperative. For example, the CDC claims on its website that “Vaccines Do Not Cause Autism” even though this broad claim is plainly not supported by the scientific literature.⁷⁴

Indeed, as part of the IOM’s 2011 review of vaccine safety, it was asked by HHS whether there is a causal relationship between autism and the DTaP vaccine administered to children at two, four, six, and fifteen months of age.⁷⁵ The IOM could not locate a single study supporting that DTaP does not cause autism.⁷⁶ The IOM therefore concluded: “The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid–, tetanus toxoid–, or acellular pertussis–containing vaccine and autism.”⁷⁷ The IOM’s full explanation for this finding is as follows:

⁶⁹ <https://www.nap.edu/read/13563/chapter/9#130>

⁷⁰ Ibid.

⁷¹ <https://www.nap.edu/read/13164/chapter/3#28>

⁷² <https://www.hhs.gov/about/budget/index.html#previous>; <https://www.statista.com/statistics/265102/revenues-in-the-global-vaccine-market/>; <https://www.ft.com/content/93374f4a-e538-11e5-a09b-1f8b0d268c39>

⁷³ For example, while in 2016 vaccine makers reported over \$33 billion from vaccine sales and the CDC reported spending over

\$5 billion promoting and purchasing vaccines (Ibid.), the CDC Immunization Safety Office’s budget is apparently only around \$20 million. [http://www.ajpmonline.org/article/S0749-3797\(15\)00314-1/pdf](http://www.ajpmonline.org/article/S0749-3797(15)00314-1/pdf)

⁷⁴ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁷⁵ <https://www.nap.edu/read/13164/chapter/2#2>

⁷⁶ <https://www.nap.edu/read/13164/chapter/12#545>

⁷⁷ Ibid.

AUTISM

Epidemiologic Evidence

The committee reviewed one study to evaluate the risk of autism after the administration of DTaP vaccine. This one study (Geier and Geier, 2004) was not considered in the weight of epidemiologic evidence because it provided data from a passive surveillance system and lacked an unvaccinated comparison population.

Weight of Epidemiologic Evidence

The epidemiologic evidence is insufficient or absent to assess an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.

Mechanistic Evidence

The committee did not identify literature reporting clinical, diagnostic, or experimental evidence of autism after the administration of vaccines containing diphtheria toxoid, tetanus toxoid, and acellular pertussis antigens alone or in combination.

Weight of Mechanistic Evidence

The committee assesses the mechanistic evidence regarding an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism as lacking.

Causality Conclusion

Conclusion 10.6: The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.⁷⁸

It is troubling that the only study the IOM could locate regarding whether DTaP causes autism, (Geier and Geier, 2004), concluded there *was* an association between DTaP and autism.⁷⁹ No research has been published since 2011 that could change the IOM's conclusion. Based on the foregoing, the CDC cannot validly make the blanket assertion that "Vaccines Do Not Cause Autism."

As with DTaP, there are also no published studies showing that autism is not caused by Hepatitis B, Rotavirus, Hib, Pneumococcal, Inactivated Poliovirus, Influenza, Varicella, or Hepatitis A vaccines – all of which HHS recommends babies receive by one year of age.⁸⁰

Instead, HHS's claim that "Vaccines Do Not Cause Autism" relies almost entirely upon studies exclusively studying only one vaccine, MMR (which is administered no earlier than one year of age), or only one vaccine ingredient, thimerosal, with regard to autism.⁸¹ Putting aside the controversy surrounding these studies, studies which focus on only one vaccine and one ingredient while ignoring the entire balance of the CDC's pediatric vaccine schedule cannot support the

⁷⁸ Ibid.

⁷⁹ Ibid. Ironically, this study was disregarded "because it provided data from a passive surveillance system [VAERS] and lacked an unvaccinated comparison population," which would be true of any study using VAERS data.

⁸⁰ <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>

⁸¹ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

CDC's overarching declaration that "Vaccines Do Not Cause Autism."

As for the MMR vaccine, the CDC's senior scientist for its seminal MMR-autism study has recently revealed that the CDC concealed an association between MMR and autism. Dr. William Thompson has been a scientist at CDC for nearly two decades and is the CDC's Senior Scientist on dozens of the CDC's peer-reviewed publications, including the core group of the CDC's vaccine-autism safety studies.⁸²

Dr. Thompson recently provided a statement through his attorney that the CDC "omitted statistically significant information" showing an association between the MMR vaccine and autism in the first and only MMR-autism study ever conducted by the CDC with American children.⁸³

Dr. Thompson, in a recorded phone call in 2014, described how the CDC concealed a finding indicating that healthy children who received the MMR vaccine may be eight times more likely to develop autism than those without the vaccine.⁸⁴ He stated: "Oh my God, I can't believe we did what we did. But we did. It's all there. It's all there. I have handwritten notes."⁸⁵ Dr. Thompson stated that "If I were forced to testify or something like that, I'm not gonna lie ... I basically have stopped lying."⁸⁶ Expressing contrition for concealing the MMR-autism association, Dr. Thompson stated:

I have great shame now when I meet families with kids with autism because I

have been part of the problem ... the CDC is so paralyzed right now by anything related to autism. They're not doing what they should be doing because they're afraid to look for things that might be associated. So anyway there's still a lot of shame with that. ... I am completely ashamed of what I did.⁸⁷

Dr. Thompson also provided the following statement explaining the CDC's concealment of the autism-MMR association with regard to African-American males:

My primary job duties while working in the immunization safety branch from 2000 to 2006, were to later co-lead three major vaccine safety studies. ... We hypothesized that if we found statistically significant effects at either 18 or 36 month thresholds, we would conclude that vaccinating children early with MMR vaccine could lead to autism-like characteristics or features. We all met and finalized the study protocol and analysis plan ... [and after implementing this plan we found] the adjusted race effect statistical significance was huge.

All the authors and I [therefore] met and decided ... to exclude reporting any race effects. The co-authors scheduled a meeting to destroy documents related to the study. The remaining four co-authors all met and brought a big garbage can into the meeting room, and reviewed and went through all the hardcopy documents that we had thought we should discard, and put them into a huge garbage can. However,

⁸² <https://www.ncbi.nlm.nih.gov/pubmed/?term=Thompson+WW%5BAuthor%5D>

⁸³ <http://www.rescuepost.com/files/william-thompson-statement-27-august-2014-3.pdf>

⁸⁴ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

⁸⁵ Ibid.

⁸⁶ Ibid.

⁸⁷ Ibid.

*because I assumed it was illegal and would violate both FOIA and DOJ requests, I kept hardcopies of all documents in my office, and I retain all associated computer files. I believe we intentionally withheld controversial findings from the final draft of the Pediatrics paper.*⁸⁸

Hence, for the only vaccine (MMR) actually studied by the CDC with regard to autism, it appears the CDC concealed an association between that vaccine and autism.

When the former Director of the National Institutes of Health, Dr. Bernadine Healy, was asked about whether public health authorities are correct to claim that vaccines do not cause autism, she answered: “You can’t say that.”⁸⁹ When asked again, Dr. Healy explained: “The more you delve into it – if you look at the basic science – if you look at the research that’s been done, in animals – if you also look at some of these individual cases – and, if you look at the evidence that there is no link - what I come away with is: *The question has not been answered.*”⁹⁰

Former NIH Director Dr. Healy goes on to explain:

This is the time when we do have the opportunity to understand whether or not there are susceptible children, perhaps genetically, perhaps they have a metabolic issue, mitochondrial disorder, immunological issue, that makes them more susceptible to vaccines plural, or to one particular vaccine, or to a component of vaccine. ... A susceptible group does not

mean that vaccines are not good. What a susceptible group will tell us is that maybe there is a group of individuals, or a group of children, that shouldn’t have a particular vaccine or shouldn’t have vaccine on the same schedule. ...

I think the government, or certain health officials in the government, are - have been too quick to dismiss the concerns of these families without studying the population that got sick. I haven’t seen major studies that focus on - three hundred kids, who got autistic symptoms within a period of a few weeks of a vaccine.

I think that the public health officials have been too quick to dismiss the hypothesis as irrational, without sufficient studies of causation. I think that they often have been too quick to dismiss studies in the animal laboratory, either in mice, in primates, that do show some concerns with regard to certain vaccines. ...

*The reason why they didn’t want to look for those susceptibility groups was because they’re afraid if they found them – however big or small they were – that that would scare the public away. First of all, I think the public’s smarter than that; the public values vaccines. But, more importantly, I don’t think you should ever turn your back on any scientific hypothesis because you’re afraid of what it might show!*⁹¹

The CDC’s claim that “Vaccines Do Not Cause Autism” also fails to address the

⁸⁸ <https://www.c-span.org/video/?c4546453/senator-posey-calls-investigation-cdc-fraud>

⁸⁹ <http://www.cbsnews.com/news/the-open-question-on-vaccines-and-autism/>

⁹⁰ Ibid.

⁹¹ Ibid.

science supporting a link between vaccines and autism.⁹² For example, the CDC has not addressed a study which found a 300% increased rate of autism among newborns receiving the hepatitis B vaccine at birth compared to those that did not.⁹³ Nor a recent and first ever vaccinated vs. unvaccinated pilot study which found vaccinated children had a 420% increased rate of autism and that vaccinated preterm babies had an even higher rate of autism.⁹⁴ There is also a persuasive body of science supporting a connection between aluminum adjuvants in vaccines and autism which the CDC has, despite request, failed to directly or persuasively address.⁹⁵

The CDC also failed to address the fact that a review of vaccine injuries compensated by HHS, through the vaccine injury compensation program established by the 1986 Act, “found eighty-three cases of autism among those compensated for vaccine-induced brain damage.”⁹⁶

The CDC ignores all the foregoing and continues to rely on its prior MMR-autism studies which, even putting aside Dr. Thompson’s claims of concealment, are not applicable to any of the 25 doses of seven vaccines the CDC advised doctors to inject into babies during the first year of life.⁹⁷

The critical need for the CDC to properly engage in vaccine safety science regarding autism is made even more vital by the fact that vaccine makers are immune from liability for vaccine injury and vaccines are not

safety-tested prior to licensure to assess whether they cause autism. Without proper *long-term* safety studies comparing those receiving the vaccine to a true placebo group, it is impossible to know prior to licensure whether these products cause autism. There are also no follow-up studies which compare vaccinated to unvaccinated individuals and hence no supportable basis to claim that vaccines do not cause any cases of autism. For the CDC to make this claim, it must demonstrate that a child receiving the entire vaccine schedule is at no greater risk of becoming autistic than a child that is unvaccinated. No such study has ever been done.

The IOM Report referenced above has confirmed that the CDC cannot make this claim even for children receiving only the DTaP, let alone the entire vaccine schedule. It is thus plain that the CDC cannot validly claim that “Vaccines Do Not Cause Autism.” The truth is, the CDC, at best, does not know.

5. CDC & IOM Ignore Massive Body of Science Supporting Vaccine Injuries

While the 2011 IOM Report has 75 pages of citations to peer-reviewed sources, there are far more peer-reviewed articles documenting vaccine injuries apparently not even considered by the 2011 IOM Report. Resources for references to these citations can be provided upon request.

⁹² <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁹³ http://hisunim.org.il/images/documents/scientific_literature/Gallagher_Goodman_HepB_2010.pdf

⁹⁴ http://www.cmsri.org/wp-content/uploads/2017/05/Mawson_StudyHealthOutcomes5.8.2017.pdf

⁹⁵ http://vaccine-safety.s3.amazonaws.com/WhitePaper-Alum_AdjuvantAutism.pdf

⁹⁶ <http://digitalcommons.pace.edu/cgi/viewcontent.cgi?article=1681&context=peir>

⁹⁷ Further, studies of MMR and autism are simply erroneous because of healthy user bias, which has been emphasized as a serious source of error in epidemiological vaccine safety studies by the CDC’s own scientists. <https://www.ncbi.nlm.nih.gov/pubmed/1415136>

A major theme among these peer-reviewed vaccine papers is the connection between vaccination and chronic disease, mainly autoimmunity and immune mediated neurological disorders and injuries. As detailed above, in the last 30 years, the CDC's childhood vaccine schedule has rapidly increased from 11 injections of 4 vaccines in 1986 to 56 injections of 30 vaccines in 2017. This upsurge has occurred in lock step with the precipitous increase in childhood chronic illness and developmental disabilities which have, during this same period, risen among American children from 12.8% to 54%.⁹⁸

Many of the same disorders that have sharply risen during this period, including neurological and autoimmune disorders, are associated with vaccination as reflected in VAERS⁹⁹, manufacturer inserts for vaccines¹⁰⁰, and claims in the Vaccine Injury Compensation Program¹⁰¹.

The causal mechanisms of these disorders are increasingly understood, and increasingly implicate vaccine exposure during early development.¹⁰² For example, it is now known that early life immune activation can cause autism, mental illnesses, and immune disorders.¹⁰³ Vaccines and vaccine adjuvants (particularly in cases of adverse reactions) can cause the types of immune activation known to cause these disorders later in life.¹⁰⁴ Accordingly, there is an urgent and long-overdue need for higher quality vaccine safety research looking at long term neurological and immune outcomes.

Nonetheless, the 2011 IOM Report makes it clear that little has been ruled out with regard to what injures are caused by vaccines. In 2013, the IOM was again engaged by HHS to review the safety of the entire vaccine schedule on a population level.¹⁰⁵ The "committee's literature searches and review were intended to identify health outcomes associated with some aspect of the childhood immunization schedule."¹⁰⁶ "Allergy and asthma, autoimmunity, autism, other neurodevelopmental disorders (e.g., learning disabilities, tics, behavioral disorders, and intellectual disability), seizures, and epilepsy were included as search terms."¹⁰⁷

Instead of answers, the IOM found that no studies had been conducted to validly assess the safety of the entire vaccine schedule or even portions of the vaccine schedule:

[F]ew studies have comprehensively assessed the association between the entire immunization schedule or variations in the overall schedule and categories of health outcomes, and no study ... compared the differences in health outcomes ... between entirely unimmunized populations of children and fully immunized children. Experts who addressed the committee pointed not to a body of evidence that had been overlooked but rather to the fact that existing research has not been designed to test the entire immunization schedule. ...

⁹⁸ <https://www.ncbi.nlm.nih.gov/pubmed/20159870>

⁹⁹ <https://wonder.cdc.gov/vaers.html>

¹⁰⁰ <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm>; See also Section III(7) below.

¹⁰¹ <http://www.usfc.uscourts.gov/aggregator/sources/7>; See also Section IV(4) below.

¹⁰² <https://www.ncbi.nlm.nih.gov/pubmed/27540164>

¹⁰³ <https://www.ncbi.nlm.nih.gov/pubmed/25311587>

¹⁰⁴ <https://www.ncbi.nlm.nih.gov/pubmed/26531688>;

<https://www.ncbi.nlm.nih.gov/pubmed/27908630>

¹⁰⁵ <https://www.nap.edu/read/13563/chapter/1>

¹⁰⁶ <https://www.nap.edu/read/13563/chapter/2#5>

¹⁰⁷ Ibid.

*[Also,] studies designed to examine the long-term effects of the cumulative number of vaccines or other aspects of the immunization schedule have not been conducted.*¹⁰⁸

While most of the 78 million children in America follow the CDC's childhood vaccine schedule, currently at 56 injections, no science has been done to confirm the safety of this schedule.¹⁰⁹ Even more alarming is that the IOM acknowledges that science does not yet even know "if there is a relationship between short-term adverse events following vaccination and long-term health issues."¹¹⁰

Due to the lack of science regarding the safety of the CDC vaccine schedule, the best the IOM could do was conclude: "There is no evidence that the schedule is not safe."¹¹¹ Left unsaid, but equally true: There is no evidence that the schedule is safe.

6. CDC Refuses to Conduct Vaccinated vs. Unvaccinated Study

The best and most efficient way to answer a large portion of the questions raised regarding vaccine safety would be a long-term, properly powered (*i.e.*, sized) study comparing the overall health outcomes of vaccinated and completely unvaccinated children. Parents and safety advocacy groups

have been demanding for decades that HHS perform such a study. Even the CDC's internal vaccine committee recognizes that assessing "adverse events require more detailed epidemiologic studies to compare the incidence of the event among vaccinees to the incidence among unvaccinated persons."¹¹²

HHS has nonetheless consistently refused to study health outcomes of the completely unvaccinated. There have been, however, small-scale studies performed outside of HHS comparing vaccinated with completely unvaccinated children. And these smaller studies have consistently reported that the unvaccinated have much better health outcomes.

Dr. Peter Aaby is renowned for studying and promoting vaccines in Africa with over 300 published studies.¹¹³ In 2017, he published a study finding children vaccinated with DTP were 10 times more likely to die in the first 6 months of life than the unvaccinated.¹¹⁴ Dr. Aaby's study therefore concluded that: "All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis."¹¹⁵ More disturbing is that children vaccinated with DTP were dying from causes never associated with this vaccine, such as respiratory infections, diarrhea, and malaria.¹¹⁶ This indicated that while DTP

increasingly recognized problem in vaccine safety studies is that subjects are typically not well-matched. People with pre-existing health problems are reluctant to receive a vaccine, and are therefore unwittingly used as controls. When this happens, the control group is sicker than the vaccine-exposed group at the outset of the study. Studies with this problem give wrong results, and make the vaccine look much safer than it really is. Dr. Aaby's study was one of the few specifically designed to avoid this error.

¹⁰⁸ Ibid.

¹⁰⁹ Ibid.

¹¹⁰ <https://www.nap.edu/read/13563/chapter/5#45>

¹¹¹ <https://www.nap.edu/read/13563/chapter/2#12>

¹¹² <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm>

¹¹³ <https://www.ncbi.nlm.nih.gov/pubmed/?term=PETER+AABY%5BAuthor+-+Full%5D>

¹¹⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/>

Dr. Aaby's study was more reliable than other vaccine safety studies because the subjects were accurately matched. An

¹¹⁵ Ibid.

¹¹⁶ Ibid.

reduced the incidence of diphtheria, tetanus, and pertussis, it increased susceptibility to other infections.¹¹⁷

It is equally troubling that Dr. Aaby's study was based on data that had been collecting dust for over 30 years.¹¹⁸ This begs the question: what other serious vaccine injuries are we missing because of neglect to conduct proper vaccine safety science?

A pilot study comparing 650 vaccinated and unvaccinated homeschooled children in the United States provides a glimpse of the potential scope of vaccine harm.¹¹⁹ The study found that, compared to completely-unvaccinated children, fully-vaccinated children had an increased risk of 390% for allergies, 420% for ADHD, 420% for autism, 290% for eczema, 520% for learning disabilities, and 370% for any neuro-developmental delay.¹²⁰ Fully-vaccinated pre-term infants had an increased risk of 1,450% for a neurodevelopmental disorder, which includes a learning disability, ADHD or autism, compared to completely unvaccinated preterm infants.¹²¹

Another recent study compared children receiving the flu shot with those receiving a saline injection in a prospective randomized double-blind study.¹²² Both groups had the same rate of influenza but the group receiving the flu shot had a 440% increased rate of non-influenza infection.¹²³

Like the DTP study, the flu vaccine increased susceptibility to other infections.

As a final example, the CDC in 2001 unwittingly conducted a narrow vaccinated versus unvaccinated study comparing children receiving the Hepatitis B vaccine during the first month of life versus those who did not.¹²⁴ The results of this study were never released by the CDC, and an abstract of the study was only recently obtained under a FOIA request.¹²⁵ Children vaccinated with Hepatitis B vaccine in the first month of life, compared to children receiving no vaccines in the first month of life, had an increased risk of 829% for ADHD, 762% for autism, 638% for ADD, 565% for tics, 498% for sleep disorders, and 206% for speech delays.¹²⁶

The foregoing limited studies should have raised alarm bells at the CDC regarding the urgency of a proper vaccinated versus unvaccinated study that stakeholders have been demanding the CDC perform for over 20 years. The IOM has even confirmed such a study can be conducted using the CDC's VSD, a database of health records for almost ten million individuals maintained by the CDC.¹²⁷ As explained by the IOM: "It is possible to make this comparison [between vaccinated and unvaccinated children] through analyses of patient information contained in large databases such as VSD."¹²⁸ Such a retrospective epidemiological study would be quick, cheap and efficient; CDC could literally

¹¹⁷ Ibid.

¹¹⁸ Ibid.

¹¹⁹ <http://www.oatext.com/pdf/JTS-3-186.pdf>

¹²⁰ Ibid.

¹²¹ <http://www.oatext.com/pdf/JTS-3-187.pdf>

¹²² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/>

¹²³ Ibid.

¹²⁴ http://vaccine-safety.s3.amazonaws.com/CDC_FOIA_Response_UnpublishedStudy.pdf The CDC's study abstract discusses comparing thimerosal exposure by one month of age.

Since the only vaccine recommended by one month of age was Hepatitis B, and since only thimerosal containing Hepatitis B vaccine was available at the time of this study, this study primarily compared children receiving Hepatitis B with children that did not receive this vaccine.

¹²⁵ Ibid.

¹²⁶ Ibid.

¹²⁷ <https://www.nap.edu/read/13563/chapter/2#13>

¹²⁸ Ibid.

conduct this study using the VSD in a matter of minutes. Yet it has never, as far as the public knows, been done.¹²⁹

Every year tens of millions of American children are compelled to receive pediatric vaccines. Yet a large-scale study with completely-unvaccinated controls has never been performed to assess the long-term safety of the CDC's recommended vaccine schedule.¹³⁰ When vaccine makers are generating over \$33 billion in vaccine revenue annually and the CDC is spending over \$5 billion annually to promote and purchase vaccines, there is no justification for not performing this study.¹³¹

7. CDC Ignores Vaccine Manufacturer Disclosures of Potential Adverse Reactions

Vaccine makers are required by law to report to the FDA complaints they receive from consumers of serious adverse reactions from their vaccines.¹³² A partial list of these serious adverse reactions is detailed below. While studies have been conducted for a few of these to confirm whether they are in fact caused by vaccines, the CDC has failed to conduct such studies for most of them.

Meningitis (acute inflammation of protective membranes covering the brain and spinal cord); Thrombocytopenia (low blood platelet count which can result from autoimmune action); Stevens-Johnson's Syndrome (severe autoimmune reaction in which the top layer of skin is burned off and dies); Alopecia Areata (autoimmune skin disease resulting in the loss of hair on the scalp and elsewhere on the body); Arthritis (painful and disabling autoimmune disease that includes joint pain, swelling and progressive stiffness in the fingers, arms, legs and wrists); Rhinitis (irritation and inflammation of nasal mucous membranes impacting ability to breathe properly); Insomnia; Lupus Erythematosus (autoimmune disease in which immune system attacks healthy tissue, including skin, joint, kidney, brain, and other organs); Hypotension (abnormally low blood pressure); Guillian-Barre Syndrome (autoimmune disease that attacks the nerves in the legs, upper body, arms and/or face); Polyarteritis Nodosa (systemic vasculitis that affect medium-sized and small muscular arteries resulting in ruptures and other damage); Encephalitis (inflammation of the brain, which can result in permanent injury); Bell's Palsy (disfiguring paralysis or weakness on one side of the face); Radiculopathy (compressed or pinched nerve); Myelitis (inflammation of spinal cord that can involve nerve pain, paralysis and incontinence); Multiple Sclerosis (immune system attacks nerve fibers, causing them to deteriorate); Optic Neuritis (inflammation

¹²⁹ The CDC's inaction does not appear to be mere neglect since CDC Senior Scientist, Dr. Thompson, recently stated that a proper large scale vaccine safety study "needs to be done" but that the CDC is "not doing what they should be doing because they're afraid to look for things that might be associated." <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio> Dr. Thompson even explained that they have the data to conduct such a study and that "we're insane to be sitting on this data and not have an independent group" conduct this study but that it will not happen because "they don't really want people to know that this data exists." Ibid.

¹³⁰ In fact, due to the CDC's refusal to act, bills have been proposed in Congress to require such a study, but, the political clout for passage could not be mustered. See, e.g., H.R. 1757 (2013) and H.R. 1636 (2015) ("to conduct or support a comprehensive study comparing total health outcomes ... in vaccinated populations in the United States with such outcomes in unvaccinated populations in the United States").

¹³¹ <https://www.hhs.gov/sites/default/files/fy2017-budget-in-brief.pdf>; <https://www.bccresearch.com/market-research/pharmaceuticals/vaccine-technologies-markets-report-phm014f.html>

¹³² [21 C.F.R. § 600.80\(c\)](#)

causing eye pain and partial or complete vision loss); Aplastic anemia (damage to the bone marrow which slows or shuts down the production of new blood cells); Aseptic Meningitis (acute inflammation of the brain and spinal cord which can lead to death); Henoch-Schonlein purpura (abnormal immune response resulting in inflammation of microscopic blood vessels which can result in multiple organ damage); Myalgia (muscle pain that can become chronic); Radial nerve and recurrent nerve paralysis (nerve injury to the radial nerve that can cause weakness or difficulty moving the wrist, hand or fingers); Encephalopathy with EEG disturbances (damage or malfunction of the brain with severity ranging from altered mental status to dementia, seizures and coma); Grand Mal Convulsion (loss of consciousness and violent muscle contractions); Sudden Infant Death Syndrome (sudden death of infant in good health); Diabetes mellitus (chronic, lifelong condition effecting ability to use

energy found in food); Pancreatitis (pancreas attacks its own digestive enzymes); Encephalomyelitis (inflammation of the brain and spinal cord); Transverse myelitis (autoimmunity causing inflamed spinal cord which may result in paralysis); Pneumonitis (inflammation of lung tissue); Ocular Palsies (damage to the nerve of the eye that controls eye movement); Ataxia (brain damage resulting loss of full control of bodily movement, impaired speech, eye movement, and swallowing); Retrobulbar Neuritis (inflammation and damage to the optic nerve between the back of the eye and the brain); Epididymitis (inflammation testicle tube which can lead to abscess formation, testicular pain, painful urination, tissue death, and decreased functionality of gonads); Orchitis (inflammation of one or more testicles that can cause infertility, testicular atrophy, pain, and severe pain); Nerve Deafness (hearing loss from damage to the nerve that runs from the ear to the brain).¹³³

IV. CONFLICTS OF INTEREST IN VACCINE SAFETY

The 1986 Act created a system in which vaccines are licensed, recommended, encouraged, subsidized, and defended by HHS (the **Vaccine Program**).

The lack of evidence supporting vaccine safety is partially the result of the 1986 Act's unfortunate scheme which places the same agency, HHS, in charge of two conflicting duties. On the one hand, HHS is responsible for vaccine safety. On the other hand, HHS is simultaneously required to promote vaccine uptake and defend against any claim that vaccines cause any harm.

Regrettably, it appears that HHS has chosen to focus almost entirely on its vaccine promotion and defense responsibilities to such a degree that it has essentially abandoned its vaccine safety responsibility.

The Vaccine Program has transformed what should be a government watchdog over the pharmaceutical industry with regard to vaccines into an industry partner, with the same interests of promoting and literally defending, with the Department of Justice (**DOJ**) as its defense firm, against any claim of

¹³³ See vaccine products inserts at <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm>

vaccine injury. The result – as reflected in scathing reports by Congress and the HHS Inspector General – is that the Vaccine Program is fraught with pervasive conflicts of interests both structurally and literally with pharmaceutical company insiders.

Usually, when a government watchdog becomes ineffective or conflicted, consumers turn to the last line of recourse against harm caused by a product: class action and product liability attorneys. But in the case of vaccines, even they have been neutered because of the immunity from financial liability given to pharmaceutical companies for harms caused by their vaccines.

The Vaccine Program created by the 1986 Act has unfortunately resulted in a complete lack of accountability for vaccine safety.

1. HHS Licenses Vaccines

The introduction of a new vaccine begins with its licensure by the FDA. A committee at the FDA, the Vaccines and Related Biological Products Advisory Committee (VRBPAC), “advises the FDA on whether or not to license new vaccines for commercial use.”¹³⁴ In reality this committee effectively decides whether a new vaccine gets licensed since its recommendations for licensure are almost always accepted by the FDA. Unfortunately, the members of this board are often pharmaceutical insiders and, as discussed in Section II above, they license vaccines with virtually no safety data.

By the year 2000, most pediatric vaccines on the CDC’s vaccine schedule were already licensed by the FDA. That same year, the U.S. House of Representatives’ Committee on Government Reform (the **Committee**) issued a report revealing serious conflicts of interest in the VRBPAC.¹³⁵ The Committee “determined that conflict of interest rules employed by the FDA and the CDC have been weak, enforcement has been lax, and committee members with substantial ties to pharmaceutical companies have been given waivers to participate in committee proceedings.”¹³⁶ The Committee further explained that:

*Perhaps one of the major problems contributing to the overall influence of the pharmaceutical industry over the vaccine approval and recommendation process may be the loose standards that are used by the agency in determining whether a conflict actually exists. In many cases, significant conflicts of interest are not deemed to be conflicts at all.*¹³⁷

For instance, the Committee found that “3 out of 5 FDA advisory committee [VRBPAC] members who voted to approve the rotavirus vaccine in December 1997 [then the most recently approved vaccine by the VRBPAC] had financial ties to pharmaceutical companies that were developing different versions of the vaccine.”¹³⁸

Among these five VRBPAC members present and voting to license the rotavirus vaccine: one member’s employer had a \$9,586,000 contract for a rotavirus vaccine;

¹³⁴ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹³⁵ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹³⁶ Ibid.

¹³⁷ Ibid.

¹³⁸ Ibid.

another member was the principal investigator for a grant from Merck for the development of a rotavirus vaccine; two other members received almost \$1,000,000 from vaccine manufacturers toward vaccine development; and even the “consumer advocate” member (an ardent vaccine supporter) had received honoraria, in addition to travel expenses, from Merck.¹³⁹

These members voted to approve this pediatric vaccine even though a temporary voting member raised the following concern: “I would ask the FDA to work with the sponsor to further quantitate what these serious side effects are – specifically the adverse effects, driven in particular by febrile illness – is inducing hospitalizations and what is that level of access. I still don’t feel like I have a good grasp of that at this point.”¹⁴⁰

Regarding the VRBPAC, the Committee concluded: “The overwhelming majority of members, both voting members and consultants, have substantial ties to the pharmaceutical industry.”¹⁴¹ Hence, even putting aside the astonishing lack of safety review prior to licensure, extensive conflicts were found to pervade the HHS committee that largely determined whether to license the pediatric vaccines currently on the market.

2. HHS Recommends Vaccines

After a pediatric vaccine is licensed with virtually no safety data by an HHS

committee rife with conflicts of interest, another HHS committee, the CDC’s Advisory Committee on Immunization Practices (ACIP), decides whether to recommend the vaccine for all children in America.

ACIP is the only federal entity to make vaccination recommendations and these recommendations are consistently approved by the CDC.¹⁴² A recommendation by ACIP “for routine use of a vaccine is tantamount to a Federal mandate for vaccine use.”¹⁴³ This is because “HHS regulations require that all grants for childhood immunizations are subject to the States’ implementation of procedures to ensure routine vaccination ... [and] vigorous enforcement of school immunization laws.”¹⁴⁴

ACIP-recommended vaccines are also subsidized by the federal government.¹⁴⁵ In fact, 41% of the entire childhood vaccine market is purchased through ACIP resolutions.¹⁴⁶ This currently amounts to over \$4 billion paid to vaccine makers by the CDC, accounting for a third of the CDC’s current budget.¹⁴⁷

Putting all this together: as a result of the 1986 Act, **when the ACIP votes to recommend a pediatric vaccine for general use, the pharmaceutical industry is handed a liability-free, captive market of 78 million children with guaranteed payment.** It is not surprising that with this economic incentive,

without needing additional Congressional appropriations. As pointed out by the CDC: “It is unusual that a federal advisory committee has the power and authority to add benefits to an entitlement program.” It is also noteworthy that another 11% of the pediatric vaccine market is purchased through other Congressional appropriations and another 5% from state and local government funding.)

¹⁴⁷ <https://www.hhs.gov/sites/default/files/fy2017-budget-in-brief.pdf>

¹³⁹ Ibid.

¹⁴⁰ Ibid.

¹⁴¹ Ibid.

¹⁴² Ibid.

¹⁴³ Ibid.

¹⁴⁴ Ibid.

¹⁴⁵ <https://doi.org/10.1086/420748>

¹⁴⁶ Ibid. (Once ACIP votes to add a vaccine to the Vaccine for Children program, payment is provided to vaccine makers

the vaccine market has catapulted from \$170 million in 1982 to over \$33 billion in 2016.¹⁴⁸

Given these economic incentives, it is obvious that the ACIP should be scrupulously shielded from even an apparent – let alone actual – conflict of interest with vaccine makers. Unfortunately, government reports have found the exact opposite.

The ACIP is comprised of 15 voting members that are *not* federal government employees. Fourteen of these voting members must be medical professionals in the area of immunization.¹⁴⁹ There are also eight non-voting members who represent federal agencies with responsibility for immunization programs and an additional 26 non-voting members of liaison organizations, many of which receive financial support from vaccine makers.¹⁵⁰ As the U.S. House Committee on Government Reform concluded:

*The absence of any consumer advocates on the ACIP has resulted in an advisory committee that is inherently not 'fairly balanced.'*¹⁵¹

Far worse than the structural conflicts in ACIP's composition are the actual conflicts of interests of its members. These conflicts have been highlighted by multiple government reports but due to gridlock and disparate influence on Congress by pharmaceutical companies, Congress has never moved to fix the issues and conflicts it has identified.

One investigation by the U.S. House Committee on Government Reform resulted in a June 15, 2000 report entitled *Conflicts of Interest in Vaccine Policy Making*.¹⁵² The Committee found that ACIP members routinely fail to disclose conflicts with vaccine manufacturers.¹⁵³ Moreover, as a matter of routine, “[t]he CDC grants blanket waivers to the ACIP members each year that allow them to deliberate on any subject, regardless of their conflicts, for the entire year.”¹⁵⁴ In the congressional inquiry, legal counsel for the ACIP *conceded* that even when serious conflicts are identified, “we generally give them [waivers] to everyone ... we give them out freely.”¹⁵⁵ The Committee on Government Reform was troubled:

*The CDC's policy of issuing annual waivers creates an environment where people do not take the conflict of interest issue as seriously as they should. This policy, in concert with sloppy monitoring of the completeness of members' financial disclosure statements, allows for a clubby environment where ethical concerns are downplayed.*¹⁵⁶

As an example of this “clubby environment,” the Committee found: “Members of the ACIP are allowed to vote on a recommendation for one company's vaccine even if they have

¹⁴⁸ <https://www.bccresearch.com/market-research/pharmaceuticals/vaccine-technologies-markets-report-phm014f.html>;

<https://www.ncbi.nlm.nih.gov/books/NBK216815/>

¹⁴⁹ <https://www.cdc.gov/vaccines/acip/committee/downloads/nominations.pdf>

¹⁵⁰ <https://www.cdc.gov/vaccines/acip/committee/acip-charter-2016.pdf>

¹⁵¹ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹⁵² Ibid.

¹⁵³ Ibid.

¹⁵⁴ Ibid.

¹⁵⁵ Ibid.

¹⁵⁶ Ibid.

financial ties to a competing firm developing a similar vaccine.”¹⁵⁷

Highlighting these conflict issues, the Committee drew focus on the vaccine most recently approved by the ACIP, a rotavirus vaccine, and whatever conflicts they could identify for the eight members of the ACIP that voted to approve that vaccine for routine pediatric use.¹⁵⁸ The Committee’s findings were damning: (1) The chairman served on Merck’s Immunization Advisory Board; (2) another member, who shared the patent on a rotavirus vaccine, had a \$350,000 grant from Merck to develop the vaccine, and was a consultant for Merck; (3) another member was under contract with the Merck Vaccine Division and received funds from various vaccine makers including Pasteur, and was a principal investigator for SmithKline; (4) another member received a salary and other payments from Merck; (5) another member participated in vaccine studies with Merck, Wyeth, and SmithKline; and (6) another member received grants from Merck and SmithKline.¹⁵⁹

The Committee was deeply troubled that these members were nonetheless allowed to vote to recommend a pediatric vaccine for universal use.¹⁶⁰

The Committee was further concerned by its finding that “ACIP liaison representatives have numerous ties to vaccine manufacturers.”¹⁶¹ The Committee found that these liaison members, through whom third-party organizations are permitted to provide

opinions regarding a vaccine under review, “provide more than just the opinions.”¹⁶² The Committee found them “more like” a voting member of ACIP “than an advisory representative.”¹⁶³ The advice of these liaison representatives “is solicited frequently by CDC personnel on issues where their organization has a financial interest.”¹⁶⁴

The ACIP also routinely forms subcommittees (called “working groups”) which convene behind closed doors and whose recommendations are typically rubber stamped by the ACIP.¹⁶⁵ The Committee was troubled by extensive and routine use of working groups since the participants in these working groups often had conflicts which would have prohibited them from voting during an actual ACIP meeting.¹⁶⁶ The Committee explained: “The ACIP’s prolific use of working groups to draft vaccine policy recommendations outside the specter of public scrutiny opens the door to undue special interest access.”¹⁶⁷ Regarding the ACIP’s most recent working group recommending approval of a vaccine, the Committee found:

The working group has ten members, seven of whom have identifiable conflicts of interest with vaccine manufacturers or vaccine interest groups. The group’s meetings were held in private with no minutes or records of the proceedings taken. It appears that members who were not allowed to vote because of conflicts of interest ... were allowed to work

¹⁵⁷ Ibid.

¹⁵⁸ Ibid.

¹⁵⁹ Ibid.

¹⁶⁰ Ibid.

¹⁶¹ Ibid.

¹⁶² Ibid.

¹⁶³ Ibid.

¹⁶⁴ Ibid.

¹⁶⁵ Ibid.

¹⁶⁶ Ibid.

¹⁶⁷ Ibid.

*extensively on the recommendation for a long period of time in the working group.*¹⁶⁸

The Committee's damning overall conclusion was that ACIP's process for recommending a vaccine reflected "a system where government officials make crucial decisions affecting American children without the advice and consent of the governed."¹⁶⁹

After the Committee's scathing report in 2000, one would expect nothing less than drastic reform of ACIP – something that would differentiate it from a biased and self-interested pharmaceutical company board so that the interests of American children are placed ahead of the companies with the resources to influence government. This expectation unfortunately has not been fulfilled.

Indeed, in December 2009, the HHS Office of Inspector General issued another report after an extensive review of the conflicts of CDC's advisory committee members, known as Special Government Employee (SGEs), with the first among these committees being the ACIP.¹⁷⁰ The Inspector General found that the "CDC had a systemic lack of oversight of the ethics program for SGEs."¹⁷¹ For example, the Inspector General found that: "Most of the experts who served on advisory panels in 2007 to evaluate vaccines for flu and cervical cancer had potential conflicts that were never resolved."¹⁷²

The Inspector General reached this conclusion after reviewing the conflict forms, Form 450's, filed by SGEs at the CDC. CDC "must obtain from SGEs" a completed Form 450, which includes "assets, sources of income, and non-income-earning activities."¹⁷³ Then, "[b]efore permitting SGEs to participate in committee meetings, CDC must review these forms and certify them to indicate that they are complete and that it has identified and resolved all conflicts of interest."¹⁷⁴ Reviewing CDC's compliance with these requirements, the Inspector General found that nothing had changed in the years since the scathing Congressional Committee on Government Reform report in 2000.¹⁷⁵

Indeed, the Inspector General found that "CDC certified OGE Forms 450 with at least one omission in 2007 for 97 percent ... of SGEs."¹⁷⁶ Almost all of these "had more than one type of omission."¹⁷⁷ Compounding this problem, the Inspector General found that "58 percent ... of SGEs had at least one potential conflict of interest that CDC did not identify."¹⁷⁸ Splicing down this 58% of unidentified conflicts, 40% involved employment or grants, 13% involved equity ownership, and 5% involved consulting.¹⁷⁹

These conflicts are serious, and the CDC "did not inform the SGEs that they would violate the criminal conflict-of-interest statute if they participated in committee work regarding particular matters affecting their specific employers' financial interests."¹⁸⁰

¹⁶⁸ Ibid.

¹⁶⁹ Ibid.

¹⁷⁰ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf>

¹⁷¹ Ibid.

¹⁷² <http://www.nytimes.com/2009/12/18/health/policy/18cdc.html?mcubz=0>

¹⁷³ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf>

¹⁷⁴ Ibid.

¹⁷⁵ Ibid.

¹⁷⁶ Ibid.

¹⁷⁷ Ibid.

¹⁷⁸ Ibid.

¹⁷⁹ Ibid.

¹⁸⁰ Ibid.

The Inspector General further concluded that even when the CDC actually identified a conflict, the CDC improperly granted broad waivers despite already being castigated for this improper practice in 2000.¹⁸¹ Even worse, “32 percent ... of SGEs with certified forms had at least one potential conflict of interest that CDC identified but did not resolve.”¹⁸² Amazingly, 13 percent of SGEs were allowed to participate in committee meetings without even having a Form 450 on file.¹⁸³

In sum, even after the blistering 2000 Committee on Government Reform report, and numerous damning Congressional hearings before that committee regarding CDC’s conflicts with vaccine makers, little changed.¹⁸⁴ Instead of resolving and avoiding these conflicts, the “incestuous relationship” between the CDC and vaccine makers has apparently become even more hardened and enmeshed.¹⁸⁵

Since an ACIP vote to recommend a vaccine hands a vaccine maker a liability-free market of 78 million American children with guaranteed payment, an ACIP vote must be completely insulated from any influence by pharmaceutical companies. Instead, the ACIP and its working groups, are inundated with conflicts of interest and ties to these companies.

3. HHS Promotes Vaccines

Not only is the process for licensing and recommending vaccines riddled with conflicts, so is HHS’s process for promoting vaccines.

While the CDC states on its website – not less than 130 times – that “CDC does not accept commercial support,” this is simply not true.¹⁸⁶ For example, in reviewing this very issue, the British Medical Journal, which it asserts is “one of the world’s most influential and widely read medical journals,” reported in 2015:

*The CDC’s image as an independent watchdog over the public health has given it enormous prestige, and its recommendations are occasionally enforced by law. Despite the agency’s disclaimer, the CDC does receive millions of dollars in industry gifts and funding, both directly and indirectly, and several recent CDC actions and recommendations have raised questions about the science it cites, the clinical guidelines it promotes, and the money it is taking.*¹⁸⁷

Explaining the concern with CDC receiving industry funding, the Journal described this as “classic stealth marketing, in which industry puts their message in the mouths of a trusted third party [here the CDC].”¹⁸⁸ The Journal quoted a methodologist and emeritus professor of medicine at UCLA stating, “Most of us were shocked to learn the CDC takes

¹⁸¹ Ibid.

¹⁸² Ibid.

¹⁸³ Ibid.

¹⁸⁴ Compare <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf> with Ibid.

¹⁸⁵ https://cdn.voiceamerica.com/health/010278/arranga_040814.mp3

¹⁸⁶ <https://search.cdc.gov/search?query=%22cdc+does+not+accept+commercial+support%22&utf8=%E2%9C%93&affiliate=cdc-main>

¹⁸⁷ <http://vapors.org.uk/wp-content/uploads/2015/05/CDC-Industry-Funding.pdf>

¹⁸⁸ Ibid.

funding from industry,” adding that, “it is outrageous that industry apparently is allowed to punish the CDC if the agency conducts research that has the potential to cut into profits.”¹⁸⁹

As another example, Congress expressly created a private foundation, the “CDC Foundation,” through which private entities, such as pharmaceutical companies, can support programs at the CDC, endow positions at the CDC, and even place individuals to work at the CDC, paid through “private funding.”¹⁹⁰

Since 1995 the CDC Foundation has raised \$620 million to pay for 824 programs at the CDC.¹⁹¹ In 2015 alone, the CDC Foundation raised \$157 million for privately funded programs at the CDC, which then obtain the stamp of legitimacy of the CDC.¹⁹² Merck, for example, funded an \$832,916 program through the CDC Foundation to “expand CDC’s ... viral hepatitis prevention and vaccination activities.”¹⁹³ As a result, the CDC is reliant on the CDC Foundation for the continued funding of these projects, and even for the services of the staff placed at the CDC by the CDC Foundation, since the CDC is only permitted to use these funds as expressly directed by the CDC Foundation.¹⁹⁴ This foundation even funds and thus directs CDC “management training courses.”¹⁹⁵

Worse, the promotion track for CDC management extends into vaccine makers.

The most prominent example is former CDC Director Dr. Julie Gerberding who headed the CDC from 2002 to 2009. Dr. Gerberding oversaw several controversial studies regarding vaccines produced by Merck, including notably the MMR vaccine, which sought to silence those calling for an increase in the safety profile of those vaccines. When she left the CDC she was rewarded with the position of President of Merck Vaccines in 2010 with a reported estimated \$2.5 million annual salary and lucrative stock options.¹⁹⁶

In contrast, the few CDC officials who have attempted to blow the whistle on how vaccine safety research is conducted and treated at the CDC have become targets of character assassination. For example, following revelations of Dr. Thompson’s statements regarding the CDC’s improper conduct¹⁹⁷ (some of which was discussed above), he soon found himself marginalized and publicly maligned, despite the CDC’s prior reliance on him for over a decade to produce most of its core vaccine safety science.¹⁹⁸

As Congressman Bill Posey explained in 2014 after investigating the CDC’s approach to vaccine safety: the CDC and vaccine industry’s “media network [will] twist the truth to disparage, to malign, to vilify, to denigrate anybody who wants any kind of accountability” and added that his review of CDC emails discussing vaccine safety “will make you absolutely sick to your stomach.”¹⁹⁹

¹⁸⁹ Ibid.

¹⁹⁰ [42 U.S.C.A. §§ 280e-11\(h\)\(1\), \(2\)](#)

¹⁹¹ <http://www.cdcfoundation.org/FY2015>

¹⁹² Ibid.

¹⁹³ Ibid.

¹⁹⁴ [42 U.S.C.A. § 280e-11\(h\)\(2\)\(a\), \(7\)\(b\)](#)

¹⁹⁵ <https://www.cdcfoundation.org/sites/default/files/upload/pdf/CDCF-Form990-2014.pdf>

¹⁹⁶ <https://www.sec.gov/cgi-bin/own-disp?action=getowner&CIK=0001628884>

¹⁹⁷ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

¹⁹⁸ <https://www.ncbi.nlm.nih.gov/pubmed/?term=Thompson+WW%5BAuthor%5D>

¹⁹⁹ <https://cdn.voiceamerica.com/health/010278/arranga040814.mp3>

4. HHS Defends Vaccines

After HHS licenses, effectively mandates, and promotes a vaccine to 78 million American children with virtually no safety data, *this very same government agency is mandated to defend against any claim that the vaccine caused harm.* There is no other product where the very agency responsible to regulate a product and assure its safety is statutorily required to defend against any claim it causes harm.

The Vaccine Injury Compensation Program (**VICP** or **Vaccine Court**) is effectively the only legal recourse in America to obtain compensation for a pediatric vaccine injury.²⁰⁰ The injured must file a claim in the VICP and litigate against HHS and the DOJ in a quasi-judicial process filed under seal where the injured child effectively cannot obtain documents from or depose vaccine makers to prove how the vaccine caused injury.²⁰¹ There is no jury, nor even a judge; special masters play the role of trial judges, with the final say.²⁰² DOJ and HHS have the government's vast resources while the injured must secure a private attorney.²⁰³ Moreover, an injured child's damages are limited to \$250,000 for death and pain and suffering.²⁰⁴

Worst of all, despite these limitations, the injured child must *still* almost always prove "causation" – the biological mechanism by which the vaccine caused the claimed injury. Requiring an injured child to prove causation adds insult to injury because, sadly, had HHS conducted the vaccine safety science it demands as proof in the VICP before

licensing a vaccine, the child's injury may have been avoided altogether.

There is a disconnect in requiring a child receiving a compulsory pharmaceutical product to medically prove how the vaccine caused his or her injury, where the science to understand vaccine injuries is not being done by the government agency tasked with this job.²⁰⁵ As confirmed by the IOM, HHS has not conducted the basic science needed to even determine whether commonly claimed vaccine injuries are caused by vaccines.²⁰⁶ It has failed to conduct even one properly sized study comparing vaccinated to unvaccinated children, despite all the resources at its disposal.²⁰⁷ It therefore may not be surprising that the Federal Circuit Court of Appeals found, medical science is "a field bereft of complete and direct proof of how vaccines affect the human body."²⁰⁸

The Committee on Government Reform explained the devastating consequences suffered by families when children are injured by a vaccine:

Every year, a number of children are seriously injured by adverse reactions to vaccines. When such a tragedy befalls a family, they are faced with devastating emotional and financial consequences. As the devastation of adverse reactions can lead to paralysis, permanent disability and death, families without adequate insurance can face enormous expenses, including

²⁰⁰ [42 U.S.C. § 300aa-10 et seq.](#)

²⁰¹ [42 U.S.C. § 300aa-12](#)

²⁰² *Ibid.*

²⁰³ [42 U.S.C. § 300aa-15](#)

²⁰⁴ *Ibid.*

²⁰⁵ See Sections II and III above.

²⁰⁶ See Section III(2) above.

²⁰⁷ See Section III(6) above.

²⁰⁸ [Althen v. Secretary of Health and Human Services, 418 F.3d 1274 \(Fed. Cir. 2005\)](#)

*residential care, therapy, medical equipment, and drugs.*²⁰⁹

Yet it is left to the injured child to prove the physiological mechanics by which the vaccine caused injury.²¹⁰

Moreover, Congress left HHS with the authority to set the rules for the VICP and so HHS has used this authority to shortcut its defense of claims for vaccine injuries by changing the rules in its favor. Indeed, the 1986 Act created a Vaccine Injury Table (the **Table**) which quickly compensated certain common injuries associated with each vaccine.²¹¹ If the petitioner suffered an injury on the Table, the burden would shift to HHS to prove the vaccine did not cause the injury.²¹² After passage of the 1986 Act, almost 90 percent of claims were Table claims and were quickly settled.²¹³ Soon after, in 1995 and 1997, HHS amended the Table such that 98% of new claims are off-Table.²¹⁴ This change greatly increased the difficulty of obtaining compensation for vaccine injuries.

While HHS changes the VICP rules in its favor, the Committee on Government Reform found “DOJ attorneys make full use of the apparently limitless resources available to them,” “pursued aggressive defenses in

compensation cases,” and “establish[ed] a cadre of attorneys specializing in vaccine injury” and “an expert witness program to challenge claims.”²¹⁵ The Committee even noted a VICP decision which stated:

*In the special master’s view, [HHS’s] counsel’s abrasive, tenacious, obstreperous litigation tactics were inappropriate in a program that is intended to be less adversarial; and hindered greatly a fair, expeditious resolution of the case. In addition, counsel lacks simply tact and compassion. Quite frankly; the special master is embarrassed that [HHS’s] counsel and ... life care planner represented the United States Government in this case.*²¹⁶

The length of time it has taken to adjudicate claims has also multiplied such that over half of claims now take over five years.²¹⁷

Even with all the foregoing barriers to obtaining compensation for a vaccine injury – notably requiring injured children to prove causation and capping damages for pain and suffering and death at \$250,000 – the VICP has paid over \$2.1 billion dollars for vaccine injury claims since 2007 and over \$3.7 billion since 1986.²¹⁸ Just a few of the serious vaccine injuries for which the VICP has paid include:

²⁰⁹ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

²¹⁰ Further compounding the above issues, babies are unable to describe their symptoms which may explain why most VICP claims are filed by adults. Most adults bring claims for injury after a single flu shot. (https://www.hrsa.gov/vaccinecompensation/data/vicpmonthlyreporttemplate8_1_17.pdf) In contrast, babies receive between five and seven injections of numerous vaccine doses at two months, four months, six months, etc. (See Section I above.) If babies could talk, they may be able to explain why they are crying inconsolably, have decreased activity/lethargy, drowsiness, irritability, fussiness, and loss of appetite – reactions that are considered “normal” side effects of vaccination. (See vaccine product inserts at <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm>

[093833.htm](https://www.gao.gov/assets/670/667136.pdf)) But since babies can’t talk, the symptoms which would explain a neurological injury, for example, are not knowable until later in life when it is too late to assert a claim.

²¹¹ <https://www.hrsa.gov/vaccinecompensation/vaccineinjurytable.pdf>

²¹² 42 U.S.C. § 300aa-13

²¹³ *Stevens v. Secretary of the Department of Health & Human Services*, No. 99-594V (Office of Special Masters 2001)

²¹⁴ <http://www.gao.gov/assets/670/667136.pdf>

²¹⁵ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

²¹⁶ *Ibid.*

²¹⁷ <http://www.gao.gov/assets/670/667136.pdf>

²¹⁸ https://www.hrsa.gov/vaccinecompensation/data/vicpmonthlyreporttemplate8_1_17.pdf; 42 U.S.C.A. § 300aa-15(a)(2), (4)

*Guillain-Barre Syndrome, Transverse Myelitis, Encephalopathy (disease altering brain function), Seizure Disorder, Death, Brachial Neuritis, CIDP (inflammation damaging the brain and spinal cord), Acute Disseminated Encephalomyelitis, Premature Ovarian Failure, Bell's Palsy, Idiopathic Thrombocytopenic Purpura (ITP) (autoimmune disease of the blood), Juvenile Diabetes, Rheumatoid Arthritis, Multiple Sclerosis, Fibromyalgia, Infantile Spasms, Anaphylaxis, Ocular Myasthenia Gravis (autoimmune condition causing visual impairments), Hypoxic Seizure*²¹⁹

Recognizing the depths of the foregoing issues and conflicts, in 2006 a bipartisan group of seven congressmen proposed a bill to create an entirely new government agency solely devoted to vaccine safety.²²⁰ The primary sponsor of this bill explained the need for this bill as follows:

Federal agencies charged with overseeing vaccine safety research have failed. They have failed to provide sufficient resources for vaccine safety research. They have failed to fund extramural research. And, they have failed to free themselves from conflicts of interest that serve to undermine public confidence in the safety of vaccines.

The American public deserves better and increasingly parents and the public at large are demanding better.

I'm a physician. ... When I first began working on this issue about seven years ago, I was shocked at the dearth of resources dedicated to vaccine safety research. ...

When I first tasked my staff with investigating this issue we got a lot of confused responses from federal agencies. The FDA told us to check in with the CDC, saying CDC did most of the vaccine safety research. The CDC referred us over to the NIH. Then, the NIH referred us back to the CDC. ...

Several issues relating to vaccine safety have persisted for years. The response from public health agencies has been largely defensive from the outset and the studies plagued by conflicts of interest. ...

Presently, vaccine safety research is an in-house function conducted predominantly by the CDC – the very agency that makes vaccine

²¹⁹ See, e.g., *Kuperus v. Sec'y of the HHS*, No. 01-0060V, 2003 U.S. Claims LEXIS 397 (Fed. Cl. Oct. 23, 2003) (Acute Disseminated Encephalitis from DTaP); *Lerwick v. Sec'y of HHS*, No. 06-847V, 2010 U.S. Claims LEXIS 398 (Fed. Cl. May 26, 2010) (Acute Disseminated Encephalitis from DTaP); *Price v. Sec'y of HHS*, No. 11-442V, 2015 U.S. Claims LEXIS 1554 (Fed. Cl. Oct. 29, 2015) (Anaphylaxis from DTaP); *Rodriguez v. Sec'y of the HHS*, No. 06-559V, 2007 U.S. Claims LEXIS 685 (Fed. Cl. Sep. 14, 2007) (Death from DTaP); *Harry Tembenis & Gina Tembenis v. Sec'y of HHS*, No. 03-2820V, 2010 U.S. Claims LEXIS 950 (Fed. Cl. Nov. 29, 2010) (Death from DTaP); *Agresti v. Sec'y of HHS*, No. 05-0752V, 2009 U.S. Claims LEXIS 517 (Fed. Cl. Mar. 17, 2009) (Encephalopathy from DTaP); *Corzine v. Sec'y of the HHS*, No.

[01-230V](#), 2004 U.S. Claims LEXIS 116 (Fed. Cl. Apr. 23, 2004) (Hypoxic seizure leading to Death from DTaP); *Loving v. Sec'y of HHS*, No. 02-469V, 2013 U.S. Claims LEXIS 1570 (Fed. Cl. Sep. 20, 2013) (Infantile Spasms and Seizure Disorder from DTaP); *Herrell v. Sec'y of the HHS*, No. 08-123V, 2009 U.S. Claims LEXIS 577 (Fed. Cl. Jan. 6, 2009) (Idopathic Thrombocytopenic Purpura from MMR); *Zatuchni v. Sec'y of HHS (In re Snyder)*, No. 94-58V, 2006 U.S. Claims LEXIS 127 (Fed. Cl. May 10, 2006) (Fibromyalgia leading to death from MMR); *Francis v. Sec'y of the HHS*, No. 99-520V, 2007 U.S. Claims LEXIS 172 (Fed. Cl. May 23, 2007) (Ocular Myasthenia Gravis from Varicella).

²²⁰ <https://www.congress.gov/bill/109th-congress/house-bill/5887>

*recommendations and promotes their uptake. This should not be.*²²¹

This bill did not get out of committee, a fact which likely reflects the ratio of over 1,000 pharma lobbyists in Washington D.C. to virtually no vaccine safety lobbyists.

Many parents, doctors and scientists, as well as politicians, are legitimately concerned about the process whereby vaccines are licensed, recommended, promoted and defended by the same department. This is not because of any conspiracy, or belief in an insidious intent. Rather, the problem is with the structural conflicts and incentive scheme this system creates. There is no incentive for research to

uncover which long-term chronic conditions, including which immune and neurological disorders – which *can* clearly result from the current vaccination schedule – are caused by vaccines. Even worse is the disincentive to uncover susceptible populations to vaccine injury. The burden of judging whether a vaccine will seriously injure a child therefore falls on the child’s parents. But unless parents can identify with scientific accuracy how a vaccine will injure their child, parents cannot obtain a medical exemption from vaccinating their child. Worse, when a child is injured, the burden again falls on the parent to prove how the vaccine injured their child. This system is inherently unfair and unjust.

CONCLUSION

We can do better. With hundreds of vaccines in the pipeline we must do better. Children susceptible to vaccine injury are as deserving of protection as any other child. Avoiding injury to these children is not only a moral and ethical duty, but will, in fact, strengthen the Vaccine Program. Every parent that does not witness their child suffer a serious reaction after vaccination, such as a seizure or paralysis, is another parent that will not add their voice to the growing chorus of parents opposed to the Vaccine Program due to safety concerns.

These parents and their kindred doctors, scientists and politicians, are also in fact correct that the system for vaccine safety is broken. While we know that vaccines can

cause serious adverse reactions, the studies to quantify the rate at which it causes these harms have never been done. While we know that certain children are predisposed to serious injury from vaccines, the studies to identify which children are so disposed have never been done. While we know that valid pre-licensure safety trials take years and must use an inert placebo control, such pre-licensure safety trials are never done for any vaccine. While we know that post-licensure surveillance of vaccines captures less than one percent of adverse reactions, the CDC refused to cooperate to automate VAERS reporting.

In the zeal to protect the Vaccine Program the primary objective of protecting every child to the greatest extent possible from

²²¹ http://vaccine-safety.s3.amazonaws.com/Weldon_Statement_Vaccine_Safety_final.pdf

harm has been lost. Every child susceptible to a vaccine injury or injured by a vaccine deserves better.

The good news is that fixing this system is not complicated and would require a tiny fraction of the resources already devoted to the Vaccine Program. The quickest solution would be to repeal the 1986 Act and let normal market forces drive vaccine safety. Alternatively, the following actions would immediately correct many of the issues identified in this white-paper:

Reduce Conflicts

1. Prohibit any conflict waivers for members of HHS's vaccine committees.²²²
2. Prohibit HHS vaccine committee members or employees from accepting any compensation from a vaccine maker for twenty years.
3. Require that vaccine safety advocates comprise at least half of HHS's vaccine committees.

Increase Safety Profile

4. Conduct prospective double-blind saline-placebo controlled studies of each vaccine recommended by the CDC as well as the entire CDC vaccine schedule.
5. Conduct properly sized and controlled retrospective and prospective safety studies

comparing total health outcomes between vaccinated children and completely unvaccinated children.

6. Create a vaccine safety agency independent of HHS with a budget equal to 50% of HHS's budget for promoting and purchasing vaccines.
7. Automate creation and transmission of adverse reactions reports at hospital/clinic to VAERS.

²²² HHS's vaccine committees include the Advisory Committee on Immunization Practices (ACIP), the Vaccine and Related

Biological Products Advisory Committee (VRBPAC), the National Vaccine Advisory Committee (NVAC), and the Advisory Commission on Childhood Vaccines (ACCV).

APPENDIX: Vaccine Ingredients

Most pediatric vaccines do not contain live viruses.²²³ For example, (i) polio vaccine (IPV) only contains a killed virus, (ii) hepatitis b vaccine contains a portion of a killed virus, and (iii) diphtheria vaccine contains only a modified toxin released by the diphtheria bacteria.²²⁴ These pieces of killed bacteria or virus or modified toxins are commonly referred to as “antigens.” An injection of antigen alone, with nothing more, produces a weak immune response insufficient for creating long-term immunity.²²⁵

Therefore, many vaccines also contain an “adjuvant,” an immune-stimulating substance that increase the immune response to the antigen, so that immunity is created. Aluminum compounds are by far the most commonly used adjuvants in vaccines. They are made of particles of aluminum hydroxide, aluminum phosphate or aluminum sulfate, or mixtures thereof.²²⁶

It is universally accepted that aluminum is a potent neurotoxin, and toxic to all life.²²⁷ Accordingly, the FDA has established strict limits for aluminum in intravenous feeding solutions (.000005 grams per kg body weight per day). Exposure in infants exceeding this limit causes long term cognitive impairment.²²⁸

A significant safety problem with aluminum adjuvants is that, because they are made of microscopic particles, they can travel into the brain.²²⁹ Once in the brain, aluminum adjuvants cause long term chronic inflammation.²³⁰

Inflammation in the brain is a cause of neurodevelopmental disorders (e.g. autism) and mental illnesses (e.g. schizophrenia).²³¹ The resulting mental illness can occur years or decades after the inflammation starts.²³²

Exposure to aluminum adjuvants has increased dramatically in the last 50 years, in parallel with the increasing incidence of neurodevelopmental disorders in children.²³³

Some vaccines also contain other biological matter, both intended and unintended.²³⁴ These include cell lines from aborted human fetuses and biological material from animal tissue.²³⁵ Before being killed in the vaccine manufacturing process, the virus, disease, or toxin (against which the vaccine is supposed to protect) is grown on these human and biological mediums.²³⁶

Human cell portions in vaccines disclosed by the CDC include “human albumin, human diploid cell cultures (WI-38), human embryonic lung cultures, WI-38 human diploid lung fibroblasts, MRC-5 (human diploid) cells, MRC-5 cells, residual components of MRC-5 cells including DNA and protein, [and] recombinant human albumin.”²³⁷ These human cell portions also include billions of strands of human DNA from these aborted fetal cells lines that are of a length capable of inserting themselves into DNA to which they are exposed.²³⁸

²²³ <https://www.vaccines.gov/basics/types/index.html>

²²⁴ Ibid.

²²⁵ <https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html>

²²⁶ Ibid.

²²⁷ <https://www.ncbi.nlm.nih.gov/pubmed/2940082>;
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819810/>;
<https://www.ncbi.nlm.nih.gov/pubmed/23932735>

²²⁸ <https://www.ncbi.nlm.nih.gov/pubmed/9164811>

²²⁹ <https://www.ncbi.nlm.nih.gov/pubmed/23557144>

²³⁰ <https://www.ncbi.nlm.nih.gov/pubmed/27908630>;

<https://www.ncbi.nlm.nih.gov/pubmed/19740540>

²³¹ <https://www.ncbi.nlm.nih.gov/pubmed/27540164>;

<https://www.ncbi.nlm.nih.gov/pubmed/25311587>

²³² Ibid.

²³³ <https://www.cdc.gov/vaccines/schedules/past.html>;

<https://www.ncbi.nlm.nih.gov/pubmed/20159870>

²³⁴ <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

²³⁵ Ibid.

²³⁶ Ibid.

²³⁷ Ibid.

²³⁸ <http://soundchoice.org/research/dna-fragments-research/>;

<http://soundchoice.org/wp-content/uploads/2012/08/DNA>

The CDC's list of ingredients for the vaccines also includes the following animal parts:

*monkey kidney cells, vero (monkey kidney) cells, embryonic guinea pig cell cultures, lactose, chick embryo cell culture, bovine calf serum, bovine serum albumin, calf serum protein, fetal bovine serum*²³⁹

These fragments of cultured human tissue and animal tissue, which have also been found to include various monkey, retro and other unintended viruses, are injected into the muscle tissue of babies and children, along with the adjuvant intended to generate a sustained immune response to the biological matter in the vaccine.²⁴⁰

[Contaminants in Vaccines Can Integrate Into Childrens Genes.pdf](#)

²³⁹ <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

²⁴⁰ <https://www.fda.gov/biologicsbloodvaccines/scienceresearch/biologicsresearchareas/ucm127327.htm>; <https://www.ncbi.nlm.nih.gov/pubmed/20375174>. Vaccines also contain, among other ingredients, the following: *2-phenoxethanol, complex*

fermentation medium, detergent, 5rdimethyl 1-beta-cyclodextrin, Eagle MEM modified medium, enzymes, formaldehyde, gelatin, glutaraldehyde, hemin chloride, hydrolyzed galtin, lactalbumin hydrolysate, Medium 199, Minimum Essential Medium, modified Mueller's growth medium, modified Stainer-Scholte liquid medium, neomycin, neomycin sulfate, phenol polymyxin B, polymyxin B sulfate, polysorbate 80, soy peptone, Stainer-Scholte medium, streptomycin, yeast, yeast protein



VACCINE **Peer Review**

**The History Of The Global Vaccination Program
In 1000 Peer Reviewed Reports And Studies**

1915-2015

A Jeff Prager Publication

“Dissent is crucial for the advancement of science.

Disagreement is at the heart of peer review and is important for uncovering unjustified assumptions, flawed methodologies and problematic reasoning.”

I. de Melo-Martín and K. Intemann, Division of Medical Ethics, Department of Public Health, Weill Cornell Medical College, New York, USA

“the harm from vaccines has seriously exceeded the benefit of disease prevention”

Dr. Harold Buttram

“No batch of vaccine can be proved safe before it is given to children”

Surgeon General of the United States, Leonard Scheele, addressing an AMA convention in 1955

“The only safe vaccine is a vaccine that is never used.”

Dr. James A. Shannon, National Institutes of Health

“Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function.

Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity. In some developed countries, by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of aluminum adjuvants through routine vaccinations.

According to the US Food and Drug Administration, safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic. Taken together, these observations raise plausible concerns about the overall safety of current childhood vaccination programs.”

Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs

Donald W. Light
Rowan University, School of Osteopathic Medicine
Harvard University - Edmond J. Safra Center for Ethics

Joel Lexchin
York University

Jonathan J. Darrow
Harvard Medical School

Donald W. Light, Ph.D., is a fellow for 2012-2013 at the Edmond J. Safra Center for Ethics at Harvard University in Cambridge, MA. He received his Ph.D. in sociology from Brandeis University and is a professor of comparative health policy at Rowan University, School of Osteopathic Medicine.

Joel Lexchin, M.Sc., M.D., has been teaching health policy for 12 years at York University in Toronto, ON. He received his M.D. from the University of Toronto in 1977 and since 1988 has been an emergency physician at the University Health Network in Toronto.

Jonathan J. Darrow, J.D., M.B.A., LL.M., S.J.D., is a research fellow at Harvard Medical School and a lecturer on law at Bentley University in Waltham, MA. He received his S.J.D. from Harvard in 2013.

~ June 1, 2013 ~

Journal of Law, Medicine and Ethics, 2013, Vol. 14, No. 3:590-610

Abstract

Over the past 35 years, patients have suffered from a largely hidden epidemic of side effects from drugs that usually have few offsetting benefits. The pharmaceutical industry has corrupted the practice of medicine through its influence over what drugs are developed, how they are tested, and how medical knowledge is created. Since 1906, heavy commercial influence has compromised Congressional legislation to protect the public from unsafe drugs. The authorization of user fees in 1992 has turned drug companies into the FDA's prime clients, deepening the regulatory and cultural capture of the agency. Industry has demanded shorter average review times and, with less time to thoroughly review evidence, increased hospitalizations and deaths have resulted. Meeting the needs of the drug companies has taken priority over meeting the needs of patients. Unless this corruption of regulatory intent is reversed, the situation will continue to deteriorate. We offer practical suggestions including: separating the funding of clinical trials from their conduct, analysis, and publication; independent FDA leadership; full public funding for all FDA activities; measures to discourage R&D on drugs with few if any new clinical benefits; and the creation of a National Drug Safety Board.

Institutional corruption is a normative concept of growing importance that embodies the systemic dependencies and informal practices that distort an institution's societal mission. An extensive range of studies and lawsuits already documents strategies by which pharmaceutical companies hide, ignore, or misrepresent evidence about new drugs; distort the medical literature; and misrepresent products to prescribing physicians. We focus on the consequences for patients: millions of adverse reactions. After defining institutional corruption, we focus on evidence that it lies behind the epidemic of harms and the paucity of benefits.

It is our thesis that institutional corruption has occurred at three levels. First, through large-scale lobbying and political contributions, the pharmaceutical industry has influenced Congress to pass legislation that has compromised the mission of the Food and Drug Administration (FDA). Second, largely as a result of industry pressure, Congress has underfunded FDA enforcement capacities since 1906, and turning to industry-paid "user fees" since 1992 has biased funding to limit the FDA's ability to protect the public from serious adverse reactions to drugs

that have few offsetting advantages. Finally, industry has commercialized the role of physicians and undermined their position as independent, trusted advisers to patients.

Institutional Integrity: The Baseline of Corruption

If “corruption” is defined as an impairment of integrity or moral principle, then institutional corruption is an institution’s deviation from a baseline of integrity. In the case of Congress, integrity demands that democratically elected representatives should be dedicated solely to the best interests of the people they represent. According to seminal essays on institutional corruption by Dennis Thompson and Larry Lessig, this baseline of integrity is corrupted because elections are not publicly funded. As a result, congressional representatives must constantly raise funds from a tiny percent of the population and respond to their priorities. This dependency corruption creates an “economy of influence,” even if individual actors are well-intentioned. Lessig’s examples portray how secrecy and rationalizations disguise distortions in the democratic process and mission.

The concept of institutional corruption highlights numerous distinctions — between what is legal and illegal; between good people doing bad things, not bad people doing bad things; between influence, not money, affecting decisions. These are the ends of continua, and there is a need to recognize degrees of corruption in between.

Special interests also influence members of Congress to make legal what has been illegal or else to game the rules, thereby blurring the line between legal and illegal as well as making it hard to determine the law’s intent.

Just as a proper electoral democracy is devoted to the public good, health care systems are founded on the moral principles of beneficence, nonmaleficence (“first, do no harm”), respect for autonomy, and the just distribution of scarce resources. Based on these principles, health care workers are obliged to use the best medical science to relieve suffering and pain, treat illness, and address risks to health. The institutional corruption of health care consists of deviations from these principles.

The major patent-based research pharmaceutical companies also nominally commit themselves to improving health and relieving suffering. For example, Merck promises “*to provide innovative, distinctive products that save and improve lives ... and to provide investors with a superior rate of return.*” Pfizer is dedicated “*to applying science and our global resources to improve health and well-being at every stage of life.*” Pharmaceutical companies continuously emphasize how deeply society depends on their development of innovative products to improve health. But in fact, these companies are mostly developing drugs that are little better than existing products but have the potential to cause widespread adverse reactions even when appropriately prescribed.

This deviation from the principles of health care by institutions allegedly dedicated to health care is institutional corruption. We present evidence that industry has a hidden business model to maximize profits on scores of drugs with clinically minor additional benefits. Physician commitment to better health is compromised as the industry spends billions to create what Lessig calls a “gift economy” of interdependent reciprocation. New research finds that truly innovative new drugs sell themselves in the absence of such gift-economy marketing.

Regulators such as the FDA and the Environmental Protection Agency arise when unregulated competition is perceived to cause serious harm to society and government regulation is needed to address the problem. The FDA was founded to protect the public’s health from the fraudulent cures peddled in the 19th century. Through a series of legislative enactments, often in response to a drug disaster, the pharmaceutical regulatory side of the FDA has acquired ever-wider responsibilities to ensure that new drugs do more good than harm. Institutional corruption consists of distortions of these responsibilities, such as approving drugs that are mostly little better than existing medications, failing to ensure sufficient testing for serious risks, and inadequately guarding the public from harmful side effects. These distortions serve commercial interests well and public health poorly.

For the past 50 years, patent-based research companies have objected to the FDA’s gate-keeping function as being too rigid and too slow. They have claimed that an obsessive concern about safety has undermined patient access to drugs that could save lives or reduce the burdens of ill health. This message is increasingly being accepted by the FDA.

Flooding the Market with Drugs of Little Benefit

In response to the emphasis by pharmaceutical companies, their lobbyists, and their trade association — the Pharmaceutical Research Manufacturers of America (PhRMA) — on the high risk and cost of research and development (R&D), Congress has authorized billions in taxpayer contributions to support R&D, exemptions from market competition, and special privileges. Patents, of course, can be found in all industries, but lobbyists for the pharmaceutical industry have successfully pressured Congress to provide several forms of market protection beyond patents.

Therapeutic Value of Drugs Marketed in France, 2002-2011

The industry measures “*innovation*” in terms of new molecular entities (NMEs), but most NMEs provide at best minor clinical advantages over existing ones and may lawfully be approved by the FDA even if they are inferior to previously approved drugs. The preponderance of drugs without significant therapeutic gain dates back at least 35 years. From the mid-1970s through the mid-1990s, multiple assessments have found that only 11 to 15.6 percent of NMEs provide an important therapeutic gain. Millions of patients benefit from the one out of six drugs that are therapeutically significant advances; but most R&D dollars are devoted to developing molecularly different but therapeutically similar drugs, which tends to involve less risk and cost for manufacturers. These drugs are then sold through competition based on brand name, patent status, and newness, rather than on their therapeutic merits.

An analysis of data from the National Science Foundation by Donald Light and Joel Lexchin indicates that patent-based pharmaceutical companies — often deemed by Congress, the press, the public, and themselves to be “innovative” — in fact devote only 1.3 percent of revenues, net of taxpayer subsidies, to discovering new molecules. The 25 percent of revenues spent on promotion is about 19 times more than the amount spent on discovering new molecules. In short, the term “R&D” as used by industry primarily means “development” of variations rather than the path-breaking “research” that onlookers might like to imagine.

The independent drug bulletin, *La revue Prescrire*, analyzes the clinical value of every

new drug product or new indication approved in France. From 1981 to 2001, it found that about 12 percent offered therapeutic advantages. But in the following decade, 2002- 2011, as shown in Figure 1, only 8 percent offered some advantages and nearly twice that many — 15.6 percent — were judged to be more harmful than beneficial. A mere 1.6 percent offered substantial advantages. Assessments by the Canadian advisory panel to the Patented Medicine Prices Review Board and by a Dutch general practice drug bulletin have come to similar conclusions. No comparable review has been done in the United States on the 229 NMEs approved by the FDA between 2002 and 2011.

This decrease does not come from the “innovation crisis” of fewer new molecules entering trials or eventually being approved but from fewer new drugs being clinically superior. The number of products put into trials has actually increased as the number of clinically superior drugs has decreased. These facts provide evidence that companies are using patents and other protections from market competition primarily to develop drugs with few if any new therapeutic benefits and to charge inflated prices protected by their strong IP rights.

Despite the small number of clinically superior drugs, sales and profits have soared as successful marketing persuades physicians to prescribe the much more costly new products that are at best therapeutically equivalent to established drugs. Both an American and a Canadian study found that 80 percent of the increase in drug expenditures went to paying for these minor-variation new drugs, not for important advances. Companies claim that R&D costs are “unsustainable.” But over the past 15 years, revenues have increased six times faster than has investment in R&D.

Almost a decade ago, Jerry Avorn, a widely respected pharmacoepidemiologist and author of a book on the risks of drugs, described how the big pharmaceutical companies exploited patents and concluded that “[l]aws designed to encourage and protect meaningful innovation had been turned into a system that rewarded trivial pseudo-innovation even more profitably than important discoveries.” He also noted that efforts in Congress to introduce a “reasonable pricing clause” that would reflect large taxpayer contributions to new drugs were defeated by industry lobbyists.

An Epidemic of Harmful Side Effects

Most new drugs approved and promoted since the 1970s lack additional clinical advantages over existing drugs and — as with all drugs — they have been accompanied by harmful side effects. A systematic review of the 39 methodologically strongest studies performed in the U.S. between 1964 and 1995 examined patients who were hospitalized due to a serious adverse drug reaction (ADR) or who experienced an ADR while in the hospital.

The review found that 4.7 percent of hospital admissions were due to serious reactions from prescription drugs that had been appropriately prescribed and used. In addition, 2.1 percent of in-hospital patients who received correctly prescribed medications experienced a serious ADR, for a total of 6.8 percent of hospital patients having serious ADRs. Applying this 6.8 percent hospital ADR rate to the 40 million annual admissions in U.S. acute care hospitals indicates that up to 2.7 million hospitalized Americans each year have experienced a serious adverse reaction. Of all hospitalized patients, 0.32 percent died due to ADRs, which means that an estimated 128,000 hospitalized patients died annually, matching stroke as the 4th leading cause of death. Deaths and serious reactions outside of hospitals would significantly increase the totals.

An analysis conducted in 2011, based on a year of ADRs reported to the FDA, came to similar conclusions: Americans experienced “2.1 million serious injuries, including 128,000 patient deaths.”

Other studies reveal that one in every five NMEs eventually caused enough serious harm in patients to warrant a severe warning or withdrawal from the market.

Of priority drugs that were reviewed in slightly more than half the normal time, at least one in three of them caused serious harm.

The public health impacts are even greater when milder adverse reactions are taken into account. Given estimates that about 30 ADRs occur for every one that leads to hospitalization, about 81 million side effects are currently experienced every year by the 170 million Americans who use pharmaceuticals. Groups such as pregnant women, elderly patients, and those who are taking multiple medications are especially at risk. Most of these medically minor adverse reactions are never brought to clinical attention, but even minor reactions can impair productivity or functioning, lead to falls, and cause potentially fatal motor vehicle accidents.

Contributors to More Harm and Less Benefit

Are the adverse side effects we have just been describing simply the “price of progress or an unavoidable risk of drug therapy?” In fact, evidence suggests that commercial distortions of the review process and aggressive marketing contribute to both undermining beneficence as health care’s *raison d’être* and to the epidemic of harm to patients.

Distorting, Limiting, and Circumventing Safety Regulations

Since at least the 1890s, the public has clamored for Congress to regulate contaminated or adulterated foods and harmful or ineffective medicines (medicines that may delay truly useful treatments). At that time, lobbyists — paid from drug profits — argued that even bills to require accurate listing of secret ingredients would destroy the industry. These lobbyists had managed to have earlier bills sent to die in the Committee on Manufactures until President Roosevelt intervened to secure passage of the 1906 Food and Drug Act, which still only required that statements on labels be true and provided no budget for enforcement.

Work on what would become the 1938 food and drug law began in 1933 with a bill that would prohibit misstatements in advertising and require manufacturers to prove to the FDA that drugs were safe before being allowed to sell them. The companies’ two trade associations launched “well-choreographed screams of protest” and letter-writing campaigns to mislead Congress and to distort its mission to protect its constituents from harm. Employees of drug makers wrote to Congress, arguing that requiring companies to make honest claims about safe drugs would put thousands out of work. The FDA staff wanted the legislation passed but were stopped by threats of prosecution if they campaigned for it. Then a manufacturer added diethylene glycol (antifreeze) to a sulfa drug to make a sweet-tasting elixir and children started dying. Public response trumped industry lobbyists and Congress passed the 1938 law, requiring that drugs be safe but leaving it to companies to decide how to define and test for safety.

For the next 25 years, drugs were approved within 180 days unless the FDA objected, based on the companies' tests and reports of safety. Some companies "tested" their products by sending samples out to providers for feedback, keeping no records of the results, and denying serious harms when reported by doctors. Daniel Carpenter, the author of a book considered to be a definitive work on the politics of the FDA, has detailed how the FDA staff dedicated themselves to enforcing the rules and developing better criteria for safety and efficacy. But as Malcolm Salter, at the Harvard Business School emphasizes, companies institutionalize corruption by getting legislative and administrative rules shaped to serve their interests, either directly or by crafting rules in ways they can game.

In his review of new pharmaceutical products in the 1940s and 1950s, Dr. Henry Dowling, an AMA senior officer and expert, found that companies launched 200-400 a year but only three on average were clinically useful. Physicians, swamped with far more drugs than they could know much about, relied on sales reps to brief them, entertain them, and leave an ample supply of free samples as gifts that the physicians could then give to their patients — a two-stage economy of reciprocity. In effect, through political pressure and lobbying, companies minimized the role of the FDA as the protector of public health for its first 56 years.

Following the 1962 amendments, propelled to passage by the thalidomide tragedy, the FDA commissioned the National Research Council, as part of the National Academy of Sciences, to review the effectiveness of all 2820 drugs (available in 4350 different versions) approved between 1938 to 1962. Companies were required to submit substantial evidence of effectiveness. The review concluded that seven percent of the drugs reviewed were completely ineffective for every claim they made and a further 50 percent were only effective for some of the claims made for them. Although the FDA has acted to remove many of these ineffective drugs from the market, some pre-1962 drugs are — more than 50 years later — still under-going review and are among the "several thousand drug products" that, according to a 2011 FDA guidance document, are today "marketed illegally without required FDA approval."

Regulatory capture begins with the dependency corruption of Congress, which passes the regulations and provides the funding for agencies to protect the public. While the 1962 amendments ushered in the modern era of testing for safety and efficacy before a drug can be approved, three key features of the modern drug-testing system actually work for industry profits and against the development of safe drugs that improve health.

First, three criteria used by the FDA contribute to the large number of new drugs approved with few therapeutic advantages. New drugs are often tested against placebos rather than against established effective treatments, and the use of surrogate or substitute end points, rather than actual effects on patients' health. Noninferiority trials that merely show that the product is not worse than another drug used to treat the same condition by more than a specified margin are accepted, rather than requiring superiority trials. Silvio Garattini, founder of the Mario Negri Institute for Pharmacological Research, points out that placebo and noninferiority trials violate international ethical standards and provide no useful information for prescribing.

Second, allowing companies to test their own products has led them — as rational economic actors — to design trials in ways that minimize detection and reporting of harms and maximize evidence of benefits. Furthermore, clinical trials for new drugs are designed

to test primarily for efficacy and generally are not able to detect less common adverse events.

Industry-friendly rules allow companies to exclude those patients most likely to have adverse reactions, while including those most likely to benefit, so that drugs look safer and more effective than they are in practice. Approvals based on scientifically compromised trials underlie the large number of heavily marketed new drugs with few or no new therapeutic benefits to offset their under-tested risks of harm.

Third, companies have created what can be characterized as the trial-journal pipeline because companies treat trials and journals as marketing vehicles. They design trials to produce results that support the marketing profile for a drug and then hire "publication planning" teams of editors, statisticians, and writers to craft journal articles favorable to the sponsor's drug. Articles that present the conclusions of commercially funded clinical trials are at least 2.5 times more likely to favor the sponsor's drug than are the conclusions in articles discussing non-commercially funded clinical trials. Yet, journal approval is deemed to certify what constitutes medical knowledge. Published papers legitimate the pharmaceutical products emerging from the R&D pipeline and provide the key marketing materials.

Furthermore, companies are much less likely to publish negative results, and they have threatened researchers who break the code of secrecy and confidentiality about those results. Positive results are sometimes published twice — or even more often — under different guises. This further biases meta-analyses — a method of statistically combining the results of multiple studies — and clinical guidelines used for prescribing. The result is "a massive distortion of the clinical evidence."

For decades, the FDA has kept silent about these practices and about the discrepancies between the data submitted to the FDA by companies and the findings published in journal articles, to the detriment of patients but much to the benefit of the companies. In sum, testing and FDA criteria approval provide little or no information to clinicians on how to prescribe new drugs, a vacuum filled by company-shaped "evidence" that misleads physicians to prescribe drugs that are less safe and effective than indicated by evidence that the FDA possesses.

PDUFA: Conflict-of-Interest Payments

In 1992, after years of underfunding and cuts in the 1980s that contributed to drug review times ballooning from 6 to 30 months, Congress passed the Prescription Drug User Fee Act (PDUFA), authorizing the FDA to collect "user fees" from drug companies that would allow it to hire 600 more reviewers and thereby speed up drug review. Supporters claimed that fees would increase incentives for innovation and improve health; but aside from clearing the backlog of NMEs waiting for approval, industry fees have not increased innovation as measured by clinically superior drugs.

In return for paying user fees, companies required the FDA to guarantee that it would review priority applications within six months and standard applications within 12 months of submission. Shortened review times led to substantial increases in serious harms. An in-depth analysis found that each 10-month reduction in review time — which could take up to 30 months — resulted in an 18.1-percent increase in serious adverse reactions, a 10.9-percent increase in hospitalizations, and a 7.2-percent increase in deaths. Now, 20 years

later, what Carpenter calls “corrosive capture” has set in — a weakened application of regulatory tools and a cultural capture of rhetoric about saving lives by getting new drugs to patients more quickly.

For the FDA, the reduction in review time combined with the fear that missing review deadlines will jeopardize continued PDUFA funding has also led to an increase in “up against the wall” approvals as review deadlines approach. Carpenter and his colleagues found that “the probability of a drug approved in the two months before the deadline receiving a new black-box warning (the most serious safety warning that the FDA can issue) is 3.27 times greater than a drug approved at some other time” and the likelihood of a drug being withdrawn from the market because of serious adverse events is 6.92 times greater.

These detailed studies corroborate what FDA staff told the Office of the Inspector General, namely, that concerns arising near the end of the review period are not adequately addressed, that needed meetings with advisory committees are not held, and that label warnings and contraindications are hastily written. As a result, there are “tens of thousands of additional hospitalizations, adverse drug reactions, and deaths.”

The 1998 withdrawal of five drugs, used by 19.8 million Americans, prompted critical reflection. Three distinguished physicians were struck by how little information had been gathered about the harmful side effects of these drugs before they were withdrawn. They attributed inaction to the FDA’s lack of interest in safety, lack of funds, and to “the lack of a proactive, comprehensive and independent system to evaluate the long-term safety, efficacy, and toxicity of drugs” after FDA approval.

To compensate for the FDA’s failures, they called for an independent National Drug Safety Board — akin to the National Transportation Safety Board that investigates each plane crash and holds public meetings — so that the same part of the FDA that approves drugs, the Center for Drug Evaluation and Research (CDER), would not later be asked to decide whether that drug should be restricted or withdrawn. In other words, public health would not depend on FDA officials’ willingness to admit their own mistakes. Such an independent board should establish an active monitoring system and gather comparative data across a given therapeutic class so it could provide objective information and develop better strategies for addressing adverse reactions as a major cause of death.

In 1997, a year before these five withdrawals, Congress had passed PDUFA II and companies had insisted that none of the fees collected be spent on post-market surveillance or on drug-safety programs. PDUFA II, III, IV, and V and related legislation provided the FDA with steeply increasing user fees but included lower criteria for approval, mandated that an industry representative be on FDA scientific advisory committees, lowered barriers to promotional efforts by companies, and required FDA officers to consult and negotiate with industry on the agency’s goals and plans.

Offsetting the harms associated with PDUFA I’s shortened approval framework are several tools created in PDUFA III through V for detecting, managing, and raising awareness of risks such as the Sentinel system and the Risk Evaluation and Mitigation Strategies; but there is no clear evidence these are reducing the epidemic of harms. These tools are inadequate to counterbalance the increase in risks — let alone to improve safety.

The additional \$10 million of funding provided by PDUFA III for the Office of Drug Safety and the \$7.5 million provided for the FDA’s advertising enforcement arm are tiny in comparison to the more than \$690

million in user fees that flow to the FDA each year. In sum, PDUFA allocates user fees overwhelmingly to ensure speedy review of new drug applications while leaving safety and enforcement dependent on grossly inadequate funding, perpetuating a history of underfunding safety.

Granting priority status to more drugs further increases the number of drugs reviewed in the shortest time and the chance of a major safety issue increases from one drug in five to one in three. Between 1999 and 2008, the FDA gave priority review status to almost 47 percent (114 of 244) of new drug applications, more than four times the proportion of drugs found to have superior clinical effects by independent review groups. Reflecting the cultural and corrosive capture of the FDA, its Commissioner said recently that “an increasing number of treatments are being approved under the agency’s fast-track, priority review ... to get critical and innovative medicines to market more rapidly.” Quicker reviews and less evidence of clinical benefit have rewarded the hidden business model of developing still more drugs with minor benefits.

The FDA’s obligation to serve the public is being corroded by pressures to serve the companies it regulates. As for post-market surveillance — “the single most important function...for protecting the public against the dangers of harmful drugs” — it is put largely in the hands of the manufacturers and the FDA Center for Drug Evaluation and Research (CDER), the part of the FDA that companies pay to review their new drug applications.

After approval, aggressive marketing of new drugs to doctors for both approved and unapproved uses before good safety information is available maximizes the number of patients exposed to risks from the roughly 25 to 40 new NMEs approved annually.

Field studies find that most drug representatives do not discuss adverse side effects. Although the law requires companies to submit some marketing materials for review, Congress and the FDA allocate only a small budget and staff to review about 75,000 submissions a year for false or misleading information. Further, the small stream of letters ordering that inaccuracies be corrected is subject to a review process that delays their reaching the companies.

Marketing for unapproved or “off-label” uses worsens the balance of harm and benefit and undermines the purpose of testing to show that a drug is effective and safe for a specific use. While trying drugs for new uses is clinically important, especially for certain populations such as children and cancer patients, 75 percent of off-label prescribing is neither supported by sound evidence nor accompanied by an organized means for gathering such evidence. Companies retain leading experts to expand use, broaden clinical guidelines, and conduct small, short sham trials that companies get published and hand out to their physician-customers as “evidence.”

A 15-month investigation by the Committee on Government Reform of the U.S. House of Representatives found “a growing laxity in FDA’s surveillance and enforcement procedures, a dangerous decline in regulatory vigilance, and an obvious unwillingness to move forward even on claims from its own field offices.” The resulting 2006 report also documented a 53.7-percent decline in warning letters. Since then, FDA leadership has shifted to talking about being a “partner” with industry to get more drugs to patients more quickly. For the reasons we explained above, the proportion of new products with clinical advantages seems to have moved from about 1 in 8 down to 1 in 12, while the proportion with serious harms has gone up from 1 in 5 towards 1 in 3 as the number of drugs given priority status increases.

Read the rest: <https://app.box.com/s/5414zf7lufhtwf3czjfo9msafnoz6ht5> or: <http://ethics.harvard.edu/news/institutional-corruption-and-pharmaceutical-policy>

Direct from author: https://www.academia.edu/6750219/Institutional_Corruption_and_the_Myth_of_Safe_and_Effective_Drugs

Medical Veritas • 2008

The truth behind the vaccine cover-up

Russell L. Blaylock, MD

Abstract

On June 7-8, 2000 a secret conference was held at the Simpsonwood Conference Center in Norcross, Georgia to discuss a study examining the link between increasing doses of Thimerosal and neurodevelopmental disorders. The study was done using the Vaccine Safety Datalink (VSD) data-base, an official governmental data bank collecting patient vaccination information on the children from the health maintenance organizations (HMOs) being paid to participate. Attending were 51 scientists, representatives of pharmaceutical vaccine manufacturing companies and a representative of the World Health Organization; the public and the media were unlawfully excluded. The conclusions of this meeting were quite startling, since it confirmed a dose-response link between Thimerosal and neurodevelopmental disorders that held up to rigorous statistical analyses.

In their discussion, they make plain why the meeting was held in secret: the conclusions would have destroyed the public's confidence in the vaccine program, and more importantly, their faith in vaccine authorities. When the results of this study were published three years later in the journal Pediatrics, the "problem" had been fixed, in that by adding another set of data from a third HMO, reorganizing the criteria for inclusion and restructuring the patient groupings, a less than statistically significant link was demonstrated. In my analysis I discuss the more outrageous statements made during the meeting and how accepted experts in the field of mercury neurotoxicity were excluded from the meeting.

I was asked to write a paper on some of the newer mechanisms of vaccine damage to the nervous system, but in the interim I came across an incredible document that should blow the lid off the cover-up being engineered by the pharmaceutical companies in conjunction with powerful governmental agencies.

continued on page 725-726

“There is a great deal of evidence to prove that immunization of children does more harm than good”

Dr. J. Anthony Morris, former Chief Vaccine Control Officer, FDA

Table of Contents

Chapter One	Manufacturing Biologics	Page 24
Chapter Two	Thimerosal • Mercury	Page 129
Chapter Three	Alum • Aluminum Salts	Page 308
Chapter Four	The HPV Vaccine	Page 489
Chapter Five	Vaccination History 1915 - 2015	Page 525
Chapter Six	On Autism	Page 980
Chapter Seven	Short Essays On Vaccination	Page 1041

Featured Full-Length Reports

- Page 186 Mercury toxicity: Genetic susceptibility and synergistic effects
- Page 199 Heavy-Metal Toxicity—With Emphasis on Mercury
- Page 430 Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?
- Page 437 Aluminum Vaccine Adjuvants: Are they Safe?
- Page 440 Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations
- Page 470 Aluminum-induced entropy in biological systems: implications for neurological disease
- Page 503 Who Profits From Uncritical Acceptance of Biased Estimates of Vaccine Efficacy and Safety?
- Page 505 No autoimmune safety signal after vaccination with quadrivalent HPV vaccine Gardasil?
- Page 507 Death after Quadrivalent Human Papillomavirus (HPV) Vaccination: Causal or Coincidental?
- Page 509 HPV vaccines and cancer prevention, science versus activism
- Page 624 Vaccines and Autism
- Page 645 Biological Evidence of Significant Vaccine Related Side-effects Resulting in Neurodevelopmental Disorders
- Page 649 Chronic Microglial Activation and Excitotoxicity Secondary to Excessive Immune Stimulation: Possible Factors in Gulf War Syndrome and Autism
- Page 697 FDA Science and Mission at Risk
- Page 698 Current childhood vaccine programs
- Page 699 Vaccines, depression, and neurodegeneration after age 50 years: another reason to avoid the recommended vaccines
- Page 705 Modeling Neurodevelopment Outcomes and Ethylmercury Exposure from Thimerosal-Containing Vaccines
- Page 720 Current childhood vaccine programs: An overview with emphasis on the Measles-Mumps-Rubella (MMR) vaccine
- Page 726 The truth behind the vaccine cover-up
- Page 818 Vaccination: Why the ‘one size fits all’ vaccination argument does not fit all!
- Page 872 Hidden in Plain Sight: Vaccines as a Major Risk Factor for Chronic Disease
- Page 912 Methodological issues and evidence of malfeasance in research purporting to show thimerosal in vaccines is safe
- Page 998 A possible central mechanism in autism spectrum disorders Part 1
- Page 999 A possible central mechanism in autism spectrum disorders Part 2
- Page 1000 A possible central mechanism in autism spectrum disorders Part 3

Introduction

Vaccines are not the product of altruistic and generous or benevolent action on the part of the manufacturers. Gardasil alone sells for well over 100 dollars per injection. As a consequence, each of us at birth immediately represents thousands of dollars worth of income across the over 188 injections we'll receive in a lifetime—according to the complete recommended US vaccination schedule—starting with 128 antigen, adjuvant and excipient injections before reaching adulthood.

Vaccines are sold under an extremely clever marketing strategy that encompasses not only a “must-have” scenario for each of us but included with that is absolutely no liability for harm. What do you suppose motivated the vaccine manufacturers to work so exceedingly hard through public and governmental processes to establish a “lawsuit-free zone” for vaccines? Was it to avoid any chance at all of legal challenges? The extraordinary harm you'll read about here is directly related to seeking that discharge of legal responsibility for damage. Many of us won't remember that years ago the lawsuits were mounting and the vaccine business was about to come to an end.

This collection of reports reveals the gruesome and stark reality that lies hidden behind what is actually “open-source and public” medical literature that, for reasons unknown, the general public will rarely see. Perhaps the difficulty in finding representative material is an obstacle. Maybe the complexities surrounding the issue are an impediment to fruitful searches. This PDF was created for these reasons. Admittedly, this is a large collection of data that can't be examined properly in a weekend. Yet the totality of the data is what's so very important. If one person told us that repeatedly injecting aluminum, mercury, antigens or excipients could be dangerous we might question the theory but when 100s of professionals make a medically supported claim, we should listen closely, don't you think?

The vaccine industry is rife with corruption and fraud and that's about the only thing that isn't actually printed. The human damage and the collateral toll from vaccination is carefully recorded and this collection discloses some of that harm. While there may be 1000 peer reviewed reports here, I can assure you that there are 1000s more just the same. This collection provides the reader with the peer review that is less complex and easier to understand. Some of you, hopefully, will research the more complex issues further on your own using terms, authors and subject matter found here.

If you take the time to read all of the reports collected here you'll come to understand certain uncomfortable realities. For example, that all of the 350-plus vaccines currently in use are nothing more than population-wide experiments. The pre-licensing trials are so short and with small cohorts and they

use only very healthy, robust people, that they can't gain any knowledge at all regarding adverse events in the general population. It's common knowledge within the industry that a vaccine isn't tested and that adverse events are virtually unknown, until after it's been used for some time in large segments of the population. Several years to a decade or more later they may find that there are serious problems related to a particular vaccine. This is what happened with Thimerosal. The scientific evidence came in decades later that autism, neurological disorders and other human diseases were promoted by and often caused by Thimerosal. You'll read peer reviewed reports here from respected journals about the epidemic human damage and the cover-up. In fact, if not for the cover-up we might have been able to reduce or even eventually halt the autism epidemic. Instead, the issue has been concealed from the public and Thimerosal was quietly replaced with aluminum.

Thimerosal was not “removed” from vaccines. All Thimerosal-containing vaccines (TCVs) were used up and the new lots of vaccine were made with a new adjuvant.

Various aluminum salts, adjuvants used in many vaccines, may be even more insidious than Thimerosal. Numerous authors from around the world believe so. A new disease, encompassing nearly 100 different disorders and affecting as many as 50 million people in the US, has been named and studied. ASIA, autoimmune/inflammatory syndrome induced by adjuvants, was officially named by the medical research community in 2013. To paraphrase one of the authors within these pages, we've reached a point in time where the damage from vaccines has exceeded the hoped for protection from disease. To paraphrase further, childhood illnesses like chicken pox, measles, mumps and others are “challenge viruses” that strengthen the immune system and we've removed a significant and very important immune fortifying evolutionary step from humankind by vaccinating.

Misleading advertising campaigns with deceptive and often times unproven claims accompanied by well organized sham-marketing strategies have completely misled the average consumer who buys vaccines like lattes. The resulting tragedy is a series of epidemics of disease and disorder that translates into nothing short of the very definition of the word “pandemic.”

Across the globe the vaccination programs have traded several childhood diseases for nearly 100 new disorders many of which were virtually unknown just a century ago. Measles, mumps, rubella, chicken pox and other tolerable, “*immune system fortifying*” childhood illnesses have been replaced by epidemics, and I'm not using that word lightly. Epidemics of Autistic Spectrum Disorder (ASD), Guillain-Barre Syndrome (GBS), Mac-

rophagic Myofasciitis (MMF), Multiple Sclerosis (MS), Alzheimers Disease (AD), Learning Disabilities (ADHD), Arthritis, Inflammatory Bowel Disease, Crohn's Disease (CD), Autoimmune And Inflammatory Syndrome Induced By Adjuvants (ASIA), Hodgkin and non-Hodgkin lymphomas, Allergies, Asthma and nearly 100 more diseases and disorders are all reaching epidemic proportions. They're all caused by vaccines.

Yet the greatest human epidemic of the 20th and 21st centuries will be the enormous spectrum of neurological and biological symptoms and complications associated with autism, ADHD and learning disabilities. Taken together, these neuro-bio-disorders affect one in 6 children in the USA and they are directly related to the US vaccine schedule.

The material collected herein will inform the reader that vaccines cause disorders that increase the profits on tablet and capsule style drugs substantially and that vaccines are not safe, nor are they effective. The collateral damage currently being caused by what the reader will come to know as a very primitive and largely unknown and unproven science, is beyond imaginable and beyond description. It requires 100s of pages of text to accurately describe the full gamut of human damage caused by the global vaccination programs and that's exactly what we've collected here.

The reports within these pages were written by many celebrated, accomplished and esteemed authors who are well known within their fields, independent authors whose integrity hasn't been compromised by influence or wealth. Represented here are hundreds of prominent and duly recognized medical professionals and specialists, scientists, clinicians and researchers from around the world, people such as Dr. Christopher Exley, one of the worlds leading experts on Aluminum, and whose sense of humor in the face of extraordinary, planet-wide adversity, is a welcomed respite. I hope you'll become acquainted with Dr. Jose Dorea, Dr. CA Shaw, Dr. Harold Buttram, Dr. Joachim Mutter, Dr. Russell Blaylock and Dr. Lucija Tomljenovic and their varied, prescient and wholly honest writing styles. There are many others. These are just some of my favorites. Look for them and read what they have to say and your understanding of vaccination will grow accordingly. After all, they're writing to you.

These issues are so critically important to these professionals that they write about them repeatedly. You can literally hear their voices in their writing. Many of the 100s of authors within these pages may be risking career advancement to expose the truth—that the harm from vaccines has seriously exceeded the benefit of disease prevention—yet none of these authors have compromised their morals. Please, listen to them.

Preface

Most of the ingredients in vaccines—including aluminum, mercury, formaldehyde, B2 glycoprotein, Triton X-100®, Polysorbate or Tween 80®, 60 and 20, 2-Phenoxyethanol, etc.—are neurotoxins, toxic to cells, cell structure and neurons. Vaccines are designed such that “tissue damage” is a necessary component of antibody creation to acquire some level of assumed immunity. Tissue damage, cell death or apoptosis are required aspects of vaccination success. The key is to cause tissue damage without damaging the person herself. After 100 years of vaccination science we are still as yet unable to achieve that goal. Vaccine damage is ubiquitous.

There are low-responders and non-responders the medical profession fails to discuss publicly and inform us about. Within every country-population cohort—people that will respond to vaccination with low or zero recognizable titers and whose immune system simply will not “take” to the vaccine—make up a normal and expected percentage of the population. Non- and low-responders can be responsible for outbreaks of disease just as fully vaccinated individuals can acquire and spread the illnesses they were vaccinated for. Vaccination is never, ever 100% and comes with no guarantees of protection or immunity to disease nor guarantees against serious harm or death.

Historically, the innate immune system was at the forefront of disease defense and it mobilized epithelial barriers (referring to the skin and the thin tissue covering the body’s surface and lining the alimentary canal and other hollow structures of the ears, eyes, nose and throat), special lymphocytes called “natural killer (NK)” cells, plasma proteins and other immune system components. Vaccination bypasses the innate immune system and directly affects only the humoral immune system (referring to antibodies in body fluids as distinct from cells).

Decades of bypassing the innate immune system along with removal of common and tolerable childhood “challenge” diseases—mumps, chicken pox, measles, etc.—has caused a reversal in the way our bodies fight viral and bacterial infection. Evolutions first line of defense and the faster, stronger primary system, the innate immune system, has been relegated to second place with vaccination causing the slower acting humoral immune system to occupy the first line of defense. The result of repeated vaccination to perturb the human immune system into developing antibodies to less than 2 dozen different tolerable childhood ailments—antibodies which have never been proven to be markers of immunity—has manifest as 100 or more human disorders after little more than 100 years of vaccination. The epidemic of disease we can now see surrounding us is staggering. The reasons for these epidemics of disease are outlined herein and are supported not by any individual report or study but by the totality of the collected evidence.

I sincerely hope that the material represented here helps you to better understand a very important aspect of life in this 21st century.

The link below accesses a collection of 44 full-length reports in PDF format that are free to download and that are also included herein in shorter abstract form:

<https://app.box.com/s/xa75ta0j9jbe05e615gd5xto9ff1mz4a>

“It is now universally recognized that we have a steadily growing epidemic of childhood autism, learning disabilities, and other developmental disorders, with comparable increases in asthma and allergies.”

Medical Veritas International Inc • 2007

**Reminiscences of America’s children in the 1930s
as compared with today, and the possible role of vaccines
in causing retrogressive changes**

Editorial

by Harold Buttram, MD, FAACP
5724 Clymer Road Quakertown, PA 18951
HButtrum@woodmed.com

Abstract

It is now universally recognized that we have a steadily growing epidemic of childhood autism, learning disabilities, and other developmental disorders, with comparable increases in asthma and allergies. By any measure now available, these conditions were rare during the 1930s and 1940s. If this trend is to be reversed, we must seek for causes.

As largely disclosed during the U.S. Congressional Hearings on issues of vaccine safety, which took place from 1999 to December, 2004, there are gross deficiencies in vaccine safety testing. Because of this lack, we have no means of identifying or proving adverse reactions when they do occur.

Almost totally lacking until now, the great need is for definitive before-and-after tests specifically designed to search for adverse effects of vaccines on the neurological and immune systems as well as genetics of our children, and in findings adverse effects to make appropriate safety modifications in vaccine programs. Over the years there have been a scattering of before-and-after vaccine tests showing that there can be harm to the immune and central nervous systems, bringing suspicion on vaccines as an underlying cause of current childhood epidemics. However, these have always been of limited scale, seldom if ever with adequate follow-up.

In the opinion of this observer, until the safety of vaccine programs can be assured by such testing, any further mandating of childhood vaccines will remain morally and ethically untenable.

<http://www.medicalveritas.com/images/00166.pdf>

Lucija Tomljenovic, PhD

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences, University of British Columbia
828 W. 10th Ave, Vancouver, BC, V5Z 1L8 tel: 604-875-4111 (68375)

Regarding H.527

Distinguished Members of the Vermont House,

The argument of forcing a parent to vaccinate their child in the name of the “greater good argument” is flawed both scientifically and ethically. Firstly, all drugs are associated with some risks of adverse reactions. Because vaccines represent a special category of drugs which are by and large given to healthy individuals, and for prophylaxis against diseases to which an individual may never be exposed, the margin of tolerance for side effects is very narrow (in fact, the U.S. Food and Drug Administration (FDA) concurs with this point [1]) and careful assessment of risks versus benefits essential in deciding whether one should be vaccinated or not. Removing the “philosophical exemption” as a means to opt out from vaccination will put vulnerable but otherwise healthy individuals at risk of serious adverse reactions to vaccinations. Such an outcome should be of concern since cases of permanent neurodevelopmental disabilities and deaths following vaccination in children with underlying genetic and other susceptibilities have been firmly established in scientific literature [2-4]. Please consider carefully whether you wish to be responsible for such potential outcomes should you facilitate this legislation to come to pass.

Secondly, medical ethics demand that vaccination should be carried out with the participant’s full and informed consent. This necessitates an objective disclosure of the known or foreseeable vaccination benefits and risks. The way in which pediatric vaccines are often promoted by various health authorities indicates that such disclosure is rarely given from the basis of best available knowledge but rather, largely unproven and/or untenable assumptions on both, vaccine safety and effectiveness. I shall herein elaborate on these arguments.

Is Vaccine Safety Evidence “Rock Solid”?

The statement by Dr Chen that “the science behind vaccination safety is rock solid” is factually inaccurate and contradicts a large body of scientific literature published on this subject [3-35]. As with any medication, vaccines can carry risks of adverse reactions (ADRs). However, in spite of the widespread notion that vaccines are largely safe and serious adverse complications are extremely rare, a close scrutiny of the scientific literature does not support this view [10-12]. For example, to date the clinical trials that could adequately address vaccine safety issues have not been conducted (i.e., comparing health outcomes in vaccinated versus non-vaccinated children). The lack of such controlled trials may be because historically, vaccines have been assumed safe [12]. There is also a view that conducting such trials would be extraordinarily difficult or unethical; the first is simply not correct, the second is not a scientific issue per se.

It is also often assumed that vaccines face a tougher safety standard than most pharmaceutical products. However, according to the U.S. FDA, “Historically, the non-clinical safety assessment for preventive vaccines has often not included toxicity studies in animal models. This is because vaccines have not been viewed as inherently toxic” [1]. This is a startling admission from an Agency which according to its own mission statement is “responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs”[36]. Essentially, what the FDA workshop [1] revealed is that not only are vaccines not adequately evaluated for toxicity but also, that the reason for such an oversight rested on a belief rather than scientific evidence. Science is not a religion

in which dogmatic statements of faith can replace adequately powered, controlled, longitudinal vaccine safety studies in animals and people. Furthermore, such assumptions of safety, in the absence of actual experimental data, are not only dangerous but have historically hampered serious scrutiny of potential vaccine harms.

To illustrate a recent example of grave consequences that resulted from pushing a poorly tested vaccine to young children, note that there have been a large numbers of major ADRs from seasonal influenza vaccines. Consequently, they have been suspended for use in children under five years of age in Australia. In a series of Rapid Responses addressing this issue, published in British Medical Journal, titled “Adverse events following influenza vaccination in Australia-should we be surprised?” Collignon (Director of Infectious Diseases & Microbiology at Australian National University) and colleagues from the Cochrane Collaboration review panel concluded: “There is poor evidence on how well influenza vaccines prevent any influenza complications in children and other age groups. There is good evidence that influenza vaccines study reports cherry pick results and achieve spurious notoriety. Exposing human beings to uncertain effects is a risky business” [25]. The authors also noted that worldwide, the recommendations from public health authorities regarding influenza vaccination has been “misguided”[26].

It important to note that even those in the scientific community who are strong proponents of vaccinations have come to question the scientific legitimacy of “one-size fits all” vaccination practices [37]. For example, Poland (Editor in Chief of the journal Vaccine and co-author of “The age-old struggle against the antivaccinationists” [38]) and colleagues rightly ask whether “with the advances coming from the new biology of the 21st Century”, it is time to consider “how might new genetic and molecular biology information inform vaccinology practices of the future?” [37]. In light of this question Poland et al. conclude that “one-size fits all” approach for all vaccines and all persons should be abandoned. According to Poland, this conclusion applies to both vaccine efficacy, as well as safety [37]. Regarding the latter, the widely held view that serious vaccine-related ADRs are rare needs revision, as current worldwide vaccination policies indeed operate on “one-size fits all” assumption. This assumption persists despite the fact that historically, vaccine trials have routinely excluded vulnerable individuals with a variety of pre-existing conditions (i.e., premature birth, personal or family history of developmental delay or neurologic disorders including epilepsy/seizures, hypersensitivity to vaccine constituents etc. [39-43]). Because of such selection bias, the occurrence of serious ADRs resulting from vaccinations may be considerably underestimated. As mentioned previously, such an outcome should be of concern in view of documented evidence of permanent neurodevelopmental disabilities and deaths following vaccination in children with underlying genetic and other susceptibilities [2-4]. Poland et al.’s current data may thus have far broader implications for understanding vaccines, not only in terms of efficacy and the desired immune response, but also in terms of safety. Indeed, vulnerable populations will neither have the same antibody response nor the same level of tolerance to serious ADRs as non-vulnerable populations [37,44].

The Quality of Existing Vaccine Safety Data

A further obfuscation of the actual rate of serious vaccine-associated ADRs may also be due to methodological inadequacy of existing vaccine trials (i.e, the frequent exclusion of individuals with potential pre-existing susceptibilities to vaccine-associated ADRs) [12], and due to the fact that the vast majority of such trials use an aluminum adjuvant-containing placebo or another aluminum-containing vaccine as the “control group” [45]. That aluminum is a demonstrated neurotoxin has been known for over 100 years [46] and in this context, it is becoming clear to a number of investigators that its use as a placebo control is scientifically untenable [45,47].

Furthermore, with regard to the studies which allegedly demonstrably show no link between autism and vaccines, it has to be emphasized that once such studies undergo proper expert scrutiny, the “evidence” against the link becomes rather flimsy. In reviewing the published literature on measles- mumps-rubella (MMR) vaccine (139

studies), the respected Cochrane Collaboration review panel concluded that, “The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate” [48]. Moreover, none of the 31 studies that were included in the review met the Cochrane Collaboration’s methodological criteria. More specifically, referring to the 2001 Fombonne and Chakrabarti study [49] which was widely regarded by medical health authorities as most persuasive in disproving the link between the MMR vaccine and autism, the Cochrane Collaboration commented the following: “The number and possible impact of biases in this study was so high that interpretation of the results is impossible” [48]. Although the Cochrane Review on the safety of MMR concluded that there was no credible link between MMR vaccination and autism and Crohn’s disease, as pointed out earlier, the majority of the studies included in the evaluation were methodologically inadequate. The question thus is what “credible” or “rock solid” evidence can be derived from inadequate studies?

Demonstrated Toxicity of Vaccine Constituents

Vaccines contain known neurotoxins (i.e., mercury, aluminum, formaldehyde), potent adjuvants designed to hyperstimulate the immune system, as well as various antigenic compounds [10,50] albeit all in relatively small amounts. Thus a typical vaccine formulation contains all the necessary biochemical components to induce both autoimmune as well as neuroimmune disorders. The question is not whether these compounds are in vaccines or if they are toxic, rather if in such concentrations alone or combined, they can harm the nervous and other systems. Experimental evidence indeed shows that some of these constituents (mercury and aluminum) can cause long-term neurological impairments in animal models when individually administered in vaccine-relevant human exposures [7,51-57].

Furthermore, data also demonstrate that over-stimulating the host’s immune system by repeated immunization with immune antigens and/or adjuvants inevitably leads to autoimmunity even in genetically non-susceptible animals [58,59]. Specifically, simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity [59]. Yet in spite of these observations, according to the current U.S. immunization schedule by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of Al adjuvants [10].

Given the scarcity of evidence of safety of the combined pediatric schedule and the fact that administration of only a few vaccines in human adults can lead to brain dysfunction and a variety of autoimmune conditions [8,16,17,19], the concerns about the overall safety of current childhood vaccination programs are scientifically plausible and thus require urgent consideration [10].

Full Report with References

<http://www.vaxchoicevt.com/wp-content/uploads/2012/04/Lucija-Tomljenovic-PhD-letter.pdf>

<https://app.box.com/s/ev8bhi6vb3rofhkavum3v3hpt2xlil9>

<http://vaccinechoicecanada.com/wp-content/uploads/Forced-Vaccinations-For-the-Greater-Good-Tomljenovic.pdf>

“According to the Autism Society of America, autism is now considered to be an epidemic.”

Journal Of Toxicology And Environmental Health Part B, Critical Review • November 2006

Evidence of toxicity, oxidative stress, and neuronal insult in autism

Author information

Kern JK1, Jones AM.
Department of Psychiatry
University of Texas Southwestern Medical Center at Dallas
Dallas, Texas 75390-9119, USA
janet.kern@UTSouthwestern.edu

Abstract

According to the Autism Society of America, autism is now considered to be an epidemic. The increase in the rate of autism revealed by epidemiological studies and government reports implicates the importance of external or environmental factors that may be changing. This article discusses the evidence for the case that some children with autism may become autistic from neuronal cell death or brain damage sometime after birth as result of insult; and addresses the hypotheses that toxicity and oxidative stress may be a cause of neuronal insult in autism. The article first describes the Purkinje cell loss found in autism, Purkinje cell physiology and vulnerability, and the evidence for postnatal cell loss. Second, the article describes the increased brain volume in autism and how it may be related to the Purkinje cell loss. Third, the evidence for toxicity and oxidative stress is covered and the possible involvement of glutathione is discussed. Finally, the article discusses what may be happening over the course of development and the multiple factors that may interplay and make these children more vulnerable to toxicity, oxidative stress, and neuronal insult.

<http://www.ncbi.nlm.nih.gov/pubmed/17090484>

Vaccination and autoimmunity: reassessing evidence

Marc Girard, MSc, MD
1 bd de la République
78000-Versailles, France
Phone:+330139670110
Fax:+330139670111
agosgirard@free.fr

Abstract

The autoimmune risks of vaccines seem frequently overlooked. Whereas most available vaccinations are supposed to produce long-lasting immunity, the fact that they can also produce long-term detrimental immune effects seems to be ignored as evidenced by the short duration of safety studies during development. Likewise, whereas it seems natural to simply rely on surrogate markers, such as antibodies, to demonstrate vaccine efficacy, the levels of evidence required to acknowledge adverse effects is far higher. Reports to the Vaccine Adverse Event Reporting System (VAERS) are deemed more conclusive when reassuring than when suggesting significant toxicity. As a result of these blatant biases in clinical and/or epidemiological research, experts on autoimmunity and vaccine critics are limited to demonstrating theoretical mechanisms because evidence in practice is lacking.

Known as the bias of the selective assessment, this unbalance in the demonstration of the benefits as compared to the risks is the *bête noire* of evidence-based medicine. Therefore, when readjusted to the demonstrative level normally viewed as sufficient in clinical research in general and in vaccine science specifically, the corpus of data on the autoimmune hazards of vaccines appears certainly more impressive than generally recognized and calls for further research, for an overall reassessment of the benefit/risk ratio of vaccines including multiple vaccinations. Because vaccines are now aimed at preventing diseases which may be quite rare, the Hippocratic principle of prudence is more than ever a very topical issue.

Many other examples of poor methodology, selective assessment or dissimulation of data could be given. This suggests that research and development on vaccines are still at the zero- level of evidence-based medicine (EBM).

As assessed with the same units of measure used with other drugs, some vaccines and specifically the hepatitis B vaccine have an unacceptable benefit/risk ratio, especially in countries where the diseases they claim to control are not endemic.

For obvious reasons of profit, the threats to the scientific and medical ethics of our job have reached a worrying level: it is the personal responsibility of each of us to resist – and to support those who are the most under pressure.

“The autoimmune risks of vaccines seem frequently overlooked. Many other examples of poor methodology, selective assessment or dissimulation of data could be given. This suggests that research and development on vaccines are still at the zero-level of evidence-based medicine (EBM) ... It is the personal responsibility of each of us to resist”

Unanswered Questions A Review of Compensated Cases of Vaccine-Induced Brain Injury

by Mary Holland, Louis Conte, Robert Krakow and Lisa Colin

Executive Summary

In 1986, Congress created the Vaccine Injury Compensation Program (VICP) under the National Childhood Vaccine Injury Act (1986 Law). This Program has original jurisdiction for children's claims of vaccine injury. Because almost all children receive multiple vaccinations for daycare and school, it is critically important that the Program provides fundamental fairness, due process and transparency.

This empirical investigation, published in a peer-reviewed law journal, examines claims that the VICP compensated for vaccine-induced encephalopathy and seizure disorder. The VICP has compensated approximately 2,500 claims of vaccine injury since the inception of the program. This study found 83 cases of acknowledged vaccine-induced brain damage that include autism, a disorder that affects speech, social communication and behavior. In 21 published cases of the Court of Federal Claims, which administers the VICP, the Court stated that the petitioners had autism or described autism unambiguously. In 62 remaining cases, the authors identified settlement agreements where Health and Human Services (HHS) compensated children with vaccine-induced brain damage, who also have autism or an autism spectrum disorder.

Parents reported the existence of autism in telephone interviews and supplied supplemental materials including medical diagnoses, school records, and completed, standard autism screening questionnaires to verify their reports. In 39 of the 83 cases, or 47% of the cases of vaccine injury reviewed, there is confirmation of autism or autism spectrum disorder beyond parental report.

This finding of autism in compensated cases of vaccine injury is significant. U.S. government spokespeople have been asserting no vaccine-autism link for more than a decade. This finding calls into question the decisions of the Court of Federal Claims in the Omnibus Autism Proceeding in 2009 and 2010 and the statement of Health and Human Services on its website that "HHS has never concluded in any case that autism was caused by vaccination."

Using publicly available information, the investigation shows that the VICP has been compensating cases of vaccine-induced brain damage associated with autism for more than twenty years. This investigation suggests that officials at HHS, the Department of Justice and the Court of Federal Claims may have been aware of this association but failed to publicly disclose it.

The study calls on Congress to thoroughly investigate the VICP, including a medical investigation of compensated claims of vaccine injury. This investigation calls on Congress to get answers to these critically important unanswered questions.

<http://www.ebcala.org/unanswered-questions>

"Using publicly available information, the investigation shows that the Vaccine Injury Compensation Program (VICP) has been compensating cases of vaccine-induced brain damage associated with autism for more than twenty years. This investigation suggests that officials at HHS, the Department of Justice and the Court of Federal Claims may have been aware of this association but failed to publicly disclose it."

“This eBook is free because the truth should always be free”

~ Jeff Prager

Chapter One

The Business Of Manufacturing Biologics

1969 - 2015

If the global vaccination programs are causing epidemic incidents of death and disease, and they are, then it's our responsibility to do something about it and revealing it using respected, independent peer review is a critically important component of that exposure. Here we provide basic insight into the highly complex and tricky business of manufacturing injectable products. Laboratory creation of safe injectable's is a dirty business fraught with risk and unpredictable circumstances at every turn. Viruses mutate and new viruses appear out of nowhere to sully the product. Most, if not all, vaccine lots are contaminated. Enteroviruses, pestiviruses, DNA and RNA fragments, bovine and porcine viruses and other components of the virus manufacturing process remain in the final product. We're told there's no harm related to injecting these vagrant particles but the truth is, there's absolutely no scientific data to support that claim. Mutating viruses with the high potential for undiscovered contamination will eventually win over man in his misguided attempt to repeatedly vaccinate every living human being. We're each faced with almost 200 vaccines in our lifetime—128 antigen, adjuvant and excipient injections by adulthood if the vaccine schedule is followed—and that extraordinary volume of repeatedly injected material is now causing devastating population-wide effects. The increase in disease and disorder is readily apparent to anyone that looks. This chapter describes the dirty business of biological manufacturing.

“A cell line (MDCK) of dog kidney origin grows on a glass surface as a mosaic of epithelium with many multicellular hemispherical vesicles. The cells lining the blisters actively secrete into the cyst cavities. Suspensions of these cells injected intravenously in the chick embryo produce brain metastases resembling adenocarcinoma.”

Science • January 1969

Secretory activity and oncogenicity of a cell line (MDCK) derived from canine kidney

A cell line (MDCK) of dog kidney origin grows on a glass surface as a mosaic of epithelium with many multicellular hemispherical vesicles. The cells lining the blisters actively secrete into the cyst cavities. Suspensions of these cells injected intravenously in the chick embryo produce brain metastases resembling adenocarcinoma.

[Editors Note: The MDCK (NBL-2) (ATCC® CCL-34™) cell line has been used since 1958 to produce influenza and other vaccines]

<http://www.sciencemag.org/content/163/3866/472.long>

MDCK cell line:

<http://www.atcc.org/products/all/CCL-34.aspx>

“The phage contamination of virus
vaccines and its possible consequences
need further investigations.”

Journal of Biological Standardization
Volume 3, Issue 3, July 1975
Pages 307–308

Bacteriophage contamination in live poliovirus vaccine

by Hedda Milch†, F. Fornosi†

Abstract

Bacteriophages lytic for *Escherichia coli* strains were isolated from two lots of oral poliomyelitis vaccine. From one ultracentrifuged sample bacteriophages of four different plaque patterns were demonstrable with *E. coli* C 3000 (2.8×10^2 PFU/ml) and *E. coli* (1.1 $\times 10^2$ PFU/ml) as indicator strains. The phage contamination of virus vaccines and its possible consequences need further investigations.

Purchase Price - \$31.50

<http://www.sciencedirect.com/science/article/pii/0092115775900347>

“The determination of the total 5,224 base-pair DNA sequence of the virus SV40 has enabled us to locate precisely the known genes on the genome.”

Nature • May 1978

Complete nucleotide sequence of SV40 DNA

Fiers W, Contreras R, Haegemann G, Rogiers R, Van de Voorde A, Van Heuverswyn H, Van Herreweghe J, Volckaert G, Ysebaert M.

Abstract

The determination of the total 5,224 base-pair DNA sequence of the virus SV40 has enabled us to locate precisely the known genes on the genome. At least 15.2% of the genome is presumably not translated into polypeptides. Particular points of interest revealed by the complete sequence are the initiation of the early t and T antigens at the same position and the fact that the T antigen is coded by two non-contiguous regions of the genome; the T antigen mRNA is spliced in the coding region. In the late region the gene for the major protein VP1 overlaps those for proteins VP2 and VP3 over 122 nucleotides but is read in a different frame. The almost complete amino acid sequences of the two early proteins as well as those of the late proteins have been deduced from the nucleotide sequence. The mRNAs for the latter three proteins are presumably spliced out of a common primary RNA transcript. The use of degenerate codons is decidedly non-random, but is similar for the early and late regions. Codons of the type NUC, NCG and CGN are absent or very rare.

<https://www.ncbi.nlm.nih.gov/pubmed/205802>

“Preservatives in multidose vaccine vials do not prevent short-term bacterial contamination.”

Pediatrics • February 1985

Outbreaks of group A streptococcal abscesses following diphtheria-tetanus toxoid-pertussis vaccination

Stetler HC, Garbe PL, Dwyer DM, Facklam RR,
Orenstein WA, West GR, Dudley KJ, Bloch AB.

Abstract

Two outbreaks of group A streptococcal abscesses following receipt of diphtheria-tetanus toxoid-pertussis (DTP) vaccine from different manufacturers were reported to the Centers for Disease Control (CDC) in 1982. The clustering of the immunization times of cases, the isolation of the same serotype of *Streptococcus* from all cases in each outbreak, and the absence of reported abscesses associated with receipt of the same lots of vaccine in other regions of the country, suggest that each outbreak was probably caused by contamination of a single 15-dose vial of vaccine. The preservative thimerosal was present within acceptable limits in unopened vials from the same lot of DTP vaccine in each outbreak. Challenge studies indicate that a strain of *Streptococcus* from one of the patients can survive up to 15 days in DTP vaccine at 4 degrees C. Contamination of vials during manufacturing would have required survival of streptococci for a minimum of 8 months. Preservatives in multidose vaccine vials do not prevent short-term bacterial contamination. Options to prevent further clusters of streptococcal abscesses are discussed. The only feasible and cost-effective preventive measure now available is careful attention to sterile technique when administering vaccine from multidose vials.

<http://www.ncbi.nlm.nih.gov/pubmed/3881728>

Lancet • April 1987

Possible Role Of Pestiviruses In Microcephaly

Author Information

BarbaraJ. Potts, JohnL. Sever, NancyR. Tzan, David Huddleston, GregoryA. Elder

Infectious Diseases Branch

National Institute of Neurological and Communicative Disorders and Stroke
National Institutes of Health, Bethesda, Maryland 20892, USA

Abstract

“The background of this suggestion was that, first, although usually a pathogen in cattle and sheep, pestivirus infection can occur in children (Yolken et al. 1989). Second, an association has been reported between pestivirus exposure and microcephaly in newborns (Potts et al. 1987), which might be due to a generalized reduction in white matter bulk. Third, dysmyelination (Potts et al. 1985, Anderson et al. 1987b), frank brain damage (Hewicker-Trautwein and Trautwein 1994), and hypothyroxinemia (Anderson et al. 1987a) are characteristics of perinatal pestivirus infection in lamb models, are found in preterm infants (Leviton and Gilles 1996, Reuss et al. 1997), and are associated with each other among preterm infants (Den Ouden et al. 1996, Leviton et al. 1999). “

Report available for purchase

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(87\)90311-4/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(87)90311-4/abstract)

“... an association has been reported between pestivirus exposure and microcephaly in newborns, which might be due to a generalized reduction in white matter bulk. Third, dysmyelination, frank brain damage and hypothyroxinemia are characteristics of perinatal pestivirus infection in lamb models, are found in preterm infants, and are associated with each other among preterm infants ...”

“Vaccine produced on contaminated cells may in turn be contaminated,
leading to seroconversion or disease in the vaccine.”

Developments In Biological Standardization • 1991

Bovine viral diarrhea virus contamination of nutrient serum, cell cultures and viral vaccines

Author information

Levings RL1, Wessman SJ.

National Veterinary Services Laboratories
Animal and Plant Health Inspection Service
USDA, Ames, IA 50010

Abstract

Bovine viral diarrhea virus (BVDV) infection is common in the bovine population. Infection in utero leads to virus and antibody contamination of the fetal bovine serum used in cell cultures. These contaminants can interfere with diagnosis of viral infection. The high frequency of virus and antibody detection in individual animal or small pool samples suggests that any large pool of unscreened sera will be contaminated. Infection of cell cultures with BVDV can lead to interference with the growth of other viruses. Vaccine produced on contaminated cells may in turn be contaminated, leading to seroconversion or disease in the vaccine. The safety, purity, and efficacy of viral vaccines require BVDV testing of ingredients, cell substrates and final product. Methods for detection of BVDV in nutrient serum, cell cultures, seed viruses, and viral vaccines, and the frequency of their detection at the National Veterinary Services Laboratories are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/1665461>

Developments In Biological Standardization • 1991

Viral contamination of fetal bovine serum used for tissue culture: risks and concerns

Author information

Erickson GA1, Bolin SR, Landgraf JG.

Rollins Animal Disease Diagnostic Laboratory
Raleigh, NC 27605

Abstract

Four viral contaminants have been routinely detected in unprocessed and commercial lots of fetal bovine serum: bacteriophage, infectious bovine rhinotracheitis, parainfluenza-3 and bovine viral diarrhea virus (BVDV). Of those, BVDV is consistently present in a majority of commercial lots of fetal bovine serum. Methods for BVDV detection and removal are reviewed. The tentative role of an unclassified pestivirus in microcephaly of infants has been reported. Its significance remains uncertain.

<http://www.ncbi.nlm.nih.gov/pubmed/1665460>

“Four viral contaminants have been routinely detected in unprocessed and commercial lots of fetal bovine serum: bacteriophage, infectious bovine rhinotracheitis, parainfluenza-3 and bovine viral diarrhea virus (BVDV). Of those, BVDV is consistently present in a majority of commercial lots of fetal bovine serum. Methods for BVDV detection and removal are reviewed. The tentative role of an unclassified pestivirus in microcephaly of infants has been reported. Its significance remains uncertain.”

Journal Of Clinical Microbiology • June 1994

Evidence of pestivirus RNA in human virus vaccines

Author information

Harasawa R1, Tomiyama T.

Animal Center for Biomedical Research
Faculty of Medicine, University of Tokyo, Japan

Abstract

We examined live virus vaccines against measles, mumps, and rubella for the presence of pestivirus RNA or of pestiviruses by reverse transcription PCR. Pestivirus RNA was detected in two measles-mumps-rubella combined vaccines and in two monovalent vaccines against mumps and rubella. Nucleotide sequence analysis of the PCR products indicated that a modified live vaccine strain used for immunization of cattle against bovine viral diarrhea is not responsible for the contamination of the vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8077414>

“Pestivirus RNA was detected
in two measles-mumps-rubella combined vaccines
and in two monovalent vaccines against
mumps and rubella.”

“Sixty-one % of the neoplastic patients positive for SV40 sequences had an age excluding exposure to SV40-contaminated polio vaccines, suggesting a contagious transmission of SV40.”

Cancer Research • October 1996

**SV40 early region and large T antigen
in human brain tumors, peripheral blood cells, and
sperm fluids from healthy individuals**

Author information

Martini F1, Iaccheri L, Lazzarin L, Carinci P, Corallini A,
Gerosa M, Iuzzolino P, Barbanti-Brodano G, Tognon M.

Institute of Histology and General Embryology
School of Medicine, University of Ferrara, Italy

Abstract

SV40 T antigen (Tag) coding sequences were detected by PCR amplification followed by Southern blot hybridization in human brain tumors and tumor cell lines, as well as in peripheral blood cells and sperm fluids of healthy donors. SV40 early region sequences were found in 83% of choroid plexus papillomas, 73% of ependymomas, 47% of astrocytomas, 33% of glioblastoma multiforme cases, 14% of meningiomas, 50% of glioblastoma cell lines, and 33% of astrocytoma cell lines and in 23% of peripheral blood cell samples and 45% of sperm fluids from normal individuals. None of the 13 normal brain tissues were positive for SV40 DNA, nor were seven oligodendrogliomas, two spongioblastomas, one neuroblastoma, one meningioma, or four neuroblastoma cell lines. Expression of SV40 early region was found by reverse transcription PCR, and SV40-specific Tag was detected by indirect immunofluorescence in glioblastoma cell lines. DNA sequence analysis, performed in four positive samples, confirmed that the amplified PCR products belong to the SV40 early region. Sixty-one % of the neoplastic patients positive for SV40 sequences had an age excluding exposure to SV40-contaminated polio vaccines, suggesting a contagious transmission of SV40. The possible role of SV40 Tag in the etiopathogenesis of human brain tumors and the spread of SV40 by horizontal infection in the human population are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/8841004>

Biologicals • December 1996

Application of PCR for detection of mycoplasma DNA and pestivirus RNA in human live viral vaccines

Author information

Sasaki T1, Harasawa R, Shintani M, Fujiwara H, Sasaki Y, Horino A, Kenri T, Asada K, Kato I, Chino F.

Department of Safety Research on Biologics
National Institute of Health, Tokyo, Japan

Abstract

PCR techniques were applied for the detection of mycoplasma DNA and pestivirus RNA to 43 lots of live viral vaccines (measles, mumps, rubella, and oral poliomyelitis) produced by six manufacturers in Japan. Although mycoplasma DNA was not detected in any of the vaccines tested, pestivirus RNA was detected in 12 lots (28%). The incidence of contamination among the four viral vaccines was in the range of 20 to 37%, and the incidence among the six manufacturers varied from 0 to 56%.

<http://www.ncbi.nlm.nih.gov/pubmed/9088554>

“The incidence of contamination among the four viral vaccines was in the range of 20 to 37%, and the incidence among the six manufacturers varied from 0 to 56%.”

“These issues have received relatively little attention hitherto but are likely to achieve greater prominence as development of such preparations proceeds.”

Developments In Biological Standardization • 1996

Reasons for instability of bacterial vaccines

Author information

Corbel MJ.

Division of Bacteriology
National Institute for Biological Standards & Control
Potters Bar, United Kingdom

Abstract

Stability problems in relation to bacterial vaccines vary widely between different types of product. Killed whole cell bacterial vaccines including pertussis, cholera and typhoid vaccines generally show a high degree of stability of potency. Reversion to toxicity may occur in incompletely inactivated pertussis vaccines. Live attenuated vaccines such as BCG and Ty21a typhoid vaccines lose potency through loss of viability when exposed to adverse conditions. Both vaccines are susceptible to ultra violet radiation but Ty21a also has low thermal stability. Its fragility is probably a consequence of multiple mutations affecting structural and metabolic factors. Diphtheria and tetanus toxoids generally show high stability of potency. Reversion to toxicity may occur if the toxoiding process is inadequate. Decline in potency may result from exposure to adverse conditions, such as freezing, that affect the interaction with the adjuvant. Similar problems may be encountered with purified subunit vaccines such as acellular pertussis preparations. Some components, in particular pertussis toxin and filamentous haemagglutinin, show inherent low stability and degrade on storage at refrigerator temperatures unless stabilized by a protein cross-linking agent. Bacterial proteases carried over from the cell cultures may also be responsible for degradation of purified components. Purified bacterial polysaccharides usually show high stability if freeze-dried under appropriate conditions. Catalytic degradation may occur however, if the stabilizers are of inadequate purity. Polysaccharide-protein conjugates such as Haemophilus influenzae b (Hib) polyribosylribityl phosphate-protein conjugates show high thermal stability if freeze dried. In the liquid state, such conjugates tend to degrade by hydrolysis of the polysaccharide chains. Combined vaccines may present special stability problems because of the interaction of the various components in the liquid state. It can be difficult to freeze-dry some components of such vaccines, particularly aluminium hydroxide-adsorbed diphtheria-tetanus-pertussis (DTP) components. Slow release vaccines based on polyglycolide-lactolide microspheres may show suboptimal stability of encapsulated antigen under both in vitro conditions as a result of gradual acidification through polymer hydrolysis. Vaccines based on the use of live recombinant strains to express heterologous protective antigens may present special stability problems. Apart from the carrier strains, heterologous genes carried on plasmids may be subject to spontaneous deletion under adverse conditions. These issues have received relatively little attention hitherto but are likely to achieve greater prominence as development of such preparations proceeds.

<http://www.ncbi.nlm.nih.gov/pubmed/8854008>

Simian virus 40 and human cancer

Author information

Mutti L1, Carbone M,
Giordano GG, Giordano A.

S. Maugeri Foundation, IRCCS
Rehabilitation Institute of Veruno/Varallo S., Italy

Abstract

Deoxyribonucleic acid (DNA) oncoviruses can induce neoplastic transformation by interfering with proliferative proteins. Simian virus 40 (SV40) has been shown to induce brain tumors, osteosarcoma, lymphoid tumors and malignant mesothelioma in hamsters and SV40-like DNA sequences corresponding to the Rb-pocket binding domain of SV40 T-antigen (Tag) have been detected in the same human tumors. Since only a small percentage of people exposed to asbestos fibers develop a malignant mesothelioma, SV40 has been suspected to co-operate with the fibers in the neoplastic transformation or even to itself induce the onset of malignant mesothelioma in patients without expositive history. The mechanism that seems to be involved in the SV40-induced carcinogenesis process is mediated by interaction of Tag, both with p53 and Rb proteins, leading to their functional inactivation that is responsible for the removal of their inhibitory cell cycle effect which determines the increase of the number of cells entering the G1-S phase. Up to now the source of SV40 human infections has not yet been completely identified even though administration from 1957-1965 of SV40 contaminated polio vaccines is highly suspected. Horizontal infection by sexual transmission has been also hypothesized. Due to the important public health implications further investigations are required in order to establish both the source and the carcinogenic role of simian virus 40 in humans.

<http://www.ncbi.nlm.nih.gov/pubmed/9689809>

“Up to now the source of SV40 human infections has not yet been completely identified even though administration from 1957-1965 of SV40 contaminated polio vaccines is highly suspected. Horizontal infection by sexual transmission has been also hypothesized.”

The biological activities of simian virus 40 large-T antigen and its possible oncogenic effects in humans

Author information

Matker CM1, Rizzo P, Pass HI, Di Resta I,
Powers A, Mutti L, Kast WM, Carbone M.

Cardinal Bernardin Cancer Center
Loyola University of Chicago
Maywood, IL 60153, USA

Abstract

Simian virus 40 (SV40) is an oncogenic virus which induces tumors in hamsters and transforms human cells in tissue culture. Between 1955 and 1963, polio vaccines and adenovaccines were contaminated with SV40; therefore, millions of people were exposed to this oncogenic virus. The SV40 proteins responsible for in vivo oncogenesis and in vitro cell transformation are encoded by the early region of the virus. These proteins are called T (tumor) antigens (Tags), because animals with tumors induced by SV40 have antibodies against these viral proteins. Recently, we and other research laboratories have found SV40 in specific types of human tumors: mesothelioma, ependymoma and choroid plexus tumors, osteosarcoma and sarcoma. The same tumor types will develop in hamsters which have been injected systemically with SV40. SV40 causes cell transformation in tissue culture and tumors in animals, because SV40 Tag binds and inactivates the cellular tumor suppressor gene products, Rb and p53. We found that SV40 Tag binds p53 and Rb in human mesotheliomas, possibly contributing to the malignant phenotype.

<http://www.ncbi.nlm.nih.gov/pubmed/9689808>

“Between 1955 and 1963,
polio vaccines and adenovaccines
were contaminated with SV40; therefore,
millions of people were exposed
to this oncogenic virus.”

The detection of simian virus 40 in human tumors by polymerase chain reaction

Author information

Rizzo P1, Di Resta I, Powers A, Matker CM, Zhang A,
Mutti L, Kast WM, Pass H, Carbone M.

Loyola University of Chicago
Cardinal Bernardin Cancer Center
Maywood, IL, USA

Abstract

Simian virus (SV) 40 is a deoxyribonucleic acid (DNA) virus that induces mesotheliomas, ependymomas, bone tumors, and lymphomas in hamsters. In recent years SV40 sequences have been detected in approximately 60% of mesotheliomas and ependymomas, in 33% of bone tumors and sarcomas, and in 13% of lymphomas. Because the amount of human specimens available for molecular studies is usually minimal, the method most commonly used to demonstrate SV40 in human specimens is the polymerase chain reaction (PCR). PCR is a highly sensitive and useful technique. In the PCR reaction, different sets of primers are used for targeting different regions of DNA. The regions of the SV40 genome targeted by PCR include the large T-antigen, the small t-antigen, the origin of replication, and viral protein-1 capsid protein. The use of these different sets of primers to test human tumor specimens for SV40 produce a different percentage of positive results. This is because these experiments revealed that some primers are more specific than others which may also detect sequences belonging to other DNA papovaviruses. Therefore, the combined use of different sets of primers is recommended when it is important to distinguish SV40 from other related papovaviruses such as BK and JC, which can also be occasionally present in human cells. Furthermore, these experiments demonstrated that polymerase chain reaction analyses for simian virus 40 can be performed better and easier when using deoxyribonucleic acid extracted from fresh and/or frozen tissue. Deoxyribonucleic acid from paraffin embedded specimens should not be used routinely for simian virus 40 testing because of the high risk of obtaining false negative results. However, these paraffin derived deoxyribonucleic acids can be used reliably in molecular laboratories specialized in these type of analyses. This paper describes the methods that we have developed to test simian virus 40 in human specimens.

“This paper describes the methods
that we have developed to test simian
virus 40 in human specimens.”

Practical considerations in converting from plasma-derived to recombinant hepatitis B vaccines

Author information

Lee PI1, Lee CY.

Department of Paediatrics
National Taiwan University Hospital
Taipei, Taiwan

Abstract

Plasma-derived and recombinant vaccines have been developed to prevent hepatitis B virus infections. Both types of vaccine perform very well with respect to safety, immunogenicity and protective efficacy. The protection afforded by both types of vaccine is satisfactory for at least 5 to 10 years after vaccination, and a further booster dose is not necessary during this period. However, the plasma-derived vaccine is costly to produce and there is an unjustified but prevalent fear that it may be contaminated by potential pathogens. The supply of human plasma for production of the plasma-derived vaccine cannot be assured once use of hepatitis B vaccines becomes universal. It is therefore inevitable that the recombinant vaccine will replace the plasma-derived vaccine. If necessary, both vaccines can be used in combination. Future directions for hepatitis B vaccine development include: determination of the need for incorporation of pre-S gene products to enhance immunogenicity; defining a practical strategy to combat the problem of escape mutants after vaccination; and development of combination vaccines containing other inactivated antigens to allow complete immunisation against several diseases with a minimal number of injections.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18020583>

“the plasma-derived vaccine is costly to produce and there is an unjustified but prevalent fear that it may be contaminated by potential pathogens. The supply of human plasma for production of the plasma-derived vaccine cannot be assured once use of hepatitis B vaccines becomes universal.”

Cell and molecular biology of simian virus 40: implications for human infections and disease

Author information

Butel JS1, Lednicky JA.

Division of Molecular Virology
Baylor College of Medicine
Houston, TX 77030-3498, USA
jbutel@bcm.tmc.edu

Abstract

Simian virus 40 (SV40), a polyomavirus of rhesus macaque origin, was discovered in 1960 as a contaminant of polio vaccines that were distributed to millions of people from 1955 through early 1963. SV40 is a potent DNA tumor virus that induces tumors in rodents and transforms many types of cells in culture, including those of human origin. This virus has been a favored laboratory model for mechanistic studies of molecular processes in eukaryotic cells and of cellular transformation. The viral replication protein, named large T antigen (T-ag), is also the viral oncoprotein. There is a single serotype of SV40, but multiple strains of virus exist that are distinguishable by nucleotide differences in the regulatory region of the viral genome and in the part of the T-ag gene that encodes the protein's carboxyl terminus. Natural infections in monkeys by SV40 are usually benign but may become pathogenic in immunocompromised animals, and multiple tissues can be infected. SV40 can replicate in certain types of simian and human cells. SV40-neutralizing antibodies have been detected in individuals not exposed to contaminated polio vaccines. SV40 DNA has been identified in some normal human tissues, and there are accumulating reports of detection of SV40 DNA and/or T-ag in a variety of human tumors. This review presents aspects of replication and cell transformation by SV40 and considers their implications for human infections and disease pathogenesis by the virus. Critical assessment of virologic and epidemiologic data suggests a probable causative role for SV40 in certain human cancers, but additional studies are necessary to prove etiology.

<http://www.ncbi.nlm.nih.gov/pubmed/9923853>

“Critical assessment
of virologic and epidemiologic data suggests
a probable causative role for SV40 in certain
human cancers, but additional studies are
necessary to prove etiology.”

“These data suggest that there may be an increased incidence of certain cancers among the 98 million persons exposed to contaminated polio vaccine in the U.S.”

Anticancer Research • May 1999

Cancer risk associated with simian virus 40 contaminated polio vaccine

Author information

Fisher SG1, Weber L, Carbone M.

Cancer Cause and Prevention Program
Loyola University Medical Center
Maywood, Illinois 60153, USA

Abstract

BACKGROUND

The presence of SV40 in monkey cell cultures used in the preparation of the polio vaccine from 1955 through 1961 is well documented. Investigations have consistently demonstrated the oncogenic behavior of SV40 in animal models. Early epidemiologic studies were inadequate in demonstrating an increase in cancer incidence associated with contaminated vaccine. Recently, investigators have provided persuasive evidence that SV40 is present in human ependymomas, choroid plexus tumors, bone tumors, and mesotheliomas, however, the etiologic role of the virus in tumorigenesis has not been established.

MATERIALS AND METHODS

Using data from SEER, we analyzed the incidence of brain tumors, bone tumors, and mesotheliomas from 1973-1993 and the possible relationship of these tumors with the administration of the SV40 contaminated vaccine.

RESULTS

Our analysis indicates increased rates of ependymomas (37%), osteogenic sarcomas (26%), other bone tumors (34%) and mesothelioma (90%) among those in the exposed as compared to the unexposed birth cohort.

CONCLUSIONS

These data suggest that there may be an increased incidence of certain cancers among the 98 million persons exposed to contaminated polio vaccine in the U.S.; further investigations are clearly justified.

<http://www.ncbi.nlm.nih.gov/pubmed/10472327>

Unique strains of SV40
in commercial poliovaccines from 1955
not readily identifiable with current testing
for SV40 infection

Author information

Rizzo P1, Di Resta I, Powers A, Ratner H, Carbone M.

Loyola University Medical Center, Cardinal Bernardin Cancer Center
Department of Pathology, Maywood, Illinois 60153, USA

Abstract

SV40 was first identified as a contaminant of poliovaccines used from 1955 until 1963. Recently, SV40 has been detected in several human tumors. The virus detected in human tumors often contained only one 72-bp enhancer in the regulatory region, in contrast to the SV40 originally isolated from poliovaccines, which contained two 72-bp enhancers. The origin of viruses with one 72-bp enhancer in humans was unknown, because it was thought that these viruses were not present in poliovaccines. It was also thought that all poliovaccine vials produced from 1955 until 1963 had been discarded, thus the possibility that one 72-bp virions contaminated those vials could not be tested. We unexpectedly obtained what appear to be the last available vials of poliovaccine produced in 1955. In these vials, we detected and sequenced SV40 containing only one 72-bp enhancer in the regulatory region. The tissue culture cytopathic test currently used in the United States to screen oral poliovaccines was designed to detect rapidly proliferating SV40 virions containing two 72-bp enhancers. We found that this test is not sensitive enough to detect low amounts of the slow-replicating SV40 virions containing one 72-bp enhancer. This virus was easily detected in the same cells by immunostaining and PCR. Twelve current vials of poliovaccines tested uniformly negative for SV40, suggesting that the precaution of preparing poliovaccines from kidneys obtained from monkeys bred in isolated colonies prevented SV40 contamination. Our data demonstrate that humans were exposed to SV40 viruses with both one 72-bp enhancer and two 72-bp enhancers SV40 through contaminated vaccines. Our data also suggest that instead of cytopathic tests, immunohistochemical and/or molecular studies should be used to screen poliovaccines for SV40 to completely eliminate the risk of occasional contamination.

<https://www.ncbi.nlm.nih.gov/pubmed/10626798>

“SV40 was first identified as a contaminant of poliovaccines used from 1955 until 1963. Recently, SV40 has been detected in several human tumors.”

“... in litigation involving the Lederle oral polio vaccine,
the manufacturer’s internal documents failed to reveal such removal in all of the seeds.”

Anticancer Research • November 2000

**Oral polio vaccine and human cancer:
a reassessment of SV40 as a contaminant based upon legal documents**

Author information

Kops SP.

stankops@aol.com

Abstract

To date, the scientific literature and research examining SV40 and cancer-related diseases has been based upon an assumption that SV40 was not present in any poliovirus vaccine administered in the United States and was removed from the killed polio vaccine by 1963. The basis for this presumption has been that the regulations for live oral polio vaccine required that SV40 be removed from the seeds and monovalent pools ultimately produced in the manufacturing process. The Division of Biologic Standards permitted an additional two tissue culture passages--from three to five--in order to allow manufacturers the ability to remove this contaminant from the oral poliovirus vaccines then awaiting licensure. The confirmation of the removal by one drug manufacturer, Lederle, has been made public at an international symposium in January 1997, where its representatives stated that all of Lederle’s seeds had been tested and screened to assure that it was free from SV40 virus. However, in litigation involving the Lederle oral polio vaccine, the manufacturer’s internal documents failed to reveal such removal in all of the seeds. The absence of confirmatory testing of the seeds, as well as testimony of a Lederle manager, indicate that this claim of removal of SV40 and the testing for SV40 in all the seeds cannot be fully substantiated. These legal documents and testimony indicate that the scientific community should not be content with prior assumptions that SV40 could not have been in the oral polio vaccine. Only further investigation by outside scientific and independent researchers who can review the test results claimed in the January 1997 meeting and who can conduct their own independent evaluations by testing all the seeds and individual mono-valent pools will assure that SV40 has not been present in commercially sold oral poliovirus vaccine manufactured by Lederle.

<http://www.ncbi.nlm.nih.gov/pubmed/11205211>

Genotypes of pestivirus RNA detected in live virus vaccines for human use

Author information

Giangaspero M1, Vacirca G, Harasawa R, Büttner M, Panuccio A,
De Giuli Morghen C, Zanetti A, Belloli A, Verhulst A.

Institute of Special Pathology and Veterinary Medical Clinic
Faculty of Veterinary Medicine, The University of Milan, Italy

Abstract

Live virus vaccines for human use, 29 monovalent vaccines against measles, mumps, rubella or polio, eight polyvalent vaccines against measles-mumps-rubella and one bacterial polyvalent vaccine against *Streptococcus pneumoniae*, were tested by reverse transcriptase-nested PCR for the presence of pestivirus or pestivirus RNA. Twenty-four samples were selected from European manufacturers, ten were from U.S.A. and four from Japan. Five (13.1%) out of 38 tested samples were positive for pestivirus RNA. Three vaccines (rubella and two measles) were from Europe and two (mumps and rubella) from Japan. The 5'-untranslated genomic region of the contaminant pestivirus RNA were amplified by reverse transcription-PCR and sequenced. Analyses based on primary nucleotide sequence homology and on secondary structures, characteristic to genotypes, revealed that the cDNA sequences belonged to bovine viral diarrhea virus (BVDV). A cDNA sequence, detected from one measles sample, belonged to BVDV-1b genotype. Pestiviral cDNA detected from the Japanese mumps and rubella vaccine samples, belonged to the BVDV genotypes 1a and 1c, respectively. Analysis on two cDNA sequences detected from measles and rubella vaccine samples from Europe showed their appurtenance to a new genotype, BVDV-1d. These findings indicate that contamination by animal pestivirus may occur in biological products for human use.

<http://www.ncbi.nlm.nih.gov/pubmed/11503899>

“Twenty-four samples were selected from European manufacturers, ten were from U.S.A. and four from Japan. Five (13.1%) out of 38 tested samples were positive for pestivirus RNA. Three vaccines (rubella and two measles) were from Europe and two (mumps and rubella) from Japan.”

What are the limits of adjuvanticity?

Author information

Del Giudice G1, Podda A, Rappuoli R.

IRIS Research Center, Chiron SpA, Via Fiorentina 1, 53100, Siena, Italy

Abstract

Vaccines developed traditionally following empirical approaches have often limited problems of immunogenicity, probably due to the low level of purity of the active component(s) they contain. The application of new technologies to vaccine development is leading to the production of purer (e.g. recombinant) antigens which, however, tend to have a poorer immunogenicity as compared to vaccines of the previous generation. The search for new vaccine adjuvants involves issues related to their potential limits. Since the introduction of aluminium salts as vaccine adjuvants more than 70 years ago, only one adjuvant has been licensed for human use. The development of some of these new vaccine adjuvants has been hampered by their unacceptable reactogenicity. In addition, some adjuvants work strongly with some antigens but not with others, thus, limiting their potentially widespread use. The need to deliver vaccines via alternative routes of administration (e.g. the mucosal routes) in order to enhance their efficacy and compliance has set new requirements in basic and applied research to evaluate their efficacy and safety. Cholera toxin (CT) and labile enterotoxin (LT) mutants given along with intranasal or oral vaccines are strong candidates as mucosal adjuvants. Their potential reactogenicity is still matter of discussions, although available data support the notion that the effects due to their binding to the cells and those due to the enzymatic activity can be kept separated. Finally, adjuvanticity is more often evaluated in terms of antigen-specific antibody titers induced after parenteral immunization. It is known that, in many instances, antigen-specific antibody titers do not correlate with protection. In addition, very little is known on parameters of cell-mediated immunity which could be considered as surrogates of protection. Tailoring of new adjuvants for the development of vaccines with improved immunogenicity/efficacy and reduced reactogenicity will represent one of the major challenges of the ongoing vaccine-oriented research.

<http://www.ncbi.nlm.nih.gov/pubmed/11587808>

“Vaccines developed traditionally following empirical approaches have often limited problems of immunogenicity, probably due to the low level of purity of the active component(s) they contain.”

Implications of prion-induced diseases for animal-derived pharmaceutical products

Author information

Erstad BL.

Department of Pharmacy Practice and Science
College of Pharmacy, University of Arizona
1703 E. Mabel Street, Tucson, AZ 85721-0207, USA

Abstract

The implications of prion-induced diseases for the use of medications that theoretically could harbor the infectious pathogens are discussed. Prions have been identified as protein particles that lack nucleic acids. There is evidence that prions cause the transmissible neurodegenerative diseases known as transmissible spongiform encephalopathies. Of these diseases, bovine spongiform encephalopathy (BSE) and the human spongiform encephalopathy to which it has been linked, new variant Creutzfeldt-Jakob disease (CJD), have generated the most attention. The first cases of new variant CJD appeared in Britain in the mid-1990s. Ingestion of prion-infected beef remains the only known cause of new variant CJD. No cases of BSE or new variant CJD have been documented in the United States. The time from exposure to the development of clinical sequelae appears to be about 10 years. The median duration of illness is 14 months, and the outcome is invariably death. There is no treatment; currently the only available approach is prevention. There is no reliable method of predicting the number of new cases that might occur because of lack of definitive information on the efficiency of transmission from animals to humans and the number of people currently infected and at risk for infection. The infectivity of medications and plasma fractionation products containing material from cattle with BSE is unknown, but the risk is believed to be very low. No cases of such transmission have been identified. Guidelines to keep the risk of transmission via medications low have been promulgated by FDA, and further research is warranted. There have been no reports of medications or plasma fractionation products being contaminated with the prions that cause new variant CJD. Ongoing vigilance and research are appropriate, however.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11862637>

“The infectivity of medications
and plasma fractionation products
containing material from cattle
with BSE is unknown, but the risk
is believed to be very low.”

“This analysis confirmed higher concentrations of endotoxin
in whole-cell DTP vaccines compared with DTaP or DT vaccines.

As high concentrations of endotoxin may be correlated with a higher incidence of adverse events ...”

Annals Of Pharmacotherapeutics • May 2002

Clinical implications of endotoxin concentrations in vaccines

Author information

Geier DA1, Geier MR.

Genetic Centers of America, 14 Redgate Court, Silver Spring, MD 20905-5726, USA

Abstract

BACKGROUND

A previous study suggested that high concentrations of endotoxin may be present in whole-cell diphtheria/tetanus/pertussis (DTP) vaccine, and the scientific literature contains many studies examining the reactivity of whole-cell DTP vaccine. The medical and scientific communities have previously reported that the presence of endotoxin in commercial vaccines may have negative effects on vaccine recipients.

OBJECTIVE

To determine the endotoxin concentrations in whole-cell DTP, acellular DTP(DTaP), and DT vaccines and determine the clinical experience with each vaccine.

METHODS

To study the endotoxin concentrations in vaccines, the Limulus amoebocyte lysate (LAL) assay was used. The vaccines analyzed with the LAL assay were whole-cell DTP vaccine lots manufactured by Connaught, Lederle, the Michigan and Massachusetts Departments of Health, and Wyeth; DTaP vaccine lots manufactured by Merieux and Takeda; and DT vaccine lots manufactured by Wyeth and Lederle. The incidence of adverse reactions following whole-cell DTP, DTaP, and DT vaccines were determined based on analysis of the Vaccine Adverse Events Reporting System (VAERS) database.

RESULTS

The results of the LAL assay showed that whole-cell DTP vaccines contained considerably more endotoxin than either DTaP or DT vaccines. The VAERS showed that statistically significantly more adverse reactions were associated with whole-cell DTP vaccine than DTaP or DT vaccines.

CONCLUSIONS

This analysis confirmed higher concentrations of endotoxin in whole-cell DTP vaccines compared with DTaP or DT vaccines. As high concentrations of endotoxin may be correlated with a higher incidence of adverse events, the switch from whole-cell DTP to DTaP for routine vaccinations in the US seems well justified.

SV40 in human tumors: new documents shed light on the apparent controversy

Author information

MacLachlan DS.
MacLachlan Law Offices LLC
487 Goffle Road
Ridgewood, New Jersey 07450, USA

Abstract

BACKGROUND

Presently there are over 61 reports from 49 different laboratories that have detected SV40 in human mesothelioma, lymphoma, brain and bone tumors, versus three reports (two from Dr. Shah's laboratory who performed his study under contract from Dr. Strickler at the Viral Epidemiology Branch (VEB) National Cancer Institute (USA) that have failed to detect SV40 in some of these same tumor types. To address whether the negative reports were caused by lack of sensitivity of the technique used in Shah's laboratory, or whether the positive reports were caused by contamination within the greater number of laboratories reporting SV40 detection, two multi-center studies were conducted. The first study, Testa et al., 1998, confirmed the presence of SV40 in mesothelioma. The second study, Strickler et al., produced irregular results indicating that: (a) though never reporting SV40 detection to date, Dr. Shah's laboratory reported the most sensitive technique of all participating laboratories; (b) all participating laboratories essentially agreed the DNA extracts provided under contract to the VEB were negative; (c) all participating laboratories agreed one-half of the negative controls prepared by the VEB contract laboratory were positive due to contamination by the contract laboratory. In addition, (d) the authors concluded the

laboratories previously detecting SV40 in human tissue specimens were not reporting contamination. Scientists in the field have since debated how these seemingly contradictory results were produced.

MATERIALS

During the course of litigation representing patients with SV40-positive tumors, the author obtained correspondence among members of the VEB multi-center study and sworn testimony by Dr. Shah that address some of the incongruities of the study.

RESULTS

Dr. Shah's laboratory technique used in 1996 was apparently not sufficiently sensitive to detect SV40 in human tumors. When this became apparent, during unilateral pre-trial testing of positive controls by Dr. Shah, the study coordinator of the VEB, Dr. Strickler, apparently compromised the blinded nature of the study and allowed Dr. Shah to modify and improve his technique. When one of the participating laboratories questioned irregularities in the data from Dr. Shah's laboratory and directly questioned Dr. Strickler, the study organizer, about the potential irregularity, Dr. Strickler and Dr. Shah offered letters stating that such irregularities had not occurred and re-confirmed that they had not deviated from the standard protocol.

CONCLUSION

The facts indicating that Dr. Shah's laboratory technique was not sufficiently sensitive to detect SV40 were not made available to the other laboratories participating in the study and were not published. Instead, according to Dr. Shah's testimony, Dr. Strickler, the VEB multi-center study coordinator, compromised the masked positive controls and knowingly permitted Dr. Shah to re-test and adjust his technique during pre-trial testing. The actual negative pre-trial test results were never published alongside the published trial results indicating Dr. Shah's laboratory had the most sensitive technique to detect SV40 among the nine participating laboratories.

“When one of the participating laboratories questioned irregularities in the data from Dr. Shah's laboratory and directly questioned Dr. Strickler, the study organizer, about the potential irregularity, Dr. Strickler and Dr. Shah offered letters stating that such irregularities had not occurred and re-confirmed that they had not deviated from the standard protocol.”

[it was found that they had lied]

Detection and characterization of pestivirus contaminations in human live viral vaccines

Author information

Studer E1, Bertoni G, Candrian U.

Official Medicines Control Laboratory Biologika and R&D Unit
Division of Biologicals, Swiss Federal Office of Public Health
P.O. Box 3003, Bern, Switzerland

Abstract

In view of the use of potentially contaminated foetal calf serum (FCS) in cell cultures pestiviruses may be present in live viral vaccines. Thirty-six lots of human live viral vaccines produced by three manufacturers were tested for the presence of pestiviruses. Bovine viral diarrhoea virus (BVDV) RNA was detected in 33% of the vaccine lots. All positive results were caused by the mumps component of a single manufacturer. Partial sequences of the 5' untranslated region of BVD viral RNA were determined. The sequences were closely related to that of the NADL strain of BVDV. The amount of BVDV RNA in the vaccines was determined by real-time RT-PCR using the LightCycler. Between 3.3×10^2 and 6.2×10^5 RNA copies per dose were found to be present in the vaccine samples. Additionally, culture tests were done with FCS and human diploid cells used in the vaccine production of the manufacturer whose vaccines were positive by PCR. All attempts to detect virus antigen in MRC-5 human diploid cells or to infect these cells with BVDV failed. This suggests that BVDV RNA detected in human live viral vaccines represents passive carry over of BVDV from contaminated FCS rather than active virus replication in human diploid cells. Our results indicate that contamination with BVDV of FCS used in vaccine production does not appear to be of immediate concern to human health. Furthermore, our results indicate that gamma-irradiation of FCS destroys BVDV particles and is also effective in preventing the presence of BVDV RNA in the vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/12421586>

“This suggests that BVDV RNA detected in human live viral vaccines represents passive carry over of BVDV from contaminated foetal calf serum rather than active virus replication in human diploid cells. Our results indicate that contamination with BVDV of foetal calf serum used in vaccine production does not appear to be of immediate concern to human health.”

Institute of Medicine (US) Immunization Safety Review Committee • 2002

**Immunization Safety Review:
SV40 Contamination of Polio Vaccine and Cancer**
Washington, DC National Academies Press

Editors
Stratton K, Almario DA, McCormick MC.

Excerpt

Some of the polio vaccine administered from 1955–1963 was contaminated with a virus, called simian virus 40 (SV40). The virus came from the monkey kidney cell cultures used to produce the vaccine. Most, but not all, of the contamination was in the inactivated polio vaccine (IPV). Once the contamination was recognized, steps were taken to eliminate it from future vaccines. Researchers have long wondered about the effects of the contaminated vaccine on people who received it. Although SV40 has biological properties consistent with a cancer-causing virus, it has not been conclusively established whether it might have caused cancer in humans. Studies of groups of people who received polio vaccine during 1955–1963 provide evidence of no increased cancer risk. However, because these epidemiologic studies are sufficiently flawed, the Institute of Medicine’s Immunization Safety Review Committee concluded that the evidence was inadequate to conclude whether or not the contaminated polio vaccine caused cancer. In light of the biological evidence supporting the theory that SV40-contamination of polio vaccines could contribute to human cancers, the committee recommends continued public health attention in the form of policy analysis, communication, and targeted biological research.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25057632>

Full Report

<http://www.ncbi.nlm.nih.gov/books/NBK221113/>

“ In light of the biological evidence supporting the theory that SV40-contamination of polio vaccines could contribute to human cancers, the committee recommends continued public health attention in the form of policy analysis, communication, and targeted biological research.”

Association between SV40 and non-Hodgkin's lymphoma

Author information

Butel JS1, Vilchez RA, Jorgensen JL, Kozinetz CA.

Department of Molecular Virology and Microbiology
Baylor College of Medicine, Mail Stop BCM385, One Baylor Plaza
Houston, TX 77030, USA
jbutel@bcm.tmc.edu

Abstract

Millions of people worldwide were inadvertently exposed to live simian virus 40 (SV40) between 1955 and 1963 through immunization with SV40-contaminated polio vaccines. Although the prevalence of SV40 infections in humans is not known, numerous studies suggest that SV40 is a pathogen resident in the human population today. SV40 is a potent DNA tumor virus that is known to induce primary brain cancers, bone cancers, mesotheliomas, and lymphomas in laboratory animals. SV40 oncogenesis is mediated by the viral large tumor antigen (T-ag), which inactivates the tumor suppressor proteins p53 and pRb. During the last decade, independent studies using different molecular biology techniques have shown the presence of SV40 DNA, T-ag, or other viral markers in primary human brain and bone cancers and malignant mesotheliomas. Evidence suggests that there may be geographic differences in the frequency of these virus-positive tumors. Recent large independent controlled studies have shown that SV40 T-ag DNA is significantly associated with human non-Hodgkin's lymphoma (NHL). In our study, we analyzed systemic NHL from 76 HIV-1-positive and 78 HIV-1-negative patients, and nonmalignant lymphoid samples from 79 HIV-1-positive and 107 HIV-1-negative patients without tumors; 54 colon and breast carcinoma samples served as cancer controls. We used polymerase chain reaction (PCR) followed by Southern blot hybridization and DNA sequence analysis to detect DNAs of polyomaviruses and herpesviruses. SV40-specific DNA sequences were detected in 64 (42%) of 154 NHL, none of 186 nonmalignant lymphoid samples, and none of 54 control cancers. For NHL from HIV-1-positive patients, 33% contained SV40 DNA and 39% Epstein Barr virus (EBV) DNA, whereas NHLs from HIV-1-negative patients were 50% positive for SV40 and 15% positive for EBV. Few tumors were positive for both SV40 and EBV. Human herpesvirus type 8 was not detected. SV40 sequences were found most frequently in diffuse large B cell and follicular-type lymphomas. We conclude that SV40 is significantly associated with some types of NHL and that lymphomas should be added to the types of human cancers associated with SV40.

<http://www.ncbi.nlm.nih.gov/pubmed/15202523>

“Millions of people worldwide were inadvertently exposed to live simian virus 40 (SV40) between 1955 and 1963 through immunization with SV40-contaminated polio vaccines. We conclude that SV40 is significantly associated with some types of non-Hodgkins Lymphoma and that lymphomas should be added to the types of human cancers associated with SV40.”

Serum antibodies to JC virus, BK virus, simian virus 40, and the risk of incident adult astrocytic brain tumors

Author information

Rollison DE1, Helzlsouer KJ, Alberg AJ,
Hoffman S, Hou J, Daniel R, Shah KV, Major EO.

Department of Epidemiology
The Johns Hopkins Bloomberg School of Public Health
Baltimore, Maryland 21205, USA

Abstract

Genomic sequences of the human polyomaviruses, JC virus (JCV) and BK virus (BKV), and simian virus 40 (SV40) have been reported from several types of human brain tumors, but there have been no population-based seroepidemiologic studies to evaluate the association between polyomavirus infection and brain tumors. We conducted a case-control study, nested within a prospective cohort, to investigate the association between antibodies to JCV, BKV, and SV40, as measured in serum collected 1-22 years before diagnosis and incident primary malignant brain tumors. Brain tumor cases (n = 44) and age-, gender-, and race-matched controls (n = 88) were identified from participants of two specimen banks in Washington County, Maryland. IgG antibodies to the capsid proteins of JCV and BKV were assessed using ELISAs. SV40-neutralizing antibodies were measured using plaque neutralization assays. Similar to the general population, the prevalence of JCV and BKV infection was high in our study population (77 and 85%, respectively). Antibodies to SV40 were less prevalent (11%). The odds ratio for subsequent brain tumor development was 1.46 [95% confidence interval (CI), 0.61-3.5] for JCV, 0.66 for BKV (95% CI, 0.22-1.95), and 1.00 for SV40 (95% CI, 0.30-3.32). Given the high prevalence of JCV and BKV infections and the millions who were potentially exposed to SV40 through contaminated polio vaccines, future studies should attempt to replicate these findings.

<http://www.ncbi.nlm.nih.gov/pubmed/12750243>

“Given the high prevalence
of JCV and BKV infections and the
millions who were potentially exposed to SV40
through contaminated polio vaccines, future studies
should attempt to replicate these findings.”

Simian virus 40 in human cancers

Author information

Vilchez RA1, Kozinetz CA, Arrington AS, Madden CR, Butel JS.

Department of Medicine, Section of Infectious Diseases
Baylor College of Medicine, BCM 286, Room N1319
One Baylor Plaza, Houston, TX 77030, USA
rvilchez@bcm.tmc.edu

Abstract

BACKGROUND

Many studies have reported the presence of simian virus 40 (SV40) deoxyribonucleic acid (DNA) or protein in human brain tumors and bone cancers, malignant mesothelioma, and non-Hodgkin's lymphoma. However, the small samples and lack of control groups in some reports have made it difficult to assess their reliability.

METHODS

Studies were included in this analysis if they met the following criteria: original studies of patients with primary brain tumors and bone cancers, malignant mesothelioma, or non-Hodgkin's lymphoma; the investigation of SV40 was performed on primary cancer specimens; the analysis included a control group; and the same technique was used for cases and controls. Included reports were published from 1975 to 2002.

RESULTS

Thirteen studies fulfilled the criteria for the investigation of primary brain cancers (661 tumors and 482 control samples). Specimens from patients with brain tumors were almost four times more likely to have evidence of SV40 infection than were those from controls (odds ratio [OR] = 3.9; 95% confidence interval [CI]: 2.6 to 5.8). The association was even stronger for mesothelioma (OR = 17; 95% CI: 10 to 28; based on 15 studies with 528 mesothelioma samples and 468 control samples) and for bone cancer (OR = 25; 95% CI: 6.8 to 88; based on four studies with 303 cancers and 121 control samples). SV40 DNA was also more frequent in samples from patients with non-Hodgkin's lymphoma (OR = 5.4; 95% CI: 3.1 to 9.3; based on three studies with 301 cases and 578 control samples) than from controls.

CONCLUSION

These results establish that SV40 is associated significantly with brain tumors, bone cancers, malignant mesothelioma, and non-Hodgkin's lymphoma. Studies are needed to assess current prevalence of SV40 infections.

“These results establish that SV40 is associated significantly with brain tumors, bone cancers, malignant mesothelioma, and non-Hodgkin's lymphoma.”

New developments about the association of SV40 with human mesothelioma

Author information

Carbone M1, Pass HI, Miele L, Bocchetta M.

Department of Pathology, Cardinal Bernardin Cancer Center
Cancer Immunology Program, Loyola University Chicago
Maywood, IL 60153, USA
mcarbon@orion.it.luc.edu

Abstract

Simian virus 40 (SV40) has been detected in human tumors in over 40 different laboratories. Many of these reports linked SV40 to human mesotheliomas. The Vaccine Safety Committee of the Institute of Medicine (IOM), National Academy of Sciences, USA, recently reviewed the evidence associating polio vaccines and/or SV40 with human tumors. The IOM conclusions about polio vaccines and human cancer were: (1) 'the evidence is inadequate to accept or reject a causal relation between SV40-containing polio vaccines and cancer' because the 'epidemiological studies are sufficiently flawed'; (2) 'the biological evidence is of moderate strength that SV40 exposure from the polio vaccines is related to SV40 infection in humans'. The epidemiological studies were considered flawed because it was not possible to distinguish reliably among exposed and nonexposed cohorts. Concerning SV40, the IOM concluded that (1) 'the evidence is strong that SV40 is a transforming virus; (2) the evidence is of moderate strength that SV40 exposure could lead to cancer in humans under natural conditions' (IOM, 2002). Similar conclusions were reached at an International consensus meeting on SV40 and human tumors held at the University of Chicago in 2001. G Klein and C Croce, who chaired the final panel that reviewed all the published evidence linking SV40 to human tumors, stated that 'the presence of SV40 in human tumors has been convincingly demonstrated' (Klein et al., 2002). In addition, a workshop organized by the Biological Carcinogenesis Branch of the National Cancer Institute, Bethesda, MD, chaired by J Paganò, has reached similar conclusions (Wong et al., 2002). Therefore, three independent scientific panels have all agreed that there is compelling evidence that SV40 is present in some human cancers and that SV40 could contribute to the pathogenesis of some of them. It should be noted that the presence of SV40 in mesothelioma and other human tumor types has been challenged by a research team that has consistently reported negative findings (Strickler et al., 2001). However, a member of this research team has recently acknowledged - in sworn testimony - sensitivity problems and possible irregularities that raise concerns about these negative reports (MacLachlan, 2002). These revelations, together with the conclusions of the three independent panels mentioned above, appear to bring to an end the apparent controversy about the presence of SV40 in human mesotheliomas and brain tumors.

“Therefore, three independent scientific panels have all agreed that there is compelling evidence that SV40 is present in some human cancers and that SV40 could contribute to the pathogenesis of some of them.”

[foetal calf serum is used in vaccine production]

Bovine viral diarrhoea virus antigen in foetal calf serum batches and consequences of such contamination for vaccine production

Author information

Makoschey B1, van Gelder PT,
Keijsers V, Goovaerts D.
Virological R&D Department
Intervet International b.v., Wim de Körverstraat 35
NL-5831 AN, Boxmeer, The Netherlands
Birgit.Makoschey@Intervet.com

Abstract

A protocol to test foetal calf serum (FCS) for contamination with bovine viral diarrhoea virus (BVDV) is described. Following this protocol, which combines cell culture methods and detection of pestivirus RNA, seven batches of FCS were tested. Infectious BVDV was detected in four of those batches. One of the remaining batches contained a relatively high number of non-infectious BVDV particles. A sample of this batch was formulated with aluminium hydroxide and aluminium phosphate as adjuvant into an experimental vaccine preparation. This product was injected twice into BVDV seronegative cattle with a 4 week interval. Blood samples taken 4 weeks after the second application were negative for BVDV specific antibodies. Our data stress that detection of BVDV RNA is not sufficient for a complete risk assessment on FCS. Discrimination between infectious and non-infectious BVDV is essential. This can only be achieved by cell culture methods.

<http://www.ncbi.nlm.nih.gov/pubmed/12935809>

“Our data stress that detection of BVDV RNA is not sufficient for a complete risk assessment on Foetal Calf Serum. Discrimination between infectious and non-infectious BVDV is essential. This can only be achieved by cell culture methods.”

Genotypes of Pestivirus RNA detected in anti-influenza virus vaccines for human use

Author information

Giangaspero M1, Vacirca G, Harasawa R, Buttner M,
Panuccio A, De Giuli Morghen C, Zanetti A, Belloli A, Verhulst A.

Dipartimento di Scienze Cliniche Veterinarie
Facoltà di Medicina Veterinaria, Università degli Studi
Milan, Italy

Abstract

Nine polyvalent human influenza virus vaccines were tested by reverse transcriptase-polymerase chain reaction (RT-PCR) for the presence of pestivirus RNA. Samples were selected from manufacturers in Europe and the USA. Three samples of the nine vaccines tested (33.3%) gave positive results for pestivirus RNA. The 5'-untranslated genomic region sequence of the contaminant pestivirus RNA was analysed based on primary nucleotide sequence homology and on secondary sequence structures characteristic to genotypes. Two sequences belonged to Pestivirus type-1 (bovine viral diarrhoea virus [BVDV]) species, genotypes BVDV-1b and BVDV-1e. These findings confirm previous reports, suggesting an improvement in preventive measures against contamination of biological products for human use.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20437384>

Full Report (In Italian)

http://www.izs.it/vet_italiana/2004/40_1/7.pdf

“Samples were selected
from manufacturers in Europe and the USA.
Three samples of the nine vaccines tested (33.3%)
gave positive results for pestivirus RNA.”

Simian virus 40 infection in humans and association with human diseases: results and hypotheses

Author information

Barbanti-Brodano G1, Sabbioni S, Martini F,
Negrini M, Corallini A, Tognon M.

Department of Experimental and Diagnostic Medicine
Section of Microbiology, Center of Biotechnology
University of Ferrara, I-44100, Ferrara, Italy

Abstract

Simian virus 40 (SV40) is a monkey virus that was introduced in the human population by contaminated poliovaccines, produced in SV40-infected monkey cells, between 1955 and 1963. Epidemiological evidence now suggests that SV40 may be contagiously transmitted in humans by horizontal infection, independent of the earlier administration of SV40-contaminated poliovaccines. This evidence includes detection of SV40 DNA sequences in human tissues and of SV40 antibodies in human sera, as well as rescue of infectious SV40 from a human tumor. Detection of SV40 DNA sequences in blood and sperm and of SV40 virions in sewage points to the hematic, sexual, and orofecal routes as means of virus transmission in humans. The site of latent infection in humans is not known, but the presence of SV40 in urine suggests the kidney as a possible site of latency, as it occurs in the natural monkey host. SV40 in humans is associated with inflammatory kidney diseases and with specific tumor types: mesothelioma, lymphoma, brain, and bone. These human tumors correspond to the neoplasms that are induced by SV40 experimental inoculation in rodents and by generation of transgenic mice with the SV40 early region gene directed by its own early promoter-enhancer. The mechanisms of SV40 tumorigenesis in humans are related to the properties of the two viral oncoproteins, the large T antigen (Tag) and the small t antigen (tag). Tag acts mainly by blocking the functions of p53 and RB tumor suppressor proteins, as well as by inducing chromosomal aberrations in the host cell. These chromosome alterations may hit genes important in oncogenesis and generate genetic instability in tumor cells. The clastogenic activity of Tag, which fixes the chromosome damage in the infected cells, may explain the low viral load in SV40-positive human tumors and the observation that Tag is expressed only in a fraction of tumor cells. "Hit and run" seems the most plausible mechanism to support this situation. The small tag, like large Tag, displays several functions, but its principal role in transformation is to bind the protein phosphatase PP2A. This leads to constitutive activation of the Wnt pathway, resulting in continuous cell proliferation. The possibility that SV40 is implicated as a cofactor in the etiology of some human tumors has stimulated the preparation of a vaccine against the large Tag. Such a vaccine may represent in the future a useful immunoprophylactic and immunotherapeutic intervention against human tumors associated with SV40.

“Simian virus 40 (SV40) is a monkey virus that was introduced in the human population by contaminated poliovaccines, produced in SV40-infected monkey cells, between 1955 and 1963. Epidemiological evidence now suggests that SV40 may be contagiously transmitted in humans by horizontal infection, independent of the earlier administration of SV40-contaminated poliovaccines.”

Multiple sclerosis and hepatitis B vaccination:
could minute contamination of the vaccine by
partial hepatitis B virus polymerase
play a role through molecular mimicry?

Author information

Faure E.

E.R. Biodiversity and Environment, case 5
University of Provence, Place Victor Hugo
13331 Marseilles cedex 3, France
eric.faure@up.univ-mrs.fr

Abstract

Reports of multiple sclerosis developing after hepatitis B vaccination have led to the concern that this vaccine might be a cause of multiple sclerosis in previously healthy subjects. Some articles evidenced that minor Hepatitis B virus (HBV) polymerase proteins could be produced by alternative transcriptional or translational strategies. Their detection is very difficult because they are in minute concentration and probably enzymatically inactive, however, it was shown that they could be exposed on the outside of the virus particles and also be immunogenic. In addition, HBV polymerase shares significant amino acid similarities with the human myelin basic protein. We hypothesise that some of the apparent adverse reactions to the vaccine could be due to a process called of molecular mimicry, the HBV polymerase, which could be a contaminant in the recombinant or plasma-derived vaccines, could act as autoantigens and induce autoimmune demyelinating diseases such as multiple sclerosis.

<http://www.ncbi.nlm.nih.gov/pubmed/15908138>

“We hypothesise that some of the apparent adverse reactions to the vaccine could be due to a process called of molecular mimicry, the Hepatitis B Virus polymerase, which could be a contaminant in the recombinant or plasma-derived vaccines, could act as autoantigens and induce autoimmune demyelinating diseases such as multiple sclerosis.”

Some oral poliovirus vaccines were contaminated with infectious SV40 after 1961

Author information

Cutrone R1, Lednický J, Dunn G, Rizzo P, Bocchetta M, Chumakov K, Minor P, Carbone M.

Thoracic Oncology Program, Cardinal Bernardin Cancer Center
Loyola University, Chicago, Illinois, USA

Abstract

Some polio vaccines prepared from 1954 to 1961 were contaminated with infectious SV40. It has been assumed that all polio vaccines were SV40 free in the United States after 1961 and in other countries after 1962. Following a WHO requirement that was prompted by the detection of SV40 in some human tumors, we conducted a multilaboratory study to test for SV40 polio vaccines prepared after 1961. Vaccine samples from 13 countries and the WHO seed were initially tested by PCR. The possible presence of intact and/or infectious SV40 DNA in PCR-positive samples was tested by transfection and infection of permissive CV-1 cells. All results were verified by immunohistochemistry, cloning, and sequencing. All the vaccines were SV40 free, except for vaccines from a major eastern European manufacturer that contained infectious SV40. We determined that the procedure used by this manufacturer to inactivate SV40 in oral poliovirus vaccine seed stocks based on heat inactivation in the presence of MgCl₂ did not completely inactivate SV40. These SV40-contaminated vaccines were produced from early 1960s to about 1978 and were used throughout the world. Our findings underscore the potential risks of using primary monkey cells for preparing poliovirus vaccines, because of the possible contamination with SV40 or other monkey viruses, and emphasize the importance of using well-characterized cell substrates that are free from adventitious agents. Moreover, our results indicate possible geographic differences in SV40 exposure and offer a possible explanation for the different percentage of SV40-positive tumors detected in some laboratories.

<http://www.ncbi.nlm.nih.gov/pubmed/16288015>

“It has been assumed that all polio vaccines were SV40 free in the United States after 1961 and in other countries after 1962.

These SV40-contaminated vaccines were produced from early 1960s to about 1978 and were used throughout the world. Our findings underscore the potential risks of using primary monkey cells for preparing poliovirus vaccines, because of the possible contamination with SV40 or other monkey viruses, and emphasize the importance of using well-characterized cell substrates that are free from adventitious agents.”

Human polyomaviruses and brain tumors

Author information

White MK1, Gordon J, Reiss K, Del Valle L,
Croul S, Giordano A, Darbinyan A, Khalili K.

Center for Neurovirology and Cancer Biology
College of Science and Technology, Temple University
1900 North 12th Street, 015-96, Room 203
Philadelphia, PA 19122, USA

Abstract

Polyomaviruses are DNA tumor viruses with small circular genomes. Three polyomaviruses have captured attention with regard to their potential role in the development of human brain tumors: JC virus (JCV), BK virus (BKV), and simian vacuolating virus 40 (SV40). JCV is a neurotropic polyomavirus that is the etiologic agent of progressive multifocal leukoencephalopathy (PML), a fatal demyelinating disease of the central nervous system occurring mainly in AIDS patients. BKV is the causative agent of polyomavirus-associated nephropathy (PVN) which occurs after renal transplantation when BKV reactivates from a latent state during immunosuppressive therapy to cause allograft failure. SV40, originating in rhesus monkeys, gained notoriety when it entered the human population via contaminated polio vaccines. All three viruses are highly oncogenic when injected into the brain of experimental animals. Reports indicate that these viruses, especially JCV, are associated with brain tumors and other cancers in humans as evidenced from the analysis of clinical samples for the presence of viral DNA sequences and expression of viral proteins. Human polyomaviruses encode three non-capsid regulatory proteins: large T-antigen, small t-antigen, and agnoprotein. These proteins interact with a number of cellular target proteins to exert effects that dysregulate pathways involved in the control of various host cell functions including the cell cycle, DNA repair, and others. In this review, we describe the three polyomaviruses, their abilities to cause brain and other tumors in experimental animals, the evidence for an association with human brain tumors, and the latest findings on the molecular mechanisms of their actions.

<http://www.ncbi.nlm.nih.gov/pubmed/15982744>

“In this review,
we describe the three polyomaviruses,
[SV40, JC virus (JCV) and BK virus (BKV)]
their abilities to cause brain and other
tumors in experimental animals, the
evidence for an association with human
brain tumors, and the latest findings on the
molecular mechanisms of their actions.”

Developments In Biologicals (Basel) • 2006

**Vaccine cell substrates:
bovine and porcine virus considerations**

Author information

Wessman SJ

USDA, APHIS, VS
Center for Veterinary Biologics
Ames, Iowa 50010, USA
stephen.j.wessman@aphis.usda.gov

Abstract

The use of materials of animal origin to supplement cell cultures used in vaccine production, viral diagnostic testing, or materials testing may lead to contamination of the vaccines, with seroconversion or disease in the vaccinated animals, and possible misdiagnosis of diagnostic samples or incorrect test results. The methods used by the Center for Veterinary Biologics to monitor serum and cell cultures are described. Considerations for the use of animal origin materials, especially bovine and porcine, as substrates or additives, plus the possibility of crossovers to humans are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/16566453>

“The use of materials of animal origin to supplement cell cultures used in vaccine production, viral diagnostic testing, or materials testing may lead to contamination of the vaccines, with seroconversion or disease in the vaccinated animals, and possible misdiagnosis of diagnostic samples or incorrect test results.”

Pharmacovigilance of vaccines

Author information

Autret-Leca E1, Bensouda-Grimaldi L,
Jonville-Béra AP, Beau-Salinas F.

Service de Pharmacologie, Hôpital Bretonneau
Université François-Rabelais de Tours
Centre Régional de Pharmacovigilance et d'Information sur le Médicament
CHRU de Tours, 2, boulevard Tonnellé, 37044 Tours, cedex 09, France
autret-leca@med.univ-tours.fr

Abstract

Safety of vaccines must be excellent to make vaccine's strategy acceptable, since it usually has a deferred individual benefit but immediate adverse drug reactions (ADRs). Pharmacovigilance of vaccines after their marketing is crucial because, prior to its availability on the market, the size of clinical trials is insufficient to identify rare or deferred adverse effects. The Pharmacovigilance is based on "spontaneous reporting" of ADRs to the Pharmacovigilance Regional Centre (PVRC) which establishes a relationship between each drug taken by the patient and the ADRs occurrence (imputability). This method is crucial to generate alerts, but under-estimates the real frequency of ADRs (1 to 10% of severe ADRs are reported). Thus pharmacoepidemiology studies are necessary to confirm the alerts identified by spontaneous reporting. ADRs can be specific, related to the antigen of an attenuated alive virus vaccine (lymphocyte meningitis after anti-mumps vaccine) or non-specific, related to a component different from the antigen (aluminium hydroxide involved in the "macrophagic myofasciitis", allergic reactions to neomycin, latex, egg or gelatine). Importance of Pharmacovigilance of vaccines is illustrated. Data, especially case-control studies, about the relationship between multiple sclerosis and hepatitis B vaccine are summarised. Data about the relationship between Crohn's disease or autism and MMR vaccine are analysed. As vaccines are used in healthy people, their safety must be excellent to be accepted. To monitor them after their marketing is the unique way to detect rare ADRs. This surveillance is made through reporting of ADRs to the PVRC. However, an active and intensive surveillance of ADRs as the one set up from the marketing of Prevenar should be systematic.

<http://www.ncbi.nlm.nih.gov/pubmed/16343870>

“Pharmacovigilance

of vaccines after their marketing

is crucial because, prior to its availability on the market,

the size of clinical trials is insufficient to identify

rare or deferred adverse effects.”

Developments In Biology, Basel • March 2006

Polio vaccines, SV40 and human tumours, an update on false positive and false negative results

Author information

Elmishad AG1, Bocchetta M, Pass HI, Carbone M.

Loyola University Medical Center
Cardinal Bernardin Cancer Center
Department of Pathology, Maywood, IL 60153, USA

Abstract

Simian virus 40 (SV40) has been detected in different human tumours in numerous laboratories. The detection of SV40 in human tumours has been linked to the administration of SV40-contaminated polio vaccines from 1954 until 1963. Many of these reports linked SV40 to human mesothelioma. Some studies have failed to detect SV40 in human tumours and this has caused a controversy. Here we review the current literature. Moreover, we present evidence showing how differences in the sensitivities of methodologies can lead to a very different interpretation of the same study. The same 20 mesothelioma specimens all tested negative, 2/20 tested positive or 7/20 tested positive for SV40 Tag by simply changing the detection method on the same immuno-precipitation/western blot membranes. These results provide a simple explanation for some of the apparent discordant results reported in the literature.

<http://www.ncbi.nlm.nih.gov/pubmed/16566440>

“we present evidence showing how differences in the sensitivities of methodologies can lead to a very different interpretation of the same study.”

High prevalence of SV40 infection
in patients with nodal non-Hodgkin's lymphoma
but not acute leukemia independent of
contaminated polio vaccines in Taiwan

Author information

Chen PM1, Yen CC, Yang MH, Poh SB, Hsiao LT, Wang WS,
Lin PC, Lee MY, Teng HW, Bai LY, Chu CJ, Chao SC,
Yang AH, Chiou TJ, Liu JH, Chao TC.

Division of Medical Oncology
Department of Medicine, Taipei Veteran General Hospital
Taipei, Taiwan, Republic of China

Abstract

Recent studies have linked simian virus 40 (SV40) to non-Hodgkin's lymphoma (NHL), especially in countries in which people were exposed to contaminated polio vaccines prior to 1963. In Taiwan, nearly all children were not exposed to contaminated polio vaccine during this period; the relationship between SV40 infection and hematological malignancies is unclear and deserves to be studied. Using PCR amplification of SV40 large T antigen DNA, confirmed by Southern blot hybridization and sequence analysis, 91 frozen lymph nodes from NHL patients were examined. Thirteen (14.3 percent) showed positive for SV40. All other test samples, including diagnostic bone marrow from patients with acute leukemia, peripheral blood from 10 relatives of SV40 positive-patients and 91 age-matched normal volunteers, and 5 reactive hyperplastic lymphoid tissues, showed negative. These results may reflect that human-to-human transmission of SV40 is independent of contaminated polio vaccines; and SV40 is possibly associated with the development of NHL in Taiwan ($p = 0.0001$). Prospective studies are needed to determine the prevalence of SV40 infections in our and other human populations and to explore the means of transmission of the virus.

<http://www.ncbi.nlm.nih.gov/pubmed/16809147>

“These results may reflect
that human-to-human transmission
of SV40 is independent of contaminated
polio vaccines; and SV40 is possibly
associated with the development of
non-Hodgkin's lymphoma in Taiwan ...”

The Legal Environment Underlying Influenza Vaccine Allocation and Distribution Strategies

Hodge, James G. Jr JD, LL.M.; O'Connell, Jessica P. JD/MPH

Abstract

In the fall of 2004, the United States faced a national shortage of influenza vaccine after a major vaccine manufacturer was unable to produce millions of doses of the vaccine due to potential contamination. Many public and private sector entities had far fewer doses of influenza vaccine to allocate than they had anticipated. In response, federal, state, and local public health officials, private vaccine distributors, and healthcare providers collaborated to distribute available doses of influenza vaccine. However, the existing legal framework through which allocations were made is murky. This article examines major legal issues regarding allocation strategies involving limited supplies of influenza vaccines, addressing in particular (1) existing legal requirements for allocating and distributing influenza vaccines among public health authorities and healthcare providers at the federal, state, and local levels; (2) the legal capacity of public health authorities to acquire existing vaccine supplies from healthcare providers; and (3) specific legal responses implemented by states in response to the 2004–2005 influenza vaccine shortage.

“In the fall of 2004, the United States faced a national shortage of influenza vaccine after a major vaccine manufacturer was unable to produce millions of doses of the vaccine due to potential contamination.”

**Crocidolite asbestos and SV40
are co-carcinogens in human mesothelial cells
and in causing mesothelioma in hamsters**

Barbara Kroczyńska,* Rochelle Cutrone,* Maurizio Bocchetta,*
Haining Yang,* Amira G. Elmishad,* Pamela Vacek,† Maria Ramos-Nino,‡
Brooke T. Mossman,‡ Harvey I. Pass,§ and Michele Carbone*

*Thoracic Oncology Program
Cardinal Bernardin Cancer Center
Loyola University Chicago, Maywood, IL 60153

Departments of †Medical Biostatistics and
‡Pathology, College of Medicine, University of Vermont, Burlington, VT 05404
and §Department of Thoracic Surgery, New York University, New York, NY 10016

ABSTRACT

Only a fraction of subjects exposed to asbestos develop malignant mesothelioma (MM), suggesting that additional factors may render some individuals more susceptible. We tested the hypothesis that asbestos and Simian virus (SV40) are cocarcinogens. Asbestos and SV40 in combination had a costimulatory effect in inducing ERK1/2 phosphorylation and activator protein-1 (AP-1) activity in both primary Syrian hamster mesothelial cells (SHM) and primary human mesothelial cells (HM). Ap-1 activity caused the expression and activation of matrix metalloprotease (MMP)-1 and MMP-9, which in turn led to cell invasion. Experiments using siRNA and chemical inhibitors confirmed the specificity of these results. The same effects were observed in HM and SHM. Experiments in hamsters showed strong cocarcinogenesis between asbestos and SV40: SV40 did not cause MM, asbestos caused MM in 20% of hamsters, and asbestos and SV40 together caused MM in 90% of hamsters. Significantly lower amounts of asbestos were sufficient to cause MM in animals infected with SV40. Our results indicate that mineral fibers and viruses can be cocarcinogens and suggest that lower amounts of asbestos may be sufficient to cause MM in individuals infected with SV40.

Full Report: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1599923/>

“Our results indicate
that mineral fibers and viruses
can be cocarcinogens and suggest that
lower amounts of asbestos may be sufficient
to cause malignant mesothelioma in
individuals infected with SV40.”

The role of SV40 in malignant mesothelioma and other human malignancies

Author information

Pershhouse MA1, Heivly S, Girtsman T.

Center for Environmental Health Sciences
Department of Biomedical and Pharmaceutical Sciences
University of Montana, Missoula, Montana 59812, USA
mark.pershhouse@umontana.edu

Abstract

SV40 is a DNA tumor virus thrust upon human populations primarily as a contaminant in various vaccine preparations. Some estimates suggest that millions of people are currently infected with the virus. The virus causes primary brain tumors, bone tumors, lymphomas, and mesotheliomas when injected into some rodent models. It has also been detected in a similar spectrum of human tumors. However, epidemiological studies have failed to conclusively demonstrate a higher incidence of disease in affected populations. To date, over 60 reports from 49 different laboratories have shown SV40 sequences in tissues from human cancer patients. Six studies, however, have failed to detect evidence of virus in similar tissues. Some have suggested that SV40 may act as a cocarcinogen with asbestos to cause mesothelioma formation, or that it may be responsible for the 10-20% of mesotheliomas with no reported history of asbestos exposure. This report briefly covers the historical evidence for SV40 carcinogenesis and then covers experiments now underway to better understand the role of SV40 in human mesotheliomas.

<https://www.ncbi.nlm.nih.gov/pubmed/16920674>

“Some have suggested that SV40 may act as a co-carcinogen with asbestos ‘to cause mesothelioma formation, or that it may be responsible for the 10-20% of mesotheliomas with no reported history of asbestos exposure.’”

“The use of materials of animal origin to supplement cell cultures used in vaccine production, viral diagnostic testing, or materials testing may lead to contamination of the vaccines ...”

Developments In Biologicals (Basel) • 2006

Vaccine cell substrates: bovine and porcine virus considerations

Author information

Wessman SJ.

USDA, APHIS, VS, Center for Veterinary Biologics, Ames, Iowa 50010, USA
stephen.j.wessman@aphis.usda.gov

Abstract

The use of materials of animal origin to supplement cell cultures used in vaccine production, viral diagnostic testing, or materials testing may lead to contamination of the vaccines, with seroconversion or disease in the vaccinated animals, and possible misdiagnosis of diagnostic samples or incorrect test results. The methods used by the Center for Veterinary Biologics to monitor serum and cell cultures are described. Considerations for the use of animal origin materials, especially bovine and porcine, as substrates or additives, plus the possibility of cross-overs to humans are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/16566453>

SV40 association with human malignancies and mechanisms of tumor immunity by large tumor antigen

Author information

Lowe DBI, Shearer MH, Jumper CA, Kennedy RC.

Department of Microbiology and Immunology
Texas Tech University Health Sciences Center
Lubbock, TX 79430-6591, USA

Abstract

SV40 was discovered as a contaminate of poliovirus vaccine lots distributed to millions of individuals in the United States between 1955 and 1963 while contaminated vaccine batches were later circulated worldwide. After SV40 was observed to cause in vitro animal and human cell transformations and in vivo tumor formations in animals, the search for a connection between the virus and human malignancies has continued to the present day. Different molecular methods have been used to detect SV40 gene products in a variety of human cancers, though SV40 causality in these tumor types has yet to be established. These data, however, are not without controversial issues related to inconclusive SV40 serological and epidemiological evidence alongside tools and methodologies that may contribute to false-positive results in human specimens. This review will also explore how vaccination against SV40 protein products may be used to help prevent and treat individuals with SV40-expressing cancers.

<http://www.ncbi.nlm.nih.gov/pubmed/17260087>

“SV40 was discovered
as a contaminate of poliovirus vaccine lots
distributed to millions of individuals in the
United States between 1955 and 1963 while
contaminated vaccine batches were
later circulated worldwide.”

Mycoplasma contamination and viral immunomodulatory activity: dendritic cells open Pandora's box

Author information

Alves MP1, Carrasco CP, Balmelli C,
Ruggli N, McCullough KC, Summerfield A.

Institute of Virology and Immunoprophylaxis
Sensemattstrasse 293, CH-3147
Mittelhäusern, Switzerland

Abstract

During in vitro investigations on the interaction of classical swine fever virus (CSFV)--an immunosuppressive viral pathogen--with monocyte-derived dendritic cells (MoDC) a soluble factor with a strong anti-proliferative activity for T lymphocytes was found. This activity, with an inhibitory dilution 50% (ID(50)) of 10(3)-10(7), was induced after virus infection of monocytes differentiating into DC. UV--inactivation of the supernatants and blocking experiments with a monoclonal antibody against the E2 envelope protein of CSFV initially indicated a virus-dependency. However, further investigations including filtration and centrifugation experiments as well as antibiotic treatment demonstrated the involvement of mycoplasma. This was confirmed by a Hoechst 33258 staining, PCR and mycoplasma cultures--Mycoplasma hyorhinis was identified as the contaminant. Elucidation of a mycoplasma presence occurred under conditions in which the original virus stocks prepared in SK6 cells were negative for mycoplasma using the above tests. Moreover, conventional passage of the virus on the SK6 cells used for this purpose did not reveal any mycoplasma. It was the passage of virus in MoDC rather than SK6 cells that was required to expose the contamination. Three passages of the anti-proliferative supernatants on MoDC cultures increased the ID(50) 10(3)-fold; only when these MoDC-derived supernatants were employed was the mycoplasma contaminant also detectable on SK6 cells. In conclusion, these data demonstrate that regular testing of cell lines and virus stocks for mycoplasma does not necessarily identify their presence, and that application of passage in MoDC cultures could prove an aid for identifying initially undetectable levels of mycoplasma contamination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17532055>

“... these data demonstrate
that regular testing of cell lines
and virus stocks for mycoplasma
does not necessarily identify their presence ...”

Oncogenic potentials of the human polyomavirus regulatory proteins

Author information

Moens U1, Van Ghelue M, Johannessen M.

Department of Microbiology and Virology
Faculty of Medicine, University of Tromsø
N-9037, Tromsø, Norway
ugom@fagmed.uit.no

Abstract

The polyomaviruses BK, JC and SV40 are common in the human population. Their DNA genomes encode large T-antigen, small t-antigen, agnoprotein, and the capsid proteins VP1-3. Studies with these viruses have contributed extensively to the understanding of processes such as replication, transcriptional and posttranscriptional regulation, and cell cycle control. All three viruses can transform human cells in vitro, can induce tumours in animal models, and are strongly associated with certain human cancers. It is generally assumed that large T-antigen is the major protein involved in neoplastic processes and that large T-antigen predominantly exerts its effect through deregulation of the tumour suppressors p53 and the retinoblastoma family members. However, additional properties of large T-antigen as well as the other viral proteins contribute to oncogenic processes. This review presents the different mechanisms by which the polyomavirus proteins can induce transformation and discusses which mechanisms may be operational in polyomavirus-positive cancers.

<https://www.ncbi.nlm.nih.gov/pubmed/17483871>

“This review presents the different mechanisms by which the polyomavirus proteins can induce transformation and discusses which mechanisms may be operational in polyomavirus-positive cancers.”

“... determining the origin of the SV40 sequences detected in human tumors might be difficult.”

Virology • January 2008

Recovery of strains of the polyomavirus SV40 from rhesus monkey kidney cells dating from the 1950s to the early 1960s

Keith Pedena, Li Shenga, Romelda Omeira, Maureen Yacobuccia,
Michael Klutchb, †, Majid Laassric, Konstantin Chumakovc, Achintya Palb, 1,
Haruhiko Murataa, b, Andrew M. Lewis Jr.b

- a. Laboratory of Retrovirus Research, Division of Viral Products, Center for Biologics Evaluation and Research
Food and Drug Administration, 29 Lincoln Drive, Bethesda, MD 20892, USA
- b. Laboratory of DNA Viruses, Division of Viral Products, Center for Biologics Evaluation and Research
Food and Drug Administration, Bethesda, MD 20892, USA
- c. Laboratory of Methods Development, Division of Viral Products, Center for Biologics Evaluation and Research
Food and Drug Administration, Bethesda, MD 20892, USA

Abstract

From stocks of adenovirus and poliovirus prepared in primary rhesus macaque kidney cells and dating from 1956 to 1961, the time when SV40 contaminated some poliovirus vaccine lots, we have recovered ten isolates of SV40. Of these ten isolates, based on the C-terminal region of T antigen, five novel strains of SV40 have been identified. Additionally, three pairs of isolates were found to be the same strain: one pair was strain 777, one pair was strain 776 archetype, and the third pair represented a novel strain. All strains had identical protein sequences for VP2 and VP3. There were two variants of agnoprotein and the small t antigen and three variants of VP1. These results, and those of others, suggest that a limited number of SV40 strains might exist in rhesus macaques in the United States, and thus determining the origin of the SV40 sequences detected in human tumors might be difficult.

Full Report: <http://www.sciencedirect.com/science/article/pii/S0042682207004321>

Strategy for identification of leachables in packaged pharmaceutical liquid formulations

Author information

Pan C1, Harmon F, Toscano K, Liu F, Vivilecchia R.

Pharmaceutical and Analytical Development
Novartis Pharmaceuticals Corporation, One Health Plaza
East Hanover, NJ 07936, USA
charles.pan@novartis.com

Abstract

Drug stability is one of the key properties to be monitored in pharmaceutical drug development. Drug degradation products, impurities and/or leachables from the drug product and packages may have significant impacts on drug efficacy, safety profile and storage conditions. In the registration stability samples of an ophthalmic pharmaceutical drug product, an unknown compound was found at a level of 0.19% by HPLC analysis. Subsequent liquid chromatography/mass spectrometry (LC/MS) analysis with electrospray ionization (ESI) indicated that the unknown was not related to the drug substance and was most likely a leachable. Identification of this unknown leachable was needed to evaluate the impact on drug safety. Through systematic extraction of various components or component combination of the packaging materials, and subsequently LC/MS analysis, the unknown was found to be a leachable coming from the varnish applied to the label. In general, using LC/MS alone is not sufficient to elucidate the structure of a complete unknown. Gas chromatography/mass spectrometry (GC/MS) was then conducted with a chemical ionization (CI) source to determine the retention time and mass of the compound of interest. Both CI and ESI sources generated the same protonated molecular ion [M+H] and similar fragmentation ions, which provides a good correlation of the unknown eluted in the liquid chromatogram and in the gas chromatogram. GC/MS with electron impact (EI) was then conducted to obtain the EI mass spectrum of this unknown. It was identified as monomethyl derivative of mephenesin through the NIST library search. The identification strategy utilized electrospray LC/MS and GC/MS with chemical and electron ionization sources which provided complimentary information for structure elucidation of this unknown compound. This combination approach in conjunction with systematic extraction was necessary for the determination of the source of this unknown in the pharmaceutical drug stability studies.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18180126>

“Drug degradation products,
impurities and/or leachables
from the drug product and packages
may have significant impacts on drug efficacy,
safety profile and storage conditions.”

Drug delivery and nanoparticles: Applications and hazards

Wim H De Jong¹ and Paul JA Borm^{2,3}

1. Laboratory for Toxicology, Pathology and Genetics,
National Institute for Public Health and the Environment (RIVM)
Bilthoven, The Netherlands
2. Zuyd University, Centre of Expertise in Life Sciences
Heerlen, The Netherlands
3. Magnamedics GmbH, Aachen, Germany

Abstract

The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery and more specifically for cancer therapy. Interestingly pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs and up to recently did not realize that carrier systems themselves may impose risks to the patient. The kind of hazards that are introduced by using nanoparticles for drug delivery are beyond that posed by conventional hazards imposed by chemicals in classical delivery matrices. For nanoparticles the knowledge on particle toxicity as obtained in inhalation toxicity shows the way how to investigate the potential hazards of nanoparticles. The toxicology of particulate matter differs from toxicology of substances as the composing chemical(s) may or may not be soluble in biological matrices, thus influencing greatly the potential exposure of various internal organs. This may vary from a rather high local exposure in the lungs and a low or neglectable exposure for other organ systems after inhalation. However, absorbed species may also influence the potential toxicity of the inhaled particles. For nanoparticles the situation is different as their size opens the potential for crossing the various biological barriers within the body. From a positive viewpoint, especially the potential to cross the blood brain barrier may open new ways for drug delivery into the brain. In addition, the nanosize also allows for access into the cell and various cellular compartments including the nucleus. A multitude of substances are currently under investigation for the preparation of nanoparticles for drug delivery, varying from biological substances like albumin, gelatine and phospholipids for liposomes, and more substances of a chemical nature like various polymers and solid metal containing nanoparticles. It is obvious that the potential interaction with tissues and cells, and the potential toxicity, greatly depends on the actual composition of the nanoparticle formulation. This paper provides an overview on some of the currently used systems for drug delivery. Besides the potential beneficial use also attention is drawn to the questions how we should proceed with the safety evaluation of the nanoparticle formulations for drug delivery. For such testing the lessons learned from particle toxicity as applied in inhalation toxicology may be of use. Although for pharmaceutical use the current requirements seem to be adequate to detect most of the adverse effects of nanoparticle formulations, it can not be expected that all aspects of nanoparticle toxicology will be detected. So, probably additional more specific testing would be needed.

“for pharmaceutical use
the current requirements
seem to be adequate to detect
most of the adverse effects
of nanoparticle formulations,
it can not be expected that all
aspects of nanoparticle toxicology
will be detected.”

Collegium Antropologicum • June 2008

The role of polio-vaccine in pleural mesothelioma— an epidemiological observation

Author information

Sarin M1, Curin K, Varnai VM.

Institute for Medical Research and Occupational Health
Zagreb, Croatia
marko@imi.hr

Abstract

From the Croatian Cancer Registry (period 1991-1997) 194 malignant pleural mesothelioma patients were collected. According to participation in polio vaccination mass campaign in 1961 that covered the entire Croatian population aged 3 months to 20 years, mesothelioma patients were divided in vaccinated (N=58), and non-vaccinated (N=136) subjects. Significantly higher percentage of those with a history of occupational exposure to asbestos was found in vaccinated (79%) compared to non-vaccinated group (63%). This is the opposite to what would be expected if potential SV40 contamination of polio vaccine used had a causative role in the development of the tumour. On the other hand, shorter latency period reflected by very high percentage of 45-year-old or younger mesothelioma patients in vaccinated group (15 out of 58), with all of them having a history of occupational asbestos exposure, raises a question for a possible enhancing effect of the vaccine used to asbestos exposure, if it was contaminated with SV40.

<http://www.ncbi.nlm.nih.gov/pubmed/18756898>

“... raises a question
for a possible enhancing effect
of the vaccine used to asbestos exposure ...”

Vaccine • June 2008

A quantitative risk assessment
of exposure to adventitious agents
in a cell culture-derived subunit influenza vaccine

Author information

Gregersen JP.

Novartis Behring, Marburg, Germany
jens-peter.gregersen@novartis.com

Abstract

A risk-assessment model has demonstrated the ability of a new cell culture-based vaccine manufacturing process to reduce the level of any adventitious agent to a million-fold below infectious levels. The cell culture-derived subunit influenza vaccine (OPTAFLU), Novartis Vaccines and Diagnostics) is produced using Madin-Darby canine kidney (MDCK) cells to propagate seasonal viral strains, as an alternative to embryonated chicken-eggs. As only a limited range of mammalian viruses can grow in MDCK cells, similar to embryonated eggs, MDCK cells can act as an effective filter for a wide range of adventitious agents that might be introduced during vaccine production. However, the introduction of an alternative cell substrate (for example, MDCK cells) into a vaccine manufacturing process requires thorough investigations to assess the potential for adventitious agent risk in the final product, in the unlikely event that contamination should occur. The risk assessment takes into account the entire manufacturing process, from initial influenza virus isolation, through to blending of the trivalent subunit vaccine and worst-case residual titres for the final vaccine formulation have been calculated for >20 viruses or virus families. Maximum residual titres for all viruses tested were in the range of 10^{-6} to 10^{-16} infectious units per vaccine dose. Thus, the new cell culture-based vaccine manufacturing process can reduce any adventitious agent to a level that is unable to cause infection.

<http://www.ncbi.nlm.nih.gov/pubmed/18485545>

“... the ability of a new
cell culture-based vaccine manufacturing process
to reduce the level of any adventitious agent
to a million-fold below infectious levels.”

“Two tetanus outbreaks in 1901 — from contaminated diphtheria antitoxin in St. Louis, Missouri, and contaminated smallpox vaccine in Camden, New Jersey — raised public concern about pharmaceutical safety.”

Perspectives In Biology And Medicine • Spring 2008

The first pharmacoepidemiologic investigations: national drug safety policy in the United States, 1901-1902

Author information

Lilienfeld DE.
lilienfeld@comcast.net

Abstract

The pharmaceutical industry developed in the late 19th century as a consequence of both scientific and commercial innovations, such as the development of diphtheria antitoxin and the commercialization of smallpox vaccine. Two tetanus outbreaks in 1901 — from contaminated diphtheria antitoxin in St. Louis, Missouri, and contaminated smallpox vaccine in Camden, New Jersey — raised public concern about pharmaceutical safety. In St. Louis, errant manufacturing processes were found to be the source of the outbreak. In Camden, investigation identified contaminated vaccine from one manufacturer as the cause. These investigations, the first known pharmacoepidemiologic studies, were widely reported. They formed the basis for the 1902 Biologics Control Act, which focused on the safety of biologics produced and sold by the pharmaceutical industry and established a precedent of federal regulation of this industry. That power, welcomed by manufacturers to restore the public's trust in their products, was enhanced in the 1906 Food and Drug Act, which created the Food and Drug Administration.

<http://www.ncbi.nlm.nih.gov/pubmed/18453724>

Virology • December 2008

SV40 DNA replication: From the A gene to a nanomachine

Author Information

Ellen Fanning* and Kun Zhao

Department of Biological Sciences and Vanderbilt-Ingram Cancer Center
Vanderbilt University, Nashville, TN 37235-1634

Abstract

Duplication of the simian virus 40 (SV40) genome is the best understood eukaryotic DNA replication process to date. Like most prokaryotic genomes, the SV40 genome is a circular duplex DNA organized in a single replicon. This small viral genome, its association with host histones in nucleosomes, and its dependence on the host cell milieu for replication factors and precursors led to its adoption as a simple and powerful model. The steps in replication, the viral initiator, the host proteins, and their mechanisms of action were initially defined using a cell-free SV40 replication reaction. Although our understanding of the vastly more complex host replication fork is advancing, no eukaryotic replisome has yet been reconstituted and the SV40 paradigm remains a point of reference. This article reviews some of the milestones in the development of this paradigm and speculates on its potential utility to address unsolved questions in eukaryotic genome maintenance.

Full Report: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2718763/>

“Duplication of the
simian virus 40 genome
is the best understood
eukaryotic DNA replication
process to date.”

BMJ • March 2009

Suspected contamination leads to recall of meningitis C vaccine

Caroline White

Two batches of meningitis C vaccine distributed to general practices across England have been recalled by the medicines watchdog amid fears that they may have been contaminated. The manufacturer, Novartis Vaccines, raised the alarm last week after routine sampling of a shipment of doses from the same two batches air freighted to the United States showed contamination with *Staphylococcus aureus*. The sterility of the solvent, aluminium hydroxide, which is used to mix the vaccine, had been compromised.

Purchase the full report for \$23

<http://www.bmj.com/content/338/bmj.b896.long>

“The sterility of the solvent, aluminium hydroxide, which is used to mix the vaccine, had been compromised.”

Safety assessment of recalled *Haemophilus influenzae* type b (Hib) conjugate vaccines United States, 2007-2008

Author information

Huang WT1, Chang S, Miller ER, Woo EJ, Hoffmaster AR,
Gee JE, Clark TA, Iskander JK, Ball R, Broder KR.

Epidemic Intelligence Service, Career Development Division
Office of the Workforce and Career Development
Centers for Disease Control and Prevention (CDC)
Atlanta, GA 30333, USA

Abstract

PURPOSE

On 13 December 2007, Merck & Co., Inc. voluntarily recalled 1.2 million doses of *Haemophilus influenzae* type b (Hib) vaccines that had been distributed since April 2007 for concerns regarding potential *Bacillus cereus* contamination. Enhanced postrecall surveillance was conducted to detect vaccine-associated *B. cereus* infections.

METHODS

We reviewed reports involving recalled Hib vaccines received by the Vaccine Adverse Event Reporting System (VAERS) during 1 April 2007-29 February 2008. For each reported death, autopsy review sought evidence of *B. cereus* infections. For each specified outcome, the proportional reporting ratios (PRRs) were calculated to compare the recalled Hib vaccines with the manufacturer's nonrecalled Hib vaccines in the VAERS databases. On 20 December 2007, we used the Epidemic Information Exchange (Epi-X) to solicit nongastrointestinal vaccine-associated *B. cereus* infections, and requested *B. cereus* isolates for genotyping to compare with the manufacturing facility isolate.

RESULTS

VAERS received 75 reports involving recalled Hib vaccines; none described a confirmed *B. cereus* infection. Comparative analyses did not reveal disproportionate reporting of specified outcomes for recalled Hib vaccines. The Epi-X posting triggered one report of vaccine-associated *B. cereus* bacteremia from a child who received a nonrecalled Hib vaccine manufactured by Merck; the genotypes of isolates from the patient and the manufacturing facility differed.

CONCLUSIONS

No evidence of vaccine-associated *B. cereus* infection had been found in recipients of recalled Hib vaccines. Conducting laboratory surveillance through Epi-X was feasible and may enhance public health response capacities for future vaccine safety emergencies.

<http://www.ncbi.nlm.nih.gov/pubmed/20084617>

“On 13 December 2007, Merck & Co., Inc.
voluntarily recalled 1.2 million doses of
Haemophilus influenzae type b (Hib) vaccines
that had been distributed since April 2007 ...”

Isolation of an Infectious Endogenous Retrovirus in a Proportion of Live Attenuated Vaccines for Pets

Takayuki Miyazawa,1,‡,* Rokusuke Yoshikawa,1,‡
Matthew Golder,2 Masaya Okada,1
Hazel Stewart,2 and Massimo Palmarini2,*

1. Laboratory of Signal Transduction
Institute for Virus Research, Kyoto University
53 Shogoin-Kawaracho, Sakyo-ku, Kyoto 606-8507, Japan
2. Institute of Comparative Medicine
University of Glasgow Faculty of Veterinary Medicine
464 Bearsden Road, Glasgow G61 1QH, Scotland2

Abstract

The genomes of all animal species are colonized by endogenous retroviruses (ERVs). Although most ERVs have accumulated defects that render them incapable of replication, fully infectious ERVs have been identified in various mammals. In this study, we isolated a feline infectious ERV (RD-114) in a proportion of live attenuated vaccines for pets. Isolation of RD-114 was made in two independent laboratories using different detection strategies and using vaccines for both cats and dogs commercially available in Japan or the United Kingdom. This study shows that the methods currently employed to screen veterinary vaccines for retroviruses should be reevaluated.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2838105/?tool=pubmed>

“ In this study, we isolated a feline infectious ERV (RD-114) in a proportion of live attenuated vaccines for pets. Isolation of RD-114 was made in two independent laboratories using different detection strategies and using vaccines for both cats and dogs commercially available in Japan or the United Kingdom. This study shows that the methods currently employed to screen veterinary vaccines for retroviruses should be reevaluated.”

Atypical 'HoBi'-like pestiviruses— recent findings and implications thereof

Author information

Ståhl K1, Beer M, Schirrneier H, Hoffmann B, Belák S, Alenius S.

The Joint R&D Division in Virology
the National Veterinary Institute (SVA) and
The Swedish University of Agricultural Sciences (SLU)
Uppsala, Sweden
karl.stahl@bvf.slu.se

Abstract

In 2004, an atypical pestivirus named D32/00_'HoBi', isolated from foetal calf serum (FCS) originating from Brazil, was described (Schirrneier et al., 2004). A few years later, a closely related virus (Th/04_KhonKaen) was detected in serum from a calf in Thailand, indicating that this group of atypical pestiviruses already is spread in cattle populations in various regions of the world. At the Friedrich-Loeffler-Institute, Insel Riems, Germany, FCS batches are regularly tested for pestivirus contamination, in general with positive PCR results, and in some cases the contaminants have been typed as 'HoBi'-like. At the National Veterinary Institute (SVA) in Uppsala, Sweden, a recent event with contaminated FCS ruined much of the ongoing cell culture work. From the FCS and the contaminated cells we were able to amplify and sequence nucleic acid from three different pestivirus strains, including BVDV-1, -2 and 'HoBi'-like; this in a commercial FCS that had been tested free from pestivirus by the manufacturer. In this short communication we review the current status of atypical 'HoBi'-like pestiviruses, describe recent findings and discuss the implications thereof.

“From the Fetal Calf Serum and the contaminated cells we were able to amplify and sequence nucleic acid from three different pestivirus strains, including BVDV-1, -2 and 'HoBi'-like; this in a commercial FCS that had been tested free from pestivirus by the manufacturer.”

Endogenous retroviruses as potential hazards for vaccines

Author information

Miyazawa T1.

Laboratory of Signal Transduction
Department of Cell Biology
Institute for Virus Research
Kyoto University, 53 Shogoin-Kawaracho
Sakyo-ku, Kyoto 606-8507, Japan
takavet@gmail.com

Abstract

Retroviruses are classified as exogenous or endogenous according to their mode of transmission. Generally, endogenous retroviruses (ERVs) are not pathogenic in their original hosts; however, some ERVs induce diseases. In humans, a novel gammaretrovirus was discovered in patients with prostate cancer or chronic fatigue syndrome. This virus was closely related to xenotropic murine leukemia virus (X-MLV) and designated as xenotropic murine leukemia virus-related virus (XMRV). The origin and transmission route of XMRV are still unknown at present; however, XMRV may be derived from ERVs of rodents because X-MLVs are ERVs of inbred and wild mice. Many live attenuated vaccines for animals are manufactured by using cell lines from animals, which are known to produce infectious ERVs; however, the risks of infection by ERVs from xenospecies through vaccination have been ignored. This brief review gives an overview of ERVs in cats, the potential risks of ERV infection by vaccination, the biological characteristics of RD-114 virus (a feline ERV), which possibly contaminates vaccines for companion animals, and the methods for detection of infectious RD-114 virus.

<http://www.ncbi.nlm.nih.gov/pubmed/20378372>

“Many live attenuated vaccines for animals are manufactured by using cell lines from animals, which are known to produce infectious ERVs; however, the risks of infection by ERVs from xenospecies through vaccination have been ignored. This brief review gives an overview of ERVs in cats, the potential risks of ERV infection by vaccination, the biological characteristics of RD-114 virus (a feline ERV), which possibly contaminates vaccines for companion animals, and the methods for detection of infectious RD-114 virus.”

Australia suspends seasonal flu vaccination of young children

by Melissa Sweet

Australia has extended a suspension of vaccination of children aged 5 years and under against seasonal flu, pending further investigations into an apparent spike in febrile convulsions associated with the vaccine.

A temporary suspension was first announced on 23 April, after concerns emerged in Western Australia about an increase in the number of young children presenting to hospitals with febrile convulsion after receiving the trivalent seasonal flu vaccine.

The federal government's chief medical officer, Jim Bishop, announced on 30 April that more time was needed to complete epidemiological and scientific investigations.

"Given the ongoing and incomplete scientific and clinical case review, the moratorium on the use of seasonal influenza vaccine in children 5 years and less will continue," he said.

Figures released by the national Department of Health and Ageing show that 77 cases of febrile convulsion in children aged 5 or under and associated with the vaccination have recently been reported to the Therapeutic Goods Administration.

Of these, 57 were in Western Australia, the only Australian state to provide free seasonal flu vaccination for all children aged 6 months to 4 years. It introduced the vaccination programme in 2008 after the highly publicised deaths of three young children with flu and because of concerns that this age group has the highest hospitalisation rates for flu. About 35% of children under 5 in Western Australia are estimated to have received at least one dose of flu vaccine in 2008 and 2009, but it is not yet known how many have been vaccinated this season, Paul Armstrong of the state's health department told the BMJ.

A range of experts have said that it is unclear whether the cases of fever relate to a specific batch or product or to inclusion of the pandemic vaccine in a trivalent vaccine. Three companies market seasonal flu vaccines in Australia. They contain the components recommended by the Australian Influenza Vaccine Committee for the 2010 season (A/H1N1, A/H3N2, and B) (www.tga.gov.au/committee/aivc.htm).

The TGA is continuing to recommend the pandemic vaccine (active only against H1N1) for adults and children (www.tga.gov.au/alerts/medicines/flu vaccine.htm).

Other possibilities being investigated are whether febrile illness has increased more broadly this winter or whether the Western Australian programme has uncovered an increased risk among young children in particular.

Peter Richmond, a paediatrician in Perth, told ABC television this week that the association of fevers with the vaccination was striking (www.abc.net.au/7.30/content/2010/s2885203.htm). "This year has been something that I've never seen in 20 years as a paediatrician," he said. "We have had a large number of children presenting to their doctors who were previously well who received the flu vaccine, and they had a very sudden onset of this high fever. And obviously for parents of young children it was very scary, and unfortunately some of these children actually had febrile convulsions."

Professor Bishop told the BMJ he had an "open mind" about whether there was a real increase in side effects. "In the meantime it is prudent and safe to proceed cautiously," he said.

An industry funded group, the Influenza Specialist Group, has said that Queensland's government is also working closely with a local coroner regarding the death of a 2 year old girl who was found dead in her cot several hours after receiving a seasonal flu vaccine in early April (www.influenzaspecialistgroup.org.au/news-recent/143-seasonal-flu-vaccination-and-in-children-5-years-and-under-). Professor Bishop said that this case had not been reported to the Therapeutic Goods Administration.

A statement from the Department of Health and Ageing said that batch testing of the vaccine by the Therapeutic Goods Administration and other independent experts had so far shown the vaccine to be satisfactory, while testing by the major flu vaccine manufacturer CSL had found no abnormalities in its product. Further testing and experiments are planned.

Meanwhile, Julie Leask, a senior research fellow at the National Centre for Immunisation Research & Surveillance, said that public confidence in flu vaccination is likely to suffer, resulting in reduced vaccination coverage across all ages.

Peter Collignon, an infectious diseases specialist at the Australian National University, Canberra, said that the situation showed the need for better surveillance and evaluation of flu vaccination. "We're in a situation now where the government can't tell us how many doses of the vaccine have been given out or how many people have side effects," he said.

Dr Armstrong said that the vaccination programme would resume in Western Australia only when it was clear that it was safe to do so. He said, "The first thing we need to do is to work out [whether there] is a problem and what the magnitude is, and then to work out what the problem is; we don't know that at the moment."

Adverse events following influenza vaccination in Australia—should we be surprised?

There have been large numbers of major adverse reactions to this year's seasonal influenza vaccine in Australia, and the vaccine has been suspended for use in children aged five and under [1,2]. These reactions have occurred across the country and involved multiple batches of vaccine [2]. In the state of Western Australia where the problem was first detected, reports suggest that of the 20,000 to 30,000 children vaccinated, more than 250 had adverse reactions and 55 had febrile convulsions before vaccination was suspended in young children [2]. Assuming all convulsions were in children, about one child in every 500 vaccinated had a febrile convulsion. Across Australia, media accounts indicate that more than 400 adverse reactions [3] including 77 cases of febrile convulsion [1] have been reported by regulators. While attention remains focused on reactions in very young children, reports suggest only one-third of the reactions may have occurred in children under five [4].

Although this situation has triggered considerable controversy in Australia, the story has attracted little to no media attention in the US and Europe. Similarly, the media has paid little attention to a US H1N1 federal vaccine safety advisory committee which recently reported detecting signals for Guillain-Barre syndrome (GBS), Bell's palsy, and thrombocytopenia in the monovalent H1N1 (swine flu) vaccine [5]. The same monovalent H1N1 antigen component under review in the US is scheduled to be added to the US trivalent seasonal vaccine and is contained in the Australian trivalent seasonal vaccine and will be given to children, pregnant women and adults [6].

Data from a previous Australian study of H1N1 vaccine show that a large percentage of children developed fevers following vaccination — in children less than 3 years, between three and six in every ten vaccinated, depending on dose [7,8]. The data also show a dose response effect — the larger the vaccine dose, the more severe the harms. There was also an age relationship: children under the age of three developed fevers at more than twice the rate of older children [7,8]. The study was however underpowered to detect febrile convulsions at the current rates in Australia, with only 162 children below the age of three. The size problem was further aggravated by stratification by age group and antigen dose.

Presumably the vaccine manufacturer CSL, which sponsored the trial, and Australia's regulatory body, the Therapeutic Goods Administration (TGA), which used this data in approving the vaccine for children, were aware of these important findings. But authors of the study published earlier this year did not discuss the high incidence of fever associated with vaccination [7]; data were instead only reported in online-only supplementary tables [8].

Overall, the percentages of children under three who developed a fever after vaccination appear very high; thirty five per cent with the 15 ug dose and 62% after a 30 ug dose [7,8]. Of those that received a 7.5 ug dose in the seasonal influenza vaccine, 23% develop a fever of >38 degrees Celsius [6].

The large number of children suffering harms — and subsequent suspension of the vaccine — challenges the assumption that regulators are ensuring the safety and efficacy of all marketed therapeutics. Should we be surprised that these problems have occurred with influenza vaccine, a vaccine used for over 60 years, said to have “an established record of safety in all age groups”? [9]

There are actually relatively little data on the effects of vaccinating young children against influenza [10]. Some manufacturers have even withheld data from public scrutiny amidst general indifference [10,11]. Evidence from all comparative influenza vaccine studies shows that harms, when they are investigated, are not reported consistently and systematically [10,11].

As pandemic vaccines are provided to governments and not individuals and manufacturers are indemnified for damages caused to users [12-14], there seem to be few incentives for investigation of harms.

Last winter, the likelihood that a child without risk factors would die from swine flu was less than one in a million [15]. When such a high proportion of children develop moderate to severe febrile reactions to the influenza vaccine, it's likely that more harm than good will occur by vaccinating the entire population.

If such a large proportion of children develop high fevers, it is also likely that a substantial number will develop febrile convulsions as a result of vaccination. It is thus surprising the vaccine was approved for this age group. It is also surprising that more explicit warnings about the high risk of adverse reactions were not given to parents when their children were being vaccinated. Passive surveillance (as in Australia and elsewhere) is a relatively weak mechanism to detect and evaluate post-vaccination adverse events [16].

Unlike most drugs, vaccines are used on a population basis triggered by public health policy. As such, evidence of their safety and efficacy needs to be extraordinarily rigorous and evaluation methods and data should be open to independent scrutiny. We need much better and larger studies on both safety and efficacy before we roll out influenza vaccine programs to all populations, especially to children who appear to have much higher rates of adverse reactions. Finally, decisions to use a vaccine in a population must consider its safety profile, but principally its effectiveness. There is poor evidence on how well influenza vaccines prevent any influenza complications in children [10] and other age groups. There is good evidence that influenza vaccines study reports cherry pick results and achieve spurious notoriety [17]. Exposing human beings to uncertain effects is a risky business.

Report available for purchase
Try a 14-day free trial at BMJ.com
or Google the title of the report for more information

“The large number of children suffering harms — and subsequent suspension of the vaccine — challenges the assumption that regulators are ensuring the safety and efficacy of all marketed therapeutics. Should we be surprised that these problems have occurred with influenza vaccine, a vaccine used for over 60 years, said to have “an established record of safety in all age groups”?

There are actually relatively little data on the effects of vaccinating young children against influenza. Some manufacturers have even withheld data from public scrutiny amidst general indifference. Evidence from all comparative influenza vaccine studies shows that harms, when they are investigated, are not reported consistently and systematically.

As pandemic vaccines are provided to governments and not individuals and manufacturers are indemnified for damages caused to users, there seem to be few incentives for investigation of harms.”

Viral Nucleic Acids in Live-Attenuated Vaccines: Detection of Minority Variants and an Adventitious Virus †

Author Information

Joseph G. Victoria,^{1,2} Chunlin Wang,³ Morris S. Jones,⁴
Crystal Jaing,⁵ Kevin McLoughlin,⁵ Shea Gardner,⁵ and Eric L. Delwart^{1,2*}

1. Blood Systems Research Institute, San Francisco, California 94118
2. Dept. of Laboratory Medicine, University of California, San Francisco, California 94118
3. Stanford Genome Technology Center, Stanford, California 94304
4. Clinical Investigation Facility, David Grant USAF Medical Center, Travis AFB, California 94535
5. Lawrence Livermore National Laboratory, Livermore, California 94551

Highly effective, safe, and relatively inexpensive, live-attenuated viruses protect against numerous human and animal viral infections. Attenuation is achieved by genetically adapting viruses for replication in a different host species or under nonphysiological conditions, such that viruses lose their pathogenic potential in their original host species while remaining sufficiently antigenic to induce lasting protective immunity. Live-attenuated vaccines are highly efficacious due to the physiologic presentation of native antigen to the host's immune system and include the earliest human vaccine developed by serial passages of rabies virus in rabbits. In very rare instances, one attenuated viral vaccine, the oral poliovirus vaccine (OPV), can accumulate mutations as well as recombine with other coinfecting enteroviruses and revert to a pathogenic state (18, 24). Attenuated live vaccines also carry a potential risk of contamination with adventitious viruses introduced during the attenuation process, from the cell lines used, and/or from the animal sera or other biologics often used in cell cultures. Very early Theiler's yellow fever attenuated virus was once "stabilized" with human plasma thought to contain hepatitis B virus, resulting in many cases of hepatitis (5, 28). Some early Sabin poliovirus vaccines were contaminated with the simian virus 40 (SV40) polyomavirus from the monkey cells used to amplify polioviruses. While carcinogenic in rodents, SV40 has no epidemiologic association with human cancers (10). Avian leukosis virus (ALV) and endogenous avian virus (AEV) have been reported in attenuated vaccines grown in chicken embryo fibroblasts (CEF), but extensive testing has also ruled out human infections (14, 15). Vaccine-associated ALV and AEV are thought to originate from endogenous retroviruses in the chicken germ line (14, 15, 17).

Because the chemical inactivation used in the manufacture of killed-virus vaccines is also likely to inactivate adventitious viruses, we focused on eight live-attenuated viruses, OPV (Biopolio), rubella (Meruvax-II), measles (Attenuvax), yellow fever (YF-Vax), human herpesvirus 3 (HHV-3) (Varivax), rotavirus (Rotarix and Rotateq), and multivalent measles/mumps/rubella (MMR-II), to resequence the attenuated viruses and test for the presence of adventitious viruses after viral particle purification, massively parallel pyrosequencing, and viral sequence similarity searches. Vaccine nucleic acids were also analyzed using a panmicrobial microarray.

Published ahead of print on 7 April 2010

† The authors have paid a fee to allow immediate free access to this article.

Full Report: <http://jvi.asm.org/content/84/12/6033.full.pdf>

“In very rare instances, one attenuated viral vaccine, the oral poliovirus vaccine (OPV), can accumulate mutations as well as recombine with other coinfecting enteroviruses and revert to a pathogenic state.”

“Recently discovered contamination of 2 rotavirus vaccines by pig viruses is unlikely to pose a human health threat, according to the US Food and Drug Administration (FDA).”

Journal Of The American Medical Association (JAMA) • July 2010
Medical News and Perspectives

**FDA:
Benefits of Rotavirus Vaccination
Outweigh Potential Contamination Risk**

by Bridget M. Kuehn

Recently discovered contamination of 2 rotavirus vaccines by pig viruses is unlikely to pose a human health threat, according to the US Food and Drug Administration (FDA). The agency recommended in May that physicians resume use of one vaccine, Rotarix, and continue use of the other vaccine, RotaTeq.

On March 22, the FDA had recommended that physicians suspend the use of Rotarix after the agency learned that academic researchers made the unexpected finding that the vaccine contained DNA from porcine circovirus 1 (PCV1), a virus that is common in US swine but not associated with illness in pigs or humans (Victoria JG et al. J Virol. 2010;84[12]:6033-6040). This finding was confirmed by scientists from the FDA and the vaccine's maker, GlaxoSmithKline.

<http://jama.jamanetwork.com/article.aspx?articleid=186166>

Expert Review Of Vaccines • October 2010

MF59; as a vaccine adjuvant: a review of safety and immunogenicity

Author information

El Sahly H.

Department of Molecular Virology and Microbiology
Baylor College of Medicine, Houston, TX 77030, USA
hanae@bcm.edu

Abstract

Approximately 70 years passed between the licensing of alum salts as vaccine adjuvants and that of MF59, an oil-in-water emulsion, is currently licensed for use in the elderly as an adjuvant in seasonal influenza vaccines. Its mechanism of action is not fully understood, but enhancement of the interaction between the antigen and the dendritic cell seems to be involved. When used with seasonal influenza vaccines, an increase occurs in the hemagglutination inhibition antibody titers against some, but not all, seasonal vaccine influenza strains. The adjuvant effect is more pronounced when MF59 is combined with novel influenza antigens such as H9 and H5. The use of the adjuvant is associated with an increase in the frequency of local and systemic early post-vaccine adverse events (3-7 days), but no increase in adverse events was observed thereafter. Currently, MF59 is under evaluation as an adjuvant with other antigens such as pandemic influenza antigens and cytomegalovirus antigens.

<http://www.ncbi.nlm.nih.gov/pubmed/20923265>

“Currently, MF59 [squalene] is under evaluation as an adjuvant with other antigens such as pandemic influenza antigens and cytomegalovirus antigens.”

Toxicology • December 2010

Interindividual variations in the efficacy and toxicity of vaccines

Author information

Thomas C1, Moridani M.

Department of Pharmaceutical Sciences
School of Pharmacy, Lake Erie College of Osteopathic Medicine
Bradenton, FL 34211, USA

Abstract

A number of currently available vaccines have shown significant differences in the magnitude of immune responses and toxicity in individuals undergoing vaccination. A number of factors may be involved in the variations in immune responses, which include age, gender, race, amount and quality of the antigen, the dose administered and to some extent the route of administration, and genetics of immune system. Hence, it becomes imperative that researchers have tools such as genomics and proteomics at their disposal to predict which set of population is more likely to be non-responsive or develop toxicity to vaccines. In this article, we briefly review the influence of pharmacogenomics biomarkers on the efficacy and toxicity of some of the most frequently reported vaccines that showed a high rate of variability in response and toxicity towards hepatitis B, measles, mumps, rubella, influenza, and AIDS/HIV.

<http://www.ncbi.nlm.nih.gov/pubmed/19837123>

“A number of currently available vaccines have shown significant differences in the magnitude of immune responses and toxicity in individuals undergoing vaccination.”

“When Eric Delwart couldn’t find the right email addresses online to contact GlaxoSmithKline ...”

Nature Medicine • 2010

Vaccine contamination prompts safety review

Megan Scudellari

When Eric Delwart couldn’t find the right email addresses online to contact GlaxoSmithKline (GSK) in early February, he posted a good old-fashioned letter to the Belgian headquarters of the pharma giant to inform the company that one of its vaccines was contaminated with a pig virus. Months earlier, Delwart, a viral...

Purchase this report full text PDF: \$18

<http://www.nature.com/nm/journal/v16/n5/full/nm0510-493.html>

Plaque purification as a method
to mitigate the risk of adventitious-agent contamination
in influenza vaccine virus seeds

Author information

Murata H1, Macauley J, Lewis AM Jr, Peden K.

Laboratory of DNA Viruses
Division of Viral Products
CBER, FDA, Bethesda, MD 20892, USA
haruhiko.murata@fda.hhs.gov

Abstract

At present, the seed viruses for the manufacture of licensed seasonal inactivated influenza vaccines in the United States are derived from primary egg isolates as a result of concerns associated with adventitious agents. According to the prevailing view, the passage of influenza viruses through eggs serves as a filtering step to remove potential contaminating viruses. We have investigated the feasibility of addressing adventitious-agent risk by subjecting influenza virus to a plaque-purification procedure using MDCK cells. SV40 and canine adenovirus-1 (representing viruses for which MDCK cells are non-permissive and permissive, respectively) were used as challenge viruses to model agents of concern that might be co-isolated along with the influenza virus. By mixing influenza virus strain A/PR/8/34 with varying amounts of each challenge virus and then performing a plaque assay for influenza virus using MDCK cells, we have attempted to determine the efficiency by which the challenge virus is removed. Our data suggest that substantial removal can be achieved even after a single round of plaque purification. If cell-derived isolates were deemed to be acceptable following a plaque-purification procedure, the manufacture of seasonal influenza vaccine would be facilitated by: (1) the expansion of the repertoire of viruses from which seed virus candidates could be generated for licensed egg-derived vaccines as well as for vaccines manufactured in mammalian cells; and (2) the mitigation of adventitious-agent risk associated with the seed virus, and hence the elimination of the need to passage seed viruses in eggs for vaccines manufactured in mammalian cells.

<http://www.ncbi.nlm.nih.gov/pubmed/21354480>

“At present, the seed viruses for the manufacture of licensed seasonal inactivated influenza vaccines in the United States are derived from primary egg isolates as a result of concerns associated with adventitious agents. According to the prevailing view, the passage of influenza viruses through eggs serves as a filtering step to remove potential contaminating viruses.”

Investigations of porcine circovirus type 1 (PCV1) in vaccine-related and other cell lines

Hailun Ma, Syed Shaheduzzaman,
Dhanya K. Williams, Yamei Gao, Arifa S. Khan

Division of Viral Products
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research
US Food and Drug Administration
Bethesda, MD 20892, USA

Abstract

Porcine circovirus type 1 (PCV1) is highly prevalent in swine and was recently reported in some rotavirus vaccines. Since animal-derived raw materials, such as cells, trypsin, and serum, can be a major source of introducing virus contamination in biological products, we have investigated PCV1 in several cell lines obtained from ATCC that have broad use in research, diagnostics, or vaccine development. It is expected that these cell lines have been exposed to bovine and porcine viruses during their establishment and passage history due to the use of serum and trypsin that was not qualified according to current testing guidances or processed using new virus-inactivation methods. This study showed that Vero, MRC-5, and CEFs, which represent cell substrates used in some U.S. licensed vaccines, and other cell lines used in investigational vaccines, such as MDCK, HEK-293, HeLa, and A549, were negative for PCV1 using a nested PCR assay; some were also confirmed negative by infectivity analysis. However, MDBK cells, which are used for some animal vaccines, contained PCV1 sequences, although no virus was isolated. Although the results showed that PCV infection may not have occurred under previous culture conditions, the recent cases of vaccine contamination emphasizes the need for continued efforts to reduce the likelihood of introducing viruses from animal-derived materials used in product manufacture.

<http://www.sciencedirect.com/science/article/pii/S0264410X1101173X>

[click Science Direct]

“Although the results showed that Porcine Circovirus infection may not have occurred under previous culture conditions, the recent cases of vaccine contamination emphasizes the need for continued efforts to reduce the likelihood of introducing viruses from animal-derived materials used in product manufacture.”

Simian virus 40 transformation, malignant mesothelioma and brain tumors

Author information

Qi F1, Carbone M, Yang H, Gaudino G.

University of Hawaii Cancer Center
Honolulu, HI, USA

Abstract

Simian virus 40 (SV40) is a DNA virus isolated in 1960 from contaminated polio vaccines, that induces mesotheliomas, lymphomas, brain and bone tumors, and sarcomas, including osteosarcomas, in hamsters. These same tumor types have been found to contain SV40 DNA and proteins in humans. Mesotheliomas and brain tumors are the two tumor types that have been most consistently associated with SV40, and the range of positivity has varied about from 6 to 60%, although a few reported 100% of positivity and a few reported 0%. It appears unlikely that SV40 infection alone is sufficient to cause human malignancy, as we did not observe an epidemic of cancers following the administration of SV40-contaminated vaccines. However, it seems possible that SV40 may act as a cofactor in the pathogenesis of some tumors. In vitro and animal experiments showing cocarcinogenicity between SV40 and asbestos support this hypothesis.

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3241931/>

“it seems possible that SV40
may act as a cofactor in the pathogenesis
of some tumors. In vitro and animal
experiments showing cocarcinogenicity
between SV40 and asbestos support
this hypothesis.”

Using an Immunization Information System to Facilitate a Vaccine Recall in New York City 2007

Papadouka, Vikki PhD, MPH; Metroka,
Amy MSW, MPH; Zucker, Jane R. MD, MSc

Abstract

Background

In December 2007, Merck & Co, Inc, initiated a voluntary recall of 10 lots of PedvaxHIB, and 2 lots of COMVAX when the potential of contamination was identified during routine testing of the manufacturing equipment. Merck recommended that providers stop vaccinating children using these vaccine lots.

Objective

To describe how the New York City (NYC) Immunization Information System was used in the effort to recall vaccines.

Methods

Immediately following Merck's announcement, NYC's Bureau of Immunization used the New York Citywide Immunization Registry (CIR) to (a) fax and e-mail all pediatric facilities a letter informing them of the recall and asking that they immediately remove recalled vaccines from their refrigerators; (b) identify facilities that had used the recalled lots, on the basis of data reported to the CIR, and contact them individually by phone; and (c) monitor the success of the recall by examining the number of recalled doses administered and reported to the CIR before and after the recall.

Results

The alert was faxed and e-mailed to 1928 pediatric facilities informing them of the recall. In addition, the Bureau of Immunization identified 105 facilities that had reported doses of vaccine from the recalled lots to the CIR and called to ask them to check their refrigerators for remaining supplies and discontinue use of this vaccine. The number of doses with the affected lot numbers reported to the CIR decreased sharply following CIR recall notification. Furthermore, the Centers for Disease Control and Prevention and Merck reported the return of nearly 50% of publicly and privately purchased vaccines from the recalled lots that had been distributed to NYC providers.

Conclusion

Immunization Information Systems can be effective tools for quickly identifying providers in possession of recalled vaccine lots, particularly when lot numbers are well reported, and for facilitating rapid vaccine recall in support of vaccine safety.

“In December 2007, Merck & Co, Inc, initiated a voluntary recall of 10 lots of PedvaxHIB, and 2 lots of COMVAX when the potential of contamination was identified during routine testing of the manufacturing equipment. Merck recommended that providers stop vaccinating children using these vaccine lots.”

“Because the product is itself a virus,
traditional viral clearance steps are generally not included in the manufacturing process ...”

PDA Journal Of Pharmaceutical Science And Technology • November 2011

**Application of Risk Assessments
in the Design of the Overall Viral Control Strategy Used
during the Manufacture and Testing of Live Virus Vaccines**

Author information

Pennathur S.

MedImmune, LLC, One MedImmune Way, Gaithersburg, MD 20878

Abstract

CONFERENCE PROCEEDING

Proceedings of the PDA/FDA Adventitious Viruses in Biologics: Detection and Mitigation Strategies Workshop in Bethesda, MD, USA; December 1-3, 2010 Guest Editors: Arifa Khan (Bethesda, MD), Patricia Hughes (Bethesda, MD) and Michael Wiebe (San Francisco, CA) It is important to include a risk assessment process in the overall viral control strategy used during the manufacture and testing of live virus vaccines. Because the product is itself a virus, traditional viral clearance steps are generally not included in the manufacturing process, and there is normally no inactivation step in the manufacturing process either. The risk assessment is therefore necessary to identify potential sources for entry of adventitious agents into the vaccine, and to develop a strategy to minimize or eliminate the sources through which adventitious agents can enter the vaccine. The risk assessment can also be used to tailor the biosafety testing that is performed on raw materials, vaccine seeds, vaccine bulk materials, and final product. Biosafety testing is normally designed to ensure the detection of both known and unknown adventitious agents, but the results of the risk assessment can be used to put in place a biosafety testing strategy designed to maximize the detection of an adventitious agent that is potentially likely to be present in the vaccine. The risk assessment therefore enables the development of a comprehensive viral control strategy and provides a higher level of assurance that the vaccine will be free from contamination by adventitious agents.

<http://www.ncbi.nlm.nih.gov/pubmed/22294607>

Contamination with gangliosides in brain-derived rabies vaccine may trigger Guillain–Barré syndrome

Author Information

Hikomichi Sakai¹, Faqeehah Mohamed Harun¹,
Naoki Yamamoto^{1,2}, Nobuhiro Yuki^{1,2}

1. Department of Microbiology, National University of Singapore, Singapore
2. Department of Medicine, National University of Singapore, Singapore

Abstract

Guillain–Barré syndrome (GBS) is an autoimmune-mediated peripheral neuropathy typically occurring after microbial infections such as *Campylobacter jejuni* enteritis. It can also occur following vaccinations such as the 1976 swine flu vaccine in the USA.¹ GBS is divided into demyelinating and axonal subtypes. There is now good evidence that gangliosides or similar components trigger the development of axonal GBS.² Axonal GBS associated with IgG anti-GM1 or anti-GD1a antibodies after bovine brain ganglioside administration have been recorded in several patients. Sensitisation of rabbits with bovine brain gangliosides or isolated GM1 produced a replica of axonal GBS. Based on these findings, it has been suggested that *C jejuni* components mimic human gangliosides GM1 and GD1a, and *C jejuni* infection induces the production of autoantibodies against the gangliosides that are expressed in the peripheral nerves, resulting in the limb weakness seen in GBS. By contrast, the mechanism by which certain vaccines elicit the development of GBS remains unresolved, although there have been studies to suggest that the 1976 swine flu vaccine could elicit anti-GM1 antibodies in mice and that the GM1 epitope was present in the influenza haemagglutinin.³ It is important to understand the pathogenesis of postvaccination GBS to allow safer vaccines to be developed.

<http://jnnp.bmj.com/content/83/4/467.extract>

“There is now good evidence that gangliosides or similar components trigger the development of axonal Guillain–Barré syndrome (GBS).”

A need for careful evaluation of endotoxin contents in acellular pertussis-based combination vaccines

Michiyo Kataoka, Masaki Ochiai, Akihiko Yamamoto, Yoshinobu Horiuchi

Department of Bacterial Pathogenesis and Infection Control
National Institute of Infectious Diseases
4-7-1 Gakuen, Musashimurayama-shi
Tokyo 208-0011, Japan

Abstract

Two batches each of diphtheria-tetanus-acellular pertussis vaccine (DTaP) and that combined with inactivated polio vaccine purchased from foreign markets were tested by mouse body weight decreasing (BWD) toxicity test and Limulus amoebocyte lysate (LAL) test. Three out of the four imported vaccine batches showed the levels of BWD toxicity even comparable to that of DT-whole cell pertussis vaccine. BWD toxicity test is based on endotoxin dose-dependent weight loss of mice and has been used for controlling endotoxin in DTaP. Although of the strong BWD toxicity of the imported vaccines, there was no marked difference in LAL test results between the imported vaccines and Japanese DTaP. However, one imported DTaP batch showed very strong interference with LAL activity of spiked lipopolysaccharide (LPS). The batch interfered not only with LAL activity but also with pyrogenicity and prostaglandin E2 induction activity. However, the pyrogenicity of the spiked LPS could be recovered from the precipitated fraction of the batch by treating with phosphate buffer to suggest the possibility of recovering in vivo toxicity. As an adequate in vitro test method could not be identified for controlling the safety of the interfering batch, an appropriate in vivo test would be required for testing such vaccines.

“However, the pyrogenicity of the spiked LPS could be recovered from the precipitated fraction of the batch by treating with phosphate buffer to suggest the possibility of recovering in vivo toxicity. As an adequate in vitro test method could not be identified for controlling the safety of the interfering batch, an appropriate in vivo test would be required for testing such vaccines.”

Vaccine discontinuation and switching following regulatory interventions in response to rotavirus vaccine contamination with porcine circovirus DNA fragments

Author information

Dore DD1, Turnbull BR, Seeger JD.

Departments of Health Services
Policy and Practice and Epidemiology
Program in Public Health
The Warren Alpert Medical School of Brown University
Providence, RI, USA
david_dore@brown.edu

Abstract

PURPOSE

The Food and Drug Administration temporarily suspended monovalent rotavirus vaccine (RV1) use following discovery of contamination with porcine circovirus fragments and subsequently announced similar contamination of the pentavalent rotavirus vaccine (RV5) but recommended continued use of the product. We assessed the utilization of these vaccines in relation to the announcements.

METHODS

Using claims submitted to a commercial health insurer for administration of RV1 and RV5, we estimated the number of administrations of the vaccines and the extent of switching between RV1 and RV5. Procedure codes on submitted claims identified vaccine administrations among infants ≤ 1 year old through 16 June 2010. Among infants who received a first dose of vaccine before the corresponding announcement, and whose second dose was anticipated following the announcement, we estimated the number who received no second dose of rotavirus vaccine.

RESULTS

There were 31 178 RV1 initiators and 514 357 RV5 initiators. We observed a 93% reduction in RV1 doses in the month following the recommended suspension of use, coupled with extensive switching to RV5 (90% of subsequent doses) and a reduction in second RV1 doses (from 35.5% incomplete to 40.9%). There was a 15% increase in number of RV5 administrations following announcement of its contamination, with little switching to RV1 but with a possible decrease in completion.

CONCLUSIONS

Recommended suspension of RV1 use led to a substantial decrease in use and extensive switching to RV5. The announcement that RV5 was similarly contaminated, but without a corresponding recommendation to suspend use, had little effect on use.

“The Food and Drug Administration temporarily suspended monovalent rotavirus vaccine (RV1) use following discovery of contamination with porcine circovirus fragments and subsequently announced similar contamination of the pentavalent rotavirus vaccine (RV5) but recommended continued use of the product.”

Investigation of porcine circovirus contamination in human vaccines

Author Information

Sarah M. Gillilanda, Lindsay Forresta,
Heather Carrea, Adrian Jenkinsb, Neil Berryb,
Javier Martina, Philip Minora, Silke Schepelmann,

Abstract

DNA from porcine circovirus type 1 (PCV1) and 2 (PCV2) has recently been detected in two vaccines against rotaviral gastroenteritis from manufacturers A and B. We investigated if PCV1 sequences are present in other viral vaccines. We screened seeds, bulks and final vaccine preparations from ten manufacturers using qRT-PCR. We detected 3.8×10^3 to 1.9×10^7 PCV1 DNA copies/milliliter in live poliovirus seeds for inactivated polio vaccine (IPV) from manufacturer A, however, following inactivation and purification, the finished IPV was PCV1-negative. PCV1 DNA was not detectable in live polio preparations from other vaccine producers. There was no detectable PCV1 DNA in the measles, mumps, rubella and influenza vaccines analysed including material supplied by manufacturer A. We confirmed that the PCV1 genome in the rotavirus vaccine from manufacturer A is near full-length. It contains two mutations in the PCV cap gene, which may result from viral adaptation to Vero cells. Bulks of this vaccine contained 9.8×10^{10} to 1.8×10^{11} PCV1 DNA copies/millilitre and between 4.1×10^7 and 5.5×10^8 DNA copies were in the final doses. We found traces of PCV1 and PCV2 DNA in the rotavirus vaccine from manufacturer B. This highlights the issue of vaccine contamination and may impact on vaccine quality control.

<http://www.sciencedirect.com/science/article/pii/S1045105612000267>

“We found traces of PCV1 and PCV2 DNA in the rotavirus vaccine from manufacturer B. This highlights the issue of vaccine contamination and may impact on vaccine quality control.”

Analysis of the cell tissue culture contamination with the bovine viral diarrhea virus and mycoplasmas

Author Information

Uryvaevaev LV, Ionova KS, Dedova AV,
Dedova LV, Selivanova TK, Parasiuk NA, Mezentseva MV, Kostina LV,
Gushchina EA, Podcherniaeva RIa, Grebennikova TV.

Abstract

Different cell tissue cultures and commercial fetal calf sera (FCS) used in biological and virological research were screened for the bovine viral diarrhea virus (BVDV, Pestivirus genus, Flaviviridae family) and mycoplasma contamination. BVDV was detected using RT-PCR and Indirect immunofluorescence (with monoclonal antibodies) methods in 33% cases of the studied cell lines and in > 60% cases of FCS. BVDV was shown to present and reproduce in high spectra of human cell lines, as well as in monkey, pig, rabbit, goat, dog, and cat cells at high levels (up to 100-1000 genome-equivalent copies per cell) and reached up to 10⁽³⁾-10⁽⁷⁾ genome-equivalent copies per serum ml. The molecular mechanisms of the long virus persistence without definite signs of destruction should be studied.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23248854>

“Bovine Viral Diarrhea Virus
was detected using RT-PCR and
Indirect immunofluorescence
(with monoclonal antibodies) methods
in 33% cases of the studied cell lines
and in > 60% cases of Fetal Calf Serum.”

A Wolf in Sheep's Clothing: SV40 Co-opts Host Genome Maintenance Proteins to Replicate Viral DNA

Gregory A. Sowd and Ellen Fanning*
Richard C. Condit, Editor

Department of Biological Sciences, Vanderbilt University
Nashville, Tennessee, USA
University of Florida, USA

Abstract

Simian virus 40 (SV40) was discovered in 1960 as a contaminant in early polio vaccines. Its discovery coincided with an explosion of knowledge in the new field of molecular biology, and SV40 was quickly adopted as a model to study eukaryotic genome structure, expression, replication, and cell growth regulation in cultured cells [1]. With a genome of only 5.2 kbp, SV40 relies heavily on host cell machinery to propagate, affording investigators a powerful tool to discover key host proteins that the virus manipulates. Indeed, a single multifunctional viral protein, the large tumor (T) antigen (Tag) (Figure 1A), is sufficient to orchestrate the replication of the viral mini-chromosome in infected monkey cells [2], [3]. The origin DNA binding domain of Tag binds specifically to the viral origin of DNA replication, and the C-terminal helicase domain of Tag unwinds parental DNA at SV40 replication forks. The development of a cell-free reaction containing purified Tag and primate cell extract enabled the identification of ten evolutionarily conserved host proteins that are necessary and sufficient, together with Tag, to replicate SV40 DNA in vitro [3], [4]. Thus, much remains to be learned about how SV40 infection activates DNA damage signaling and uses it to facilitate viral propagation.

Full Report: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3493471/>

“Simian virus 40 (SV40)

was discovered in 1960 as a contaminant
in early polio vaccines ... much remains to be learned
about how SV40 infection activates DNA damage
signaling and uses it to facilitate viral propagation.”

Detection of human papillomavirus (HPV) L1 gene DNA possibly bound to particulate aluminum adjuvant in the HPV vaccine Gardasil

Author information

Lee SH.

Milford Hospital and Milford Molecular Laboratory
2044 Bridgeport Avenue, Milford, CT 06460, USA
shlee01@snet.net

Abstract

Medical practitioners in nine countries submitted samples of Gardasil (Merck & Co.) to be tested for the presence of human papillomavirus (HPV) DNA because they suspected that residual recombinant HPV DNA left in the vaccine might have been a contributing factor leading to some of the unexplained post-vaccination side effects. A total of 16 packages of Gardasil were received from Australia, Bulgaria, France, India, New Zealand, Poland, Russia, Spain and the United States. A nested polymerase chain reaction (PCR) method using the MY09/MY11 degenerate primers for initial amplification and the GP5/GP6-based nested PCR primers for the second amplification were used to prepare the template for direct automated cycle DNA sequencing of a hypervariable segment of the HPV L1 gene which is used for manufacturing of the HPV L1 capsid protein by a DNA recombinant technology in vaccine production. Detection of HPV DNA and HPV genotyping of all positive samples were finally validated by BLAST (Basic Local Alignment Search Tool) analysis of a 45-60 bases sequence of the computer-generated electropherogram. The results showed that all 16 Gardasil samples, each with a different lot number, contained fragments of HPV-11 DNA, or HPV-18 DNA, or a DNA fragment mixture from both genotypes. The detected HPV DNA was found to be firmly bound to the insoluble, proteinase-resistant fraction, presumably of amorphous aluminum hydroxyphosphate sulfate (AAHS) nanoparticles used as adjuvant. The clinical significance of these residual HPV DNA fragments bound to a particulate mineral-based adjuvant is uncertain after intramuscular injection, and requires further investigation for vaccination safety.

<http://www.ncbi.nlm.nih.gov/pubmed/23078778>

“Medical practitioners in nine countries submitted samples of Gardasil (Merck & Co.) to be tested for the presence of human papillomavirus (HPV) DNA because they suspected that residual recombinant HPV DNA left in the vaccine might have been a contributing factor leading to some of the unexplained post-vaccination side effects. A total of 16 packages of Gardasil were received from Australia, Bulgaria, France, India, New Zealand, Poland, Russia, Spain and the United States.

The results showed that all 16 Gardasil samples, each with a different lot number, contained fragments of HPV-11 DNA, or HPV-18 DNA, or a DNA fragment mixture from both genotypes. The detected HPV DNA was found to be firmly bound to the insoluble, proteinase-resistant fraction, presumably of amorphous aluminum hydroxyphosphate sulfate (AAHS) nanoparticles used as adjuvant. The clinical significance of these residual HPV DNA fragments bound to a particulate mineral-based adjuvant is uncertain after intramuscular injection ...”

“This enables quick, safe, and cost-effective vaccine production that would be required in case of a pandemic.”

Journal of Laboratory Automation • December 2012

Automated production of plant-based vaccines and pharmaceuticals

Author information

Wirz H1, Sauer-Budge AF, Briggs J, Sharpe A, Shu S, Sharon A.

Fraunhofer CMI, Brookline, MA 02446, USA

Abstract

A fully automated “factory” was developed that uses tobacco plants to produce large quantities of vaccines and other therapeutic biologics within weeks. This first-of-a-kind factory takes advantage of a plant viral vector technology to produce specific proteins within the leaves of rapidly growing plant biomass. The factory’s custom-designed robotic machines plant seeds, nurture the growing plants, introduce a viral vector that directs the plant to produce a target protein, and harvest the biomass once the target protein has accumulated in the plants—all in compliance with Food and Drug Administration (FDA) guidelines (e.g., current Good Manufacturing Practices). The factory was designed to be time, cost, and space efficient. The plants are grown in custom multiplant trays. Robots ride up and down a track, servicing the plants and delivering the trays from the lighted, irrigated growth modules to each processing station as needed. Using preprogrammed robots and processing equipment eliminates the need for human contact, preventing potential contamination of the process and economizing the operation. To quickly produce large quantities of protein-based medicines, we transformed a laboratory-based biological process and scaled it into an industrial process. This enables quick, safe, and cost-effective vaccine production that would be required in case of a pandemic.

<http://www.ncbi.nlm.nih.gov/pubmed/23015521>

Genetic characterization of bovine viral diarrhoea (BVD) viruses: confirmation of the presence of BVD genotype 2 in Africa

Author information

Ularamu HG1, Sibeko KP, Bosman AB, Venter EH, van Vuuren M.

Department of Veterinary Tropical Diseases
Faculty of Veterinary Science, University of Pretoria
Onderstepoort 0110, South Africa
ularamuhussaini@yahoo.co.uk

Abstract

Bovine viral diarrhoea virus (BVDV) has emerged as one of the economically important pathogens in cattle populations, with a worldwide distribution and causing a complex of disease syndromes. Two genotypes, BVDV 1 and 2, exist and are discriminated on the basis of the sequence of the 5' non-coding region (5' NCR) using real-time PCR. Real-time PCR is more sensitive, specific, and less time-consuming than conventional PCR, and it has less risk of cross-contamination of samples. Limited information exists on BVDV genetic subtypes in South Africa. The aim of this study was to determine the genotypes of BVDV currently circulating in South African feedlots. A total of 279 specimens (219 tissue samples, 59 trans-tracheal aspirates and 1 blood sample) were collected from dead and living cattle with lesions or clinical signs compatible with BVDV infection. Pooled homogenates from the same animals were prepared, and total RNA was extracted. A screening test was performed on the pooled samples, and positive pools were investigated individually. A Cador BVDV Type 1/2 RT-PCR Kit (QIAGEN, Hilden, Germany) was used for the real-time PCR assay on a LightCycler(®) V2.0 real-time PCR machine (Roche Diagnostics, Mannheim, Germany). The results were read at 530 and 640 nm for BVDV 1 and 2, respectively. Bovine viral diarrhoea virus was detected in a total of 103 samples that included 91 tissue samples, 1 blood sample and 11 trans-tracheal aspirates. Eighty-five (82.5 %) of the strains were genotype 1 and 18 (17.5 %) were genotype 2. Comparing the sequencing data, genotypes 1 and 2 from the field strains did not cluster with vaccine strains currently used in feedlots in South Africa. The present study revealed the presence of BVDV genotype 2 in cattle in South Africa based on the high sequence similarity between genotype 2 field strains and strain 890 from North America. The presence of genotype 2 viruses that phylogenetically belong to different clusters and coexist in feedlots is consistent with the possibility of multiple virus introductions. These results represent the first documented evidence for the presence of BVDV genotype 2 in African cattle.

“These results represent the first documented evidence for the presence of BVDV genotype 2 in African cattle.”

HoBi-like viruses: an emerging group of pestiviruses

Author information

Bauermann FV1, Ridpath JF, Weiblen R, Flores EF.

Department of Preventive Veterinary Medicine, Virus Section
Federal University of Santa Maria, Santa Maria, Rio Grande do Sul, Brazil

Abstract

The genus Pestivirus is composed of 4 important pathogens of livestock: Bovine viral diarrhea virus 1 and 2 (BVDV-1 and BVDV-2), Classical swine fever virus (CSFV), and Border disease virus of sheep (BDV). BVDV are major pathogens of cattle, and infection results in significant economic loss worldwide. A new putative pestivirus species, tentatively called “HoBi-like,” “BVDV-3,” or “atypical pestiviruses,” was first identified in Europe in fetal bovine serum (FBS) imported from Brazil. HoBi-like viruses are related to BVDV at the genetic and antigenic levels. Further, the disease caused by these new viruses resembles clinical presentations historically associated with BVDV infection, including growth retardation, reduced milk production, respiratory disease, reduced reproductive performance, and increased mortality among young stock. Current BVDV diagnostic tests may fail to detect HoBi-like viruses or to differentiate between BVDV and HoBi-like viruses. Further, commercial tests for BVDV exposure, based on serological response, do not reliably detect HoBi-like virus exposure, and cross protection against HoBi-like viruses conferred by current BVDV vaccines is likely limited. As many HoBi-like viruses, characterized to date, were isolated from FBS originating from Brazil, it is assumed that the agent is probably widespread in Brazilian herds. Nevertheless, reports of natural infection in Southeast Asia and Europe demonstrate that these viruses are not restricted to South America. Increased demand for FBS has led to widespread distribution of FBS originating in HoBi-like virus endemic regions. The contamination of such FBS with HoBi-like viruses may lead to spread of this virus to other regions.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23345268>

Full Report

<http://vdi.sagepub.com/content/25/1/6.long>

“Increased demand for fetal bovine serum has led to widespread distribution of fetal bovine serum originating in HoBi-like virus endemic regions. The contamination of such fetal bovine serum with HoBi-like viruses may lead to spread of this virus to other regions.”

[fetal bovine serum is an important element of cell research and cell culture applications, especially in vaccine research. Estimated sales of fetal bovine serum in 2008 reached 700,000 liters globally]

Nanoparticles for Brain Drug Delivery

Massimo Masserini

Department of Health Sciences
University of Milano-Bicocca
Via Cadore 48, 20900 Monza, Italy

Abstract

The central nervous system, one of the most delicate microenvironments of the body, is protected by the blood-brain barrier (BBB) regulating its homeostasis. BBB is a highly complex structure that tightly regulates the movement of ions of a limited number of small molecules and of an even more restricted number of macromolecules from the blood to the brain, protecting it from injuries and diseases. However, the BBB also significantly precludes the delivery of drugs to the brain, thus, preventing the therapy of a number of neurological disorders. As a consequence, several strategies are currently being sought after to enhance the delivery of drugs across the BBB. Within this review, the recently born strategy of brain drug delivery based on the use of nanoparticles, multifunctional drug delivery systems with size in the order of one-billionth of meters, is described. The review also includes a brief description of the structural and physiological features of the barrier and of the most utilized nanoparticles for medical use. Finally, the potential neurotoxicity of nanoparticles is discussed, and future technological approaches are described. The strong efforts to allow the translation from preclinical to concrete clinical applications are worth the economic investments.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4392984/>

“several strategies
are currently being sought after to enhance the
delivery of drugs across the Blood Brain Barrier ...
based on the use of nanoparticles ... the potential
neurotoxicity of nanoparticles is discussed”

Transposon leads to contamination of clinical pDNA vaccine

Author information

van der Heijden I1, Gomez-Eerland R,
van den Berg JH, Oosterhuis K, Schumacher TN,
Haanen JB, Beijnen JH, Nuijen B.

Department of Pharmacy & Pharmacology
Slotervaart Hospital/The Netherlands Cancer Institute
Amsterdam, The Netherlands
Iris.vanderHeijden@slz.nl

Abstract

We report an unexpected contamination during clinical manufacture of a Human Papillomavirus (HPV) 16 E6 encoding plasmid DNA (pDNA) vaccine, with a transposon originating from the *Escherichia coli* DH5 host cell genome. During processing, presence of this transposable element, insertion sequence 2 (IS2) in the plasmid vector was not noticed until quality control of the bulk pDNA vaccine when results of restriction digestion, sequencing, and CGE analysis were clearly indicative for the presence of a contaminant. Due to the very low level of contamination, only an insert-specific PCR method was capable of tracing back the presence of the transposon in the source pDNA and master cell bank (MCB). Based on the presence of an uncontrolled contamination with unknown clinical relevance, the product was rejected for clinical use. In order to prevent costly rejection of clinical material, both in-process controls and quality control methods must be sensitive enough to detect such a contamination as early as possible, i.e. preferably during plasmid DNA source generation, MCB production and ultimately during upstream processing. However, as we have shown that contamination early in the process development pipeline (source pDNA, MCB) can be present below limits of detection of generally applied analytical methods, the introduction of “engineered” or transposon-free host cells seems the only 100% effective solution to avoid contamination with movable elements and should be considered when searching for a suitable host cell-vector combination.

<http://www.ncbi.nlm.nih.gov/pubmed/23707695>

“We report an unexpected contamination during clinical manufacture of a Human Papillomavirus (HPV) 16 E6 encoding plasmid DNA (pDNA) vaccine, with a transposon originating from the *Escherichia coli* DH5 host cell genome. During processing, presence of this transposable element, insertion sequence 2 (IS2) in the plasmid vector was not noticed until quality control of the bulk pDNA vaccine when results of restriction digestion, sequencing, and CGE analysis were clearly indicative for the presence of a contaminant. Due to the very low level of contamination, only an insert-specific PCR method was capable of tracing back the presence of the transposon in the source pDNA and master cell bank (MCB).”

Investigation of a regulatory agency enquiry into potential porcine circovirus type 1 contamination of the human rotavirus vaccine, Rotarix: approach and outcome

Author information

Dubin G1, Toussaint JF, Cassart JP, Howe B,
Boyce D, Friedland L, Abu-Elyazeed R, Poncelet S, Han HH, Debrus S.

GlaxoSmithKline Vaccines; King of Prussia, PA USA

Abstract

In January 2010, porcine circovirus type 1 (PCV1) DNA was unexpectedly detected in the oral live-attenuated human rotavirus vaccine, Rotarix (GlaxoSmithKline [GSK] Vaccines) by an academic research team investigating a novel, highly sensitive analysis not routinely used for adventitious agent screening. GSK rapidly initiated an investigation to confirm the source, nature and amount of PCV1 in the vaccine manufacturing process and to assess potential clinical implications of this finding. The investigation also considered the manufacturer's inactivated poliovirus (IPV)-containing vaccines, since poliovirus vaccine strains are propagated using the same cell line as the rotavirus vaccine strain. Results confirmed the presence of PCV1 DNA and low levels of PCV1 viral particles at all stages of the Rotarix manufacturing process. PCV type 2 DNA was not detected at any stage. When tested in human cell lines, productive PCV1 infection was not observed. There was no immunological or clinical evidence of PCV1 infection in infants who had received Rotarix in clinical trials. PCV1 DNA was not detected in the IPV-containing vaccine manufacturing process beyond the purification stage. Retrospective testing confirmed the presence of PCV1 DNA in Rotarix since the initial stages of its development and in vaccine lots used in clinical studies conducted pre- and post-licensure. The acceptable safety profile observed in clinical trials of Rotarix therefore reflects exposure to PCV1 DNA. The investigation into the presence of PCV1 in Rotarix could serve as a model for risk assessment in the event of new technologies identifying adventitious agents in the manufacturing of other vaccines and biological products.

“In January 2010,
porcine circovirus type 1 (PCV1) DNA was
unexpectedly detected in the oral live-attenuated
human rotavirus vaccine, Rotarix (GlaxoSmith-
Kline [GSK] Vaccines) by an academic research
team investigating a novel, highly sensitive
analysis not routinely used for adventitious
agent screening.”

Detection of contaminants in cell cultures, sera and trypsin

Author information

Pinheiro de Oliveira TF1, Fonseca AA Jr, Camargos MF,
de Oliveira AM, Pinto Cottorello AC, Souza Ados R, de Almeida IG, Heinemann MB.

Laboratório de Biologia Molecular/Laboratório de Diagnóstico de Doenças Virais
Laboratório Nacional Agropecuário de Minas Gerais
Pedro Leopoldo, Minas Gerais, Brazil
oliveiratfp@yahoo.com.br

Abstract

The aim of this study was standardization and application of polymerase chain reaction (PCR) for the detection of contaminants in cell cultures, sera and trypsin. Five PCR protocols were standardized to assess the presence of genetic material from mycoplasma, porcine circovirus 1 (PCV1), bovine leukemia virus (BLV) or bovine viral diarrhea virus (BVDV) in cell culture samples. PCR reactions for the genes GAPDH and beta-actin were used to evaluate the efficiency of nucleic acid extraction. The PCR protocols were applied to 88 cell culture samples from eight laboratories. The tests were also used to assess potential contamination in 10 trypsin samples and 13 fetal calf serum samples from different lots from five of the laboratories. The results showed the occurrence of the following as DNA cell culture contaminants: 34.1% for mycoplasma, 35.2% for PCV1, 23.9% for BVDV RNA and 2.3% for BLV. In fetal calf sera and trypsin samples BVDV RNA and PCV1 DNA was detected. The results demonstrated that cell culture, sera and trypsin used by different laboratories show a high rate of contaminants. The results highlight the need for monitoring cell cultures and controlling for biological contaminants in laboratories and cell banks working with these materials.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24071554>

“The results showed the occurrence of the following as DNA cell culture contaminants: 34.1% for mycoplasma, 35.2% for porcine circovirus 1, 23.9% for bovine viral diarrhea virus RNA and 2.3% for bovine leukemia virus. The results demonstrated that cell culture, sera and trypsin used by different laboratories show a high rate of contaminants.”

Mechanism of a decrease in potency for the recombinant influenza A virus hemagglutinin H3 antigen during storage

Author information

Hickey JM1, Holtz KM, Manikwar P, Joshi SB, McPherson CE, Buckland B,
Srivastava IK, Middaugh CR, Volkin DB.

Department of Pharmaceutical Chemistry
Macromolecule and Vaccine Stabilization Center
University of Kansas, Lawrence, Kansas, 66047

Abstract

The recombinant hemagglutinin (rHA)-based influenza vaccine Flublok® has recently been approved in the United States as an alternative to the traditional egg-derived flu vaccines. Flublok is a purified vaccine with a hemagglutinin content that is threefold higher than standard inactivated influenza vaccines. When rHA derived from an H3N2 influenza virus was expressed, purified, and stored for 1 month, a rapid loss of in vitro potency ($\approx 50\%$) was observed as measured by the single radial immunodiffusion (SRID) assay. A comprehensive characterization of the rHA protein antigen was pursued to identify the potential causes and mechanisms of this potency loss. In addition, the biophysical and chemical stability of the rHA in different formulations and storage conditions was evaluated over time. Results demonstrate that the potency loss over time did not correlate with trends in changes to the higher order structure or hydrodynamic size of the rHA. The most likely mechanism for the early loss of potency was disulfide-mediated cross-linking of rHA, as the formation of non-native disulfide-linked multimers over time correlated well with the observed potency loss. Furthermore, a loss of free thiol content, particularly in specific cysteine residues in the antigen's C-terminus, was correlated with potency loss measured by SRID.

<http://www.ncbi.nlm.nih.gov/pubmed/24425059>

“When rHA derived from an H3N2 influenza virus was expressed, purified, and stored for 1 month, a rapid loss of in vitro potency ($<50\%$) was observed as measured by the single radial immunodiffusion (SRID) assay.”

Melting profiles may affect detection of residual HPV L1 gene DNA fragments in Gardasil

Author information

Lee SH.

Milford Hospital and Milford Molecular Laboratory
2044 Bridgeport Avenue, Milford, CT 06460, USA
shlee01@snet.net

Abstract

Gardasil® is a quadrivalent human papillomavirus (HPV) protein-based vaccine containing genotype-specific L1 capsid proteins of HPV-16, HPV-18, HPV-6 and HPV-11 in the form of virus-like-particles (VLPs) as the active ingredient. The VLPs are produced by a DNA recombinant technology. It is uncertain if the residual HPV L1 gene DNA fragments in the vaccine products are considered contaminants or excipients of the Gardasil® vaccine. Because naked viral DNA fragments, if present in the vaccine, may bind to the insoluble amorphous aluminum hydroxy-phosphate sulfate (AAHS) adjuvant which may help deliver the foreign DNA into macrophages, causing unintended pathophysiologic effects, experiments were undertaken to develop tests for HPV L1 gene DNA fragments in the final products of Gardasil® by polymerase chain reaction (PCR) and direct DNA sequencing. The results showed that while the HPV-11 and HPV-18 L1 gene DNA fragments in Gardasil® were readily amplified by the common GP6/MY11 degenerate consensus primers, the HPV-16 L1 gene DNA may need specially designed non-degenerate PCR primers for amplification at different regions of the L1 gene and different stringency conditions for detection. These variable melting profiles of HPV DNA in the insoluble fraction of the Gardasil® vaccine suggest that the HPV DNA fragments are firmly bound to the aluminum AAHS adjuvant. All methods developed for detecting residual HPV DNA in the vaccine Gardasil® for quality assurance must take into consideration the variable melting profiles of the DNA to avoid false negative results.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24083601>

“All methods developed for detecting residual HPV DNA in the vaccine Gardasil® for quality assurance must take into consideration the variable melting profiles of the DNA to avoid false negative results.”

The role of media and the Internet on vaccine adverse event reporting: a case study of human papillomavirus vaccination

Author information

Eberth JM1, Kline KN2, Moskowitz DA3, Montealegre JR4, Scheurer ME5.

1. South Carolina Cancer Prevention and Control Program, University of South Carolina
Columbia, South Carolina; Department of Epidemiology and Biostatistics, University of South Carolina
Columbia, South Carolina; Department of Communication, University of Texas at San Antonio, San Antonio TX
2. Department of Epidemiology and Biostatistics, University of South Carolina, Columbia, South Carolina
Department of Communication, University of Texas at San Antonio, San Antonio, Texas
3. Department of Epidemiology and Community Health, New York Medical College, NY, New York
4. Department of Epidemiology, Human Genetics and Environmental Sciences, University of Texas School of
Public Health, Houston, Texas; Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, Texas
5. Dan L. Duncan Cancer Center, Baylor College of Medicine, Houston, Texas, Department of Pediatrics
Baylor College of Medicine, Houston, Texas

Abstract

PURPOSE

This study aimed to determine the temporal association of print media coverage and Internet search activity with adverse events reports associated with the human papillomavirus vaccine Gardasil (HPV4) and the meningitis vaccine Menactra (MNQ) among United States adolescents.

METHODS

We used moderated linear regression to test the relationships between print media reports in top circulating newspapers, Internet search activity, and reports to the Vaccine Adverse Event Reporting System (VAERS) for HPV4 and MNQ during the first 2.5 years after Food and Drug Administration approval.

RESULTS

Compared with MNQ, HPV4 had more coverage in the print media and Internet search activity, which corresponded with the frequency of VAERS reports. In February 2007, we observed a spike in print media for HPV4. Although media coverage waned, Internet search activity remained stable and predicted the rise in HPV4-associated VAERS reports.

CONCLUSIONS

We demonstrate that media coverage and Internet search activity, in particular, may promote increased adverse event reporting. Public health officials who have long recognized the importance of proactive engagement with news media must now consider strategies for meaningful participation in Internet discussions.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3943880/>

“We demonstrate that media coverage and Internet search activity, in particular, may promote increased adverse event reporting. Public health officials who have long recognized the importance of proactive engagement with news media must now consider strategies for meaningful participation in Internet discussions.”

“Porcine circovirus-1 (PCV1) was recently identified as a contaminant in live Rotavirus vaccines ...”

Vaccine • April 2014

Reduction of spiked porcine circovirus during the manufacture of a Vero cell-derived vaccine

Author information

Lackner C, Leydold SM, Modrof J, Farcet MR, Grillberger L, Schäfer B, Anderle H, Kreil TR.

Global Pathogen Safety, Baxter BioScience, Vienna, Austria
Cell Culture Fermentation, Baxter BioScience, Orth/Donau, Austria
Vaccine R&D, Baxter BioScience, Orth/Donau, Austria
Biologicals R&D, Baxter BioScience, Vienna, Austria
Global Pathogen Safety, Baxter BioScience, Vienna, Austria

Abstract

Porcine circovirus-1 (PCV1) was recently identified as a contaminant in live Rotavirus vaccines, which was likely caused by contaminated porcine trypsin. The event triggered the development of new regulatory guidance on the use of porcine trypsin which shall ensure that cell lines and porcine trypsin in use are free from PCV1. In addition, manufacturing processes of biologicals other than live vaccines include virus clearance steps that may prevent and mitigate any potential virus contamination of product. In this work, artificial spiking of down-scaled models for the manufacturing process of an inactivated pandemic influenza virus vaccine were used to investigate inactivation of PCV1 and the physico-chemically related porcine parvovirus (PPV) by formalin and ultraviolet-C (UV-C) treatment as well as removal by the purification step sucrose gradient ultracentrifugation. A PCV1 infectivity assay, using a real-time PCR infectivity readout was established. The formalin treatment (0.05% for 48h) showed substantial inactivation for both PCV1 and PPV with reduction factors of $3.0\log_{10}$ and $6.8\log_{10}$, respectively, whereas UV-C treatment resulted in complete PPV ($\geq 5.9\log_{10}$) inactivation already at a dose of 13mJ/cm but merely $1.7\log_{10}$ at 24mJ/cm² for PCV1. The UV-C inactivation results with PPV were confirmed using minute virus of mice (MVM), indicating that parvoviruses are far more sensitive to UV-C than PCV1. The sucrose density gradient ultracentrifugation also contributed to PCV1 clearance with a reduction factor of $2\log_{10}$. The low pH treatment during the production of porcine trypsin was investigated and showed effective inactivation for both PCV1 ($4.5\log_{10}$) and PPV ($6.4\log_{10}$). In conclusion, PCV1 in general appears to be more resistant to virus inactivation than PPV. Still, the inactivated pandemic influenza vaccine manufacturing process provides for robust virus reduction, in addition to the already implemented testing for PCV1 to avoid any contaminations.

<http://www.ncbi.nlm.nih.gov/pubmed/24560672>

Systematic evaluation
of in vitro and in vivo adventitious virus assays
for the detection of viral contamination of
cell banks and biological products

Author Information

James Gombolda, Stephen Karakasidisa, Paula Niksab,
John Podczasya, Kitti Neumann, James Richardsonc, Nandini Sanec,
Renita Johnson-Levac, Valerie Randolphd, Jerald Sadoffe, Phillip Minorf,
Alexander Schmidtg, Paul Duncanh, Rebecca L. Sheetsi

- a. Charles River Laboratories, 358 Technology Drive, Malvern, PA 19355, United States
- b. Charles River Laboratories, 251 Ballardvale St. Wilmington, MA 01887, United States
- c. Advanced BioScience Laboratories, 9800 Medical Center Dr. Bldg. D, Rockville, MD 20850, United States
- d. Wyeth, 401N Middletown Rd., Pearl River, NY 10965, United States
- e. Crucell, Newtonweg 1, 2333 CP Leiden, PO Box 2048, 2301 CA Leiden, The Netherlands
- f. National Institute for Biologics Standards and Control, Blanche Lane, South Mimms, Potters Bar, UK
- g. GSK Vaccines, Rue de l'Insitut 89, 1330 Rixensart, Belgium (formerly NIH/NIAID)
- h. Merck and Co., Inc., WP17-101, 770 Sumneytown Pike, P.O. Box 4, West Point, PA 19486, United States
- i. NIH/NIAID Division of AIDS, 6700B Rockledge Dr., Rm. 5145, Bethesda, MD 20892, United States

Abstract

Viral vaccines and the cell substrates used to manufacture them are subjected to tests for adventitious agents, including viruses, contaminate. Some of the compendial methods (in vivo and in vitro in cell culture) were established in the mid-20th century. These methods have not been subjected to current assay validation, as new methods would need to be. This study was undertaken to provide insight into the breadth (selectivity) and sensitivity (limit of detection) of the routine methods, two such validation parameters. Sixteen viral stocks were prepared and characterized. These stocks were tested in serial dilutions by the routine methods to establish which viruses were detected by which methods and above what limit of detection. Sixteen out of sixteen viruses were detected in vitro, though one (bovine viral diarrhea virus) required special conditions to detect and another (rubella virus) was detected with low sensitivity. Many were detected at levels below 1 TCID₅₀ or PFU (titers were established on the production cell line in most cases). In contrast, in vivo, only 6/11 viruses were detected, and 4 of these were detected only at amounts one or more logs above 1 TCID₅₀ or PFU. Only influenza virus and vesicular stomatitis virus were detected at lower amounts in vivo than in vitro. Given the call to reduce, refine, or replace (3Rs) the use of animals in product safety testing and the emergence of new technologies for the detection of viruses, a re-examination of the current adventitious virus testing strategies seems warranted. Suggested pathways forward are offered.

“Given the call to reduce, refine, or replace (3Rs) the use of animals in product safety testing and the emergence of new technologies for the detection of viruses, a re-examination of the current adventitious virus testing strategies seems warranted. Suggested pathways forward are offered.”

“The biopharmaceutical industry continues to face enormous pressure to accelerate time to market, improve productivity and efficiency, and reduce costs.”

PDA Journal Of Pharmaceutical Science And Technology • July 2014

Advantages of single-use technology for vaccine fill-finish operations

Author information

Jenness E, Walker S.

Process Solutions, Mobius Product Manager
EMD Millipore Corporation, 80 Ashby Road, Bedford, MA
sue.walker@emdmillipore.com

Abstract

The biopharmaceutical industry continues to face enormous pressure to accelerate time to market, improve productivity and efficiency, and reduce costs. Vaccine manufacturers face additional challenges, including small batch sizes, varied product portfolios, pandemic outbreaks that require rapid responses and highly potent ingredients that place large demands on cleaning processes. Given these pressures, single-use fill-finish assemblies can represent an attractive option for vaccine manufacturing facilities. This article describes the implementation of a single-use fill-finish system at a large vaccine manufacturer. The new assembly enabled flexibility while reducing set-up time, capital investment, cross-contamination risk, and cleaning requirements.

LAY ABSTRACT

Overall the biopharmaceutical industry is constantly being challenged to bring new products more quickly and efficiently to market while keeping costs as low as possible. One specific segment of this industry is the companies that manufacture vaccines. Vaccines present unique challenges because they tend to be made in smaller amounts for a larger number of individual products. The products can also be very potent, which can require special handling methods. Another challenge is the potential outbreak of a disease that may affect a large area or a large part of the population and would require immediate action. Single-use assemblies for filling the product into its final container are an attractive option for vaccine manufacturing facilities. This article describes the implementation of a single-use filling system at a large vaccine manufacturer. The new assembly was flexible enough to meet the demands of the manufacturer while allowing quick and efficient implementation with low upfront investment.

<http://www.ncbi.nlm.nih.gov/pubmed/25035260>

Adventitious agents in viral vaccines: Lessons learned from 4 case studies

Author Information

John Petricciana, Rebecca Sheetsb, Elwyn Griffiths, Ivana Knezevicd

IABS, POB 1925, Palm Springs, CA 92263, USA
Grimalkin Partners, 13401 Norden Drive, Silver Spring, MD 20906, USA
The Farthings, Kingston Upon Thames, Surrey KT2 7PT, UK
Group Lead, Norms and Standards for Biologicals
Department of Essential Medicines and Health Products (EMP)
Health Systems and Innovation (HIS) Cluster
WHO L276, Avenue Appia 20, 1211 Geneva 27, Switzerland

Abstract

Since the earliest days of biological product manufacture, there have been a number of instances where laboratory studies provided evidence for the presence of adventitious agents in a marketed product. Lessons learned from such events can be used to strengthen regulatory preparedness for the future. We have therefore selected four instances where an adventitious agent, or a signal suggesting the presence of an agent, was found in a viral vaccine, and have developed a case study for each. The four cases are: a) SV40 in polio vaccines; b) bacteriophage in measles and polio vaccines; c) reverse transcriptase in measles and mumps vaccines; and d) porcine circovirus and porcine circovirus DNA sequences in rotavirus vaccines. The lessons learned from each event are discussed. Based in part on those experiences, certain scientific principles have been identified by WHO that should be considered in regulatory risk evaluation if an adventitious agent is found in a marketed vaccine in the future.

<http://www.sciencedirect.com/science/article/pii/S1045105614000748>

“We have therefore selected four instances where an adventitious agent, or a signal suggesting the presence of an agent, was found in a viral vaccine, and have developed a case study for each.

The four cases are: a) SV40 in polio vaccines; b) bacteriophage in measles and polio vaccines; c) reverse transcriptase in measles and mumps vaccines; and d) porcine circovirus and porcine circovirus DNA sequences in rotavirus vaccines.”

Viral safety of biological medicinal products

Author information

Stühler A1, Blümel J.

Paul-Ehrlich-Institut
Paul-Ehrlich-Straße 51-59
63225, Langen, Deutschland

Abstract

Viral safety of blood donations, plasma products, viral vaccines and gene therapy medicinal products, biotechnical-derived products and tissue and cell therapy products is a particular challenge. These products are manufactured using a variety of human or animal-derived starting materials and reagents; therefore, extensive testing of donors and of cell banks established for production is required. Furthermore, the viral safety of reagents, such as bovine sera, porcine trypsin and human transferrin or albumin needs to be considered. Whenever possible, manufacturing steps for inactivation or removal of viruses should be introduced; however, sometimes it is not possible to introduce such steps for tissues or cell-based medicinal products as the activity and viability of cells will be compromised. It might be possible to implement steps for inactivation or removal of potential contaminating enveloped viruses only for production of small and stable non-enveloped viral gene vectors.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25123140>

“Viral safety of blood donations,
plasma products, viral vaccines
and gene therapy medicinal products,
biotechnical-derived products and tissue
and cell therapy products is a
particular challenge.”

Historical Data Analyses and Scientific Knowledge Suggest Complete Removal of the Abnormal Toxicity Test as a Quality Control Test

Joerg H O Garbe,¹ Susanne Ausborn,¹ Claire Beggs,²
Martin Bopst,³ Angelika Joos,⁴ Alexandra A Kitashova,⁵
OLga Kovbasenco,⁶ Claus-Dieter Schiller,¹ Martina Schwinger,⁷
Natalia Semenova,⁸ Lilia Smirnova,⁹ Fraser Stodart,¹⁰
Thomas Visalli,¹¹ and Lisette Vromans⁴

1. F. Hoffmann-La Roche Ltd., Pharma Global Technical Operations, Basel, Switzerland
2. AbbVie Ltd., Maidenhead, England
3. F. Hoffmann-La Roche Ltd., Roche Pharma and Early Development, Roche Innovation Center, Basel, Switzerland
4. MSD Europe Inc., Brussels, Belgium
5. GlaxoSmithKline, Moscow, Russian Federation
6. Genzyme, Moscow, Russian Federation
7. Novartis Pharma AG, Basel, Switzerland
8. Bristol-Myers Squibb, Moscow, Russian Federation
9. MSD Pharmaceuticals, Moscow, Russian Federation
10. Eisai Ltd, Hatfield, England
11. Eisai Inc, Woodcliff Lake, New Jersey

Abstract

In the early 1900s, the abnormal toxicity test (ATT) was developed as an auxiliary means to ensure safe and consistent antiserum production. Today, the ATT is utilized as a quality control (QC) release test according to pharmacopoeial or other regulatory requirements. The study design has not been changed since around 1940. The evidence of abnormal toxicity testing as a prediction for harmful batches is highly questionable and lacks a scientific rationale. Numerous reviews of historical ATT results have revealed that no reliable conclusions can be drawn from this QC measure. Modern pharmaceutical manufacturers have thorough control of the manufacturing process and comply with good manufacturing practice rules. Contaminants are appropriately controlled by complying with the validated manufacturing processes and strict QC batch release confirming batch-to-batch consistency. Recognizing that product safety, efficacy, and stability can be ensured with strict QC measures, nowadays most regulatory authorities do not require the ATT for most product classes. In line with the replacement, reduction, and refinement (3Rs) initiative, the test requirement has been deleted from approximately 80 monographs of the European Pharmacopoeia and for the majority of product classes in the United States. For these reasons, it is recommended that the ATT should be consistently omitted world-wide and be removed from pharmacopoeias and other regulatory requirements.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278562/>

[Here, several divisions of F. Hoffman-La Roche Ltd.,
AbbVie Ltd., divisions of MSD Europe inc.,
GlaxoSmithKline, Genzyme, Novartis Pharma AG,
Bristol-Myers-Squibb and divisions of Eisai Ltd.,
write a report justifying the removal of the
“Abnormal Toxicity Test” as a quality control
element of vaccine production]

**Annual World Vaccine Congress 2014:
a re-evaluation of the value proposition
for increasing vaccine thermostability**

Author information

Derwand R.

Leukocare AG; Martinsried
Munich, Germany

Abstract

The 14th Annual World Vaccine Congress was held in Washington DC, March 24-26, 2014 (<http://www.terrapinn.com/vaccine2014>). More than 400 experts from different regions participated in this scientific event for vaccine professionals from industry, academia, non-profit organizations and government to discuss challenges and successes from all the major vaccine stakeholders. In more than 70 presentations, round tables, and plenary discussions major topics like emerging and re-emerging infectious disease, vaccine production, and innovative technologies were debated. While most contributions focused on specific questions in vaccine research development, some like the one by a representative of the Bill and Melinda Gates Foundation (BMGF) reported about supply chain, logistics topics, and challenges in vaccine implementation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483655>

“While most contributions focused on specific questions in vaccine research development, some like the one by a representative of the Bill and Melinda Gates Foundation (BMGF) reported about supply chain, logistics topics, and challenges in vaccine implementation.”

Adjuvants and myeloid-derived suppressor cells: enemies or allies in therapeutic cancer vaccination

Author information

Fernández A1, Oliver L, Alvarez R, Fernández LE, Lee KP, Mesa C.

Immunobiology Division
Center of Molecular Immunology; Havana, Cuba

Abstract

Adjuvants are a critical but largely overlooked and poorly understood component included in vaccine formulations to stimulate and modulate the desired immune responses to an antigen. However, unlike in the protective infectious disease vaccines, adjuvants for cancer vaccines also need to overcome the effect of tumor-induced suppressive immune populations circulating in tumor-bearing individuals. Myeloid-derived suppressor cells (MDSC) are considered to be one of the key immunosuppressive populations that inhibit tumor-specific T cell responses in cancer patients. This review focuses on the different signals for the activation of the immune system induced by adjuvants, and the close relationship to the mechanisms of recruitment and activation of MDSC. This work explores the possibility that a cancer vaccine adjuvant may either strengthen or weaken the effect of tumor-induced MDSC, and the crucial need to address this in present and future cancer vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483674>

“This work explores the possibility
that a cancer vaccine adjuvant may
either strengthen or weaken the effect
of tumor-induced Myeloid-derived suppressor cells ...”

“This may affect the integrity of the adjuvant, alter its interaction with the drug substance or change the physical characteristics of the drug product.”

Journal Of Pharmaceutical Sciences • February 2015

Shear effects on aluminum phosphate adjuvant particle properties in vaccine drug products

Author information

Kolade OO1, Jin W, Tengroth C, Green KD, Bracewell DG.

The Advanced Centre for Biochemical Engineering
Department of Biochemical Engineering
University College London, Gordon Street, London
WC1H 0AH, UK

Abstract

Adjuvant-containing drug products can be exposed to high levels of interfacial shear during manufacture. This may affect the integrity of the adjuvant, alter its interaction with the drug substance or change the physical characteristics of the drug product. In this study, a solid-liquid interfacial shear device was used to investigate the shear response of aluminum phosphate adjuvant alone and two adjuvant containing vaccine drug products (DP1 and DP2). The relationship between the shear sensitivity of each and its resuspension properties was determined. Changes in the particle dimensions of the bulk adjuvant were minimal at shear strain rates of 10,900 s⁻¹. However, at 25,500 s⁻¹, the median particle diameter was reduced from 6.2 to 3.5 μm and was marked by the presence of sub-micron fines. A formulation without drug substance and DP2 produced similar shear responses but with less impact on particle diameter. The behavior of DP1 was less predictable. Sheared DP1 was characterized by prolonged sedimentation because of the presence of fine particulates and required in excess of 300 rotations to resuspend after extended storage. The study confirms that the solid-liquid interfacial shear device may be applied to understand product shear sensitivity associated with vaccine manufacturing.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25175154>

“The ability to accurately measure and report trace amounts of residual formaldehyde impurity in a vaccine product is not only critical in the product release but also a regulatory requirement.”

Journal Of Pharmaceutical And Biomedical Analysis • March 2015

**Determining trace amounts and the origin of formaldehyde impurity
in Neisseria meningitidis A/C/Y/W-135-DT conjugate vaccine
formulated in isotonic aqueous 1× PBS by improved C18-UPLC method**

Author information

Gudlavalleti SK, Crawford EN, Tran NN, Orten DJ, Harder JD, Reddy JR.

JN International Medical Corporation, 2720 N 84th Street, Omaha, NE 68134 USA

Abstract

The ability to accurately measure and report trace amounts of residual formaldehyde impurity in a vaccine product is not only critical in the product release but also a regulatory requirement. In many bacterial or viral vaccine manufacturing procedures, formaldehyde is used either at a live culture inactivation step or at a protein de-toxification step or at both. Reported here is a validated and improved C18-UPLC method (developed based on previously published C-8 HPLC method) to determine the traces of formaldehyde process impurity in a liquid form Neisseria meningitidis A/C/Y/W-135-DT conjugate vaccine formulated in isotonic aqueous 1× PBS. UPLC C-18 column and the conditions described distinctly resolved the 2,4-DNPH-HCHO adduct from the un-reacted 2,4-DNPH as detected by TUV detector at 360 nm. This method was shown to be compatible with PBS formulation and extremely sensitive (with a quantitation limit of 0.05 ppm) and aided to determine formaldehyde contamination sources by evaluating the in-process materials as a track-down analysis. Final nanogram levels of formaldehyde in the formulated single dose vial vaccine mainly originated from the diphtheria toxoid carrier protein used in the production of the conjugate vaccine, whereas relative contribution from polysaccharide API was minimal.

<http://www.ncbi.nlm.nih.gov/pubmed/25668795>

Genetic detection and characterization of emerging HoBi-like viruses in archival foetal bovine serum batches

Author Information

M. Giammariolia, J.F. Ridpath^b, E. Rossia, M. Bazzucchia, C. Casciaria, G.M. De Miaa

a. Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, via Salvemini 1, 06126 Perugia, Italy

b. Ruminant Diseases and Immunology Research Unit, National Animal Disease Center, Agricultural Research Service, U.S. Department of Agriculture, 1920 Dayton Avenue, Ames, IA 50010, USA

Abstract

Bovine viral diarrhoea viruses (BVDV) are members of the Pestivirus genus within the family Flaviviridae. Based on antigenic and nucleotide differences, BVDV are classified into two recognized species, BVDV-1 and BVDV-2. More recently, a new putative pestivirus species, tentatively called “HoBi-like”, has been associated with bovine viral diarrhoea. HoBi-like viruses were first identified in fetal bovine serum (FBS) imported from Brazil. Subsequently, a number of HoBi-like viruses have been detected as contaminants in FBS or cell culture and in live ruminants. To further investigate the possible pestivirus contamination in commercially available FBS batches, 26 batches of FBS with various countries of origin, were tested in this study for the presence of bovine pestiviruses. All the 26 batches were positive by RT-PCR for at least one species of bovine pestiviruses. HoBi-like viruses were detected in 15 batches. Analysis of the 5'UTR and Npro sequences of 15 newly identified HoBi-like viruses combined with analysis of additional sequences from GenBank, identified 4 genetic groups tentatively named 3a–3d. The current study confirmed the presence of the emerging HoBi-like viruses in FBS products labeled with different geographic origins. This finding has obvious implications for the safety of biological products, such as cell lines and vaccines.

<http://www.sciencedirect.com/science/article/pii/S1045105615000536>

“... a new putative pestivirus species, tentatively called “HoBi-like”, has been associated with bovine viral diarrhoea.

To further investigate the possible pestivirus contamination in commercially available Fetal Bovine Serum (FBS) batches, 26 batches of FBS with various countries of origin, were tested in this study for the presence of bovine pestiviruses. All the 26 batches were positive by RT-PCR for at least one species of bovine pestiviruses. HoBi-like viruses were detected in 15 batches.”

Pestivirus control programs: how far have we come and where are we going?

Author information

Moennig V1, Becher P1.

Department of Infectious Diseases, Institute for Virology
University of Veterinary Medicine
Bünteweg 17, D-30559
Hannover, Germany

Abstract

Classical swine fever (CSF) is endemic in large parts of the world and it is a major threat to the pig industry in general. Vaccination and stamping out have been the most successful tools for the control and elimination of the disease. The systematic use of modified live vaccines (MLV), which are very efficacious and safe, has often preceded the elimination of CSF from regions or countries. Oral vaccination using MLV is a powerful tool for the elimination of CSF from wild boar populations. Bovine virus diarrhea (BVD) is endemic in bovine populations worldwide and programs for its control are only slowly gaining ground. With two genotypes BVD virus (BVDV) is genetically more diverse than CSF virus (CSFV). BVDV crosses the placenta of pregnant cattle resulting in the birth of persistently infected (PI) calves. PI animals shed enormous amounts of virus for the rest of their lives and they are the reservoir for the spread of BVDV in cattle populations. They are the main reason for the failure of conventional control strategies based on vaccination only. In Europe two different approaches for the successful control of BVD are being used: Elimination of PI animals without or with the optional use of vaccines, respectively.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26050577>

“They are the main reason for the failure of conventional control strategies based on vaccination only. In Europe two different approaches for the successful control of Bovine virus diarrhea are being used: Elimination of persistently infected animals without or with the optional use of vaccines, respectively.”

Central nervous system toxicity of metallic nanoparticles

Xiaoli Feng,¹ Aijie Chen,¹ Yanli Zhang,¹
Jianfeng Wang,² Longquan Shao,¹ and Limin Wei²

1. Nanfang Hospital, Southern Medical University
Guangzhou, People's Republic of China

2. School and Hospital of Stomatology, Wenzhou Medical University
Wenzhou, People's Republic of China

Abstract

Nanomaterials (NMs) are increasingly used for the therapy, diagnosis, and monitoring of disease- or drug-induced mechanisms in the human biological system. In view of their small size, after certain modifications, NMs have the capacity to bypass or cross the blood–brain barrier. Nanotechnology is particularly advantageous in the field of neurology. Examples may include the utilization of nanoparticle (NP)-based drug carriers to readily cross the blood–brain barrier to treat central nervous system (CNS) diseases, nanoscaffolds for axonal regeneration, nanoelectromechanical systems in neurological operations, and NPs in molecular imaging and CNS imaging. However, NPs can also be potentially hazardous to the CNS in terms of nano-neurotoxicity via several possible mechanisms, such as oxidative stress, autophagy, and lysosome dysfunction, and the activation of certain signaling pathways. In this review, we discuss the dual effect of NMs on the CNS and the mechanisms involved. The limitations of the current research are also discussed.

Summary

There are still many unanswered questions concerning nanoneurotoxicity. For instance, after bypassing the BBB, where do NPs go? How do they leave the brain? The degradation of NP coatings and NP cores inside the cell environment is an important issue that deserves serious consideration when designing safe and functional NMs. No results have been reported on this issue to date.

When NPs enter the body, the surface properties of NPs may change by adsorbing proteins from biological fluids (such as blood, plasma, or interstitial fluid), leading to a distinct new epitope, for example, protein corona exposure in the biological microenvironment. Furthermore, serum protein binding to the NPs can alter the surface charge and accelerate the cellular uptake of NPs through receptor-regulated endocytosis. However, so far, studies addressing the cell surface protein corona interactions with NPs remain limited.

Data regarding the distribution of metal-based NPs in the brain parenchyma are scarce, including data regarding the disruption of the BBB and adverse brain alterations caused by metal-based NPs. The effects of the persistence of poorly soluble metal-based NPs are of particular concern, and few studies have considered the effect of NPs on the CNS.

“The effects of the persistence of poorly soluble metal-based nano-particles are of particular concern, and few studies have considered the effect of nano-particles on the Central Nervous System.”

“Endotoxin was present in all tested samples and the final product.”

PDA Journal Of Pharmaceutical Science And Technology • July 2015

Quality Control Testing for Tracking Endotoxin-Producing Gram-Negative Bacteria during the Preparation of Polyvalent Snake Antivenom Immunoglobulin

Author information

Sheraba NS1, Diab MR1, Yassin AS2, Amin MA3, Zedan HH3.

Vacsera, The Holding Company for Biological Products and Vaccines, Giza, Egypt
Department of Microbiology and Immunology, Faculty of Pharmacy, Cairo University, Cairo, Egypt

Abstract

Snake bites represent a serious public health problem, particularly in rural areas worldwide. Antitoxic sera preparations are antibodies from immunized animals and are considered to be the only treatment option. The purification of antivenom antibodies should aim at obtaining products of consistent quality, safety, efficacy, and adherence to good manufacturing practice principles. Endotoxins are an integral component of the outer cell surface of Gram-negative bacteria. They are common contaminants of the raw materials and processing equipment used in the manufacturing of antivenoms. In this work, and as a part of quality control testing, we establish and examine an environmental monitoring program for identification of potential sources of endotoxin-producing Gram-negative bacteria throughout the whole steps of antivenom preparation. In addition, we follow all the steps of preparation starting from crude plasma till finished product using a validated sterility and endotoxin testing. Samples from air, surface, and personnel were collected and examined through various stages of manufacturing for the potential presence of Gram-negative bacteria. A validated sterility and endotoxin test was carried out in parallel at the different production steps. The results showed that air contributed to the majority of bacterial isolates detected (48.43%), followed by surfaces (37.5%) and then personnel (14%). The most common bacterial isolates detected were *Achromobacter xylosoxidans*, *Ochrobactrum anthropi*, and *Pseudomonas aeruginosa*, which together with *Burkholderia cepacia* were both also detected in cleaning water and certain equipment parts. A heavy bacterial growth with no fungal contamination was observed in all stages of antivenom manufacturing excluding the formulation stage. All samples were positive for endotoxin including the

finished product. Implementation and continued evaluation of quality assurance and quality improvement programs in aseptic preparation is essential in ensuring the safety and quality of these products.

LAY ABSTRACT

Antitoxic sera preparations are the only treatment option for snake bites worldwide. They are prepared by immunizing animals, usually horses, with snake venom and collecting horse plasma, which is then subjected to several purification steps in order to finally prepare the purified immunoglobulins. Components of the bacterial cell wall known as endotoxins can constitute a potential hazardous contamination known as pyrogen in antisera, which can lead to fever and many other adverse reactions to the person subjected to it. In this work, we monitored the environment associated with the different steps of production and purification of snake antivenom prepared from immunized horses. We examined the air quality, surface, and personnel for possible sources of contamination, particularly the presence of Gram-negative bacteria, which is the major source of endotoxin presence. We also monitored all stages of preparation by sterility and endotoxin testing. Our results showed that air contributed to the majority of bacterial isolates. Sterility testing revealed the presence of bacterial contamination in all the intermediate steps, as only the final preparation after filtration was sterile. Endotoxin was present in all tested samples and the final product. Good manufacturing practice procedures are essential in any facility involved in antisera production.

“A possible disadvantage of using human cell lines
is the potential for human-specific viral contamination ...”

Critical Reviews In Biotechnology • September 2015

Human cell lines for biopharmaceutical manufacturing: history, status, and future perspectives

Author information

Dumont J1, Euwart D1, Mei B1, Estes S1, Kshirsagar R1.

1. Biogen, Cambridge, MA, USA

Abstract

Biotherapeutic proteins represent a mainstay of treatment for a multitude of conditions, for example, autoimmune disorders, hematologic disorders, hormonal dysregulation, cancers, infectious diseases and genetic disorders. The technologies behind their production have changed substantially since biotherapeutic proteins were first approved in the 1980s. Although most biotherapeutic proteins developed to date have been produced using the mammalian Chinese hamster ovary and murine myeloma (NS0, Sp2/0) cell lines, there has been a recent shift toward the use of human cell lines. One of the most important advantages of using human cell lines for protein production is the greater likelihood that the resulting recombinant protein will bear post-translational modifications (PTMs) that are consistent with those seen on endogenous human proteins. Although other mammalian cell lines can produce PTMs similar to human cells, they also produce non-human PTMs, such as galactose- α 1,3-galactose and N-glycolylneuraminic acid, which are potentially immunogenic. In addition, human cell lines are grown easily in a serum-free suspension culture, reproduce rapidly and have efficient protein production. A possible disadvantage of using human cell lines is the potential for human-specific viral contamination, although this risk can be mitigated with multiple viral inactivation or clearance steps. In addition, while human cell lines are currently widely used for biopharmaceutical research, vaccine production and production of some licensed protein therapeutics, there is a relative paucity of clinical experience with human cell lines because they have only recently begun to be used for the manufacture of proteins (compared with other types of cell lines). With additional research investment, human cell lines may be further optimized for routine commercial production of a broader range of biotherapeutic proteins.

<http://www.ncbi.nlm.nih.gov/pubmed/26383226>

High rate of vaccine failure after administration of acellular pertussis vaccine pre- and post-liver transplantation in children at a children's hospital in Japan

Author information

Ito K1,2, Kasahara M3, Saitoh A1,4, Honda H5, Miyairi I1.

1. Division of Pediatric Infectious Diseases, Department of Medical Specialties, National Center for Child Health and Development, Tokyo, Japan
2. Department of Infectious Diseases, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan
3. Division of Transplant Surgery, Department of Surgical Subspecialties, National Center for Child Health and Development, Tokyo, Japan
4. Department of Pediatrics, Niigata University Graduate School of Medical and Dental Science, Niigata, Japan
5. Division of Infectious Diseases, Tokyo Metropolitan Tama General Medical Center, Tokyo, Japan

Abstract

We assessed the serological response to pertussis vaccines administered pre- and post-liver transplantation in 58 pediatric patients at a children's hospital in Japan. A high rate of pertussis vaccine failure was observed, 44.8% against the pertussis toxin and 69.0% against filamentous hemagglutinin, with no difference in the seropositivity rate with respect to the timing of the vaccination during the peritransplant period.

<http://www.ncbi.nlm.nih.gov/pubmed/26565897>

“A high rate of pertussis vaccine failure was observed, 44.8% against the pertussis toxin and 69.0% against filamentous hemagglutinin ...”

Chapter Two Thimerosal • Ethyl Mercury 1972 - 2015

Environmental Sources Of Mercury

Mercury Concentration	Form	Biological Significance
0.4ppb	MetHg	Median chronic intake of contaminated fish (0.4ug/kg body weight) causes delayed speech and autistic-like symptoms in male children (Corbett & Poor, 2008)
1.6ppb	MetHg	Provisional Tolerable Weekly Intake (PTWI) based on body weight for infants and pregnant women (1.6ug/kg; Food & Agricultural Association/World Health Organization 2006)
2.0ppb	Inorganic Mercury	US EPA limit for drinking water (US EPA, 2011)
200ppb	Various	Level in liquid that the US EPA classifies as hazardous waste based on toxicity characteristics (US EPA, 2010)
600ppb	EtHg	Concentration of mercury in vaccines containing trace amounts of thimerosal (0.3ug/0.5 ml. dose, or 600ug/L;Halsey, 1999)
25,000-50,000ppb	EtHg	Concentration in Thimerosal containing multi-dose influenza, meningococcal pneumococcal polysaccharide and diphtheria-tetanus vaccines (Offit & Jew, 2003)

“The ubiquitous and largely unchecked place of Thimerosal in pharmaceuticals, therefore, represents a medical crisis.”

Quoted from:

“A review of Thimerosal (Merthiolate) and its ethyl mercury breakdown product: specific historical considerations regarding safety and effectiveness”

by DA Geier, LK Sykes and MR Geier

Postgraduate Medical Journal • July 1972

Six cases of poisoning after a parenteral organic mercurial compound (Merthiolate)

J. H. M. Axton

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2495252/?page=5>

Bulletin Of The World Health Organization • May 1976

An outbreak of organomercury poisoning among Iraqi farmers

Al-Tikriti K, Al-Mufti AW.

Abstract

An outbreak of organomercury poisoning due to the consumption of treated grain by farmers and their families occurred in Iraq in 1971-72. A total of 6530 cases were admitted to hospital and of these 459 died. However, there were many more with minor symptoms of poisoning who consulted outpatient departments. This outbreak constituted the largest poisoning epidemic ever recorded. No age was exempt and no pronounced sex difference was apparent. The latent period of up to 60 days between dosage and the onset of symptoms was probably the major factor contributing to the size of the epidemic. Measures taken to limit the outbreak are outlined.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2366398/>

“A total of 6530 cases
were admitted to hospital
and of these 459 died.”

American Journal Of Obstetrics And Gynecology • October 1976

Mercury toxicity in the pregnant woman,
fetus, and newborn infant
A review

Koos BJ, Longo LD.

Abstract

This paper reviews the reported cases of mercury poisoning in pregnancy and the data based on sources of contamination, maternal uptake, and distribution. It analyzes current knowledge of placental transfer of various mercury compounds, fetal uptake, and distribution. It identifies the embryopathic and fetal toxic effects of mercury in general while emphasizing the greater toxicity of methylmercury compounds. Since maternal exposure to methylmercury is primarily through fish consumption, it recommends that women of childbearing age should not consume more than 350 Gm. of fish per week. In addition, they should not be occupationally exposed to air concentrations of mercury vapor greater than 0.01 mg. per cubic meter, of inorganic and phenylmercuric compounds greater than 0.02 mg. per cubic meter, or any detectable concentration of methylmercury.

<http://www.ncbi.nlm.nih.gov/pubmed/786026>

“This paper reviews the reported cases of mercury poisoning in pregnancy and the data based on sources of contamination, maternal uptake, and distribution. It analyzes current knowledge of placental transfer of various mercury compounds, fetal uptake, and distribution.”

British Journal Of Industrial Medicine • May 1982

Elemental mercury exposure: peripheral neurotoxicity

Levine SP, Cavender GD,
Langolf GD, Albers JW.

Abstract

Nerve conduction tests were performed on the right ulnar nerve of factory workers exposed to elemental mercury vapour. Time integrated urine mercury indices were used to measure the degree of exposure. Workers with prolonged distal latencies had significantly higher urine mercury concentrations when compared with those with normal latencies. Significant correlations between increasing urine mercury concentrations and prolonged motor and sensory distal latencies were established. Elemental mercury can affect both motor and sensory peripheral nerve conduction and the degree of involvement may be related to time-integrated urine mercury concentrations.

<http://www.ncbi.nlm.nih.gov/pubmed/6279139>

“Significant correlations between increasing urine mercury concentrations and prolonged motor and sensory distal latencies were established. Elemental mercury can affect both motor and sensory peripheral nerve conduction and the degree of involvement may be related to time-integrated urine mercury concentrations.”

Neurological abnormalities associated with remote occupational elemental mercury exposure

Author information

Albers JW1, Kallenbach LR, Fine LJ, Langolf GD,
Wolfe RA, Donofrio PD, Alessi AG, Stolp-Smith KA, Bromberg MB.

Department of Neurology
University of Michigan, Ann Arbor

Abstract

We examined 502 subjects, 247 of whom had occupational elemental mercury exposures 20 to 35 years previously, to identify potential exposure-related neurological abnormalities. Few significant (p less than 0.05) differences existed between exposed and unexposed subjects. However, multiple linear regression analysis demonstrated several significant correlations between declining neurological function and increasing exposure as determined by urine mercury measurements from the exposure interval. Subjects with urine mercury peak levels above 0.6 mg/L demonstrated significantly decreased strength, decreased coordination, increased tremor, decreased sensation, and increased prevalence of Babinski and snout reflexes when compared with the remaining subjects. Furthermore, subjects with clinical polyneuropathy had significantly higher peak levels than normal subjects (0.85 vs 0.61 mg/L; $p = 0.04$), but not increased exposure duration (20.1 vs 20.8 quarters; $p = 0.34$), and 28% of subjects with peak levels above 0.85 mg/L had clinical evidence of polyneuropathy, compared with 10% of remaining subjects ($p = 0.005$). Although exposure was not age dependent, several neurological measures showed significant age-mercury interaction, suggesting that natural neuronal attrition may unmask prior exposure-related subclinical abnormalities.

<http://www.ncbi.nlm.nih.gov/pubmed/2849369>

“... multiple linear regression analysis demonstrated several significant correlations between declining neurological function and increasing exposure as determined by urine mercury measurements from the exposure interval. Subjects with urine mercury peak levels above 0.6 mg/L demonstrated significantly decreased strength, decreased coordination, increased tremor, decreased sensation, and increased prevalence of Babinski and snout reflexes when compared with the remaining subjects.”

Brain and tissue levels of mercury after chronic methylmercury exposure in the monkey

Author information

Rice DC1.

Toxicology Research Division
Health Protection Branch
Health and Welfare
Ottawa, Ontario, Canada

Abstract

Estimated half-lives of mercury following methylmercury exposure in humans are 52-93 d for whole body and 49-164 d for blood. In its most recent 1980 review, the World Health Organization concluded that there was no evidence to suggest that brain half-life differed from whole-body half-life. In the present study, female monkeys (*Macaca fascicularis*) were dosed for at least 1.7 yr with 10, 25, or 50 micrograms/kg.d of mercury as methylmercuric chloride. Dosing was discontinued, and blood half-life was determined to be about 14 d. Approximately 230 d after cessation of dosing, monkeys were sacrificed and organ and regional brain total mercury levels determined. One monkey that died while still being dosed had brain mercury levels three times higher than levels in blood. Theoretical calculations were performed assuming steady-state brain: blood ratios of 3, 5, or 10. Brain mercury levels were at least three orders of magnitude higher than those predicted by assuming the half-life in brain to be the same as that in blood. Estimated half-lives in brain were between 56 (brain: blood ratio of 3) and 38 (brain: blood ratio of 10) d. In addition, there was a dose-dependent difference in half-lives for some brain regions. These data clearly indicate that brain half-life is considerably longer than blood half-life in the monkey under conditions of chronic dosing.

<http://www.ncbi.nlm.nih.gov/pubmed/2499694>

“These data
clearly indicate
that brain half-life
is considerably longer
than blood half-life
in the monkey under
conditions of chronic dosing.”

“This review gives an up-to-date account of mercury’s physical and chemical properties and its interaction with biologically active sites pertinent to transport across the blood-brain barrier ...”

Neuroscience & Biobehavioral Reviews • Summer 1990

Mercury neurotoxicity: Mechanisms of blood-brain barrier transport

Michael Aschner *, 1, Judy Lynn Aschner

*Department of Pharmacology and Toxicology and the Interdisciplinary Neuroscience Program
Medical College, Albany, NY 12208, USA

†Department of Pediatrics, Division of Neonatal Medicine Albany Medical College
Albany, NY 12208, USA

Abstract

Mercury exists in a wide variety of physical and chemical states, each of which has unique characteristics of target organ toxicity. The classic symptoms associated with exposure to elemental mercury vapor (Hg_0) and methylmercury (CH_3Hg^+ ; MeHg) involve the central nervous system (CNS), while the kidney is the target organ for the mono- and divalent salts of mercury (Hg^+ and Hg^{++} , respectively). Physical properties and redox potentials determine the qualitative and quantitative differences in toxicity among inorganic mercury compounds, while the ability of MeHg to cross the blood-brain barrier accounts for its accumulation in the CNS and a clinical picture that is dominated by neurological disturbances. This review gives an up-to-date account of mercury’s physical and chemical properties and its interaction with biologically active sites pertinent to transport across the blood-brain barrier, a major regulator of the CNS milieu.

<http://www.sciencedirect.com/science/article/pii/S0149763405802179>

A probable role for vaccines containing thimerosal in thimerosal hypersensitivity

Author information

Osawa J1, Kitamura K, Ikezawa Z, Nakajima H.

Department of Dermatology
Yokohama City University School of Medicine
Kanagawa, Japan

Abstract

We patch tested 141 patients with 0.05% aq. thimerosal and 222 patients with 0.05% aq. mercuric chloride, including 63 children. The frequency of positive patch test reactions to thimerosal was 16.3%. There was a marked preponderance in the young age groups after vaccination, while none of 36 infants (aged 3-48 months) reacted to thimerosal. Positive reactions to mercuric chloride were found in 23 (10.4%) of 222 patients. We also sensitized guinea pigs with diphtheria-pertussis-tetanus (DPT) vaccine containing 0.01% thimerosal and succeeded in inducing hypersensitivity to thimerosal. From patch testing in humans and animal experiments, it is suggested that 0.01% thimerosal in vaccines can sensitize children, and that hypersensitivity to thimerosal is due to the thiosalicylic part of the molecule and correlates with photosensitivity to piroxicam.

<http://www.ncbi.nlm.nih.gov/pubmed/1868700?dopt=Abstract>

“... it is suggested that 0.01% thimerosal
in vaccines can sensitize children ...”

Psychological effects
of low exposure to mercury vapor:
application of a computer-administered
neurobehavioral evaluation system

Author information

Liang YX1, Sun RK, Sun Y, Chen ZQ, Li LH.

Department of Occupational Health
Shanghai Medical University
People's Republic of China

Abstract

A computer-administered neurobehavioral evaluation system in a Chinese language version (NES-C) and a mood inventory of the profile of mood states (POMS) were applied to assess the psychological effects of low-level exposure to mercury vapor in a group of 88 workers (19 males and 69 females, with mean age of 34.2 years) exposed to mercury vapor (average duration of exposure 10.4 years). The well-matched group of 97 nonexposed workers was treated as the control. The intensity of current mercury vapor was relatively mild as reflected by the average level of mercury in the air of the workplace (0.033 mg/m³) and in urine (0.025 mg/liter). The results indicated that the profile of mood states posed was moving to the negative side in Hg-exposed group and most of the NES-C performances, in particular, the mental arithmetic, two-digit search, switching attention, visual choice reaction time, and finger tapping, were also significantly affected compared with those obtained from controls ($P < 0.05-0.01$). The present study and the previous study on the validation of the system suggest that the NES-C we developed is valid for the neurotoxicity screening among the working population exposed to neurotoxic agents.

<http://www.ncbi.nlm.nih.gov/pubmed/8472661>

“The results indicated that the profile of mood states posed was moving to the negative side in mercury-exposed group and most of the NES-C performances, in particular, the mental arithmetic, two-digit search, switching attention, visual choice reaction time, and finger tapping, were also significantly affected compared with those obtained from controls ...”

“... neurotoxic effects of inorganic mercury could be partially due to the irreversible blockade of voltage-activated calcium channels.”

Brain Research • December 1993

Mercury (Hg²⁺) decreases voltage-gated calcium channel currents in rat DRG and Aplysia neurons

M. Pekel, B. Platt, D. Büsselberg

Abstract

Inorganic mercury (Hg²⁺) reduced voltage-gated calcium channel currents irreversibility in two different preparations. In cultured rat dorsal root ganglion (DRG) neurons, studied with the whole cell patch clamp technique, a rapid concentration-dependent decrease in the L/N-type currents to a steady state was observed with an IC₅₀ of 1.1 μM and a Hill coefficient of 1.3 T-currents were blocked with Hg²⁺ in the same concentration range (0.5–2 μM). With increasing Hg²⁺ concentrations a slow membrane current was additionally activated most obviously at concentrations over 2 μM Hg²⁺. This current was irreversible and might be due to the opening of other (non-specific) ion channels by Hg²⁺. The current-voltage (I–V) relation of DRG neurons shifted to more positive values, suggesting a binding of Hg²⁺ to the channel protein and/or modifying its gating properties. In neurons of the abdominal ganglion of *Aplysia californica*, studied with the two electrode voltage clamp technique, a continuous decrease of calcium channel currents was seen even with the lowest used concentration of Hg²⁺ (5 μM). A steady state was not reached and the effect was irreversible without any change on resting membrane currents, even with high concentrations (up to 50 μM). No shift of the I–V relation of the calcium channel currents was observed. Effects on voltage-activated calcium channel currents with Hg²⁺ concentrations such low have not been reported before. We conclude that neurotoxic effects of inorganic mercury could be partially due to the irreversible blockade of voltage-activated calcium channels.

<http://www.sciencedirect.com/science/article/pii/000689939391146J>

Mercury burden of human fetal and infant tissues

Author information

Drasch G1, Schupp I, Höfl H, Reinke R, Roider G.

Institut für Rechtsmedizin
München, Germany

Abstract

The total mercury concentrations in the liver (Hg-L), the kidney cortex (Hg-K) and the cerebral cortex (Hg-C) of 108 children aged 1 day-5 years, and the Hg-K and Hg-L of 46 fetuses were determined. As far as possible, the mothers were interviewed and their dental status was recorded. The results were compared to mercury concentrations in the tissues of adults from the same geographical area. The Hg-K (n = 38) and Hg-L (n = 40) of fetuses and Hg-K (n = 35) and Hg-C (n = 35) of older infants (11-50 weeks of life) correlated significantly with the number of dental amalgam fillings of the mother. The toxicological relevance of the unexpected high Hg-K of older infants from mothers with higher numbers of dental amalgam fillings is discussed.

CONCLUSION

Future discussion on the pros and cons of dental amalgam should not be limited to adults or children with their own amalgam fillings, but also include fetal exposure. The unrestricted application of amalgam for dental restorations in women before and during the child-bearing age should be reconsidered.

<http://www.ncbi.nlm.nih.gov/pubmed/7957411>

“The mercury of fetuses and mercury of older infants (11-50 weeks of life) correlated significantly with the number of dental amalgam fillings of the mother. The toxicological relevance of the unexpected high kidney cortex of older infants from mothers with higher numbers of dental amalgam fillings is discussed.”

The effect of mercury vapour
on cholinergic neurons in the fetal brain:
studies on the expression of nerve growth factor
and its low- and high-affinity receptors

Author information

Söderström S1, Fredriksson A, Dencker L, Ebendal T.

Department of Developmental Neuroscience
Uppsala University, Sweden

Abstract

The effects of mercury vapour on the production of nerve growth factor during development have been examined. Pregnant rats were exposed to two different concentrations of mercury vapour during either embryonic days E6-E11 (early) or E13-E18 (late) in pregnancy, increasing the postnatal concentration of mercury in the brain from 1 ng/g tissue to 4 ng/g tissue (low-dose group) or 11 ng/g (high-dose group). The effect of this exposure in offspring was determined by looking at the NGF concentration at postnatal days 21 and 60 and comparing these levels to age-matched controls from sham-treated mothers. Changes in the expression of mRNA encoding NGF, the low- and high-affinity receptors for NGF (p75 and p140 trk, respectively) and choline acetyltransferase (ChAT) were also determined. When rats were exposed to high levels of mercury vapour during early embryonic development there was a significant (62%) increase in hippocampal NGF levels at P21 accompanied by a 50% decrease of NGF in the basal forebrain. The expression of NGF mRNA was found to be unaltered in the dentate gyrus. The expression of p75 mRNA was significantly decreased to 39% of control levels in the diagonal band of Broca (DB) and to approximately 50% in the medial septal nucleus (MS) whereas no alterations in the level of trk mRNA expression were detectable in the basal forebrain. ChAT mRNA was slightly decreased in the DB and MS, significantly in the striatum. These findings suggest that low levels of prenatal mercury vapour exposure can alter the levels of the NGF and its receptors, indicating neuronal damage and disturbed trophic regulations during development.

<http://www.ncbi.nlm.nih.gov/pubmed/7781173>

“These findings suggest that low levels of prenatal mercury vapour exposure can alter the levels of the NGF and its receptors, indicating neuronal damage and disturbed trophic regulations during development.”

Altered porphyrin metabolism as a biomarker of mercury exposure and toxicity

Author information

Woods JS.

Department of Environmental Health
University of Washington, Seattle, USA

Abstract

Changes in urinary porphyrin excretion patterns (porphyrin profiles) have been described in response to a variety of drugs and chemicals. The present studies were conducted to define the specific changes in the urinary porphyrin profile associated with prolonged exposure to mercury and mercury compounds. In rats, exposure for a prolonged period to mercury as methyl mercury hydroxide was associated with urinary porphyrin changes, which were uniquely characterized by highly elevated levels of 4- and 5-carboxyl porphyrins and by the expression of an atypical porphyrin ("precoproporphyrin") not found in urine of unexposed animals. These distinct changes in urinary porphyrin concentrations were observed as early as 1-2 weeks after initiation of mercury exposure, and increased in a dose- and time-related fashion with the concentration of mercury in the kidney, a principal target organ of mercury compounds. Following cessation of mercury exposure, urinary porphyrin concentrations reverted to normal levels, consistent with renal mercury clearance. In human studies, a comparable change in the urinary porphyrin profile was observed among subjects with occupational exposure to mercury as mercury vapor sufficient to elicit urinary mercury levels greater than 20 micrograms/L. Urinary porphyrin profiles were also shown to correlate significantly with mercury body burden and with specific neurobehavioral deficits associated with low level mercury exposure. These findings support the utility of urinary porphyrin profiles as a useful biomarker of mercury exposure and potential health effects in human subjects.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8723034>

"These findings support
the utility of urinary porphyrin
profiles as a useful biomarker of
mercury exposure and potential
health effects in human subjects."

Demonstration of mercury in the human brain and other organs 17 years after metallic mercury exposure

Author information

Opitz H1, Schweinsberg F, Grossmann T,
Wendt-Gallitelli MF, Meyermann R.

Department of Neuropathology
University of Tübingen, Germany

Abstract

A male subject became exposed to metallic mercury vapor at work in 1973. He excreted 1,850 mg Hg/l urine initially. Controls of urine mercury excretion after D-penicillamine administration led to the assumption of a total body clearance of mercury latest since 1976. Subsequently he developed an organic psychosyndrome without detectable signs of classical mercurialism. He never returned to work again and died of lung cancer in 1990. In different organs (brain, kidney, and lung) which were sampled at autopsy elevated levels of mercury were documented by atomic absorption analysis. Histological examination of the tissue by the Danscher and Schroder method, which is specific for mercury, showed a highly positive staining in the majority of nerve cells and cells of other organs. Ultrastructurally mercury could be demonstrated by elemental x-ray analysis within lipofuscin deposits. The lipofuscin content was increased in the mercury positive nerve cells as demonstrated by a strong positive autofluorescence.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8793247>

“He never returned to work again and died of lung cancer in 1990. In different organs (brain, kidney, and lung) which were sampled at autopsy elevated levels of mercury were documented by atomic absorption analysis.”

Neurotoxicology • Fall 1996

Effect of subchronic mercury exposure on electrocorticogram of rats

Author information

Dési I1, Nagymajtényi L, Schulz H.

Department of Public Health
Albert Szent-Györgyi Medical University
Szeged, Hungary

Abstract

Mercury is a neurotoxic compound causing irreversible disorders of the central and peripheral nervous system. In some of the previous human and experimental studies mercury also affected some functional neurological parameters such as EEG, and cortical evoked potentials. In the present study, the effect of subchronic (4, 8, and 12 weeks) relatively low-level (0.4, 0.8, and 1.6 mg/kg mercury in form of HgCl₂, per os by gavage) treatment on the basic cortical activity was investigated. Certain parameters of electrocorticogram (ECoG) recorded simultaneously from the primary somatosensory, visual and auditory centres were analyzed. The results showed that mercury had a dose- and time-dependent effect on the examined ECoG parameters, and the changes became significant by the end of the experiment of week 12.

<http://www.ncbi.nlm.nih.gov/pubmed/9086494>

“Mercury is a neurotoxic compound
causing irreversible disorders of the
central and peripheral nervous system.”

Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury

Author information

Grandjean P1, Weihe P, White RF, Debes F, Araki S, Yokoyama K, Murata K, Sørensen N, Dahl R, Jørgensen PJ.

Institute of Community Health
Odense University, Denmark
p.grandjean@winsloew.ou.dk

Abstract

A cohort of 1022 consecutive singleton births was generated during 1986-1987 in the Faroe Islands. Increased methylmercury exposure from maternal consumption of pilot whale meat was indicated by mercury concentrations in cord blood and maternal hair. At approximately 7 years of age, 917 of the children underwent detailed neurobehavioral examination. Neuropsychological tests included Finger Tapping; Hand-Eye Coordination; reaction time on a Continuous Performance Test; Wechsler Intelligence Scale for Children-Revised Digit Spans, Similarities, and Block Designs; Bender Visual Motor Gestalt Test; Boston Naming Test; and California Verbal Learning Test (Children). Clinical examination and neurophysiological testing did not reveal any clear-cut mercury-related abnormalities. However, mercury-related neuropsychological dysfunctions were most pronounced in the domains of language, attention, and memory, and to a lesser extent in visuospatial and motor functions. These associations remained after adjustment for covariates and after exclusion of children with maternal hair mercury concentrations above 10 microgram(s) (50 nmol/g). The effects on brain function associated with prenatal methylmercury exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe.

<http://www.ncbi.nlm.nih.gov/pubmed/9392777>

“The effects on brain function associated with prenatal methylmercury exposure therefore appear widespread, and early dysfunction is detectable at exposure levels currently considered safe.”

**Thimerosal:
a versatile sulfhydryl reagent,
calcium mobilizer, and cell function-modulating agent**

Author information

Elferink JG.

Department of Molecular Cell Biology, University of Leiden, The Netherlands

Abstract

An overview of the literature concerning the effects of thimerosal is presented. Because of its antibacterial effect, thimerosal is used for a variety of practical purposes such as anti-septic and preservative. In biomedical studies, thimerosal is used as a sulfhydryl reagent, and as a calcium-mobilizing agent. The ability of thimerosal to act as a sulfhydryl group is related to the presence of mercury. Relatively little study has been devoted to the mechanism of the reaction of thimerosal with the sulfhydryl group; the sulfhydryl reactive capacity is mostly concluded on the basis of inactivation of the effect by dithiothreitol (DTT). Thimerosal causes a release of calcium from intracellular stores in many cell types; this is followed by an influx of extracellular calcium. Both InsP₃- and ryanodine-sensitive calcium stores may be affected. Studies with permeabilized cells or organelles show that the effect of thimerosal on calcium is dependent on the concentration: low concentrations of thimerosal stimulate calcium release, high concentrations are inhibitory. This dependence is not found in intact cells. Thimerosal may activate or inhibit a number of cell functions. These are often related to the ability to release calcium or with the sulfhydryl reactivity. In platelets, thimerosal causes aggregation, increase of arachidonic acid metabolism, and exocytotic release of serotonin. In neutrophils, thimerosal causes, besides an increase of cytosolic free calcium, an increase of formyl-methionyl-leucyl-phenylalanine (fMLP)-activated leukotriene release, and a modulation of chemotactic migration and exocytosis. At low concentrations, thimerosal induces chemotactic migration of neutrophils, in the absence of other chemoattractants. The effect is also observed with thiosalicylic acid, indicating that the stimulation of migration was due to the thiosalicylic acid moiety of the thimerosal molecule. At higher concentrations, thimerosal causes inhibition of fMLP-activated migration. Low concentrations of thimerosal, but not of thiosalicylic acid, induced exocytotic enzyme release from neutrophils. High concentrations of thimerosal inhibited fMLP-activated exocytosis. The results point to an involvement of calcium mobilization and calcium influx of activation, and reaction with sulfhydryl groups for inhibition.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10428009>

“Thimerosal may
activate or inhibit a
number of cell functions.”

Mercury induces cell cytotoxicity and oxidative stress and increases beta-amyloid secretion and tau phosphorylation in SHSY5Y neuroblastoma cells

Author information

Olivieri G1, Brack C, Müller-Spahn F, Stähelin HB, Herrmann M, Renard P, Brockhaus M, Hock C.

Neurobiology Laboratory
Psychiatric University Hospital
Basel, Switzerland
Olivieri@ubaclu.unibas.ch

Abstract

Concentrations of heavy metals, including mercury, have been shown to be altered in the brain and body fluids of Alzheimer's disease (AD) patients. To explore potential pathophysiological mechanisms we used an in vitro model system (SHSY5Y neuroblastoma cells) and investigated the effects of inorganic mercury (HgCl₂) on oxidative stress, cell cytotoxicity, beta-amyloid production, and tau phosphorylation. We demonstrated that exposure of cells to 50 microg/L (180 nM) HgCl₂ for 30 min induces a 30% reduction in cellular glutathione (GSH) levels (n = 13, p<0.001). Preincubation of cells for 30 min with 1 microM melatonin or premixing melatonin and HgCl₂ appeared to protect cells from the mercury-induced GSH loss. Similarly, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cytotoxicity assays revealed that 50 microg/L HgCl₂ for 24 h produced a 50% inhibition of MTT reduction (n = 9, p<0.001). Again, melatonin preincubation protected cells from the deleterious effects of mercury, resulting in MTT reduction equaling control levels. The release of beta-amyloid peptide (Abeta) 1-40 and 1-42 into cell culture supernatants after exposure to HgCl₂ was shown to be different: Abeta 1-40 showed maximal (15.3 ng/ml) release after 4 h, whereas Abeta 1-42 showed maximal (9.3 ng/ml) release after 6 h of exposure to mercury compared with untreated controls (n = 9, p<0.001). Preincubation of cells with melatonin resulted in an attenuation of Abeta 1-40 and Abeta 1-42 release. Tau phosphorylation was significantly increased in the presence of mercury (n = 9, p<0.001), whereas melatonin preincubation reduced the phosphorylation to control values. These results indicate that mercury may play a role in pathophysiological mechanisms of AD.

<http://www.ncbi.nlm.nih.gov/pubmed/10617124>

“These results indicate that mercury may play a role in pathophysiological mechanisms of Alzheimer's disease.”

Journal Of Pediatrics • May 2000

Iatrogenic exposure to mercury after hepatitis B vaccination in preterm infants

Author information

Stajich GV1, Lopez GP, Harry SW, Sexson WR.

Mercer University
Southern School of Pharmacy
Atlanta, Georgia 30341, USA

Abstract

Thimerosal, a derivative of mercury, is used as a preservative in hepatitis B vaccines. We measured total mercury levels before and after the administration of this vaccine in 15 preterm and 5 term infants. Comparison of pre- and post-vaccination mercury levels showed a significant increase in both preterm and term infants after vaccination. Additionally, post-vaccination mercury levels were significantly higher in preterm infants as compared with term infants. Because mercury is known to be a potential neurotoxin to infants, further study of its pharmacodynamics is warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/10802503>

“Comparison of pre- and post-vaccination mercury levels showed a significant increase in both preterm and term infants after vaccination.”

Summary of the joint statement on thimerosal in vaccines
American Academy of Family Physicians
American Academy of Pediatrics
Advisory Committee on Immunization Practices
Public Health Service

Centers for Disease Control and Prevention (CDC)

Abstract

In June 2000, a joint statement on thimerosal in vaccines was prepared by the American Academy of Family Physicians (AAFP), the American Academy of Pediatrics (AAP), the Advisory Committee on Immunization Practices (ACIP), and the Public Health Service (PHS) in response to 1) the progress in achieving the national goal declared in July 1999 to remove thimerosal from vaccines in the recommended childhood vaccination schedule, and 2) results of recent studies that examined potential associations between exposure to mercury in thimerosal-containing vaccines and health effects. In this statement, AAFP, AAP, ACIP, and PHS recommend continuation of the current policy of moving rapidly to vaccines that are free of thimerosal as a preservative. Until adequate supplies are available, use of vaccines that contain thimerosal as a preservative is acceptable.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10914930>

“AAFP, AAP, ACIP, and PHS recommend continuation of the current policy of moving rapidly to vaccines that are free of thimerosal as a preservative. Until adequate supplies are available, use of vaccines that contain thimerosal as a preservative is acceptable.”

Vaccines without thiomersal: why so necessary, why so long coming?

Author information

van't Veen AJ.

Department of Dermatology and Venereology
Erasmus University Hospital Rotterdam-Dijkzigt
Rotterdam, The Netherlands

Abstract

The inorganic mercurial thiomersal (merthiolate) has been used as an effective preservative in numerous medical and non-medical products since the early 1930s. Both the potential toxicity of thiomersal and sensitisation to thiomersal in relation to the application of thiomersal-containing vaccines and immunoglobulins, especially in children, have been debated in the literature. The very low thiomersal concentrations in pharmacological and biological products are relatively non-toxic, but probably not in utero and during the first 6 months of life. The developing brain of the fetus is most susceptible to thiomersal and, therefore, women of childbearing age, in particular, should not receive thiomersal-containing products. Definitive data of doses at which developmental effects occur are not available. Moreover, revelation of subtle effects of toxicity needs long term observation of children. The ethylmercury radical of the thiomersal molecule appears to be the prominent sensitiser. The prevalence of thiomersal hypersensitivity in mostly selected populations varies up to 18%, but higher figures have been reported. The overall exposure to thiomersal differs considerably between countries. In many cases a positive routine patch test to thiomersal should be considered an accidental finding without or, probably more accurately, with low clinical relevance. In practice, some preventive measures can be taken with respect to thiomersal hypersensitivity. However, with regard to the debate on primary sensitisation during childhood and renewed attention for a reduction of children's exposure to mercury from all sources, the use of thiomersal should preferably be eliminated or at least be reduced. In 1999 the manufacturers of vaccines and immunoglobulins in the US and Europe were approached with this in mind. The potential toxicity in children seems to be of much more concern to them than the hidden sensitising properties of thiomersal. In The Netherlands, unlike many other countries, the exposure to thiomersal from pharmaceutical sources has already been reduced. Replacement of thiomersal in all products should have a high priority in all countries.

“The potential toxicity in children seems to be of much more concern to them [the vaccine manufacturers] than the hidden sensitising properties of thiomersal. Replacement of thiomersal in all products should have a high priority in all countries. In 1999 the manufacturers of vaccines and immunoglobulins in the US and Europe were approached with this in mind.”

Medical Hypotheses • April 2001

Autism: a novel form of mercury poisoning

Author information

Bernard S1, Enayati A, Redwood L, Roger H, Binstock T.

ARC Research, Cranford, New Jersey 07901, USA

Abstract

Autism is a syndrome characterized by impairments in social relatedness and communication, repetitive behaviors, abnormal movements, and sensory dysfunction. Recent epidemiological studies suggest that autism may affect 1 in 150 US children. Exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism, and the similarities extend to neuroanatomy, neurotransmitters, and biochemistry. Thimerosal, a preservative added to many vaccines, has become a major source of mercury in children who, within their first two years, may have received a quantity of mercury that exceeds safety guidelines. A review of medical literature and US government data suggests that: (i) many cases of idiopathic autism are induced by early mercury exposure from thimerosal; (ii) this type of autism represents an unrecognized mercurial syndrome; and (iii) genetic and non-genetic factors establish a predisposition whereby thimerosal's adverse effects occur only in some children.

<http://www.ncbi.nlm.nih.gov/pubmed/11339848>

“A review of medical literature and US government data suggests that many cases of idiopathic autism are induced by early mercury exposure from thimerosal.”

Retrograde degeneration of neurite membrane structural integrity of nerve growth cones following in vitro exposure to mercury

Author information

Leong CC1, Syed NI, Lorscheider FL.

Faculty of Medicine
Department of Physiology and Biophysics
University of Calgary, Alberta, Canada

Abstract

Inhalation of mercury vapor (Hg⁰) inhibits binding of GTP to rat brain tubulin, thereby inhibiting tubulin polymerization into microtubules. A similar molecular lesion has also been observed in 80% of brains from patients with Alzheimer disease (AD) compared to age-matched controls. However the precise site and mode of action of Hg ions remain illusive. Therefore, the present study examined whether Hg ions could affect membrane dynamics of neurite growth cone morphology and behavior. Since tubulin is a highly conserved cytoskeletal protein in both vertebrates and invertebrates, we hypothesized that growth cones from animal species could be highly susceptible to Hg ions. To test this possibility, the identified, large Pedal A (PeA) neurons from the central ring ganglia of the snail *Lymnaea stagnalis* were cultured for 48 h in 2 ml brain conditioned medium (CM). Following neurite outgrowth, metal chloride solution (2 microl) of Hg, Al, Pb, Cd, or Mn (10⁻⁷ M) was pressure applied directly onto individual growth cones. Time-lapse images with inverted microscopy were acquired prior to, during, and after the metal ion exposure. We demonstrate that Hg ions markedly disrupted membrane structure and linear growth rates of imaged neurites in 77% of all nerve growth cones. When growth cones were stained with antibodies specific for both tubulin and actin, it was the tubulin/microtubule structure that disintegrated following Hg exposure. Moreover, some denuded neurites were also observed to form neurofibrillary aggregates. In contrast, growth cone exposure to other metal ions did not effect growth cone morphology, nor was their motility rate compromised. To determine the growth suppressive effects of Hg ions on neuronal sprouting, cells were cultured either in the presence or absence of Hg ions. We found that in the presence of Hg ions, neuronal somata failed to sprout, whereas other metallic ions did not effect growth patterns of cultured PeA cells. We conclude that this visual evidence and previous biochemical data strongly implicate Hg as a potential etiological factor in neurodegeneration.

“We found that in the presence of mercury ions, neuronal somata failed to sprout, whereas other metallic ions did not effect growth patterns of cultured PeA cells. We conclude that this visual evidence and previous biochemical data strongly implicate mercury as a potential etiological factor in neurodegeneration.”

Predicted mercury concentrations in hair from infant immunizations: cause for concern

Author information

Redwood L1, Bernard S, Brown D.

Coalition for Safe Minds, Cranford, NJ 07016, USA
tlredwood@mindspring.com

Abstract

Mercury (Hg) is considered one of the world's most toxic metals. Current thinking suggests that exposure to mercury occurs primarily from seafood contamination and rare catastrophic events. Recently, another common source of exposure has been identified. Thimerosal (TMS), a preservative found in many infant vaccines, contains 49.6% ethyl mercury (EtHg) by weight and typically contributes 25 microg of EtHg per dose of infant vaccine. As part of an ongoing review, the Food and Drug Administration (FDA) announced in 1999 that infants who received multiple TMS-preserved vaccines may have been exposed to cumulative Hg in excess of Federal safety guidelines. According to the Centers for Disease Control (CDC) recommended immunization schedule, infants may have been exposed to 12.5 microg Hg at birth, 62.5 microg EtHg at 2 months, 50 microg EtHg at 4 months, 62.5 microg EtHg at 6 months, and 50 microg EtHg at approximately 18 months, for a total of 237.5 microg EtHg during the first 18 months of life, if all TMS-containing vaccines were administered. Neurobehavioral alterations, especially to the more susceptible fetus and infant, are known to occur after relatively low dose exposures to organic mercury compounds. In effort, to further elucidate the levels of ethyl mercury resulting from exposure to vaccinal TMS, we estimated hair Hg concentrations expected to result from the recommended CDC schedule utilizing a one compartment pharmacokinetic model. This model was developed to predict hair concentrations from acute exposure to methylmercury (MeHg) in fish. Modeled hair Hg concentrations in infants exposed to vaccinal TMS are in excess of the Environmental Protection Agency (EPA) safety guidelines of 1 ppm for up to 365 days, with several peak concentrations within this period. More sensitive individuals and those with additional sources of exposure would have higher Hg concentrations. Given that exposure to low levels of mercury during critical stages of development has been associated with neurological disorders in children, including ADD, learning difficulties, and speech delays, the predicted hair Hg concentration resulting from childhood immunizations is cause for concern. Based on these findings, the impact which vaccinal mercury has had on the health of American children warrants further investigation.

“Given that exposure to low levels of mercury during critical stages of development has been associated with neurological disorders in children, including ADD, learning difficulties, and speech delays, the predicted hair ethyl mercury concentration resulting from childhood immunizations is cause for concern.”

The role of mercury in the pathogenesis of autism

S Bernard, A Enayati, H Roger, T Binstock and L

Redwood Safe Minds, Cranford, NJ, USA

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder of unknown etiology in most cases. Studies of monozygotic twins report an average 60% concordance rate, indicating a role for both genetic and environmental factors in disease expression.¹ Recent reviews in environmental health have suggested that early exposure to hazardous substances may underlie some cases of neurodevelopmental disorders, including ADHD, learning disabilities, and speech/language difficulties.² In 1999, thimerosal used as a vaccine preservative was identified as a widespread source of organic mercury exposure in infants.³ Mercury (Hg), a heavy metal, is considered highly neurotoxic.⁴ The amount of mercury in vaccines, while small, exceeded USEPA safety guidelines on a cumulative basis.³ Certain individuals may exhibit severe adverse reactions to low doses of Hg which are otherwise largely benign to the majority of those exposed.⁵ Some individuals with idiopathic autism spectrum disorder may represent such a sensitive population. As summarized in this paper, disease characteristics suggest this possibility: (a) ASD traits are known to arise from mercury exposure; (b) onset of ASD symptoms is temporally associated with administration of immunizations; (c) the reported increase in the prevalence of autism in the 1990s closely follows the introduction of two mercury-containing vaccines; and (d) elevated mercury has been detected in biological samples of autistic patients. Since ASD may now affect as many as one in 150 US children,⁶ and since thimerosal is still used in many products worldwide, confirmation of thimerosal as an environmental agent in autism pathogenesis has important societal and patient implications.

Full Report

<http://www.nature.com/mp/journal/v7/n2s/pdf/4001177a.pdf>

“... onset of ASD symptoms is temporally associated with administration of immunizations; the reported increase in the prevalence of autism in the 1990s closely follows the introduction of two mercury-containing vaccines; and elevated mercury has been detected in biological samples of autistic patients.”

Biochemical and molecular basis of thimerosal-induced apoptosis in T cells: a major role of mitochondrial pathway

Author information

Makani S1, Gollapudi S, Yel L, Chiplunkar S, Gupta S.

Cellular and Molecular Immunology Laboratories
Division of Basic and Clinical Immunology
University of California, Irvine 92697, USA

Abstract

The major source of thimerosal (ethyl mercury thiosalicylate) exposure is childhood vaccines. It is believed that the children are exposed to significant accumulative dosage of thimerosal during the first 2 years of life via immunization. Because of health-related concerns for exposure to mercury, we examined the effects of thimerosal on the biochemical and molecular steps of mitochondrial pathway of apoptosis in Jurkat T cells. Thimerosal and not thiosalicylic acid (non-mercury component of thimerosal), in a concentration-dependent manner, induced apoptosis in T cells as determined by TUNEL and propidium iodide assays, suggesting a role of mercury in T cell apoptosis. Apoptosis was associated with depolarization of mitochondrial membrane, release of cytochrome c and apoptosis inducing factor (AIF) from the mitochondria, and activation of caspase-9 and caspase-3, but not of caspase-8. In addition, thimerosal in a concentration-dependent manner inhibited the expression of XIAP, cIAP-1 but did not influence cIAP-2 expression. Furthermore, thimerosal enhanced intracellular reactive oxygen species and reduced intracellular glutathione (GSH). Finally, exogenous glutathione protected T cells from thimerosal-induced apoptosis by upregulation of XIAP and cIAP1 and by inhibiting activation of both caspase-9 and caspase-3. These data suggest that thimerosal induces apoptosis in T cells via mitochondrial pathway by inducing oxidative stress and depletion of GSH.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12140745>

“The major source of thimerosal (ethyl mercury thiosalicylate) exposure is childhood vaccines. It is believed that the children are exposed to significant accumulative dosage of thimerosal during the first 2 years of life via immunization. These data suggest that thimerosal induces apoptosis in T cells via mitochondrial pathway by inducing oxidative stress and depletion of intracellular glutathione.”

Neurodevelopmental Disorders after Thimerosal-Containing Vaccines: A Brief Communication

Mark Geier And David A. Geier
The Genetic Centers of America
Silver Spring, Maryland 20905

Abstract

We were initially highly skeptical that differences in the concentrations of thimerosal in vaccines would have any effect on the incidence rate of neurodevelopmental disorders after childhood immunization. This study presents the first epidemiologic evidence, based upon tens of millions of doses of vaccine administered in the United States, that associates increasing thimerosal from vaccines with neurodevelopmental disorders. Specifically, an analysis of the Vaccine Adverse Events Reporting System (VAERS) database showed statistical increases in the incidence rate of autism (relative risk [RR] = 6.0), mental retardation (RR = 6.1), and speech disorders (RR = 2.2) after thimerosal-containing diphtheria, tetanus, and acellular pertussis (DTaP) vaccines in comparison with thimerosal-free DTaP vaccines. The male/female ratio indicated that autism (17) and speech disorders (2.3) were reported more in males than females after thimerosal-containing DTaP vaccines, whereas mental retardation (1.2) was more evenly reported among male and female vaccine recipients. Controls were employed to determine if biases were present in the data, but none were found. It was determined that overall adverse reactions were reported in similar-aged populations after thimerosal-containing DTaP (2.4 ± 3.2 years old) and thimerosal-free DTaP (2.1 ± 2.8 years old) vaccinations. Acute control adverse reactions such as deaths (RR = 1.0), vasculitis (RR = 1.2), seizures (RR = 1.6), ED visits (RR = 1.4), total adverse reactions (RR = 1.4), and gastroenteritis (RR = 1.1) were reported similarly after thimerosal-containing and thimerosal-free DTaP vaccines. An association between neurodevelopmental disorders and thimerosal-containing DTaP vaccines was found, but additional studies should be conducted to confirm and extend this study.

In recent years, thimerosal, an organic mercury compound that is metabolized to ethylmercury and thiosalicylate and has been present since the 1930s as a preservative in some vaccines and pharmaceutical products to prevent bacterial and fungal contamination, has come under scrutiny. It was determined by the U.S. Food and Drug Administration (FDA) in 1999 under the recommended childhood immunization schedule that infants might be exposed to cumulative doses of ethylmercury that exceed some federal safety guidelines established for exposure to methylmercury, another form of organic mercury (1).

The hypothesis that exposure to thimerosal-containing vaccines could be associated with neurodevelopmental disorders is not established and rests on indirect and incomplete information, primarily from analogies with methylmercury and levels of maximum mercury exposure from vaccines given in children. The hypothesis is biologically possible, but the possible relationship between thimerosal from vaccines and neurodevelopmental disorders of autism, attention deficit/hyperactivity disorder (ADHD), and speech or language delay remains seriously suspect. As of the present, there are no peer-reviewed epidemiological studies in the scientific literature examining the potential association between thimerosal-containing vaccines and neurodevelopmental disorders. Here, we show the first epidemiologic evidence, based upon tens of millions of doses of vaccine administered in the United States, that associates increasing thimerosal from vaccines with neurodevelopmental disorders.

Full Report: <http://www.autismhelpforyou.com/EXPERT%20PAPER%20-%20Geier%20-%20Internet%20File.pdf>

“... we show the first epidemiologic evidence, based upon tens of millions of doses of vaccine administered in the United States, that associates increasing thimerosal from vaccines with neurodevelopmental disorders.”

Neurotoxicity of organomercurial compounds

Author information

Sanfeliu C1, Sebastià J, Cristòfol R, Rodríguez-Farré E.

Department of Pharmacology and Toxicology
Institut d'Investigacions Biomèdiques de Barcelona, CSIC, IDIBAPS
Rossellò 161, 08036 Barcelona, Spain
cspfai@iibb.csic.es

Abstract

Mercury is a ubiquitous contaminant, and a range of chemical species is generated by human activity and natural environmental change. Elemental mercury and its inorganic and organic compounds have different toxic properties, but all them are considered hazardous in human exposure. In an equimolecular exposure basis, organomercurials with a short aliphatic chain are the most harmful compounds and they may cause irreversible damage to the nervous system. Methylmercury (CH₃Hg⁽⁺⁾) is the most studied following the neurotoxic outbreaks identified as Minamata disease and the Iraq poisoning. The first description of the CNS pathology dates from 1954. Since then, the clinical neurology, the neuropathology and the mechanisms of neurotoxicity of organomercurials have been widely studied. The high thiol reactivity of CH₃Hg⁽⁺⁾, as well as all mercury compounds, has been suggested to be the basis of their harmful biological effects. However, there is clear selectivity of CH₃Hg⁽⁺⁾ for specific cell types and brain structures, which is not yet fully understood. The main mechanisms involved are inhibition of protein synthesis, microtubule disruption, increase of intracellular Ca⁽²⁺⁾ with disturbance of neurotransmitter function, oxidative stress and triggering of excitotoxicity mechanisms. The effects are more damaging during CNS development, leading to alterations of the structure and functionality of the nervous system. The major source of CH₃Hg⁽⁺⁾ exposure is the consumption of fish and, therefore, its intake is practically unavoidable. The present concern is on the study of the effects of low level exposure to CH₃Hg⁽⁺⁾ on human neurodevelopment, with a view to establishing a safe daily intake. Recommendations are 0.4 micro g/kg body weight/day by the WHO and US FDA and, recently, 0.1 micro g/kg body weight/day by the US EPA. Unfortunately, these levels are easily attained with few meals of fish per week, depending on the source of the fish and its position in the food chain.

<http://www.ncbi.nlm.nih.gov/pubmed/12835120>

“Elemental mercury

and its inorganic and organic compounds

have different toxic properties, but all them

are considered hazardous in human exposure.

Recommendations are 0.4 micro g/kg body weight/day by

the WHO and US FDA and, recently, 0.1 micro g/kg body

weight/day by the US EPA. Unfortunately, these levels are

easily attained with few meals of fish per week, depending

on the source of the fish and its position in the food chain.”

“The evidence presented here shows that the occurrence of neurodevelopmental disorders following thimerosal-containing childhood vaccines does not appear to be coincidental.”

Pediatric Rehabilitation • April 2003

An assessment of the impact of thimerosal on childhood neurodevelopmental disorders

Author information

Geier DA1, Geier MR.

The Genetic Centers of America
14 Redgate Court, Silver Spring, MD 20905, USA

Abstract

The prevalence of autism in the US has risen from 1 in approximately 2500 in the mid-1980s to 1 in approximately 300 children in the mid-1990s. The purpose of this study was to evaluate whether mercury from thimerosal in childhood vaccines contributed to neurodevelopmental disorders. Neurodevelopmental disorder dose-response curves for increasing mercury doses of thimerosal in childhood vaccines were determined based upon examination of the Vaccine Adverse Events Reporting System (VAERS) database and the 2001 US' Department of Education Report. The instantaneous dosage of mercury children received in comparison to the Food and Drug Administration (FDA)'s maximum permissible dose for the oral ingestion of methylmercury was also determined. The dose-response curves showed increases in odds ratios of neurodevelopmental disorders from both the VAERS and US Department of Education data closely linearly correlated with increasing doses of mercury from thimerosal-containing childhood vaccines and that for overall odds ratios statistical significance was achieved. Similar slopes and linear regression coefficients for autism odds ratios in VAERS and the US Department of Education data help to mutually validate each other. Controls employed in the VAERS and US Department of Education data showed minimal biases. The evidence presented here shows that the occurrence of neurodevelopmental disorders following thimerosal-containing childhood vaccines does not appear to be coincidental.

<http://www.ncbi.nlm.nih.gov/pubmed/14534046>

“An association between neurodevelopmental disorders
and thimerosal-containing DTaP vaccines was found ...”

Experiments In Biological Medicine • June 2003

Neurodevelopmental disorders after thimerosal-containing vaccines: a brief communication

Author information

Geier MR1, Geier DA.

The Genetic Centers of America, Silver Spring, Maryland 20905, USA
mgeier@erols.com

Abstract

We were initially highly skeptical that differences in the concentrations of thimerosal in vaccines would have any effect on the incidence rate of neurodevelopmental disorders after childhood immunization. This study presents the first epidemiologic evidence, based upon tens of millions of doses of vaccine administered in the United States, that associates increasing thimerosal from vaccines with neurodevelopmental disorders. Specifically, an analysis of the Vaccine Adverse Events Reporting System (VAERS) database showed statistical increases in the incidence rate of autism (relative risk [RR] = 6.0), mental retardation (RR = 6.1), and speech disorders (RR = 2.2) after thimerosal-containing diphtheria, tetanus, and acellular pertussis (DTaP) vaccines in comparison with thimerosal-free DTaP vaccines. The male/female ratio indicated that autism (17) and speech disorders (2.3) were reported more in males than females after thimerosal-containing DTaP vaccines, whereas mental retardation (1.2) was more evenly reported among male and female vaccine recipients. Controls were employed to determine if biases were present in the data, but none were found. It was determined that overall adverse reactions were reported in similar-aged populations after thimerosal-containing DTaP (2.4 +/- 3.2 years old) and thimerosal-free DTaP (2.1 +/- 2.8 years old) vaccinations. Acute control adverse reactions such as deaths (RR = 1.0), vasculitis (RR = 1.2), seizures (RR = 1.6), ED visits (RR = 1.4), total adverse reactions (RR = 1.4), and gastroenteritis (RR = 1.1) were reported similarly after thimerosal-containing and thimerosal-free DTaP vaccines. An association between neurodevelopmental disorders and thimerosal-containing DTaP vaccines was found, but additional studies should be conducted to confirm and extend this study.

<http://www.ncbi.nlm.nih.gov/pubmed/12773696>

Environmental exposure to mercury and its toxicopathologic implications for public health

Author information

Tchounwou PB1, Ayensu WK, Ninashvili N, Sutton D.

Cellomics and Toxicogenomics Research Laboratory
NIH Center for Environmental Health, School of Science and Technology
Jackson State University, 1400 Lynch Street, Box 18540
Jackson, Mississippi 39217, USA. paul.b.tchounwou@jsums.edu

Abstract

Mercury is a toxic and hazardous metal that occurs naturally in the earth's crust. Natural phenomena such as erosion and volcanic eruptions, and anthropogenic activities like metal smelting and industrial production and use may lead to substantial contamination of the environment with mercury. Through consumption of mercury in food, the populations of many areas, particularly in the developing world, have been confronted with catastrophic outbreaks of mercury-induced diseases and mortality. Countries such as Japan, Iraq, Ghana, the Seychelles, and the Faroe Islands have faced such epidemics, which have unraveled the insidious and debilitating nature of mercury poisoning. Its creeping neurotoxicity is highly devastating, particularly in the central and peripheral nervous systems of children. Central nervous system defects and erethism as well as arrhythmias, cardiomyopathies, and kidney damage have been associated with mercury exposure. Necrotizing bronchitis and pneumonitis arising from inhalation of mercury vapor can result in respiratory failure. Mercury is also considered a potent immunostimulant and -suppressant, depending on exposure dose and individual susceptibility, producing a number of pathologic sequelae including lymphoproliferation, hypergammaglobulinemia, and total systemic hyper- and hyporeactivities. In this review we discuss the sources of mercury and the potential for human exposure; its biogeochemical cycling in the environment; its systemic, immunotoxic, genotoxic/carcinogenic, and teratogenic health effects; and the dietary influences on its toxicity; as well as the important considerations in risk assessment and management of mercury poisoning.

<http://www.ncbi.nlm.nih.gov/pubmed/12740802>

“Its creeping neurotoxicity
is highly devastating, particularly
in the central and peripheral nervous
systems of children.”

“... the present study provides further insight into one possible mechanism by which early mercury exposures could increase the risk of autism.”

International Journal Of Toxicology • July 2003

Reduced levels of mercury in first baby haircuts of autistic children

Author information

Holmes AS1, Blaxill MF, Haley BE.

SafeMinds, Cambridge, Massachusetts, USA

Abstract

Reported rates of autism have increased sharply in the United States and the United Kingdom. One possible factor underlying these increases is increased exposure to mercury through thimerosal-containing vaccines, but vaccine exposures need to be evaluated in the context of cumulative exposures during gestation and early infancy. Differential rates of postnatal mercury elimination may explain why similar gestational and infant exposures produce variable neurological effects. First baby haircut samples were obtained from 94 children diagnosed with autism using Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM IV) criteria and 45 age- and gender-matched controls. Information on diet, dental amalgam fillings, vaccine history, Rho D immunoglobulin administration, and autism symptom severity was collected through a maternal survey questionnaire and clinical observation. Hair mercury levels in the autistic group were 0.47 ppm versus 3.63 ppm in controls, a significant difference. The mothers in the autistic group had significantly higher levels of mercury exposure through Rho D immunoglobulin injections and amalgam fillings than control mothers. Within the autistic group, hair mercury levels varied significantly across mildly, moderately, and severely autistic children, with mean group levels of 0.79, 0.46, and 0.21 ppm, respectively. Hair mercury levels among controls were significantly correlated with the number of the mothers' amalgam fillings and their fish consumption as well as exposure to mercury through childhood vaccines, correlations that were absent in the autistic group. Hair excretion patterns among autistic infants were significantly reduced relative to control. These data cast doubt on the efficacy of traditional hair analysis as a measure of total mercury exposure in a subset of the population. In light of the biological plausibility of mercury's role in neurodevelopmental disorders, the present study provides further insight into one possible mechanism by which early mercury exposures could increase the risk of autism.

<http://www.ncbi.nlm.nih.gov/pubmed/12933322>

Thimerosal induces DNA breaks, caspase-3 activation, membrane damage, and cell death in cultured human neurons and fibroblasts

Author information

Baskin DS1, Ngo H, Didenko VV.

Department of Neurosurgery
Baylor College of Medicine
6560 Fannin Suite 944
Houston, Texas 77030, USA
dbaskin@tmh.tmc.edu

Abstract

Thimerosal is an organic mercurial compound used as a preservative in biomedical preparations. Little is known about the reactions of human neuronal and skin cells to its micro- and nanomolar concentrations, which can occur after using thimerosal-containing products. A useful combination of fluorescent techniques for the assessment of thimerosal toxicity is introduced. Short-term thimerosal toxicity was investigated in cultured human cerebral cortical neurons and in normal human fibroblasts. Cells were incubated with 125-nM to 250-microM concentrations of thimerosal for 45 min to 24 h. A 4', 6-diamidino-2-phenylindole dihydrochloride (DAPI) dye exclusion test was used to identify nonviable cells and terminal transferase-based nick-end labeling (TUNEL) to label DNA damage. Detection of active caspase-3 was performed in live cell cultures using a cell-permeable fluorescent caspase inhibitor. The morphology of fluorescently labeled nuclei was analyzed. After 6 h of incubation, the thimerosal toxicity was observed at 2 microM based on the manual detection of the fluorescent attached cells and at a 1-microM level with the more sensitive GENios Plus Multi-Detection Microplate Reader with Enhanced Fluorescence. The lower limit did not change after 24 h of incubation. Cortical neurons demonstrated higher sensitivity to thimerosal compared to fibroblasts. The first sign of toxicity was an increase in membrane permeability to DAPI after 2 h of incubation with 250 microM thimerosal. A 6-h incubation resulted in failure to exclude DAPI, generation of DNA breaks, caspase-3 activation, and development of morphological signs of apoptosis. We demonstrate that thimerosal in micromolar concentrations rapidly induce membrane and DNA damage and initiate caspase-3-dependent apoptosis in human neurons and fibroblasts. We conclude that a proposed combination of fluorescent techniques can be useful in analyzing the toxicity of thimerosal.

“We demonstrate that thimerosal in micromolar concentrations rapidly induce membrane and DNA damage and initiate caspase-3-dependent apoptosis in human neurons and fibroblasts.”

“This study provides strong epidemiological evidence for a link between increasing mercury from thimerosal-containing childhood vaccines and neurodevelopment disorders and heart disease.”

Journal of American Physicians and Surgeons • Volume 8, Number 1 • Spring 2003

Thimerosal in Childhood Vaccines, Neurodevelopment Disorders, and Heart Disease in the United States

Mark R. Geier, M.D., Ph.D. David A. Geier

Abstract

In this study, we evaluated doses of mercury from thimerosal-containing childhood immunizations in comparison to US Federal Safety Guidelines and the effects of increasing doses of mercury on the incidence of neurodevelopment disorders and heart disease. This study showed that children received mercury from this source in excess of the Federal Safety Guidelines for the oral ingestion of methylmercury. Our analyses showed increasing relative risks for neurodevelopment disorders and heart disease with increasing doses of mercury. This study provides strong epidemiological evidence for a link between mercury exposure from thimerosal-containing childhood vaccines and neurodevelopment disorders.

Conclusion

This study provides strong epidemiological evidence for a link between increasing mercury from thimerosal-containing childhood vaccines and neurodevelopment disorders and heart disease. In light of voluminous literature supporting the biologic mechanisms for mercury-induced adverse reactions, the presence of amounts of mercury in thimerosal-containing childhood vaccines exceeding Federal Safety Guidelines for the oral ingestion of mercury, and previous epidemiological studies showing adverse reactions from such vaccines, a causal relationship between thimerosal-containing childhood vaccines and neurodevelopment disorders and heart disease appears to be confirmed. It is to be hoped that complete removal of thimerosal from all childhood vaccines will help to stem the tragic, apparently iatrogenic epidemic of autism and speech disorders that the United States is now facing.

Full Report

<http://www.jpands.org/vol8no1/geier.pdf>

Brain barrier systems: a new frontier in metal neurotoxicological research

Author information

Zheng W1, Aschner M, Gherzi-Egea JF.

School of Health Sciences
Purdue University
West Lafayette, IN 47907, USA
wz18@purdue.edu

Abstract

The concept of brain barriers or a brain barrier system embraces the blood-brain interface, referred to as the blood-brain barrier, and the blood-cerebrospinal fluid (CSF) interface, referred to as the blood-CSF barrier. These brain barriers protect the CNS against chemical insults, by different complementary mechanisms. Toxic metal molecules can either bypass these mechanisms or be sequestered in and therefore potentially deleterious to brain barriers. Supportive evidence suggests that damage to blood-brain interfaces can lead to chemical-induced neurotoxicities. This review article examines the unique structure, specialization, and function of the brain barrier system, with particular emphasis on its toxicological implications. Typical examples of metal transport and toxicity at the barriers, such as lead (Pb), mercury (Hg), iron (Fe), and manganese (Mn), are discussed in detail with a special focus on the relevance to their toxic neurological consequences. Based on these discussions, the emerging research needs, such as construction of the new concept of blood-brain regional barriers, understanding of chemical effect on aged or immature barriers, and elucidation of the susceptibility of tight junctions to toxicants, are identified and addressed in this newly evolving field of neurotoxicology. They represent both clear challenges and fruitful research domains not only in neurotoxicology, but also in neurophysiology and pharmacology.

<http://www.ncbi.nlm.nih.gov/pubmed/14554098>

“This review article examines the unique structure, specialization, and function of the brain barrier system, with particular emphasis on its toxicological implications. Typical examples of metal transport and toxicity at the barriers, such as ... mercury ... are discussed in detail with a special focus on the relevance to their toxic neurological consequences.”

Dose-response study of thimerosal-induced murine systemic autoimmunity

Author information

Havarinasab S1, Lambertsson L, Qvarnström J, Hultman P.

Molecular and Immunological Pathology (AIR)
Department of Molecular and Clinical Medicine
Linköping University, SE-581 85 Linköping, Sweden

Abstract

The organic compound ethylmercurithiosalicylate (thimerosal), which is primarily present in the tissues as ethylmercury, has caused illness and several deaths due to erroneous handling when used as a disinfectant or as a preservative in medical preparations. Lately, possible health effects of thimerosal in childhood vaccines have been much discussed. Thimerosal is a well-known sensitizing agent, although usually of no clinical relevance. In rare cases, thimerosal has caused systemic immune reactions including acrodynia. We have studied if thimerosal might induce the systemic autoimmune condition observed in genetically susceptible mice after exposure to inorganic mercury. A.SW mice were exposed to 1.25-40 mg thimerosal/l drinking water for 70 days. Antinucleolar antibodies, targeting the 34-kDa protein fibrillarin, developed in a dose-related pattern and first appeared after 10 days in the two highest dose groups. The lowest observed adverse effect level (LOAEL) for antifibrillarin antibodies was 2.5 mg thimerosal/l, corresponding to an absorbed dose of 147 microg Hg/kg bw and a concentration of 21 and 1.9 microg Hg/g in the kidney and lymph nodes, respectively. The same LOAEL was found for tissue immune-complex deposits. The total serum concentration of IgE, IgG1, and IgG2a showed a significant dose-related increase in thimerosal-treated mice, with a LOAEL of 5 mg thimerosal/l for IgG1 and IgE, and 20 mg thimerosal/l for IgG2a. The polyclonal B-cell activation showed a significant dose-response relationship with a LOAEL of 10 mg thimerosal/l. Therefore, thimerosal induces in genetically susceptible mice a systemic autoimmune syndrome very similar to that seen after treatment with inorganic mercury, although a higher absorbed dose of Hg is needed using thimerosal. The autoimmune syndrome induced by thimerosal is different from the weaker and more restricted autoimmune reaction observed after treatment with an equipotent dose of methylmercury.

<http://www.ncbi.nlm.nih.gov/pubmed/14736497>

“... thimerosal induces
in genetically susceptible mice
a systemic autoimmune syndrome ...”

Effect of thimerosal,
a preservative in vaccines,
on intracellular Ca²⁺ concentration
of rat cerebellar neurons

Author information

Ueha-Ishibashi T1, Oyama Y, Nakao H, Umabayashi C,
Nishizaki Y, Tatsuishi T, Iwase K, Murao K, Seo H.

Laboratory of Cellular Signaling
Faculty of Integrated Arts and Sciences
The University of Tokushima
Tokushima 770-8502, Japan

Abstract

The effect of thimerosal, an organomercurial preservative in vaccines, on cerebellar neurons dissociated from 2-week-old rats was compared with those of methylmercury using a flow cytometer with appropriate fluorescent dyes. Thimerosal and methylmercury at concentrations ranging from 0.3 to 10 microM increased the intracellular concentration of Ca²⁺ ([Ca²⁺]_i) in a concentration-dependent manner. The potency of 10 microM thimerosal to increase the [Ca²⁺]_i was less than that of 10 microM methylmercury. Their effects on the [Ca²⁺]_i were greatly attenuated, but not completely suppressed, under external Ca(2+)-free condition, suggesting a possibility that both agents increase membrane Ca²⁺ permeability and release Ca²⁺ from intracellular calcium stores. The effect of 10 microM thimerosal was not affected by simultaneous application of 30 microM L-cysteine whereas that of 10 microM methylmercury was significantly suppressed. The potency of thimerosal was similar to that of methylmercury in the presence of L-cysteine. Both agents at 1 microM or more similarly decreased the cellular content of glutathione in a concentration-dependent manner, suggesting an increase in oxidative stress. Results indicate that thimerosal exerts some cytotoxic actions on cerebellar granule neurons dissociated from 2-week-old rats and its potency is almost similar to that of methylmercury.

<http://www.ncbi.nlm.nih.gov/pubmed/14698570>

“Results indicate that thimerosal exerts some cytotoxic actions on cerebellar granule neurons ... its potency is almost similar to that of methylmercury.”

A comparative evaluation of the effects of MMR immunization and mercury doses from thimerosal-containing childhood vaccines on the population prevalence of autism

Author information

Geier DA1, Geier MR.
President, MedCon, Inc, Silver Spring, MD, USA

Abstract

BACKGROUND

The purpose of the study was to evaluate the effects of MMR immunization and mercury from thimerosal-containing childhood vaccines on the prevalence of autism.

MATERIAL/METHODS

Evaluations of the Biological Surveillance Summaries of the Centers for Disease Control and Prevention (CDC), the U.S. Department of Education datasets, and the CDC's yearly live birth estimates were undertaken.

RESULTS

It was determined that there was a close correlation between mercury doses from thimerosal-containing childhood vaccines and the prevalence of autism from the late 1980s through the mid-1990s. In contrast, there was a potential correlation between the number of primary pediatric measles-containing vaccines administered and the prevalence of autism during the 1980s. In addition, it was found that there were statistically significant odds ratios for the development of autism following increasing doses of mercury from thimerosal-containing vaccines (birth cohorts: 1985 and 1990-1995) in comparison to a baseline measurement (birth cohort: 1984). The contribution of thimerosal from childhood vaccines (>50% effect) was greater than MMR vaccine on the prevalence of autism observed in this study.

CONCLUSIONS

The results of this study agree with a number of previously published studies. These studies have shown that there is biological plausibility and epidemiological evidence showing a direct relationship between increasing doses of mercury from thimerosal-containing vaccines and neurodevelopmental disorders, and measles-containing vaccines and serious neurological disorders. It is recommended that thimerosal be removed from all vaccines, and additional research be undertaken to produce a MMR vaccine with an improved safety profile.

<http://www.ncbi.nlm.nih.gov/pubmed/14976450>

“The results of this study

agree with a number of previously published studies.

These studies have shown that there is biological plausibility

and epidemiological evidence showing a direct relationship

between increasing doses of mercury from

thimerosal-containing vaccines and neurodevelopmental

disorders, and measles-containing vaccines and serious

neurological disorders.”

Medical Hypotheses • March 2004

Thimerosal and autism? A plausible hypothesis that should not be dismissed

Author information

Blaxill MF1, Redwood L, Bernard S.

Safe Minds (Sensible Action For Ending Mercury-Induced Neurological Disorders)
14 Commerce Drive, PH Cranford, New Jersey 07016, USA
blaxill@comcast.net

Abstract

The autism-mercury hypothesis first described by Bernard et al. has generated much interest and controversy. The Institute of Medicine (IOM) reviewed the connection between mercury-containing vaccines and neurodevelopmental disorders, including autism. They concluded that the hypothesis was biologically plausible but that there was insufficient evidence to accept or reject a causal connection and recommended a comprehensive research program. Without citing new experimental evidence, a number of observers have offered opinions on the subject, some of which reject the IOM's conclusions. In a recent review, Nelson and Bauman argue that a link between the preservative thimerosal, the source of the mercury in childhood vaccines, is improbable. In their defense of thimerosal, these authors take a narrow view of the original hypothesis, provide no new evidence, and rely on selective citations and flawed reasoning. We provide evidence here to refute the Nelson and Bauman critique and to defend the autism-mercury hypothesis.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15082108>

“We provide evidence here
to refute the Nelson and Bauman critique
and to defend the autism-mercury hypothesis.”

Activation of methionine synthase
by insulin-like growth factor-1 and dopamine:
a target for neurodevelopmental toxins and thimerosal

Author information

Waly M1, Olteanu H, Banerjee R, Choi SW, Mason JB,
Parker BS, Sukumar S, Shim S, Sharma A, Benzecry JM,
Power-Charnitsky VA, Deth RC.

Department of Pharmaceutical Sciences
Northeastern University, Boston, MA 02115, USA

Abstract

Methylation events play a critical role in the ability of growth factors to promote normal development. Neurodevelopmental toxins, such as ethanol and heavy metals, interrupt growth factor signaling, raising the possibility that they might exert adverse effects on methylation. We found that insulin-like growth factor-1 (IGF-1)- and dopamine-stimulated methionine synthase (MS) activity and folate-dependent methylation of phospholipids in SH-SY5Y human neuroblastoma cells, via a PI3-kinase- and MAP-kinase-dependent mechanism. The stimulation of this pathway increased DNA methylation, while its inhibition increased methylation-sensitive gene expression. Ethanol potently interfered with IGF-1 activation of MS and blocked its effect on DNA methylation, whereas it did not inhibit the effects of dopamine. Metal ions potently affected IGF-1 and dopamine-stimulated MS activity, as well as folate-dependent phospholipid methylation: Cu(2+) promoted enzyme activity and methylation, while Cu(+), Pb(2+), Hg(2+) and Al(3+) were inhibitory. The ethyl-mercury-containing preservative thimerosal inhibited both IGF-1- and dopamine-stimulated methylation with an IC(50) of 1 nM and eliminated MS activity. Our findings outline a novel growth factor signaling pathway that regulates MS activity and thereby modulates methylation reactions, including DNA methylation. The potent inhibition of this pathway by ethanol, lead, mercury, aluminum and thimerosal suggests that it may be an important target of neurodevelopmental toxins.

<http://www.ncbi.nlm.nih.gov/pubmed/14745455>

“The potent inhibition of this pathway
by ethanol, lead, mercury, aluminum
and thimerosal suggests that it may
be an important target of
neurodevelopmental toxins.”

Amalgam studies: disregarding basic principles of mercury toxicity

Author information

Mutter J1, Naumann J, Sadaghiani C, Walach H, Drasch G.

Institute for Environmental Medicine and Hospital Epidemiology
University Hospital, Freiburg, Germany
jmutter@iuk3.ukl.uni-freiburg.de

Abstract

Dental amalgam, which has been used for over 150 years in dental practice, consists of about 50% metallic mercury. Studies on animal and humans show that mercury is continuously released from dental amalgam and absorbed by several body tissues. It is widely accepted that the main source of mercury vapor is dental amalgam and it contributes substantially to mercury load in human body tissues. There is still a controversy about the consequences of this additional mercury exposure from amalgam to human health. Many studies were performed to evaluate possible adverse effects. In this comment, these studies were analyzed with regard to their methodical quality by considering the newest findings on mercury toxicity and metabolism. In sum, a number of studies are methodically flawed drawing inaccurate conclusions as to the safety of dental amalgam.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15471104>

“Studies on animal and humans show that mercury is continuously released from dental amalgam and absorbed by several body tissues. It is widely accepted that the main source of mercury vapor is dental amalgam and it contributes substantially to mercury load in human body tissues. In sum, a number of studies are methodically flawed drawing inaccurate conclusions as to the safety of dental amalgam.”

Neurotoxic effects of postnatal thimerosal are mouse strain dependent

Author information

Hornig M1, Chian D, Lipkin WI.

Jerome L and Dawn Greene Infectious Disease Laboratory
Department of Epidemiology, Mailman School of Public Health
Columbia University, New York, NY 10032, USA
mady.hornig@columbia.edu

Abstract

The developing brain is uniquely susceptible to the neurotoxic hazard posed by mercurials. Host differences in maturation, metabolism, nutrition, sex, and autoimmunity influence outcomes. How population-based variability affects the safety of the ethylmercury-containing vaccine preservative, thimerosal, is unknown. Reported increases in the prevalence of autism, a highly heritable neuropsychiatric condition, are intensifying public focus on environmental exposures such as thimerosal. Immune profiles and family history in autism are frequently consistent with autoimmunity. We hypothesized that autoimmune propensity influences outcomes in mice following thimerosal challenges that mimic routine childhood immunizations. Autoimmune disease-sensitive SJL/J mice showed growth delay; reduced locomotion; exaggerated response to novelty; and densely packed, hyperchromic hippocampal neurons with altered glutamate receptors and transporters. Strains resistant to autoimmunity, C57BL/6J and BALB/cJ, were not susceptible. These findings implicate genetic influences and provide a model for investigating thimerosal-related neurotoxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15184908>

“These findings implicate genetic influences and provide a model for investigating thimerosal-related neurotoxicity.”

Property of thimerosal-induced decrease
in cellular content of glutathione in rat thymocytes:
a flow cytometric study with 5-chloromethylfluorescein diacetate

Author information

Ueha-Ishibashi T1, Tatsuishi T, Iwase K, Nakao H,
Umebayashi C, Nishizaki Y, Nishimura Y, Oyama Y, Hirama S, Okano Y.

Laboratory of Cellular Signaling, Faculty of Integrated Arts and Sciences
The University of Tokushima, Minami-Jyosanjima 1-1
Tokushima 770-8502, Japan

Abstract

There is a concern on the part of public health community that adverse health consequences by thimerosal, a preservative in vaccines for infants, may occur among infants during immunization schedule. Therefore, the effect of thimerosal on cellular content of glutathione was examined on thymocytes obtained from 4-week-old rats using a flow cytometer and 5-chloromethylfluorescein diacetate. Thimerosal at concentrations ranging from 1 to 10 microM reduced the cellular content of glutathione in a concentration-dependent manner, and the complete depletion of cellular glutathione was observed when the cells were treated with 30 microM thimerosal. L-Cysteine significantly attenuated the actions of thimerosal to reduce the glutathione content and to increase the intracellular Ca²⁺ concentration. Prolonged incubation (24 h) with 1-3 microM thimerosal induced the apoptosis. The cytotoxic action of thimerosal was greatly augmented when the cells suffered oxidative stress induced by H₂O₂. It may be unlikely that thimerosal exerts potent cytotoxic action under the in vivo condition because the blood concentration of thimerosal after receiving vaccines does not seem to reach micromolar range and nonprotein thiols at micromolar concentrations are present in the blood.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15251173>

“Thimerosal at concentrations ranging from 1 to 10 microM reduced the cellular content of glutathione in a concentration-dependent manner, and the complete depletion of cellular glutathione was observed when the cells were treated with 30 microM thimerosal.”

“The present study provides additional epidemiological evidence supporting previous epidemiological, clinical and experimental evidence that administration of thimerosal-containing vaccines in the United States resulted in a significant number of children developing Neurological Disorders.”

International Journal Of Toxicology • November 2004

Neurodevelopmental disorders following thimerosal-containing childhood immunizations: a follow-up analysis

Author information

Geier D1, Geier MR.
MedCon, Inc., Maryland, USA

Abstract

The authors previously published the first epidemiological study from the United States associating thimerosal from childhood vaccines with neurodevelopmental disorders (NDs) based upon assessment of the Vaccine Adverse Event Reporting System (VAERS). A number of years have gone by since their previous analysis of the VAERS. The present study was undertaken to determine whether the previously observed effect between thimerosal-containing childhood vaccines and NDs are still apparent in the VAERS as children have had a chance to further mature and potentially be diagnosed with additional NDs. In the present study, a cohort of children receiving thimerosal-containing diphtheria-tetanus-acellular pertussis (DTaP) vaccines in comparison to a cohort of children receiving thimerosal-free DTaP vaccines administered from 1997 through 2000 based upon an assessment of adverse events reported to the VAERS were evaluated. It was determined that there were significantly increased odds ratios (ORs) for autism (OR = 1.8, $p < .05$), mental retardation (OR = 2.6, $p < .002$), speech disorder (OR = 2.1, $p < .02$), personality disorders (OR = 2.6, $p < .01$), and thinking abnormality (OR = 8.2, $p < .01$) adverse events reported to the VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Potential confounders and reporting biases were found to be minimal in this assessment of the VAERS. It was observed, even though the media has reported a potential association between autism and thimerosal exposure, that the other NDs analyzed in this assessment of the VAERS had significantly higher ORs than autism following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. The present study provides additional epidemiological evidence supporting previous epidemiological, clinical and experimental evidence that administration of thimerosal-containing vaccines in the United States resulted in a significant number of children developing NDs.

<http://www.ncbi.nlm.nih.gov/pubmed/15764492>

Washington, D.C. • 2004

Vaccines And Autism

Immunization Safety Review Committee
Board on Health Promotion and Disease Prevention
Institute Of Medicine Of The National Academies
The National Academies Press

<http://www.nap.edu/read/10997/chapter/1>

“It has been estimated that about 15% of the population may show enhanced susceptibility to mercury exposure.”

“We provide evidence here to refute the Nelson and Bauman critique
and to defend the autism-mercury hypothesis.”

Medical Hypotheses • 2004

**Thimerosal and autism?
A plausible hypothesis that should not be dismissed**

Author information

Blaxill MF1, Redwood L, Bernard S.

Sensible Action For Ending Mercury-Induced Neurological Disorders
SAFE MINDS 14 Commerce Drive, PH Cranford, New Jersey 07016, USA
blaxill@comcast.net

Abstract

The autism-mercury hypothesis first described by Bernard et al. has generated much interest and controversy. The Institute of Medicine (IOM) reviewed the connection between mercury-containing vaccines and neurodevelopmental disorders, including autism. They concluded that the hypothesis was biologically plausible but that there was insufficient evidence to accept or reject a causal connection and recommended a comprehensive research program. Without citing new experimental evidence, a number of observers have offered opinions on the subject, some of which reject the IOM's conclusions. In a recent review, Nelson and Bauman argue that a link between the preservative thimerosal, the source of the mercury in childhood vaccines, is improbable. In their defense of thimerosal, these authors take a narrow view of the original hypothesis, provide no new evidence, and rely on selective citations and flawed reasoning. We provide evidence here to refute the Nelson and Bauman critique and to defend the autism-mercury hypothesis.

<http://www.ncbi.nlm.nih.gov/pubmed/15082108>

Thimerosal neurotoxicity is associated with glutathione depletion: protection with glutathione precursors

Author information

James SJ1, Slikker W 3rd, Melnyk S,
New E, Pogribna M, Jernigan S.

Department of Pediatrics
University of Arkansas for Medical Sciences and
Arkansas Children's Hospital Research Institute
Little Rock, AR 72202 USA
jamesjill@uams.edu

Abstract

Thimerosal is an antiseptic containing 49.5% ethyl mercury that has been used for years as a preservative in many infant vaccines and in flu vaccines. Environmental methyl mercury has been shown to be highly neurotoxic, especially to the developing brain. Because mercury has a high affinity for thiol (sulfhydryl (-SH)) groups, the thiol-containing antioxidant, glutathione (GSH), provides the major intracellular defense against mercury-induced neurotoxicity. Cultured neuroblastoma cells were found to have lower levels of GSH and increased sensitivity to thimerosal toxicity compared to glioblastoma cells that have higher basal levels of intracellular GSH. Thimerosal-induced cytotoxicity was associated with depletion of intracellular GSH in both cell lines. Pretreatment with 100 microM glutathione ethyl ester or N-acetylcysteine (NAC), but not methionine, resulted in a significant increase in intracellular GSH in both cell types. Further, pretreatment of the cells with glutathione ethyl ester or NAC prevented cytotoxicity with exposure to 15 microM Thimerosal. Although Thimerosal has been recently removed from most children's vaccines, it is still present in flu vaccines given to pregnant women, the elderly, and to children in developing countries. The potential protective effect of GSH or NAC against mercury toxicity warrants further research as possible adjunct therapy to individuals still receiving Thimerosal-containing vaccinations.

<http://www.ncbi.nlm.nih.gov/pubmed/15527868>

“Although Thimerosal has been recently removed from most children's vaccines, it is still present in flu vaccines given to pregnant women, the elderly, and to children in developing countries.”

Genetic influences on the retention of inorganic mercury

Author information

Custodio HM1, Harari R, Gerhardsson L, Skerfving S, Broberg K.

Department of Occupational and Environmental Medicine
Lund University Hospital, Lund, Sweden

Abstract

Mercury is eliminated as glutathione (GSH) conjugates. GSH production is mediated by glutamyl-cysteine ligase (GCL), and conjugation by glutathione S-transferases (GST). This study tested if polymorphisms in GCL and GST genes modify mercury retention in humans exposed to elemental mercury vapor. Total mercury concentrations in whole blood, plasma and urine, and genotypes for GCLC, GCLM, GSTA1, GSTM1, GSTP1, and GSTT1 were determined in 309 gold miners, gold buyers and controls. The presence of the GCLM-588T allele was associated with increased blood, plasma and urine mercury levels. These results indicate that genotypes with decreased GSH availability for mercury conjugation affect the metabolism of inorganic mercury.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16961004>

“These results indicate
that genotypes with decreased glutathione
availability for mercury conjugation
affect the metabolism of
inorganic mercury.”

A two-phased population epidemiological study of the safety of thimerosal-containing vaccines: a follow-up analysis

Author information

Geier DA1, Geier MR.
MedCon, Inc., USA

Abstract

BACKGROUND

Thimerosal is an ethylmercury-containing preservative in vaccines. Toxicokinetic studies have shown children received doses of mercury from thimerosal-containing vaccines (TCVs) that were in excess of safety guidelines. Previously, an ecological study showing a significant association between TCVs and neurodevelopmental disorders (NDs) in the US was published in this journal.

MATERIAL/METHODS

A two phased population-based epidemiological study was undertaken. Phase one evaluated reported NDs to the Vaccine Adverse Event Reporting System (VAERS) following thimerosal-containing Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccines in comparison to thimerosal-free DTaP vaccines administered from 1997 through 2001. Phase two evaluated the automated Vaccine Safety Datalink (VSD) for cumulative exposures to mercury from TCVs at 1-, 2-, 3-, and 6-months-of-age for infants born from 1992 through 1997 and the eventual risk of developing NDs.

RESULTS

Phase one showed significantly increased risks for autism, speech disorders, mental retardation, personality disorders, and thinking abnormalities reported to VAERS following thimerosal-containing DTaP vaccines in comparison to thimerosal-free DTaP vaccines. Phase two showed significant associations between cumulative exposures to thimerosal and the following types of NDs: unspecified developmental delay, tics, attention deficit disorder (ADD), language delay, speech delay, and neurodevelopmental delays in general.

CONCLUSIONS

This study showed that exposure to mercury from TCVs administered in the US was a consistent significant risk factor for the development of NDs. It is clear from these data and other recent publications linking TCVs with NDs that additional ND research should be undertaken in the context of evaluating mercury-associated exposures and thimerosal-free vaccines should be made available.

“This study showed
that exposure to mercury from
Thimerosal containing vaccines
administered in the US was a
consistent significant risk factor
for the development of NDs.”

Mitochondrial mediated thimerosal-induced apoptosis in a human neuroblastoma cell line (SK-N-SH)

Author information

Humphrey ML1, Cole MP,
Pendergrass JC, Kinningham KK.

Department of Pharmacology
Joan C. Edwards School of Medicine
Marshall University
Huntington, WV 25704-9388, USA

Abstract

Environmental exposure to mercurials continues to be a public health issue due to their deleterious effects on immune, renal and neurological function. Recently the safety of thimerosal, an ethyl mercury-containing preservative used in vaccines, has been questioned due to exposure of infants during immunization. Mercurials have been reported to cause apoptosis in cultured neurons; however, the signaling pathways resulting in cell death have not been well characterized. Therefore, the objective of this study was to identify the mode of cell death in an in vitro model of thimerosal-induced neurotoxicity, and more specifically, to elucidate signaling pathways which might serve as pharmacological targets. Within 2 h of thimerosal exposure (5 microM) to the human neuroblastoma cell line, SK-N-SH, morphological changes, including membrane alterations and cell shrinkage, were observed. Cell viability, assessed by measurement of lactate dehydrogenase (LDH) activity in the medium, as well as the 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay, showed a time- and concentration-dependent decrease in cell survival upon thimerosal exposure. In cells treated for 24 h with thimerosal, fluorescence microscopy indicated cells undergoing both apoptosis and oncosis/necrosis. To identify the apoptotic pathway associated with thimerosal-mediated cell death, we first evaluated the mitochondrial cascade, as both inorganic and organic mercurials have been reported to accumulate in the organelle. Cytochrome c was shown to leak from the mitochondria, followed by caspase 9 cleavage within 8 h of treatment. In addition, poly(ADP-ribose) polymerase (PARP) was cleaved to form a 85 kDa fragment following maximal caspase 3 activation at 24 h. Taken together these findings suggest deleterious effects on the cytoarchitecture by thimerosal and initiation of mitochondrial-mediated apoptosis.

<http://www.ncbi.nlm.nih.gov/pubmed/15869795>

“Taken together these findings suggest deleterious effects on the cytoarchitecture by thimerosal and initiation of mitochondrial-mediated apoptosis.”

Effects of thimerosal on NGF signal transduction and cell death in neuroblastoma cells

Author information

Parran DK1, Barker A, Ehrich M.

Virginia-Maryland Regional College of Veterinary Medicine
Laboratory for Neurotoxicity Studies, Virginia Tech
1 Duckpond Drive, Blacksburg, Virginia 24061-0442, USA

Abstract

Signaling through neurotrophic receptors is necessary for differentiation and survival of the developing nervous system. The present study examined the effects of the organic mercury compound thimerosal on nerve growth factor signal transduction and cell death in a human neuroblastoma cell line (SH-SY5Y cells). Following exposure to 100 ng/ml NGF and increasing concentrations of thimerosal (1 nM-10 microM), we measured the activation of TrkA, MAPK, and PKC-delta. In controls, the activation of TrkA MAPK and PKC-delta peaked after 5 min of exposure to NGF and then decreased but was still detectable at 60 min. Concurrent exposure to increasing concentrations of thimerosal and NGF for 5 min resulted in a concentration-dependent decrease in TrkA and MAPK phosphorylation, which was evident at 50 nM for TrkA and 100 nM for MAPK. Cell viability was assessed by the LDH assay. Following 24-h exposure to increasing concentrations of thimerosal, the EC50 for cell death in the presence or absence of NGF was 596 nM and 38.7 nM, respectively. Following 48-h exposure to increasing concentrations of thimerosal, the EC50 for cell death in the presence and absence of NGF was 105 nM and 4.35 nM, respectively. This suggests that NGF provides protection against thimerosal cytotoxicity. To determine if apoptotic versus necrotic cell death was occurring, oligonucleosomal fragmented DNA was quantified by ELISA. Control levels of fragmented DNA were similar in both the presence and absence of NGF. With and without NGF, thimerosal caused elevated levels of fragmented DNA appearing at 0.01 microM (apoptosis) to decrease at concentrations >1 microM (necrosis). These data demonstrate that thimerosal could alter NGF-induced signaling in neurotrophin-treated cells at concentrations lower than those responsible for cell death.

Full Report

<http://toxsci.oxfordjournals.org/content/86/1/132.long>

“These data demonstrate that thimerosal could alter NGF-induced signaling in neurotrophin-treated cells at concentrations lower than those responsible for cell death.”

The association between
genetic polymorphisms of coproporphyrinogen oxidase
and an atypical porphyrinogenic response
to mercury exposure in humans

Author information

Woods JS1, Echeverria D, Heyer NJ,
Simmonds PL, Wilkerson J, Farin FM.

Department of Environmental and Occupational Health Sciences
University of Washington, Seattle, WA 98101, USA
Battelle Centers for Public Health Research and Evaluation
Seattle, WA 98105, USA
jwoods@u.washington.edu

Abstract

Previous studies have demonstrated highly specific urinary porphyrin profile (UPP) changes in response to mercury (Hg) exposure in animals and human subjects and have defined the biochemical etiology of this effect as selective alteration of the heme pathway enzymes, uroporphyrinogen decarboxylase (UROD), and coproporphyrinogen oxidase (CPOX) by Hg in the kidney. Ongoing validation studies in a population of dental practitioners with low-level occupational Hg exposure have demonstrated the predicted UPP change among approximately 85% of subjects. This study focused on the genetic etiology of an atypical porphyrinogenic response (APR) seen among the remaining 15% of Hg-exposed subjects, characterized by excess excretion of 4- and 5-carboxyl porphyrins and also of the atypical ketoisocoporphyrin (KICP). Automated DNA-sequencing-based assays were developed to examine the 7 exons and flanking intron-exon boundaries of the CPOX gene. Among several polymorphisms identified, an A814C variant in exon 4 encoding a N272H substitution was found to be predominant among subjects with the APR. Studies suggest that this variant CPOX preferentially converts the upstream 5-carboxylporphyrin (5-CP) to KICP. By partially inhibiting the 5- to 4-decarboxylation step of UROD, Hg promotes 5-CP accumulation, accounting for excess KICP excretion and the APR in Hg-exposed subjects carrying the variant CPOX gene. This finding represents the first report of a polymorphism in a human gene that modifies the effect of Hg on a biological process. The APR might serve as a biomarker of both Hg exposure and susceptibility to Hg toxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15967199>

“This finding represents
the first report of a polymorphism
in a human gene that modifies the effect of ethyl mercury
on a biological process. The atypical porphyrinogenic
response might serve as a biomarker of both mercury
exposure and susceptibility to mercury toxicity.”

“The results indicate that methyl mercury
is not a suitable reference for risk assessment from exposure to thimerosal-derived ethyl mercury.”

Environmental Health Perspectives • August 2005

Comparison of blood and brain mercury levels in infant monkeys exposed to methylmercury or vaccines containing thimerosal

Author information

Burbacher TM1, Shen DD, Liberato N, Grant KS, Cernichiari E, Clarkson T.

Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine
University of Washington, Seattle, Washington 98195, USA
tmb@u.washington.edu

Thimerosal is a preservative that has been used in manufacturing vaccines since the 1930s. Reports have indicated that infants can receive ethylmercury (in the form of thimerosal) at or above the U.S. Environmental Protection Agency guidelines for methylmercury exposure, depending on the exact vaccinations, schedule, and size of the infant. In this study we compared the systemic disposition and brain distribution of total and inorganic mercury in infant monkeys after thimerosal exposure with those exposed to MeHg. Monkeys were exposed to MeHg (via oral gavage) or vaccines containing thimerosal (via intramuscular injection) at birth and 1, 2, and 3 weeks of age. Total blood Hg levels were determined 2, 4, and 7 days after each exposure. Total and inorganic brain Hg levels were assessed 2, 4, 7, or 28 days after the last exposure. The initial and terminal half-life of Hg in blood after thimerosal exposure was 2.1 and 8.6 days, respectively, which are significantly shorter than the elimination half-life of Hg after MeHg exposure at 21.5 days. Brain concentrations of total Hg were significantly lower by approximately 3-fold for the thimerosal-exposed monkeys when compared with the MeHg infants, whereas the average brain-to-blood concentration ratio was slightly higher for the thimerosal-exposed monkeys (3.5 +/- 0.5 vs. 2.5 +/- 0.3). A higher percentage of the total Hg in the brain was in the form of inorganic Hg for the thimerosal-exposed monkeys (34% vs. 7%). The results indicate that MeHg is not a suitable reference for risk assessment from exposure to thimerosal-derived Hg. Knowledge of the toxicokinetics and developmental toxicity of thimerosal is needed to afford a meaningful assessment of the developmental effects of thimerosal-containing vaccines.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1280342/>

Editors note: most current risk assessments of biological thimerosal (ethyl mercury) use are based on the false assumption that ethyl mercury and methyl mercury behave similarly in vivo and in vitro

Low dose mercury toxicity and human health

Author information

Zahir F1, Rizwi SJ, Haq SK, Khan RH.

Interdisciplinary Brain Research Centre
JN Medical College, AMU, Aligarh, U.P., India

Abstract

Post Minamata incident there has been awareness about mercury toxicity even among the general public. Previous researches contributed a vast amount of data regarding acute mercury exposure, but gradually information about the low dose [Ninomiya, T., Ohmori, H., Hashimoto, K., Tsuruta, K., Ekino, S., 1995. Expansion of methylmercury poisoning outside minamata: an epidemiological study on chronic methylmercury poisoning outside of Minamata. *Environ. Res.* 70 (1) 47-50; Lebel, J., Mergler, D., Lucotte, M., Amorim, M., Dolbec, J., Miranda, D., Arantes, G., Rheault, I., Pichet, P., 1996. Evidence of early nervous system dysfunction in Amazonian populations exposed to low-levels of methylmercury. *Neurotoxicology* 17 (1) 157-167] of mercury toxicity has been trickling in. With mercury contaminating rain-, ground- and sea-water no one is safe. Polluted water leads to mercury laced fish, meat and vegetable. In aquatic environments, inorganic mercury is microbiologically transformed into lipophilic organic compound 'methylmercury'. This transformation makes mercury more prone to biomagnification in food chains. Consequently, populations with traditionally high dietary intake of food originating from fresh or marine environment have highest dietary exposure to mercury. Extensive research done on locals across the globe have already established this, persons who routinely consume fish or a particular species of fish are at an increased risk of methylmercury poisoning. The easy access of the toxicant to man through multiple pathways air, water, food, cosmetic products and even vaccines increase the exposure. Foetus and children are more susceptible towards mercury toxicity. Mothers consuming diet containing mercury pass the toxicant to foetus and to infants through breast milk. Decreased performance in areas of motor function and memory has been reported among children exposed to presumably safe mercury levels. Similarly, disruption of attention, fine motor function and verbal memory was also found in adults on exposure to low mercury levels. It is an occupational hazard for dental staff, chloralkali factory workers and goldminers, etc. Mercury has been found to be a causative agent of various sorts of disorders, including neurological, nephrological, immunological, cardiac, motor, reproductive and even genetic. Recently heavy metal mediated toxicity has been linked to diseases like Alzheimer's, Parkinson's, Autism, Lupus, Amyotrophic lateral sclerosis, etc. Besides this, it poses danger to wildlife. Therefore, it becomes imperative to spread the information regarding the threat of mercury exposure amongst the scientists and masses.

“Recently heavy metal mediated toxicity has been linked to diseases like Alzheimer's, Parkinson's, Autism, Lupus, Amyotrophic lateral sclerosis, etc. Besides this, it poses danger to wildlife. Therefore, it becomes imperative to spread the information regarding the threat of mercury exposure amongst the scientists and masses.”

“Repetitive doses of thimerosal leads to neurobehavioral deteriorations ...”

Neuro Endocrinology Letters • October 2005

Mercury and autism: accelerating evidence?

Author information

Mutter J1, Naumann J, Schneider R, Walach H, Haley B.

Institute for Environmental Medicine and Hospital Epidemiology
University Hospital Freiburg, Germany
joachim.mutter@uniklinik-freiburg.de

Abstract

The causes of autism and neurodevelopmental disorders are unknown. Genetic and environmental risk factors seem to be involved. Because of an observed increase in autism in the last decades, which parallels cumulative mercury exposure, it was proposed that autism may be in part caused by mercury. We review the evidence for this proposal. Several epidemiological studies failed to find a correlation between mercury exposure through thimerosal, a preservative used in vaccines, and the risk of autism. Recently, it was found that autistic children had a higher mercury exposure during pregnancy due to maternal dental amalgam and thimerosal-containing immunoglobulin shots. It was hypothesized that children with autism have a decreased detoxification capacity due to genetic polymorphism. In vitro, mercury and thimerosal in levels found several days after vaccination inhibit methionine synthetase (MS) by 50%. Normal function of MS is crucial in biochemical steps necessary for brain development, attention and production of glutathione, an important antioxidative and detoxifying agent. Repetitive doses of thimerosal leads to neurobehavioral deteriorations in autoimmune susceptible mice, increased oxidative stress and decreased intracellular levels of glutathione in vitro. Subsequently, autistic children have significantly decreased level of reduced glutathione. Promising treatments of autism involve detoxification of mercury, and supplementation of deficient metabolites.

<http://www.ncbi.nlm.nih.gov/pubmed/16264412>

Thimerosal induces neuronal cell apoptosis by causing cytochrome c and apoptosis-inducing factor release from mitochondria

Author information

Yel L1, Brown LE, Su K, Gollapudi S, Gupta S.

Department of Medicine
University of California, Irvine, CA 92697, USA
lyel@uci.edu

Abstract

There is a worldwide increasing concern over the neurological risks of thimerosal (ethylmercury thiosalicylate) which is an organic mercury compound that is commonly used as an antimicrobial preservative. In this study, we show that thimerosal, at nanomolar concentrations, induces neuronal cell death through the mitochondrial pathway. Thimerosal, in a concentration- and time-dependent manner, decreased cell viability as assessed by calcein-ethidium staining and caused apoptosis detected by Hoechst 33258 dye. Thimerosal-induced apoptosis was associated with depolarization of mitochondrial membrane, generation of reactive oxygen species, and release of cytochrome c and apoptosis-inducing factor (AIF) from mitochondria to cytosol. Although thimerosal did not affect cellular expression of Bax at the protein level, we observed translocation of Bax from cytosol to mitochondria. Finally, caspase-9 and caspase-3 were activated in the absence of caspase-8 activation. Our data suggest that thimerosal causes apoptosis in neuroblastoma cells by changing the mitochondrial microenvironment.

<http://www.ncbi.nlm.nih.gov/pubmed/16273274>

“Our data suggest
that thimerosal causes apoptosis
in neuroblastoma cells by changing the
mitochondrial microenvironment.”

Mercury toxicity: Genetic susceptibility and synergistic effects

Boyd E. Haley, PhD

Professor and Chair • Department of Chemistry
University of Kentucky

Abstract

Mercury toxicity and intoxication (poisoning) are realities that every American needs to face. Both the Environmental Protection Agency and National Academy of Science state that between 8 to 10% of American women have mercury levels that would render any child they gave birth to neurological disorders. One of six children in the USA have a neurodevelopmental disorder according to the Centers for Disease Control and Prevention. Yet our dentistry and medicine continue to expose all patients to mercury. This article discusses the obvious sources of mercury exposures that can be easily prevented. It also points out that genetic susceptibility and exposures to other materials that synergistically enhance mercury and ethyl-mercury toxicity need to be evaluated, and that by their existence prevent the actual determination of a “safe level” of mercury exposure for all. The mercury sources we consider are from dentistry and from drugs, mainly vaccines, that, in today’s world are not only unnecessary sources, but also sources that are being increasingly recognized as being significantly deleterious to the health of many.

Excerpts

3. Synergistic effects:

Thimerosal, aluminum hydroxide and Neomycin

It is well documented in the literature that mercury toxicity is synergistic with other heavy metals such as cadmium and lead. It is also known that certain antibiotics greatly enhance the toxicity of thimerosal in ocular solutions and that antibiotics prevent test animals from effectively excreting mercury. The major known difference between males and females is their hormones. We therefore investigated the possible involvement of aluminum cation (found in vaccines), antibiotics (neomycin) and male versus female (estrogen versus testosterone) on the toxic effects of 50 nanomolar (nM) thimerosal on neurons in culture. Neurons can be cultured for 24 hours without much death (Fig. 6). Fifty nanomolar thimerosal alone (solid

circles will cause the death of about 70% of the neurons within 24 hours. The synergistic effects of aluminum, neomycin and testosterone are shown (Fig. 6) and are as follows:

Aluminum: Aluminum hydroxide alone at 500 nM showed no significant death of cells at 6 hours, and only slight toxicity over the 24-hour period. Thimerosal at 50 nM effected only a slight increase in neuron death at 6 hours. However, in the presence of 50 nM thimerosal plus 500 nM aluminum hydroxide (open triangles [Δ]), the neuronal death increases to roughly 60%, an amazing increase and clearly demonstrates the synergistic effects of other metals on mercury toxicity and certainly thimerosal toxicity.

Neomycin: At 1.75 mcg neomycin alone (solid squares) did not cause a significant increase in neuronal death after 12 hours. In the presence of 50 nM thimerosal (open squares) the rate of death at same point increased from about 40% to 60%, a 20% increase in rate of death.

4. Hormonal effects: Testosterone and Estrogen

Testosterone and estrogen-like compounds give vastly different results. Using female hormones we found them not toxic to the neurons alone and to be consistently protective against thimerosal toxicity. In fact, at high levels they could afford total protection for 24 hours against neuronal death in this test system (data not plotted). However, testosterone which appeared protective at very low levels (0.01 to 0.1 micromolar), dramatically increased neuron death at higher levels (0.5 to 1.0 micromolar). In fact, 1.0 micromolar levels of testosterone that by itself did not significantly increase neuron death (red flattened oval), within 3 hours when added with 50 nanomolar thimerosal (solid circles) caused 100% neuron death. Fifty nanomolar thimerosal at this time point did not significantly cause any cell death.

“In fact,

1.0 micromolar levels of testosterone that by itself did not significantly increase neuron death, within 3 hours when added with 50 nanomolar thimerosal caused 100% neuron death.”

Full Report

<http://www.1796kotok.com/pdfs/haley.pdf>

“... there are a number of other diseases that may have a chronic mercury toxicity component, such as Alzheimer’s disease, heart disease, obesity, ALS, asthma, and other various forms of autoimmune disorders ...”

Medical Hypotheses • 2005

The potential importance of steroids in the treatment of autistic spectrum disorders and other disorders involving mercury toxicity

Author information

Geier MR1, Geier DA.
The Genetic Centers of America, 14 Redgate Ct., Silver Spring, MD 20905, USA
mgeier@comcast.net

Abstract

Autism is a neurodevelopmental disorder that according to the Centers for Disease Control and Prevention (CDC) affects 1 in 150 children in the United States. Autism is characterized by impairments in social relatedness and communication, repetitive behaviors, abnormal movements, and sensory dysfunction. Recently emerging evidence suggests that mercury, especially from childhood vaccines, appears to be a factor in the development of the autistic disorders, and that autistic children have higher than normal body-burdens of mercury. In considering mercury toxicity, it has previously been shown that testosterone significantly potentates mercury toxicity, whereas estrogen is protective. Examination of autistic children has shown that the severity of autistic disorders correlates with the amount of testosterone present in the amniotic fluid, and an examination of a case-series of autistic children has shown that some have plasma testosterone levels that were significantly elevated in comparison neurotypical control children. A review of some of the current biomedical therapies for autistics, such as glutathione and cysteine, chelation, secretin, and growth hormone, suggests that they may in fact lower testosterone levels. We put forward the medical hypothesis that autistic disorders, in fact, represents a form of testosterone mercury toxicity, and based upon this observation, one can design novel treatments for autistics directed towards higher testosterone levels in autistic children. We suggest a series of experiments that need to be conducted in order to evaluate the exact mechanisms for mercury-testosterone toxicity, and various types of clinical manipulations that may be employed to control testosterone levels. It is hoped by devising therapies that address the steroid hormone pathways, in addition to the current treatments that successful lower heavy metal body-burdens of mercury, will work synergistically to improve clinical outcomes. In light of the fact that there are a number of other diseases that may have a chronic mercury toxicity component, such as Alzheimer’s disease, heart disease, obesity, ALS, asthma, and other various forms of autoimmune disorders, it is imperative that further research should be conducted to understand mercury-testosterone toxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/15780490>

A cascade analysis of the interaction of mercury and coproporphyrinogen oxidase (CPOX) polymorphism on the heme biosynthetic pathway and porphyrin production

Author information

Heyer NJ1, Bittner AC Jr, Echeverria D, Woods JS.

Battelle Centers for Public Health Research and Evaluation
1100 Dexter Avenue N, Suite 400, Seattle, WA 98109, USA

Abstract

Mercury (Hg) exposure in various forms remains a persistent public health concern in many parts of the world. In previous studies, we have described a biomarker of mercury exposure characterized by increased urinary concentrations of specific porphyrins, pentacarboxyporphyrin (5-CP) and coproporphyrin (4-CP), and the atypical keto-isocoproporphyrin (KICP), based on selective interference with the fifth (uroporphyrinogen decarboxylase, UROD) and sixth (coproporphyrinogen oxidase, CPOX) enzymes of the heme biosynthetic pathway. Whereas this response occurs in a predictable manner among approximately 85% of subjects with Hg exposure, an atypical porphyrinogenic response (APR) has been observed in approximately 15% of Hg-exposed persons, in which the three porphyrins that are affected by Hg, i.e., 5-CP, 4-CP and, KICP, are excreted in substantial excess of that predicted on the basis of Hg exposure alone. This APR has been attributed to a specific polymorphism in exon 4 of the CPOX gene (CPOX4). In the present study, we sought to further confirm the hypothesis that the observed changes in porphyrin excretion patterns might serve as a biomarker of Hg exposure and potential toxicity by statistically modeling the cascading effects on porphyrin concentrations within the heme biosynthetic pathway of Hg exposure and CPOX4 polymorphism in a human population with long-term occupational exposure to elemental mercury. Our results are highly consistent with this hypothesis. After controlling for precursor porphyrin concentrations, we demonstrated that 5-CP and 4-CP are independently associated with Hg concentration, while KICP is associated only with the CPOX4. An unpredicted association of Hg with heptacarboxyporphyrin (7-CP) may indicate a previously unidentified point of mercury inhibition of UROD. These findings lend further support to the proposed utility of urinary porphyrin changes as a biomarker of exposure and potential toxicity in subjects with mercury exposure. Additionally, these findings demonstrate the successful application of a computational model for characterizing complex metabolic responses and interactions associated with both toxicant exposure and genetic variation in human subjects.

“Mercury (Hg) exposure in various forms remains a persistent public health concern in many parts of the world ... these findings demonstrate the successful application of a computational model for characterizing complex metabolic responses and interactions associated with both toxicant exposure and genetic variation in human subjects.”

Metal-specific lymphocyte reactivity is downregulated after dental metal replacement

Author information

Yaqob A1, Danersund A,
Stejskal VD, Lindvall A, Hudecek R, Lindh U.

Foundation for Metal Biology, Uppsala, Sweden

Abstract

OBJECTIVES

This study was done to evaluate the results and clinical relevance of an optimized lymphocyte proliferation test, MELISA, for metal-induced inflammation in patients with CFS-like symptoms. The treatment of patients consisted of the replacement of incompatible dental materials (RID) together with supportive anti-oxidant therapy.

DESIGN OF THE STUDY

513 patients were tested by MELISA at the beginning of the study. Out of this group, 248 patients were available for follow-up MELISA after RID.

METHODS

In MELISA, lymphocytes are isolated from the blood and cultivated with different metal salts in tissue culture medium containing 10% inactivated human AB+ serum or autologous serum. After 5 days, the presence of metal-reactive lymphocytes are measured by isotope labelling of newly formed DNA in growing lymphoblasts and evaluated by calculating the Stimulation Index.

RESULTS

Nickel was the most common sensitizer, followed by inorganic mercury, thimerosal, lead, cadmium, palladium and gold. After RID treatment, a decrease of metal-specific lymphocyte responses in patients who reacted to metals at the beginning of the study could be observed. The cultivation of lymphocytes in autologous and homologous serum did not significantly affect the results. Simultaneous, the health status of patients improved as well.

CONCLUSIONS

Replacement of incompatible dental materials resulted in down-regulation of metal-induced lymphocyte sensitivity in vitro, as well as in the improvement of health status of majority of patients with unspecific CFS-like symptoms.

“Replacement of incompatible dental materials resulted in down-regulation of metal-induced lymphocyte sensitivity in vitro, as well as in the improvement of health status of majority of patients with unspecific Chronic Fatigue-like symptoms.”

Thimerosal Induces Apoptosis in a Neuroblastoma Model via the cJun N-Terminal Kinase Pathway

Author Information

Michelle L. Herdman*, Aileen Marcelo*, Ying Huang†
Richard M. Niles†, Sanjit Dhar‡ and Kinsley Kelley Kinningham*

Departments of *Pharmacology, Physiology
and Toxicology and †Biochemistry and Microbiology
Joan C. Edwards School of Medicine, Marshall University
Huntington, West Virginia 25704
‡Graduate Center for Toxicology
University of Kentucky
Lexington, Kentucky 40536
kinningham@marshall.edu.

Abstract

The cJun N-terminal kinase (JNK)-signaling pathway is activated in response to a variety of stimuli, including environmental insults, and has been implicated in neuronal apoptosis. In this study, we investigated the role that the JNK pathway plays in neurotoxicity caused by thimerosal, an ethylmercury-containing preservative. SK-N-SH cells treated with thimerosal (0–10 μ M) showed an increase in the phosphorylated (active) form of JNK and cJun with 5 and 10 μ M thimerosal treatment at 2 and 4 h. To examine activator protein-1 (AP-1) transcription, cells were transfected with a pGL2 vector containing four AP-1 consensus sequences and then treated with thimerosal (0–2.5 μ M) for 24 h. Luciferase studies showed an increase in AP-1 transcriptional activity upon thimerosal administration. To determine the components of the AP-1 complex, cells were transfected with a dominant negative to either cFos (A-Fos) or cJun (TAM67). Reporter analysis showed that TAM67, but not A-Fos, decreased AP-1 transcriptional activity, indicating a role for cJun in this pathway. To assess which components are essential to apoptosis, cells were treated with a cell-permeable JNK inhibitor II (SP600125) or transfected with TAM67, and the downstream effectors of apoptosis were analyzed. Cells pretreated with SP600125 showed decreases in activation of caspases 9 and 3, decreases in degradation of poly(ADP-ribose) polymerase (PARP), and decreased levels of proapoptotic Bim, in comparison to cells treated with thimerosal alone. However, cells transfected with TAM67 showed no changes in those same components. Taken together, these results indicate that thimerosal-induced neurotoxicity occurs through the JNK-signaling pathway, independent of cJun activation, leading ultimately to apoptotic cell death.

“Taken together,
these results indicate that thimerosal-induced
neurotoxicity occurs through the JNK-signaling
pathway, independent of cJun activation, leading
ultimately to apoptotic cell death.”

An assessment of downward trends in neurodevelopmental disorders in the USA following removal of Thimerosal from childhood vaccines

Author Information

Geier DA1, Geier MR.

Department of Biochemistry
George Washington University, Washington, DC, USA

Abstract

BACKGROUND

The US is in the midst of an epidemic of neurodevelopmental disorders (NDs). Thimerosal is an ethylmercury-containing compound added to some childhood vaccines. Several previous epidemiological studies conducted in the US have associated Thimerosal-containing vaccine (TCV) administration with NDs.

MATERIAL/METHODS

An ecological study was undertaken to evaluate NDs reported to the Vaccine Adverse Event Reporting System (VAERS) from 1991 through 2004 by date of receipt and by date of vaccine administration. The NDs examined included autism, mental retardation, and speech disorders. Statistical trend analysis was employed to evaluate the effects of removal of Thimerosal on the proportion of NDs reported to VAERS.

RESULTS

There was a peak in the proportion of ND reports received by VAERS in 2001-2002 and in the proportion of ND reports by date of vaccine administration in 1998. There were significant reductions in the proportion of NDs reported to VAERS as Thimerosal was begun to be removed from childhood vaccines in the US from mid-1999 onwards.

CONCLUSIONS

The present study provides the first epidemiological evidence showing that as Thimerosal was removed from childhood vaccines, the number of NDs has decreased in the US. The analysis techniques utilized attempted to minimize chance or bias/confounding. Additional research should be conducted to further evaluate the relationship between TCVs and NDs. This is especially true because the handling of vaccine safety data from the National Immunization Program of the CDC has been called into question by the Institute of Medicine of the National Academy of Sciences in 2005.

“The present study provides the first epidemiological evidence showing that as Thimerosal was removed from childhood vaccines, the number of neurodevelopmental disorders has decreased in the US.

A meta-analysis epidemiological assessment of neurodevelopmental disorders following vaccines administered from 1994 through 2000 in the United States

Author information

Geier DA1, Geier MR.
The Institute for Chronic Illnesses, Inc., Silver Spring, MD 20905, USA
mgeier@comcast.net

Abstract

BACKGROUND

Thimerosal is an ethylmercury-containing compound (49.6% mercury by weight) used as at the preservative level in vaccines (0.005% to 0.01%).

METHODS

Statistical modeling in a meta-analysis epidemiological assessment of the Vaccine Adverse Event Reporting System (VAERS) for neurodevelopment disorders (NDs) reported following Diphtheria-Tetanus-whole-cell-Pertussis (DTP) vaccines in comparison to Diphtheria-Tetanus-whole-cell-Pertussis-Haemophilus Influenzae Type b (DTPH) vaccines (administered: 1994-1997) and following Thimerosal-containing Diphtheria-Tetanus-acellular-Pertussis (DTaP), vaccines in comparison to Thimerosal-free DTaP vaccines (administered: 1997-2000), was undertaken.

RESULTS

Significantly increased adjusted (sex, age, vaccine type, vaccine manufacturer) risks of autism, speech disorders, mental retardation, personality disorders, thinking abnormalities, ataxia, and NDs in general, with minimal systematic error or confounding, were associated with TCV exposure.

CONCLUSION

It is clear from the results of the present epidemiological study and other recently published data associating mercury exposure with childhood NDs, additional ND research should be undertaken in the context of evaluating mercury-associated exposures, especially from Thimerosal-containing vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/16807526>

“It is clear from the results of the present epidemiological study and other recently published data associating mercury exposure with childhood neurological disorders.”

“Autism was recently associated with a urinary porphyrin pattern indicative of mercury toxicity ...”

Neurotoxicity Research • August 2006

A prospective assessment of porphyrins in autistic disorders: a potential marker for heavy metal exposure

Author information

Geier DA1, Geier MR.

The Institute for Chronic Illnesses, Silver Spring, MD 20905, USA

Abstract

Autism was recently associated with a urinary porphyrin pattern indicative of mercury toxicity in a large cohort of French children. The IRB of the Institute for Chronic Illnesses approved the present study. A total of 37 consecutive American patients ($>$ or $=$ 7 years-old) with autism spectrum disorders (ASDs) (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-DSM IV), born from 1983-1998, that presented to the Genetic Centers of America for outpatient genetic evaluations were prospectively examined for urinary porphyrin levels (LabCorp, Inc.) from June 2005-June 2006. Imaging and laboratory testing were conducted on each patient to rule-out other causal factors for their ASDs. As controls, age-, sex-, and race-matched neurotypical ASD siblings were examined. An apparent dose-response effect was observed between autism severity and increased urinary coproporphyrins. Patients with non-chelated autism (2.25-fold, 83% had levels $>$ 2 SD above the control mean) and non-chelated ASDs (2-fold, 58% had levels $>$ 2 SD above the control mean), but not patients with non-chelated pervasive developmental delay-not otherwise specified (PDD-NOS) or Asperger's disorder (1.4-fold, 46% had levels $>$ 2 SD above the control mean), had significantly increased median coproporphyrin levels versus controls. A significant increase (1.7-fold) in median coproporphyrin levels was observed among non-chelated ASD patients versus chelated ASD patients. Porphyrins should be routinely clinically measured in ASDs, and potential ASD treatments should consider monitoring porphyrin levels. Additional research should be conducted to evaluate the potential role for mercury exposure in some ASDs.

<http://www.ncbi.nlm.nih.gov/pubmed/17000470>

“Significantly increased odds ratios for autism, speech disorders, mental retardation, infantile spasms, and thinking abnormalities reported to VAERS were found following DTP vaccines in comparison to DTPH vaccines with minimal bias or systematic error.”

Journal Of Toxicology And Environmental Health Part A • August 2006

An evaluation of the effects of thimerosal on neurodevelopmental disorders reported following DTP and Hib vaccines in comparison to DTPH vaccine in the United States

Author information

Geier DA1, Geier MR.
The Genetic Centers of America, Silver Spring, Maryland 20905, USA
mgeier@comcast.net

Abstract

Thimerosal is an ethylmercury (49.55% mercury by weight) preservative historically added to some vaccines. Toxicokinetic studies showed children in the United States received doses of mercury from Thimerosal-containing vaccines (TCVs) in excess of safety guidelines. In the United States during the 1990s, diphtheria-tetanus-pertussis (DTP) and Haemophilus influenzae type b (Hib) vaccines (maximally, 50 mug mercury per joint administration) and diphtheria-tetanus-pertussis-Haemophilus influenzae type b (DTPH) vaccines (25 mug mercury per administration) were given to children in the same childhood vaccination schedule at 2, 4, 6, and 15-18 mo, so that children receiving DTP and Hib vaccines may have maximally received an additional 100 mug more mercury exposure from TCVs than children administered DTPH vaccines. A case-control epidemiological study of neurodevelopmental disorders (NDs) reported to the Vaccine Adverse Event Reporting System (VAERS) (online public access version; updated 31 August 2004) following administration of DTP vaccines in comparison DTPH vaccines manufactured by Lederle Laboratories (Pearl River, NY) from 1994 through 1998 was undertaken. Significantly increased odds ratios for autism, speech disorders, mental retardation, infantile spasms, and thinking abnormalities reported to VAERS were found following DTP vaccines in comparison to DTPH vaccines with minimal bias or systematic error. Additional ND research should be undertaken in the context of evaluating mercury-associated exposures, especially since in 2005 the Institute of Medicine issued a report calling into question handling of vaccine safety data by the National Immunization Program of the Centers for Disease Control and Prevention.

<http://www.ncbi.nlm.nih.gov/pubmed/16766480>

Thimerosal induces oxidative stress in HeLa S epithelial cells

Author information

Lee S1, Mian MF, Lee HJ, Kang CB,
Kim JS, Ryu SH, Suh PG, Kim E.

Laboratory of Toxicology
Institute of Animal Medicine
College of Veterinary Medicine
Gyeongsang National University
Gajwa-Dong, Jinju 660-701
Republic of Korea

Abstract

Thimerosal is one of the most widely used preservatives and is found in a variety of biological products, including vaccines, contact lens cleaning solutions, and cosmetics. It has been reported to have harmful effects on epithelial tissues, such as causing conjunctivitis or contact dermatitis. However, the molecular mechanism of its toxicity has not been characterized using epithelial tissues. In the present study, we report that reactive oxygen species play a key role in thimerosal-induced cytotoxicity in HeLa S epithelial cells. Thimerosal significantly reduced HeLa S cell viability and it was associated with a decrease in intracellular glutathione levels. Flow cytometric cell cycle analysis showed a marked increase in the hypodiploidic cell population, indicating apoptosis of thimerosal-treated cells. The apoptotic cell death of epithelial cells was confirmed by observing a significant increase of caspase-3 activity in the cytosolic fraction of the treated cells. Thimerosal also induced a concentration-dependent increase of genomic DNA fragmentation, a biochemical hallmark of apoptosis. Hoechst 33342 nuclear staining demonstrated apoptotic-fragmented multinuclei in thimerosal-treated cells. All the thimerosal-mediated toxic responses observed in the present study were almost completely suppressed by pretreating cells with N-acetyl-L-cysteine, a radical scavenger. Taken together, these results suggest for the first time that epithelial cytotoxicity of thimerosal is mediated by oxidative stress.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21783709>

“[thimerosal] has been reported to have harmful effects on epithelial tissues, such as causing conjunctivitis or contact dermatitis. Thimerosal also induced a concentration-dependent increase of genomic DNA fragmentation, a biochemical hallmark of apoptosis. Taken together, these results suggest for the first time that epithelial cytotoxicity of thimerosal is mediated by oxidative stress.”

“... some autism spectrum disorders may result from ... exposure to mercury.”

Neuro Endocrinology Letters • December 2006

**A clinical trial
of combined anti-androgen and anti-heavy metal therapy
in autistic disorders**

Author information

Geier DA1, Geier MR.
Institute of Chronic Illnesses, Silver Spring, MD 20905, USA

Abstract

BACKGROUND

A medical hypothesis has suggested that some autism spectrum disorders (ASDs) may result from interactions between the methionine cycle-transsulfuration and androgen pathways following exposure to mercury.

METHODS

The IRB of the Institute for Chronic Illnesses approved the present study. A novel treatment was utilized combining LUPRON (leuprolide acetate, TAP Pharmaceuticals, Inc.) and CHEMET (meso-2, 3-dimercaptosuccinic acid--DMSA, McNeil Consumer Products Company) on 11 consecutive children with ASDs.

RESULTS

A significant ($p < 0.01$) overall improvement from the 70-79th percentile of severity (median baseline score=87) at baseline to the 40-49th percentile of severity (median end of study period score=63) at the end of the study was observed for patients treated for a median of approximately 4 months. Significant improvements in sociability, cognitive awareness, behavior, and clinical symptoms/behaviors of hyperandrogenemia were also observed. Significant decreases in blood androgens and increases in urinary heavy metal concentrations were observed. Minimal drug adverse effects were found.

CONCLUSION

This study provides the first clinical evidence for the benefit that combined anti-androgen and anti-heavy metal therapy may have on some children with ASDs. Additional studies should examine androgen and heavy metal mechanisms of action in ASDs, and future ASD treatment protocols should consider androgens and heavy metals.

<http://www.ncbi.nlm.nih.gov/pubmed/17187010>

[an example of disagreement within the research community]

Critical Reviews In Toxicology • December 2006

The toxicology of mercury and its chemical compounds

Author information

Clarkson TW1, Magos L.

Department of Environmental Medicine
University of Rochester School of Medicine
New York, USA
Twc30@aol.co

Abstract

This review covers the toxicology of mercury and its compounds. Special attention is paid to those forms of mercury of current public health concern. Human exposure to the vapor of metallic mercury dates back to antiquity but continues today in occupational settings and from dental amalgam. Health risks from methylmercury in edible tissues of fish have been the subject of several large epidemiological investigations and continue to be the subject of intense debate. Ethylmercury in the form of a preservative, thimerosal, added to certain vaccines, is the most recent form of mercury that has become a public health concern. The review leads to general discussion of evolutionary aspects of mercury, protective and toxic mechanisms, and ends on a note that mercury is still an “element of mystery.”

<http://www.ncbi.nlm.nih.gov/pubmed/16973445>

Critical Reviews In Toxicology • December 2007

Comments on the article “the toxicology of mercury and its chemical compounds” by Clarkson and Magos (2006)

Author information

Mutter J1, Naumann J, Guethlin C.

University Hospital
Institute for Environmental Medicine and Hospital Epidemiology
Freiburg, Germany
joachim.mutter@uniklinik-freiburg.de

Abstract

Clarkson and Magos (2006) provide their perspectives on the toxicology of mercury vapor and dental amalgam. As scientists who are involved in preparing a German federal guideline regarding dental amalgam, we welcome additional scientific data on this issue. However, Clarkson and Magos do not present all the relevant studies in their review.

The additional data provided here show that: (a) Dental amalgam is the main source of human total mercury body burden, because individuals with amalgam have 2-12 times more mercury in their body tissues compared to individuals without amalgam; (b) there is not necessarily a correlation between mercury levels in blood, urine, or hair and in body tissues, and none of the parameters correlate with severity of symptoms; (c) the half-life of mercury deposits in brain and bone tissues could last from several years to decades, and thus mercury accumulates over time of exposure; (d) mercury, in particular mercury vapor, is known to be the most toxic nonradioactive element, and is toxic even in very low doses, and (e) some studies which conclude that amalgam fillings are safe for human beings have important methodological flaws.

Therefore, they have no value for assessing the safety of amalgam.

<http://www.ncbi.nlm.nih.gov/pubmed/17661216>

Cell death and cytotoxic effects in YAC-1 lymphoma cells following exposure to various forms of mercury

Author information

Yole M1, Wickstrom M, Blakley B.

Department of Veterinary Biomedical Sciences
Western College of Veterinary Medicine
52 Campus Drive, University of Saskatchewan
Saskatoon SK S7N 5B4, Canada
yole@sask.usask.ca

Abstract

The effects of 1 min-4 h exposures to four Hg compounds (mercuric chloride [HgCl₂], methyl mercuric chloride [CH₃HgCl], p-chloromercuribenzoate [p-CMB] and thimerosal [TMS; ethylmercurithiosalicylate]) on cell death, microtubules, actin, CD3 receptor expression, protein tyrosine phosphorylation (PTyr-P) and intracellular calcium ([Ca²⁺]_i) levels were investigated in YAC-1 lymphoma cells using flow cytometry. YOPRO-1 (YP) and propidium iodide (PI) dye uptake indicated all forms of Hg tested were toxic at concentrations ranging from 25.8-48.4 microM, with two distinct patterns of effects. Early apoptosis was prolonged for CH₃HgCl- and TMS-treated cells, with more than 50% remaining YP+/PI- after 4h. Both CH₃HgCl and TMS induced complete loss of beta-tubulin fluorescence, indicative of microtubule depolymerization and inhibition of tubulin synthesis and/or beta-tubulin degradation, while F-actin fluorescence diminished to a lesser degree and only after loss beta-tubulin. CH₃HgCl and TMS induced an almost immediate two-fold increase in CD3 fluorescence, with levels returning to baseline within minutes. With continued exposure, CD3 fluorescence was reduced to approximately 50% of baseline values. Both compounds also increased PTyr-P two- to three-fold immediately, with levels returning to baseline at 4h. Similarly, two- to three-fold increases in [Ca²⁺]_i were noted after 1 min exposure. [Ca²⁺]_i increased progressively, reaching levels five- to eight-fold greater than control values. In contrast, dye uptake was delayed with HgCl₂ and p-CMB, although cell death proceeded rapidly, with almost all non-viable cells being late apoptotic (YP+/PI+) by 4h. p-CMB produced early reductions in F-actin, and after 4h, complete loss of F-actin with only partial reduction of total beta-tubulin was seen with both p-CMB and HgCl₂. HgCl₂ reduced CD3 expression and PTyr-P slightly within minutes, while p-CMB produced similar effects on CD3 only at 4h, at which time PTyr-P was increased two- to three-fold. Both compounds increased [Ca²⁺]_i within minutes, though levels remained under twice the baseline concentration after 15 min exposure. With continued exposure, [Ca²⁺]_i increased to levels two- to five-fold greater than control values. These findings indicate the two groups of Hg compounds may induce cell death by distinct pathways, reflecting interactions with different cellular targets leading to cell death.

“These findings indicate the two groups of mercury compounds may induce cell death by distinct pathways, reflecting interactions with different cellular targets leading to cell death.”

Integrative Medicine • Vol. 6, No. 2 • April 2007

Heavy-Metal Toxicity—With Emphasis on Mercury

by John Neustadt, ND, and Steve Piezenik, MD, PhD

• Recommended Report •

http://montanaim.com/pubs/Heavy_Metals_Article.pdf

“8 of 9 patients examined were exposed to significant mercury from Thimerosal-containing biologic/vaccine preparations during their fetal/infant developmental periods, and subsequently, between 12 and 24 mo of age, these previously normally developing children suffered mercury toxic encephalopathies that manifested with clinical symptoms consistent with regressive Autistic Spectrum Disorders.”

Journal Of Toxicology And Environmental Health Part A • May 2007

A case series of children with apparent mercury toxic encephalopathies manifesting with clinical symptoms of regressive autistic disorders

Author information

Geier DA1, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA

Abstract

Impairments in social relatedness and communication, repetitive behaviors, and stereotypic abnormal movement patterns characterize autism spectrum disorders (ASDs). It is clear that while genetic factors are important to the pathogenesis of ASDs, mercury exposure can induce immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with ASDs. The Institutional Review Board of the Institute for Chronic Illnesses (Office for Human Research Protections, U.S. Department of Health and Human Services, IRB number IRB00005375) approved the present study. A case series of nine patients who presented to the Genetic Centers of America for a genetic/developmental evaluation are discussed. Eight of nine patients (one patient was found to have an ASD due to Rett's syndrome) (a) had regressive ASDs; (b) had elevated levels of androgens; (c) excreted significant amounts of mercury post chelation challenge; (d) had biochemical evidence of decreased function in their glutathione pathways; (e) had no known significant mercury exposure except from Thimerosal-containing vaccines/Rho(D)-immune globulin preparations; and (f) had alternate causes for their regressive ASDs ruled out. There was a significant dose-response relationship between the severity of the regressive ASDs observed and the total mercury dose children received from Thimerosal-containing vaccines/Rho(D)-immune globulin preparations. Based upon differential diagnoses, 8 of 9 patients examined were exposed to significant mercury from Thimerosal-containing biologic/vaccine preparations during their fetal/infant developmental periods, and subsequently, between 12 and 24 mo of age, these previously normally developing children suffered mercury toxic encephalopathies that manifested with clinical symptoms consistent with regressive ASDs. Evidence for mercury intoxication should be considered in the differential diagnosis as contributing to some regressive ASDs.

<http://www.ncbi.nlm.nih.gov/pubmed/17454560>

A prospective study of thimerosal-containing Rho(D)-immune globulin administration as a risk factor for autistic disorders

Author information

Geier DA1, Geier MR.
The Institute of Chronic Illnesses, Silver Spring, MD, USA

Abstract

BACKGROUND

This study evaluated the relationship between prenatal mercury exposure from thimerosal (49.55% mercury by weight)-containing Rho(D)-immune globulins (TCRs) and autism spectrum disorders (ASDs).

METHODS

The Institutional Review Board of the Institute for Chronic Illnesses approved the present study. A total of 53 consecutive non-Jewish Caucasian patients with ASDs (Diagnostic and statistical manual of mental disorders, fourth ed. - DSM IV) born between 1987 and 2001 who presented to the Genetic Centers of America for outpatient genetic/developmental evaluations were prospectively collected from June 1, 2005 through March 31, 2006. Imaging and laboratory testing were conducted on each patient to rule out other causal factors for their ASDs. As race-matched controls, the frequency of Rh negativity was determined from 926 non-Jewish Caucasian pregnant women who had presented for outpatient prenatal genetics care to the Genetic Centers of America between 1980 and 1989.

RESULTS

Children with ASDs (28.30%) were significantly more likely (odds ratio 2.35, 95% confidence interval 1.17-4.52, $p < 0.01$) to have Rh-negative mothers than controls (14.36%). Each ASD patient's mother was determined to have been administered a TCR during her pregnancy.

CONCLUSION

The results provide insights into the potential role prenatal mercury exposure may play in some children with ASDs.

<http://www.ncbi.nlm.nih.gov/pubmed/17674242>

“Each Autistic Spectrum Disorder patient’s mother was determined to have been administered a Thimerosal-containing vaccine during her pregnancy ... The results provide insights into the potential role prenatal mercury exposure may play in some children with Autistic Spectrum Disorders.”

Exposure to mercury
during the first six months via human milk and vaccines:
modifying risk factors

Author information

Dórea JG.

Faculty of Health Sciences
Universidade de Brasília
Brasília, Brazil

Abstract

Breastfeeding is the best natural protection infants have against morbidity and mortality, and the development of safe and effective vaccines has made it possible to immunize children against infectious disease. Both of these mechanisms for ensuring good health in children may be compromised by contact with mercury (Hg). Maternal exposure to environmental Hg during pregnancy can predispose nursing children to neurodevelopmental disorders. Despite the World Health Organization assurance that thimerosal-preserved vaccines are safe to use in infants, the United States, the European Union, and dozens of other countries have eliminated thimerosal as a vaccine preservative and stopped the immunization of children with such vaccines. Because of the increase in environmental pollution and the need to produce cheap and safe vaccines, there is a need to address the uncertainty of vaccine-ethylmercury risk of toxicity and Hg exposure during breastfeeding.

<http://www.ncbi.nlm.nih.gov/pubmed/17564957>

“Maternal exposure
to environmental mercury
during pregnancy can predispose
nursing children to
neurodevelopmental disorders.”

Hair mercury in breast-fed infants exposed to thimerosal-preserved vaccines

Author information

Marques RC1, Dórea JG, Fonseca MF, Bastos WR, Malm O.

Fundação Universidade Federal de Rondônia
Porto Velho, RO, Brazil

Abstract

Because of uncertainties associated with a possible rise in neuro-developmental deficits among vaccinated children, thimerosal-preserved vaccines have not been used since 2004 in the USA (with the exception of thimerosal-containing influenza vaccines which are routinely recommended for administration to pregnant women and children), and the EU but are widely produced and used in other countries. We investigated the impact of thimerosal on the total Hg in hair of 82 breast-fed infants during the first 6 months of life. The infants received three doses of the hepatitis-B vaccine (at birth, 1 and 6 months) and three DTP (diphtheria, tetanus, and pertussis) doses at 2, 4 and 6 months, according to the immunization schedule recommended by the Ministry of Health of Brazil. The thimerosal in vaccines provided an ethylmercury (EtHg) exposure of 25 microgHg at birth, 30, 60 and 120 days, and 50 microgHg at 180 days. The exposure to vaccine-EtHg represents 80% of that expected from total breast milk-Hg in the first month but only 40% of the expected exposure integrated in the 6 months of breastfeeding. However, the Hg exposure corrected for body weight at the day of immunization was much higher from thimerosal- EtHg (5.7 to 11.3 microgHg/kg b.w.) than from breastfeeding (0.266 microgHg/kg b.w.). While mothers showed a relative decrease (-57%) in total hair-Hg during the 6 months lactation there was substantial increase in the infant's hair-Hg (446%). We speculate that dose and parenteral mode of thimerosal-EtHg exposure modulated the relative increase in hair-Hg of breast-fed infants at 6 months of age.

<http://www.ncbi.nlm.nih.gov/pubmed/17237965>

“Because of uncertainties associated with a possible rise in neuro-developmental deficits among vaccinated children, thimerosal-preserved vaccines have not been used since 2004 in the USA (with the exception of thimerosal-containing influenza vaccines which are routinely recommended for administration to pregnant women and children) ...”

A prospective study of mercury toxicity biomarkers in autistic spectrum disorders

Author information

Geier DA1, Geier MR.

Institute of Chronic Illnesses
Silver Spring, Maryland, USA

Abstract

Porphyrins are derivatives formed in the heme synthesis pathway and porphyrins afford a measure of xenobiotic exposure. The steps in the heme pathway most vulnerable to heavy metal inhibition are uroporphyrin decarboxylase (UROD) and coproporphyrinogen oxidase (CPOX) reactions. Mercury toxicity was associated with elevations in urinary coproporphyrin (cP), pentacarboxyporphyrin (5cxP), and precoproporphyrin (prcP) (also known as keto-isocoproporphyrin) levels. Two cohorts of autistic patients in the United States and France had urine porphyrin levels associated with mercury toxicity. A prospective study of urinary porphyrin testing at LabCorp (United States) and the Laboratoire Philippe Auguste (France) involving 71 autism spectrum disorder (ASD) patients, neurotypical sibling controls, and general population controls was undertaken. ASD patients had significant elevations in urinary levels of cP, 5cxP, and prcP relative to controls, and > 50% of ASD patients had urinary cP levels more than 2 standard deviations above the mean values for neurotypical sibling controls. Significant reductions in urinary 5cxP and cP levels were observed in ASD patients following chelation. A significant correlation was found between urinary porphyrins measured at LabCorp and those measured at the Laboratoire Philippe Auguste on individual ASD patients. The established developmental neurotoxicity attributed to mercury and biochemical/genomic evidence for mercury susceptibility/toxicity in ASDs indicates a causal role for mercury. Urinary porphyrin testing is clinically available, relatively inexpensive, and noninvasive. Porphyrins need to be routinely measured in ASDs to establish if mercury toxicity is a causative factor and to evaluate the effectiveness of chelation therapy.

<http://www.ncbi.nlm.nih.gov/pubmed/17885929>

“The established developmental neurotoxicity attributed to mercury and biochemical/genomic evidence for mercury susceptibility/toxicity in Autistic Spectrum Disorders indicates a causal role for mercury”

Modeling Neurodevelopment Outcomes and Ethylmercury Exposure from Thimerosal-Containing Vaccines

Author Information

José G. Dórea*,¹ and Rejane C. Marques†

*Universidade de Brasília, Brasília, DF, Brazil

†Fundação Universidade Federal de Rondônia, Porto Velho, RO, Brazil
dorea@rudah.com.br

Dear Editor

The neurotoxic effects of ethylmercury (EtHg) accidentally consumed in Iraq were sufficient to withdraw ethylmercury-containing fungicides as seed dressing. Despite that, not only did thimerosal continue to be used in pharmaceutical preparations but also toxicological interest in EtHg-derived substances diminished considerably and was never addressed with regard to the small quantities used as a vaccine preservative. Thimerosal-containing vaccines (TCV) have no record of overt clinical neurological consequences due to EtHg, and the plausibility of subtle neurotoxic effects in children has been recognized only recently by the United States and other industrialized countries. In this context, we welcome the interesting work of Berman et al. (2008); it is clear that this assiduous study (in immunologically susceptible mice) took into consideration doses and schedules of TCV-Hg concentrations that had been used in infants in the United States. Their mice model does not, however, cover the full extent of modifying factors associated with TCV-Hg exposure in the majority of immature and newborns around the world that still have to depend on TCV.

According to Berman et al. (2008), the United States vaccination schedule exposed a total of 125 µgHg distributed at 2, 2, and 6 months through TCV (hepatitis B and DTP). This type of vaccine is no longer used in industrialized countries but it is still used all over the world. We know that thimerosal concentrations vary among brands of vaccines and also that immunization schedules vary depending on a country's health policy; not only that but new outbreaks of disease introduce additional new vaccines (which may contain thimerosal) during the first year of life. As an example, the public health services of Brazil, like other countries, still uses several brands of hepatitis B vaccine (containing thimerosal as preservative) with concentrations ranging from 12.5 to 50 µgHg per 0.5 ml shot. Another salient difference between countries that use TCV (like Brazil) and the United States is that in the former country hepatitis B inoculation starts within the first 12–24 h after birth (Marques et al., 2007) and is administered to low-birth weight ≥ 2000 g (Ministério, da Saúde, 2006) and premature babies who are also recommended a fourth shot as an additional booster (DI/DH/CVE, 2006). In such situations, not only toxicokinetics (TK) but especially toxicodynamics (TD) of EtHg are entirely different between a 1-day-old (with different stages of immaturity and birth weight) and a 60-day-old child (as modeled).

The newborn presents several physiological degrees of immaturity in the excretory system (kid-

neys and bile formation) and target organ (central nervous system, CNS) that are important modifiers of EtHg TK and TD. These features are inversely accentuated by gestational age and birth weight. Under such circumstances, unbound circulating EtHg in a newborn (and immature) may not be eliminated as fast as in a 2-month-old baby and thus will be readier to cross the more vulnerable blood-brain barrier (BBB). The newborn BBB increases in effectiveness with age; therefore, the free EtHg can more easily penetrate the immature CNS (Dorea, 2007). As a consequence, the smaller the body size and blood volume, the more altered the TD and TK of EtHg. Indeed, Stajich et al. (2000) showed that preterm infants do not metabolize Hg efficiently. Collectively, studies show that larger babies have significantly higher mean liver metallothionein than smaller babies (Dorea, 2007).

Factors associated with protein-binding capacity, excretion mechanisms, and enzyme activities are immature in the neonate and modulate differences in adverse effects between newborns and infants exposed to neurotoxic substances. During the period of immaturity, not only plasma albumin but also total protein concentrations decrease (Dorea, 2007). The best example in differences between neurotoxic effects is the type of albumin and competition for binding sites (due to increased circulatory concentrations of bilirubin). Albumin binding (to bilirubin) is less effective during the first postnatal days and, as a consequence, excess free bilirubin can cross the BBB at early stages of the postnatal CNS immaturity and cause brainstem abnormalities; albumin priming can be effective in attenuating effects caused by unbound bilirubin (Dorea, 2007).

We do not dispute the conclusions drawn by Berman et al. regarding Hg and the neurobiology of autism; however, we think it is possible to take their findings one step further in regards to thimerosal neurotoxicity. We contend that these findings are appropriate for U.S.-like scenarios (as intended by the authors) but are not sufficient to address the current TCV schedules in the majority of newborns and infants around the world. TCV are used worldwide in vaccination schedules that include more of these vaccines at an earlier age. Unfortunately, the differences that set newborns (especially low-birth-weights and prematures) apart from 2-month-old infants have not yet been modeled in experimental studies and remain neglected in TK and TD knowledge of TCV-EtHg exposure. We hope that studies like Berman et al. (2008) can inspire conventional toxicology to address uncertainties regarding current serial EtHg exposure in newborns and infants that have to take TCV.

“the hair sample analysis results offer some support for the idea that persons with autism may be less efficient and more variable at eliminating mercury from the blood.”

Journal Of Child Neurology • November 2007

Blood levels of mercury are related to diagnosis of autism: a reanalysis of an important data set

Author information

Desoto MC1, Hitlan RT.

Department of Psychology
University of Northern Iowa
Cedar Falls, Iowa 50614, USA
cathy.desoto@uni.edu

Abstract

The question of what is leading to the apparent increase in autism is of great importance. Like the link between aspirin and heart attack, even a small effect can have major health implications. If there is any link between autism and mercury, it is absolutely crucial that the first reports of the question are not falsely stating that no link occurs. We have reanalyzed the data set originally reported by Ip et al. in 2004 and have found that the original p value was in error and that a significant relation does exist between the blood levels of mercury and diagnosis of an autism spectrum disorder. Moreover, the hair sample analysis results offer some support for the idea that persons with autism may be less efficient and more variable at eliminating mercury from the blood.

<http://www.ncbi.nlm.nih.gov/pubmed/18006963>

A review of Thimerosal (Merthiolate)
and its ethylmercury breakdown product:
specific historical considerations regarding
safety and effectiveness

Author Information

Geier DA1, Sykes LK, Geier MR.
The Institute of Chronic Illnesses, Inc.
Silver Spring, Maryland, USA

Abstract

Thimerosal (Merthiolate) is an ethylmercury-containing pharmaceutical compound that is 49.55% mercury and that was developed in 1927. Thimerosal has been marketed as an antimicrobial agent in a range of products, including topical antiseptic solutions and antiseptic ointments for treating cuts, nasal sprays, eye solutions, vaginal spermicides, diaper rash treatments, and perhaps most importantly as a preservative in vaccines and other injectable biological products, including Rho(D)-immune globulin preparations, despite evidence, dating to the early 1930s, indicating Thimerosal to be potentially hazardous to humans and ineffective as an antimicrobial agent. Despite this, Thimerosal was not scrutinized as part of U.S. pharmaceutical products until the 1980s, when the U.S. Food and Drug Administration finally recognized its demonstrated ineffectiveness and toxicity in topical pharmaceutical products, and began to eliminate it from these. Ironically, while Thimerosal was being eliminated from topicals, it was becoming more and more ubiquitous in the recommended immunization schedule for infants and pregnant women. Furthermore, Thimerosal continues to be administered, as part of mandated immunizations and other pharmaceutical products, in the United States and globally. The ubiquitous and largely unchecked place of Thimerosal in pharmaceuticals, therefore, represents a medical crisis.

<http://www.ncbi.nlm.nih.gov/pubmed/18049924>

“The ubiquitous and largely unchecked
place of Thimerosal in pharmaceuticals, therefore,
represents a medical crisis.”

Neurotoxic effects of thimerosal at vaccines doses on the encephalon and development in 7 day-old hamsters

Laurente, Jonny, et al.

Objectives

To determine if thimerosal administration in amounts equivalent to vaccines content produces neurotoxic effects on the encephalon in postnatal hamsters and on experimentation animals' development.

Design

Experimental, prospective, biotapic study.

Setting

San Fernando Faculty of Medicine, Universidad Nacional Mayor de San Marcos.

Biologic material

Seven-day old hamsters.

Material

We divided 45 postnatal hamsters in three groups: group A (n = 15), group B (n = 15) and group C (n = 15). We administered three intramuscular equivalent doses of sucrose and thimerosal in 20 µL of physiological serum respectively to groups B and C on birth-days 7 (0,227 µg), 9 (0,216 µg) and 11 (0,220 µg). Group A received only 20 µL of saline solution.

Main outcome measures

Body weight, encephalon weight, hamster's stature and encephalon histopathological alterations.

Results

Anova and student t tests showed statistical significance in favor of low body weight, low encephalon weight and smaller stature in group C with respect to groups A and B hamsters (p<0,000). □2 statistical significance in relation to the presence of histopathological alterations in group C was also obtained (p<0,000). We observed greater relative risk of encephalic alterations in group C.

Conclusions

The administration of thimerosal in doses equivalent to vaccines content was associated with low corporal weight, low encephalon weight and smaller stature in postnatal hamsters. Neurotoxic effects were also produced at encephalic level, at hippocampus (regions CA1, CA3, DG), cerebral cortex and cerebellum (Purkinje cells and granuloses cells) with decrease in neuronal density, neuronal necrosis, axonal dismyelinization and gliosis. In addition, risk increase in developing any of these alterations was high in the animal group receiving thimerosal.

“The administration of thimerosal in doses equivalent to vaccines content was associated with low corporal weight, low encephalon weight and smaller stature in postnatal hamsters. Neurotoxic effects were also produced at encephalic level, at hippocampus (regions CA1, CA3, DG), cerebral cortex and cerebellum (Purkinje cells and granuloses cells) with decrease in neuronal density, neuronal necrosis, axonal dismyelinization and gliosis. In addition, risk increase in developing any of these alterations was high in the animal group receiving thimerosal.”

Mercury levels in newborns and infants after receipt of thimerosal-containing vaccines

Author information

Pichichero ME1, Gentile A, Giglio N, Umido V, Clarkson T, Cernichiari E, Zareba G, Gotelli C, Gotelli M, Yan L, Treanor J.

Department of Microbiology/Immunology, Pediatrics and Medicine
University of Rochester, Rochester, New York 14642, USA
michael_pichichero@urmc.rochester.edu

Abstract

OBJECTIVES

Thimerosal is a mercurial preservative that was widely used in multidose vaccine vials in the United States and Europe until 2001 and continues to be used in many countries throughout the world. We conducted a pharmacokinetic study to assess blood levels and elimination of ethyl mercury after vaccination of infants with thimerosal-containing vaccines.

METHODS

Blood, stool, and urine samples were obtained before vaccination and 12 hours to 30 days after vaccination from 216 healthy children: 72 newborns (group 1), 72 infants aged 2 months (group 2), and 72 infants aged 6 months (group 3). Total mercury levels were measured by atomic absorption. Blood mercury pharmacokinetics were calculated by pooling the data on the group and were based on a 1-compartment first-order pharmacokinetics model.

RESULTS

For groups 1, 2, and 3, respectively, (1) mean \pm SD weights were 3.4 \pm 0.4, 5.1 \pm 0.6, and 7.7 \pm 1.1 kg; (2) maximal mean \pm SD blood mercury levels were 5.0 \pm 1.3, 3.6 \pm 1.5, and 2.8 \pm 0.9 ng/mL occurring at 0.5 to 1 day after vaccination; (3) maximal mean \pm SD stool mercury levels were 19.1 \pm 11.8, 37.0 \pm 27.4, and 44.3 \pm 23.9 ng/g occurring on day 5 after vaccination for all groups; and (4) urine mercury levels were mostly nondetectable. The blood mercury half-life was calculated to be 3.7 days and returned to prevaccination levels by day 30.

CONCLUSIONS

The blood half-life of intramuscular ethyl mercury from thimerosal in vaccines in infants is substantially shorter than that of oral methyl mercury in adults. Increased mercury levels were detected in stools after vaccination, suggesting that the gastrointestinal tract is involved in ethyl mercury elimination. Because of the differing pharmacokinetics of ethyl and methyl mercury, exposure guidelines based on oral methyl mercury in adults may not be accurate for risk assessments in children who receive thimerosal-containing vaccines.

“Because of the differing pharmacokinetics of ethyl and methyl mercury, exposure guidelines based on oral methyl mercury in adults may not be accurate for risk assessments in children who receive thimerosal-containing vaccines.”

Thiol-modulated mechanisms of the cytotoxicity of thimerosal and inhibition of DNA topoisomerase II alpha

Author information

Wu X1, Liang H, O'Hara KA,
Yalowich JC, Hasinoff BB.

Faculty of Pharmacy
University of Manitoba
50 Sifton Road, Winnipeg
Manitoba, R3T 2N2, Canada

Abstract

Thimerosal is an organic mercury compound that is widely used as a preservative in vaccines and other solution formulations. The use of thimerosal has caused concern about its ability to cause neurological abnormalities due to mercury accumulation during a normal schedule of childhood vaccinations. While the chemistry and the biological effects of methylmercury have been well-studied, those of thimerosal have not. Thimerosal reacted rapidly with cysteine, GSH, human serum albumin, and single-stranded DNA to form ethylmercury adducts that were detectable by mass spectrometry. These results indicated that thimerosal would be quickly metabolized in vivo because of its reactions with protein and nonprotein thiols. Thimerosal also potently inhibited the decatenation activity of DNA topoisomerase II alpha, likely through reaction with critical free cysteine thiol groups. Thimerosal, however, did not act as a topoisomerase II poison and the lack of cross-resistance with a K562 cell line with a decreased level of topoisomerase II alpha (K/VP.5 cells) suggested that inhibition of topoisomerase II alpha was not a significant mechanism for the inhibition of cell growth. Depletion of intracellular GSH with buthionine sulfoximine treatment greatly increased the K562 cell growth inhibitory effects of thimerosal, which showed that intracellular glutathione had a major role in protecting cells from thimerosal. Pretreatment of thimerosal with glutathione did not, however, change its K562 cell growth inhibitory effects, a result consistent with the rapid exchange of the ethylmercury adduct among various thiol-containing cellular reactants. Thimerosal-induced single and double strand breaks in K562 cells were consistent with a rapid induction of apoptosis. In conclusion, these studies have elucidated some of the chemistry and biological activities of the interaction of thimerosal with topoisomerase II alpha and protein and nonprotein thiols and with DNA.

<http://www.ncbi.nlm.nih.gov/pubmed/18197631>

“Thimerosal-induced single and double strand breaks in K562 cells were consistent with a rapid induction of apoptosis. In conclusion, these studies have elucidated some of the chemistry and biological activities of the interaction of thimerosal with topoisomerase II alpha and protein and nonprotein thiols and with DNA.”

“This study associates Thimerosal-containing Rho(D) immune globulins exposure with some Neurodevelopmental Disorders in children.”

Neuro Endocrinology Letters • April 2008

Neurodevelopmental disorders, maternal Rh-negativity, and Rho(D) immune globulins: a multi-center assessment

Author information

Geier DA1, Mumper E, Gladfelter B, Coleman L, Geier MR.
The Institute of Chronic Illnesses, Inc., Silver Spring, MD 20905, USA

Abstract

BACKGROUND

Many formulations of Thimerosal (49.55% mercury by weight)-containing Rho(D) immune globulins (TCRs) were routinely administered to Rh-negative mothers in the US prior to 2002.

OBJECTIVES

It was hypothesized: (1) if prenatal Rho(D)-immune globulin preparation exposure was a risk factor for neurodevelopmental disorders (NDs) then more children with NDs would have Rh-negative mothers compared to controls; and (2) if Thimerosal in the Rho(D)-immune globulin preparations was the ingredient associated with NDs, following the removal of Thimerosal from all manufactured Rho(D)-immune globulin preparations from 2002 in the US the frequency of maternal Rh-negativity among children with NDs should be similar to control populations.

METHODS

Maternal Rh-negativity was assessed at two sites (Clinic A-Lynchburg, VA; Clinic B-Rockville and Baltimore, MD) among 298 Caucasian children with NDs and known Rh-status. As controls, maternal Rh-negativity frequency was determined from 124 Caucasian children (born 1987-2001) without NDs at Clinic A, and the Rh-negativity frequency was determined from 1,021 Caucasian pregnant mothers that presented for prenatal genetic care at Clinic B (1980-1989). Additionally, 22 Caucasian patients with NDs born from 2002 onwards (Clinics A and B) were assessed for maternal Rh-negativity.

RESULTS

There were significant and comparable increases in maternal Rh-negativity among children with NDs (Clinic: A=24.2%), autism spectrum disorders (Clinic: A=28.3%, B=25.3%), and attention-deficit-disorder/attention-deficit-hyperactivity-disorder (Clinic: A=26.3%) observed at both clinics in comparison to both control groups (Clinic: A=12.1%, B=13.9%) employed. Children with NDs born post-2001 had a maternal Rh-negativity frequency (13.6%) similar to controls.

CONCLUSION

This study associates TCR exposure with some NDs in children.

<http://www.ncbi.nlm.nih.gov/pubmed/18404135>

Thimerosal exposure in infants
and neurodevelopmental disorders:
an assessment of computerized medical records
in the Vaccine Safety Datalink

Author information

Young HA1, Geier DA, Geier MR.

The George Washington University School of Public Health and Health Services
Department of Epidemiology and Biostatistics, United States

Abstract

The study evaluated possible associations between neurodevelopmental disorders (NDs) and exposure to mercury (Hg) from Thimerosal-containing vaccines (TCVs) by examining the automated Vaccine Safety Datalink (VSD). A total of 278,624 subjects were identified in birth cohorts from 1990-1996 that had received their first oral polio vaccination by 3 months of age in the VSD. The birth cohort prevalence rate of medically diagnosed International Classification of Disease, 9th revision (ICD-9) specific NDs and control outcomes were calculated. Exposures to Hg from TCVs were calculated by birth cohort for specific exposure windows from birth-7 months and birth-13 months of age. Poisson regression analysis was used to model the association between the prevalence of outcomes and Hg doses from TCVs. Consistent significantly increased rate ratios were observed for autism, autism spectrum disorders, tics, attention deficit disorder, and emotional disturbances with Hg exposure from TCVs. By contrast, none of the control outcomes had significantly increased rate ratios with Hg exposure from TCVs. Routine childhood vaccination should be continued to help reduce the morbidity and mortality associated with infectious diseases, but efforts should be undertaken to remove Hg from vaccines. Additional studies should be conducted to further evaluate the relationship between Hg exposure and NDs.

<http://www.ncbi.nlm.nih.gov/pubmed/18482737>

“Consistent significantly increased rate ratios were observed for autism, autism spectrum disorders, tics, attention deficit disorder, and emotional disturbances with ethyl mercury exposure from thimerosal containing vaccines.”

A comprehensive review of mercury provoked autism

Author information

Geier DA1, King PG, Sykes LK, Geier MR.

The Institute of Chronic Illnesses, Silver Spring, MD, USA
mgeier@comcast.net

Abstract

Emerging evidence supports the theory that some autism spectrum disorders (ASDs) may result from a combination of genetic/biochemical susceptibility, specifically a reduced ability to excrete mercury (Hg), and exposure to Hg at critical developmental periods. Elemental/inorganic Hg is released into the air/water where it becomes methylated and accumulates in animal tissues. The US population is primarily exposed to methyl-Hg by fish consumption. In addition, many pharmaceuticals have been, and some continue to be, a ubiquitous source of danger because they contain mercurials. Mercurials may be found in drugs for the eye, ear, nose, throat, and skin; in bleaching creams; as preservatives in cosmetics, tooth pastes, lens solutions, vaccines, allergy test and immunotherapy solutions; in antiseptics, disinfectants, and contraceptives; in fungicides and herbicides; in dental fillings and thermometers; and many other products. Hg has been found to cause immune, sensory, neurological, motor, and behavioural dysfunctions similar to traits defining/associated with ASDs, and that these similarities extend to neuroanatomy, neurotransmitters, and biochemistry. Furthermore, a review of molecular mechanisms indicates that Hg exposure can induce death, disorganization and/or damage to selected neurons in the brain similar to that seen in recent ASD brain pathology studies, and this alteration may likely produce the symptoms by which ASDs are diagnosed. Finally, a review of treatments suggests that ASD patients who undergo protocols to reduce Hg and/or its effects show significant clinical improvements in some cases. In conclusion, the overwhelming preponderance of the evidence favours acceptance that Hg exposure is capable of causing some ASDs.

<http://www.ncbi.nlm.nih.gov/pubmed/19106436>

“In conclusion,
the overwhelming preponderance of the evidence
favours acceptance that ethyl mercury exposure
is capable of causing some Autistic Spectrum Disorders.”

A possible central mechanism in autism spectrum disorders, part 1

Author information

Blaylock RL.

Belhaven College
Jackson, Mississippi, USA

Abstract

The autism spectrum disorders (ASD) are a group of related neurodevelopmental disorders that have been increasing in incidence since the 1980s. Despite a considerable amount of data being collected from cases, a central mechanism has not been offered. A careful review of ASD cases discloses a number of events that adhere to an immunoexcitotoxic mechanism. This mechanism explains the link between excessive vaccination, use of aluminum and ethylmercury as vaccine adjuvants, food allergies, gut dysbiosis, and abnormal formation of the developing brain. It has now been shown that chronic microglial activation is present in autistic brains from age 5 years to age 44 years. A considerable amount of evidence, both experimental and clinical, indicates that repeated microglial activation can initiate priming of the microglia and that subsequent stimulation can produce an exaggerated microglial response that can be prolonged. It is also known that one phenotypic form of microglia activation can result in an outpouring of neurotoxic levels of the excitotoxins, glutamate and quinolinic acid. Studies have shown that careful control of brain glutamate levels is essential to brain pathway development and that excesses can result in arrest of neural migration, as well as dendritic and synaptic loss. It has also been shown that certain cytokines, such as TNF-alpha, can, via its receptor, interact with glutamate receptors to enhance the neurotoxic reaction. To describe this interaction I have coined the term immunoexcitotoxicity, which is described in this article.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19043938>

“This mechanism explains the link between excessive vaccination, use of aluminum and ethylmercury as vaccine adjuvants, food allergies, gut dysbiosis, and abnormal formation of the developing brain.”

Kawasaki's disease, acrodynia, and mercury

Author information

Mutter JI, Yeter D.

Department of Environmental and Complementary Medicine
Salusmed Medical Center, Wieslstrasse 34,
CH - 8267 Berlingen, Switzerland
jo.mutter@web.de

Abstract

A superantigen or autoimmunity has been hypothesized to be the main cause of the Kawasaki's Disease but the etiology is unknown. Medical literature, epidemiological findings, and some case reports have suggested that mercury may play a pathogenic role. Several patients with Kawasaki's Disease have presented with elevated urine mercury levels compared to matched controls. Most symptoms and diagnostic criteria which are seen in children with acrodynia, known to be caused by mercury, are similar to those seen in Kawasaki's Disease. Genetic depletion of glutathione S-transferase, a susceptibility marker for Kawasaki's Disease, is known to be also a risk factor for acrodynia and may also increase susceptibility to mercury. Coinciding with the largest increase (1985-1990) of thimerosal (49.6% ethyl mercury) in vaccines, routinely given to infants in the U.S. by 6 months of age (from 75microg to 187.5microg), the rates of Kawasaki's Disease increased ten times, and, later (1985-1997), by 20 times. Since 1990 88 cases of patients developing Kawasaki's Disease some days after vaccination have been reported to the Centers of Disease Control (CDC) including 19% manifesting symptoms the same day. The presented pathogenetic model may lead to new preventive- and therapeutic strategies for Kawasaki's disease.

<http://www.ncbi.nlm.nih.gov/pubmed/19075648>

“Coinciding with the largest increase (1985-1990) of thimerosal in vaccines, routinely given to infants in the U.S. by 6 months of age (from 75microg to 187.5microg), the rates of Kawasaki's Disease increased ten times, and, later (1985-1997), by 20 times. Since 1990 eighty-eight cases of patients developing Kawasaki's Disease some days after vaccination have been reported to the Centers of Disease Control (CDC) including 19% manifesting symptoms the same day.”

An investigation of porphyrinuria in Australian children with autism

Author information

Austin DW1, Shandley K.

Swinburne Autism Bio-Research Initiative (SABRI)
Faculty of Life and Social Sciences, Swinburne University of Technology
Melbourne, Australia
daustin@swin.edu.au

Abstract

Two recent studies, from France (Nataf et al., 2006) and the United States (Geier & Geier, 2007), identified atypical urinary porphyrin profiles in children with an autism spectrum disorder (ASD). These profiles serve as an indirect measure of environmental toxicity generally, and mercury (Hg) toxicity specifically, with the latter being a variable proposed as a causal mechanism of ASD (Bernard et al., 2001; Mutter et al., 2005). To examine whether this phenomenon occurred in a sample of Australian children with ASD, an analysis of urinary porphyrin profiles was conducted. A consistent trend in abnormal porphyrin levels was evidenced when data was compared with those previously reported in the literature. The results are suggestive of environmental toxic exposure impairing heme synthesis. Three independent studies from three continents have now demonstrated that porphyrinuria is concomitant with ASD, and that Hg may be a likely xenobiotic to produce porphyrin profiles of this nature.

<http://www.ncbi.nlm.nih.gov/pubmed/18704827>

“These profiles serve as an indirect measure of environmental toxicity generally, and mercury toxicity specifically, with the latter being a variable proposed as a causal mechanism of Autistic Spectrum Disorder (Bernard et al., 2001; Mutter et al., 2005).”

“... present observations are compatible with increased oxidative stress and a decreased detoxification capacity, particularly of mercury, in patients diagnosed with Autistic Spectrum Disorders.”

Neurochemical Research • February 2009

A prospective study of transsulfuration biomarkers in autistic disorders

Author information

Geier DA1, Kern JK, Garver CR, Adams JB, Audhya T, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA

Abstract

The goal of this study was to evaluate transsulfuration metabolites in participants diagnosed with autism spectrum disorders (ASDs). Transsulfuration metabolites, including: plasma reduced glutathione (GSH), plasma oxidized glutathione (GSSG), plasma cysteine, plasma taurine, plasma sulfate, and plasma free sulfate among participants diagnosed with ASDs (n = 38) in comparison to age-matched neurotypical controls were prospectively evaluated. Testing was conducted using Vitamin Diagnostics, Inc. (CLIA-approved). Participants diagnosed with ASDs had significantly ($P < 0.001$) decreased plasma reduced GSH, plasma cysteine, plasma taurine, plasma sulfate, and plasma free sulfate relative to controls. By contrast, participants diagnosed with ASDs had significantly ($P < 0.001$) increased plasma GSSG relative to controls. The present observations are compatible with increased oxidative stress and a decreased detoxification capacity, particularly of mercury, in patients diagnosed with ASDs. Patients diagnosed with ASDs should be routinely tested to evaluate transsulfuration metabolites, and potential treatment protocols should be evaluated to potentially correct the transsulfuration abnormalities observed.

<http://www.ncbi.nlm.nih.gov/pubmed/18612812>

Gender-selective toxicity of thimerosal

Author information

Branch DR

Departments of Medicine and Laboratory Medicine and Pathobiology
University of Toronto, Ontario, Canada
don.branch@utoronto.ca

Abstract

A recent report shows a correlation of the historical use of thimerosal in therapeutic immunizations with the subsequent development of autism; however, this association remains controversial. Autism occurs approximately four times more frequently in males compared to females; thus, studies of thimerosal toxicity should take into consideration gender-selective effects. The present study was originally undertaken to determine the maximum tolerated dose (MTD) of thimerosal in male and female CD1 mice. However, during the limited MTD studies, it became apparent that thimerosal has a differential MTD that depends on whether the mouse is male or female. At doses of 38.4-76.8mg/kg using 10% DMSO as diluent, seven of seven male mice compared to zero of seven female mice tested succumbed to thimerosal. Although the thimerosal levels used were very high, as we were originally only trying to determine MTD, it was completely unexpected to observe a difference of the MTD between male and female mice. Thus, our studies, although not directly addressing the controversy surrounding thimerosal and autism, and still preliminary due to small numbers of mice examined, provide, nevertheless, the first report of gender-selective toxicity of thimerosal and indicate that any future studies of thimerosal toxicity should take into consideration gender-specific differences.

<http://www.ncbi.nlm.nih.gov/pubmed/18771903>

“Thus, our studies, although not directly addressing the controversy surrounding thimerosal and autism, and still preliminary due to small numbers of mice examined, provide, nevertheless, the first report of gender-selective toxicity of thimerosal and indicate that any future studies of thimerosal toxicity should take into consideration gender-specific differences.”

[autism occurs at a 4-1 ratio for boys to girls. Four boys to every one girl are damaged with autism]

Proximity to point sources of environmental mercury release as a predictor of autism prevalence

Author information

Palmer RF1, Blanchard S, Wood R.

University of Texas Health Science Center
San Antonio Department of Family and Community Medicine
7703 Floyd Curl Drive, San Antonio Texas
Mail Code 7794, TX 78229-3900, USA
palmerr@uthscsa.edu

Abstract

The objective of this study was to determine if proximity to sources of mercury pollution in 1998 were related to autism prevalence in 2002. Autism count data from the Texas Educational Agency and environmental mercury release data from the Environmental Protection Agency were used. We found that for every 1000 pounds of industrial release, there was a corresponding 2.6% increase in autism rates ($p < .05$) and a 3.7% increase associated with power plant emissions ($P < .05$). Distances to these sources were independent predictors after adjustment for relevant covariates. For every 10 miles from industrial or power plant sources, there was an associated decreased autism Incident Risk of 2.0% and 1.4%, respectively ($p < .05$). While design limitations preclude interpretation of individual risk, further investigations of environmental risks to child development issues are warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/18353703>

“We found that for every 1000 pounds of industrial release, there was a corresponding 2.6% increase in autism rates ($p < .05$) and a 3.7% increase associated with power plant emissions ($P < .05$). For every 10 miles from industrial or power plant sources, there was an associated decreased autism Incident Risk of 2.0% and 1.4%, respectively ($p < .05$).”

Biomarkers of environmental toxicity and susceptibility in autism

Author information

Geier DA1, Kern JK, Garver CR, Adams JB, Audhya T, Nataf R, Geier MR.

Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA

Abstract

Autism spectrum disorders (ASDs) may result from a combination of genetic/biochemical susceptibilities in the form of a reduced ability to excrete mercury and/or increased environmental exposure at key developmental times. Urinary porphyrins and transsulfuration metabolites in participants diagnosed with an ASD were examined. A prospective, blinded study was undertaken to evaluate a cohort of 28 participants with an ASD diagnosis for Childhood Autism Rating Scale (CARS) scores, urinary porphyrins, and transsulfuration metabolites. Testing was conducted using Vitamin Diagnostics, Inc. (CLIA-approved) and Laboratoire Philippe Auguste (ISO-approved). Participants with severe ASDs had significantly increased mercury intoxication-associated urinary porphyrins (pentacarboxyporphyrin, precoproporphyrin, and coproporphyrin) in comparison to participants with mild ASDs, whereas other urinary porphyrins were similar in both groups. Significantly decreased plasma levels of reduced glutathione (GSH), cysteine, and sulfate were observed among study participants relative to controls. In contrast, study participants had significantly increased plasma oxidized glutathione (GSSG) relative to controls. Mercury intoxication-associated urinary porphyrins were significantly correlated with increasing CARS scores and GSSG levels, whereas other urinary porphyrins did not show these relationships. The urinary porphyrin and CARS score correlations observed among study participants suggest that mercury intoxication is significantly associated with autistic symptoms. The transsulfuration abnormalities observed among study participants indicate that mercury intoxication was associated with increased oxidative stress and decreased detoxification capacity.

<http://www.ncbi.nlm.nih.gov/pubmed/18817931>

“The urinary porphyrin and CARS score correlations observed among study participants suggest that mercury intoxication is significantly associated with autistic symptoms.”

Mitochondrial dysfunction, impaired oxidative-reduction activity, degeneration, and death in human neuronal and fetal cells induced by low-level exposure to thimerosal and other metal compounds

Author information

Geier DA1, King PG2, Geier MR3.

1. Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA
2. CoMeD, Inc., Silver Spring, Maryland, USA
3. The Genetic Centers of America, Silver Spring, Maryland, USA

Abstract

Thimerosal (ethylmercurithiosalicylic acid), an ethylmercury (EtHg)-releasing compound (49.55% mercury (Hg)), was used in a range of medical products for more than 70 years. Of particular recent concern, routine administering of Thimerosal-containing biologics/childhood vaccines have become significant sources of Hg exposure for some fetuses/infants. This study was undertaken to investigate cellular damage among in vitro human neuronal (SH-SY-5Y neuroblastoma and 1321N1 astrocytoma) and fetal (nontransformed) model systems using cell vitality assays and microscope-based digital image capture techniques to assess potential damage induced by Thimerosal and other metal compounds (aluminum (Al) sulfate, lead (Pb)(II) acetate, methylmercury (MeHg) hydroxide, and mercury (Hg)(II) chloride) where the cation was reported to exert adverse effects on developing cells. Thimerosal-associated cellular damage was also evaluated for similarity to pathophysiological findings observed in patients diagnosed with autistic disorders (ADs). Thimerosal-induced cellular damage as evidenced by concentration- and time-dependent mitochondrial damage, reduced oxidative-reduction activity, cellular degeneration, and cell death in the in vitro human neuronal and fetal model systems studied. Thimerosal at low nanomolar (nM) concentrations induced significant cellular toxicity in human neuronal and fetal cells. Thimerosal-induced cytotoxicity is similar to that observed in AD pathophysiologic studies. Thimerosal was found to be significantly more toxic than the other metal compounds examined. Future studies need to be conducted to evaluate additional mechanisms underlying Thimerosal-induced cellular damage and assess potential co-exposures to other compounds that may increase or decrease Thimerosal-mediated toxicity.

“Thimerosal at low nanomolar concentrations induced significant cellular toxicity in human neuronal and fetal cells. Thimerosal-induced cytotoxicity is similar to that observed in Autistic Disorder pathophysiologic studies. Thimerosal was found to be significantly more toxic than the other metal compounds examined.”

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3924342/>

Neonate exposure to thimerosal mercury from hepatitis B vaccines

Author information

Dórea JG1, Marques RC, Brandão KG.

Universidade de Brasília, DF, Brazil
dorea@rudah.com.br

Abstract

Infant exposure to ethylmercury (EtHg) has not only increased but is starting earlier as a result of the current immunization schedule that uses thimerosal-containing vaccines (TCVs). Although vaccination schedule varies considerably between countries, infants in less-developed countries continue to be exposed to EtHg derived from more affordable TCVs. We studied the exposure of newborns to EtHg from hepatitis B vaccines; hospital records (21,685) were summarized for the years 2001 to 2005 regarding date of birth, vaccination date, and birth weight. Most of the vaccinations occurred in the first 24 hours postdelivery; over the 5 years, there was an increase in vaccinations within hours of birth (same day), from 7.4% (2001) to 87.8% (2005). Nearly 94.6% of infants are now being vaccinated within the first 24 hours. Range of mercury exposure spread from 4.2 to 21.1 microg mercury/kg body weight for those receiving TCVs with the highest thimerosal concentration; these exposure levels are conservative for 2% of children receiving vaccines within 2 to 3 postnatal days, when they are still going through physiological postnatal weight loss. Because of the particular timing (transitioning from in utero to ex utero metabolism) and specific aspects of exposure (i.e., parenteral mode, bypassing gastroenteric barriers) and dose (related to vaccine manufacturer and with variation in birth weight), this study reveals critical issues that can modulate toxicokinetics and toxicodynamics of organomercurials in neonates.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19283656>

“Infant exposure to ethylmercury (EtHg) has not only increased but is starting earlier as a result of the current immunization schedule that uses thimerosal-containing vaccines (TCVs) ... this study reveals critical issues that can modulate toxicokinetics and toxicodynamics of organomercurials in neonates.”

Increase in intracellular Zn²⁺ concentration
by thimerosal in rat thymocytes:
intracellular Zn²⁺ release induced by oxidative stress

Author information

Hashimoto E1, Oyama TB, Oyama K, Nishimura Y,
Oyama TM, Ueha-Ishibashi T, Okano Y, Oyama Y.

Laboratory of Cellular Signaling
Faculty of Integrated Arts and Sciences
The University of Tokushima
Tokushima 770-8502, Japan

Abstract

Thimerosal (TMR), an ethylmercury-containing preservative in pharmaceutical products, was recently reported to increase intracellular Zn(2+) concentration. Therefore, some health concerns about the toxicity of TMR remain because of physiological and pathological roles of Zn(2+). To reveal the property of TMR-induced increase in intracellular Zn(2+) concentration, the effect of TMR on FluoZin-3 fluorescence, an indicator of intracellular Zn(2+), of rat thymocytes was examined. TMR at concentrations ranging from 0.3 microM to 10 microM increased the intensity of FluoZin-3 fluorescence in a concentration-dependent manner under external Ca(2+)- and Zn(2+)-free condition. The threshold concentration was 0.3-1 microM. The increase in the intensity was significant when TMR concentration was 1 microM or more. N,N,N',N'-Tetrakis(2-pyridylmethyl)ethylenediamine (TPEN), a chelator for intracellular Zn(2+), completely attenuated the TMR-induced augmentation of FluoZin-3 fluorescence. Hydrogen peroxide (H(2)O(2)) and N-ethylmaleimide, reducing cellular thiol content, significantly increased FluoZin-3 fluorescence intensity and decreased 5-chloromethylfluorescein (5-CMF) fluorescence intensity, an indicator for cellular thiol. The correlation coefficient between TMR-induced augmentation of FluoZin-3 fluorescence and attenuation of 5-CMF fluorescence was -0.882. TMR also attenuated the 5-CMF fluorescence in the presence of TPEN. Simultaneous application of H(2)O(2) and TMR synergistically augmented the FluoZin-3 fluorescence. It is suggested that TMR increases intracellular Zn(2+) concentration via decreasing cellular thiol content.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19497362>

“It is suggested that Thimerosal
increases intracellular Zn(2+) concentration
via decreasing cellular thiol content.”

Assessment of chronic mercury exposure
within the U.S. population,
National Health and Nutrition Examination Survey
1999–2006

Author information

Laks DR.

Mental Retardation Research Center
David Geffen School of Medicine at UCLA
635 Charles E. Young Dr. South
Neuroscience Research Bldg., Room 379 (lab)
Los Angeles, CA 90095-7332, USA
dlaks@mednet.ucla.edu

Abstract

The purpose of this study was to assess chronic mercury exposure within the US population. Time trends were analyzed for blood inorganic mercury (I-Hg) levels in 6,174 women, ages 18-49, in the NHANES, 1999-2006 data sets. Multivariate logistic regression distinguished a significant, direct correlation within the US population between I-Hg detection and years since the start of the survey (OR = 1.49, $P < 0.001$). Within this population, I-Hg detection rose sharply from 2% in 1999-2000 to 30% in 2005-2006. In addition, the population averaged mean I-Hg concentration rose significantly over that same period from 0.33 to 0.39 μL (Anova, $P < 0.001$). In a separate analysis, multivariate logistic regression indicated that I-Hg detection was significantly associated with age (OR = 1.02, $P < 0.001$). Furthermore, multivariate logistic regression revealed significant associations of both I-Hg detection and mean concentration with biomarkers for the main targets of mercury deposition and effect: the liver, immune system, and pituitary. This study provides compelling evidence that I-Hg deposition within the human body is a cumulative process, increasing with age and in the population over time, since 1999, as a result of chronic mercury exposure. Furthermore, our results indicate that I-Hg deposition is associated with the significant biological markers for main targets of exposure, deposition, and effect. Accumulation of focal I-Hg deposits within the human body due to chronic mercury exposure provides a mechanism which suggests a time dependent rise in the population risks for associated disease.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19697139>

“Within this population,
inorganic mercury detection rose sharply
from 2% in 1999-2000 to 30% in 2005-2006.
In addition, the population averaged mean
inorganic mercury concentration rose
significantly over that same period
from 0.33 to 0.39 μL (Anova, $P < 0.001$).”

“... thimerosal administration to suckling or adult rats impairs sensitivity to pain ...”

Brain Research • December 2009

Neonatal administration of a vaccine preservative, thimerosal,
produces lasting impairment of nociception and apparent activation
of opioid system in rats

Author information

Olczak M1, Duszczyk M, Mierzejewski P, Majewska MD.

Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology
Warsaw, Poland

Abstract

Thimerosal (THIM), an organomercury preservative added to many child vaccines is a suspected factor in pathogenesis of neurodevelopmental disorders. We examined the pharmacokinetics of Hg in the brain, liver and kidneys after i.m. THIM injection in suckling rats and we tested THIM effect on nociception. THIM solutions were injected to Wistar and Lewis rats in a vaccination-like mode on PN days 7, 9, 11 and 15 in four equal doses. For Wistar rats these were: 12, 48, 240, 720, 1440, 2160, 3000 microg Hg/kg and for Lewis: 54, 216, 540 and 1080 microg Hg/kg. Pharmacokinetic analysis revealed that Hg from THIM injections accumulates in the rat brain in significant amounts and remains there longer than 30 days after the injection. At the 6th week of age animals were examined for pain sensitivity using the hot plate test. THIM treated rats of both strains and sexes manifested statistically significantly elevated pain threshold (latency for paw licking, jumping) on a hot plate (56 degrees C). Wistar rats were more sensitive to this effect than Lewis rats. Protracted THIM-induced hypoalgesia was reversed by naloxone (5 mg/kg, i.p.) injected before the hot plate test, indicative of involvement of endogenous opioids. This was confirmed by augmented catalepsy after morphine (2.5 mg/kg, s.c.) injection. Acute THIM injection to 6-week-old rats also produced hypoalgesia, but this effect was transient and was gone within 14 days. Present findings show that THIM administration to suckling or adult rats impairs sensitivity to pain, apparently due to activation the endogenous opioid system.

<http://www.ncbi.nlm.nih.gov/pubmed/19747466>

A prospective study of prenatal mercury exposure from maternal dental amalgams and autism severity

Author information

Geier DA1, Kern JK, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA

Abstract

Dental amalgams containing 50% mercury (Hg) have been used in dentistry for the last 150 years, and Hg exposure during key developmental periods was associated with autism spectrum disorders (ASDs). This study examined increased Hg exposure from maternal dental amalgams during pregnancy among 100 qualifying participants born between 1990-1999 and diagnosed with DSM-IV autism (severe) or ASD (mild). Logistic regression analysis (age, gender, race, and region of residency adjusted) by quintile of maternal dental amalgams during pregnancy revealed the ratio of autism:ASD (severe:mild) were about 1 (no effect) for < or =5 amalgams and increased for > or =6 amalgams. Subjects with > or =6 amalgams were 3.2-fold significantly more likely to be diagnosed with autism (severe) in comparison to ASD (mild) than subjects with < or =5 amalgams. Dental amalgam policies should consider Hg exposure in women before and during the child-bearing age and the possibility of subsequent fetal exposure and adverse outcomes.

Full Report

<http://www.ncbi.nlm.nih.gov/pubmed/19593333>

“Hg [ethyl mercury] exposure during key developmental periods was associated with autism spectrum disorders ... Subjects with > or =6 amalgams were 3.2-fold significantly more likely to be diagnosed with autism (severe) in comparison to ASD (mild) than subjects with < or =5 amalgams.”

“A significant correlation was observed between increasing cP levels and CARS scores.”

Journal Of Toxicology And Environmental Health Part A • 2009

A prospective blinded evaluation of urinary porphyrins verses the clinical severity of autism spectrum disorders

Author information

Geier DA1, Kern JK, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA
mgeier@comcast.net

Abstract

A prospective, blinded study evaluated the relationship between autism spectrum disorder (ASD) severity measured by Childhood Autism Rating Scale (CARS) scores and urinary porphyrins among a cohort of participants (n = 26). LabCorp (CLIA-approved) tested for uroporphyrins, heptacarboxylporphyrins, hexacarboxylporphyrins, pentacarboxylporphyrins, coproporphyrin (cP) I, and cP III levels. Participants with severe ASD had significantly increased cP I, cP III, and total cP levels in comparison to participants with mild ASD. A significant correlation was observed between increasing cP levels and CARS scores. Significant correlations were also noted for comparative urinary porphyrin testing between LabCorp and the Laboratoire Philippe Auguste (ISO-approved) for total cP. Finally, total cP measured at LabCorp was found to significantly correlate with precoproporphyrin (a specific porphyrin marker for mercury toxicity) measured at the Laboratoire Philippe Auguste. Since urinary porphyrin testing is clinically available, relatively inexpensive, and noninvasive, it may be used to help suggest whether heavy metal toxicity is associated with ASD.

<http://www.ncbi.nlm.nih.gov/pubmed/20077233>

Mercury toxicokinetics dependency on strain and gender

Author information

Ekstrand JI, Nielsen JB, Havarinasab S,
Zalups RK, Söderkvist P, Hultman P.

Molecular and Immunological Pathology
Department of Clinical and Experimental Medicine
Linköping University, SE-58185 Linköping, Sweden

Abstract

Mercury (Hg) exposure from dental amalgam fillings and thimerosal in vaccines is not a major health hazard, but adverse health effects cannot be ruled out in a small and more susceptible part of the exposed population. Individual differences in toxicokinetics may explain susceptibility to mercury. Inbred, H-2-congenic A.SW and B10.S mice and their F1- and F2-hybrids were given HgCl₂ with 2.0 mg Hg/L drinking water and traces of (203)Hg. Whole-body retention (WBR) was monitored until steady state after 5 weeks, when the organ Hg content was assessed. Despite similar Hg intake, A.SW males attained a 20-30% significantly higher WBR and 2- to 5-fold higher total renal Hg retention/concentration than A.SW females and B10.S mice. A selective renal Hg accumulation but of lower magnitude was seen also in B10.S males compared with females. Differences in WBR and organ Hg accumulation are therefore regulated by non-H-2 genes and gender. Lymph nodes lacked the strain- and gender-dependent Hg accumulation profile of kidney, liver and spleen. After 15 days without Hg A.SW mice showed a 4-fold higher WBR and liver Hg concentration, but 11-fold higher renal Hg concentration, showing the key role for the kidneys in explaining the slower Hg elimination in A.SW mice. The trait causing higher mercury accumulation was not dominantly inherited in the F1 hybrids. F2 mice showed a large inter-individual variation in Hg accumulation, showing that multiple genetic factors influence the Hg toxicokinetics in the mouse. The genetically heterogeneous human population may therefore show a large variation in mercury toxicokinetics.

<http://www.ncbi.nlm.nih.gov/pubmed/19732784>

“The genetically heterogeneous human population may therefore show a large variation in mercury toxicokinetics.”

Mercury induces inflammatory mediator release from human mast cells

Author information

Kempuraj D1, Asadi S, Zhang B, Manola A,
Hogan J, Peterson E, Theoharides TC.

Molecular Immunopharmacology and Drug Discovery Laboratory
Department of Pharmacology and Experimental Therapeutics
Tufts University School of Medicine and Tufts Medical Center
Boston, MA 02111, USA

Abstract

BACKGROUND

Mercury is known to be neurotoxic, but its effects on the immune system are less well known. Mast cells are involved in allergic reactions, but also in innate and acquired immunity, as well as in inflammation. Many patients with Autism Spectrum Disorders (ASD) have “allergic” symptoms; moreover, the prevalence of ASD in patients with mastocytosis, characterized by numerous hyperactive mast cells in most tissues, is 10-fold higher than the general population suggesting mast cell involvement. We, therefore, investigated the effect of mercuric chloride (HgCl₂) on human mast cell activation.

METHODS

Human leukemic cultured LAD2 mast cells and normal human umbilical cord blood-derived cultured mast cells (hCBMCs) were stimulated by HgCl₂ (0.1-10 microM) for either 10 min for beta-hexosaminidase release or 24 hr for measuring vascular endothelial growth factor (VEGF) and IL-6 release by ELISA.

RESULTS

HgCl₂ induced a 2-fold increase in beta-hexosaminidase release, and also significant VEGF release at 0.1 and 1 microM (311 +/- 32 pg/106 cells and 443 +/- 143 pg/106 cells, respectively) from LAD2 mast cells compared to control cells (227 +/- 17 pg/106 cells, n = 5, p < 0.05). Addition of HgCl₂ (0.1 microM) to the proinflammatory neuropeptide substance P (SP, 0.1 microM) had synergistic action in inducing VEGF from LAD2 mast cells. HgCl₂ also stimulated significant VEGF release (360 +/- 100 pg/106 cells at 1 microM, n = 5, p < 0.05) from hCBMCs compared to control cells (182 +/- 57 pg/106 cells), and IL-6 release (466 +/- 57 pg/106 cells at 0.1 microM) compared to untreated cells (13 +/- 25 pg/106 cells, n = 5, p < 0.05). Addition of HgCl₂ (0.1 microM) to SP (5 microM) further increased IL-6 release.

CONCLUSIONS

HgCl₂ stimulates VEGF and IL-6 release from human mast cells. This phenomenon could disrupt the blood-brain-barrier and permit brain inflammation. As a result, the findings of the present study provide a biological mechanism for how low levels of mercury may contribute to ASD pathogenesis.

Full Report:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2850891/>

“... the findings of the present study provide a biological mechanism for how low levels of mercury may contribute to Autistic Spectrum Disorder pathogenesis.”

“... association between premature puberty and exposure to mercury from thimerosal-containing vaccines ...”

Indian Journal Of Medical Research • April 2010

Thimerosal exposure & increasing trends of premature puberty in the vaccine safety datalink

Author information

Geier DA1, Young HA, Geier MR.
The Institute of Chronic Illnesses, Inc., Silver Spring, MD 20905, USA
mgeier@comcast.net

Abstract

BACKGROUND & OBJECTIVES

The US Agency for Toxic Substances and Disease Registry (ATSDR) reports that mercury (Hg) is a known endocrine disruptor and it adversely affects the steroid synthesis pathway in animals and humans, and may interact to enhance the risk for a child developing premature puberty. An association between premature puberty and exposure to Hg from thimerosal-containing vaccines (TCVs) was evaluated in computerized medical records within the Vaccine Safety Datalink (VSD).

METHODS

A total of 278,624 subjects were identified in birth cohorts from 1990-1996. The birth cohort prevalence rates of medically diagnosed International Classification of Disease, 9(th) revision (ICD-9) premature puberty and control outcomes were calculated. Exposures to Hg from TCVs were calculated by birth cohort for specific exposure windows from birth-7 months and birth-13 months of age. Poisson regression analysis was used to model the association between the prevalence of outcomes and Hg doses from TCVs.

RESULTS

Significantly increased ($P < 0.0001$) rate ratios were observed for premature puberty for a 100 microg difference in Hg exposure from TCVs in the birth-7 months (rate ratio=5.58) and birth-13 months (rate ratio=6.45) of age exposure windows. By contrast, none of the control outcomes had significantly increased rate ratios with Hg exposure from TCVs.

INTERPRETATION & CONCLUSIONS

Routine childhood vaccination should be continued to help reduce the morbidity and mortality associated with infectious diseases, but efforts should be undertaken to remove Hg from vaccines. Additional studies should be done to evaluate the relationship between Hg exposure and premature puberty.

Full report available at this link: <http://www.ncbi.nlm.nih.gov/pubmed/20424300>

Exposure to low-dose mercury (from thimerosal) & premature puberty - a new avenue for research with the vaccine safety datalink

Author information

Dórea JG.

Universidade de Brasilia, Brasilia, DF. Brazil
dorea@rudah.com.br

Abstract

The paper by Geier et al¹ addresses the plausible association of premature puberty after a typical pattern of exposure to ethylmercury in thimerosal-containing vaccines (TCVs) taken by young children in the USA before TCVs were discontinued. Both precocious puberty and low-level mercury are per se high-profile topics of public health interest. Given that TCVs are still currently given to pregnant women, infants and young children around the world, the paper raises a unique opportunity for discussing the role of mercury-based preservatives.

The study took advantage of the vaccine-safety datalink (VSD) system of the USA. Black et al² summarized the advantage of the VSD over the former Vaccine Adverse Event Reporting System (VAERS) in use until 1991 in the USA. Until then, potential vaccine safety issues could only be evaluated by the passive data collected through the VAERS. The current VSD system links outcome and vaccine exposure information, demographic and other covariate information, from the automated clinical databases within several Health Maintenance Organizations (HMOs). As pointed out by Black et al² this data bank can be utilized to screen for possible associations of events after vaccination and also, as in the case of Geier et al¹, to evaluate hypotheses. Geier et al¹ analyzed the data from 1990 to 1996 (n = 278,624) and explored a possible link of premature puberty to TCV received at young ages by comparing this outcome to outcomes not related to mercury exposure (controls). It is worth mentioning the disproportionate percentage of males (7%) in the sample. If encountered in future studies, this information confirms gender differences in thimerosal toxicity³. Constitutional differences in gender determine hormonal balance and represent a biologic variable⁴ to be considered in reproductive and neurologic outcomes.

Premature sexual development is a topic of current interest because of social and attendant health-associated issues, especially for girls. Unwanted teenage pregnancy and sexually transmitted diseases are among the important social and biological issues affecting poor countries and disadvantaged segments of rich countries. Reports from different parts of the world indicate that precocious gynaecological-age is significantly associated with early sexual initiation⁵ and with teenage pregnancy^{6,7}. Additionally, as reviewed by Karaolis-Danckert et al⁸, an accelerated age of puberty onset may influence the life-time risk for breast and testicular cancer, insulin resistance, and adiposity. It is becoming clear that environmental factors are strongly associated with precocious puberty⁹. Studies indicate that increasing rates of precocious puberty are among the endocrine-system related effects of endocrine-disruptor chemicals found in the environment¹⁰.

Generally described as endocrine disruptors, there are a broad range of these substances capable of affecting the endocrine system. Some of these can act specifically on the reproductive system having estrogenic, anti-estrogenic, androgenic, and anti-androgenic activity. Besides that, these chemicals can also interfere with the hypothalamo-pituitary unit, and also disrupt estrous cyclicity. The endocrine-disrupting activity of these pollutants on developmental toxicology depends on timing and dosage. However, since these occur as mixtures, it is not yet possible to know if their end-point effects are additive or antagonistic. Therefore, this type of exposure is difficult to study because of the variety of possible outcomes¹⁰. A wide range of endocrine disruptors listed by Abaci et al¹⁸ include biocides (herbicides, fungicides, insecticides, nematocides), and industrial compounds made up of organic substances and metals (that includes mercury).

Full report available at this link: <http://www.ncbi.nlm.nih.gov/pubmed/20424297>

Sensitization effect of thimerosal is mediated in vitro via reactive oxygen species and calcium signaling

Author information

Migdal C1, Foggia L, Tailhardat M, Courtellemont P,
Haftak M, Serres M.

EA 41-69, Université Lyon 1, Pavillon R
Hôpital Edouard Herriot
69437 Lyon Cedex 03, France

Abstract

Thimerosal, a mercury derivative composed of ethyl mercury chloride (EtHgCl) and thio-salicylic acid (TSA), is widely used as a preservative in vaccines and cosmetic products and causes cutaneous reactions. Since dendritic cells (DCs) play an essential role in the immune response, the sensitization potency of chemicals was studied in vitro using U937, a human promyelomonocytic cell line that is used as a surrogate of monocytic differentiation and activation. Currently, this cell line is under ECVAM (European Center for the Validation of Alternative Methods) validation as an alternative method for discriminating chemicals. Thimerosal and mercury derivatives induced in U937 an overexpression of CD86 and interleukin (IL)-8 secretion similarly to 1-chloro-2,4-dinitrobenzene (DNCB), a sensitizer used as a positive control for DC activation. Non-sensitizers, dichloronitrobenzene (DCNB), TSA and sodium dodecyl sulfate (SDS), an irritant, had no effect. U937 activation was prevented by cell pretreatment with N-acetyl-L-cysteine (NAC) but not with thiol-independent antioxidants except vitamin E which affected CD86 expression by preventing lipid peroxidation of cell membranes. Thimerosal, EtHgCl and DNCB induced glutathione (GSH) depletion and reactive oxygen species (ROS) within 15 min; another peak was detected after 2h for mercury compounds only. MitoSOX, a specific mitochondrial fluorescent probe, confirmed that ROS were essentially produced by mitochondria in correlation with its membrane depolarization. Changes in mitochondrial membrane permeability induced by mercury were reversed by NAC but not by thiol-independent antioxidants. Thimerosal and EtHgCl also induced a calcium (Ca²⁺) influx with a peak at 3h, suggesting that Ca²⁺ influx is a secondary event following ROS induction as Ca²⁺ influx was suppressed after pretreatment with NAC but not with thiol-independent antioxidants. Ca²⁺ influx was also suppressed when culture medium was deprived of Ca²⁺ confirming the specificity of the measure. In conclusion, these data suggest that thimerosal induced U937 activation via oxidative stress from mitochondrial stores and mitochondrial membrane depolarization with a primordial effect of thiol groups. A cross-talk between ROS and Ca²⁺ influx was demonstrated.

<http://www.ncbi.nlm.nih.gov/pubmed/20457211>

“In conclusion, these data suggest that thimerosal induced U937 activation via oxidative stress from mitochondrial stores and mitochondrial membrane depolarization with a primordial effect of thiol groups. A cross-talk between ROS and Ca²⁺ in ux was demonstrated.”

Urinary porphyrin excretion in neurotypical and autistic children

Author information

Woods JS1, Armel SE, Fulton DI, Allen J, Wessels K,
Simmonds PL, Granpeesheh D, Mumper E, Bradstreet JJ,
Echeverria D, Heyer NJ, Rooney JP.

Department of Environmental and Occupational Health Sciences
University of Washington, Seattle, Washington 98105, USA
jwoods@u.washington.edu

Abstract

BACKGROUND

Increased urinary concentrations of pentacarboxyl-, precopro- and copro-porphyrins have been associated with prolonged mercury (Hg) exposure in adults, and comparable increases have been attributed to Hg exposure in children with autism (AU).

OBJECTIVES

This study was designed to measure and compare urinary porphyrin concentrations in neurotypical (NT) children and same-age children with autism, and to examine the association between porphyrin levels and past or current Hg exposure in children with autism.

METHODS

This exploratory study enrolled 278 children 2-12 years of age. We evaluated three groups: AU, pervasive developmental disorder-not otherwise specified (PDD-NOS), and NT. Mothers/caregivers provided information at enrollment regarding medical, dental, and dietary exposures. Urine samples from all children were acquired for analyses of porphyrin, creatinine, and Hg. Differences between groups for mean porphyrin and Hg levels were evaluated. Logistic regression analysis was conducted to determine whether porphyrin levels were associated with increased risk of autism.

RESULTS

Mean urinary porphyrin concentrations are naturally high in young children and decline by as much as 2.5-fold between 2 and 12 years of age. Elevated copro- ($p < 0.009$), hexacarboxyl- ($p < 0.01$) and pentacarboxyl- ($p < 0.001$) porphyrin concentrations were significantly associated with AU but not with PDD-NOS. No differences were found between NT and AU in urinary Hg levels or in past Hg exposure as determined by fish consumption, number of dental amalgam fillings, or vaccines received.

CONCLUSIONS

These findings identify disordered porphyrin metabolism as a salient characteristic of autism. Hg exposures were comparable between diagnostic groups, and a porphyrin pattern consistent with that seen in Hg-exposed adults was not apparent.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957928/>

“Increased urinary concentrations of pentacarboxyl-, precopro- and copro-porphyrins have been associated with prolonged mercury (Hg) exposure in adults, and comparable increases have been attributed to Hg exposure in children with autism.”

“These data document that exposure to thimerosal during early postnatal life produces lasting alterations in the densities of brain opioid receptors along with other neuropathological changes, which may disturb brain development.”

Neurochemistry Research • November 2010

Neonatal administration of thimerosal causes persistent changes in mu opioid receptors in the rat brain

Author information

Olczak M1, Duszczyk M, Mierzejewski P, Bobrowicz T, Majewska MD.

Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology, Warsaw, Poland

Abstract

Thimerosal added to some pediatric vaccines is suspected in pathogenesis of several neurodevelopmental disorders. Our previous study showed that thimerosal administered to suckling rats causes persistent, endogenous opioid-mediated hypoalgesia. Here we examined, using immunohistochemical staining technique, the density of μ -opioid receptors (MORs) in the brains of rats, which in the second postnatal week received four i.m. injections of thimerosal at doses 12, 240, 1,440 or 3,000 $\mu\text{g Hg/kg}$. The periaqueductal gray, caudate putamen and hippocampus were examined. Thimerosal administration caused dose-dependent statistically significant increase in MOR densities in the periaqueductal gray and caudate putamen, but decrease in the dentate gyrus, where it was accompanied by the presence of degenerating neurons and loss of synaptic vesicle marker (synaptophysin). These data document that exposure to thimerosal during early postnatal life produces lasting alterations in the densities of brain opioid receptors along with other neuropathological changes, which may disturb brain development.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957583/>

“our data demonstrated that the toxicokinetics of Thimerosal (ethyl mercury) is completely different from that of methyl mercury.”

Archives of Toxicology • Inorganic Compounds • November 2010

Identification and distribution of mercury species in rat tissues following administration of thimerosal or methylmercury

Jairo L. Rodrigues, Juliana M. Serpeloni, Bruno L. Batista, Samuel S. Souza, Fernando Barbosa Jr

Abstract

Methylmercury (Met-Hg) is one the most toxic forms of Hg, with a considerable range of harmful effects on humans. Sodium ethyl mercury thiosalicylate, thimerosal (TM) is an ethylmercury (Et-Hg)-containing preservative that has been used in manufacturing vaccines in many countries. Whereas the behavior of Met-Hg in humans is relatively well known, that of ethylmercury (Et-Hg) is poorly understood. The present study describes the distribution of mercury as (-methyl, -ethyl and inorganic mercury) in rat tissues (brain, heart, kidney and liver) and blood following administration of TM or Met-Hg. Animals received one dose/day of Met-Hg or TM by gavage (0.5 mg Hg/kg). Blood samples were collected after 6, 12, 24, 48, 96 and 120 h of exposure. After 5 days, the animals were killed, and their tissues were collected. Total blood mercury (THg) levels were determined by ICP-MS, and methylmercury (Met-Hg), ethylmercury (Et-Hg) and inorganic mercury (Ino-Hg) levels were determined by speciation analysis with LC-ICP-MS. Mercury remains longer in the blood of rats treated with Met-Hg compared to that of TM-exposed rats. Moreover, after 48 h of the TM treatment, most of the Hg found in blood was inorganic. Of the total mercury found in the brain after TM exposure, 63% was in the form of Ino-Hg, with 13.5% as Et-Hg and 23.7% as Met-Hg. In general, mercury in tissues and blood following TM treatment was predominantly found as Ino-Hg, but a considerable amount of Et-Hg was also found in the liver and brain. Taken together, our data demonstrated that the toxicokinetics of TM is completely different from that of Met-Hg. Thus, Met-Hg is not an appropriate reference for assessing the risk from exposure to TM-derived Hg. It also adds new data for further studies in the evaluation of TM toxicity.

<http://link.springer.com/article/10.1007%2Fs00204-010-0538-4>

Making sense of epidemiological studies of young children exposed to thimerosal in vaccines

Author information

Dórea JG.

C.P. 04322, Universidade de Brasilia
70919-970 Brasilia, DF, Brazil
dorea@rudah.com.br

Abstract

OBJECTIVE:

To compare epidemiological studies dealing with neurological issues (compatible with Hg toxicity) linked to exposing newborns and infants to intramuscular doses of preservative-Hg resulting from vaccination with thimerosal-containing vaccines (TCV).

METHODS:

Major databases were searched for studies that addressed neurodevelopment outcomes other than autism. Eight studies were identified and compared.

RESULTS:

Information extracted from the studies done in the USA, the UK, and Italy is important in understanding the complex interplay of variables but insufficient to establish non-toxicity for infants and young children still receiving TCV: a) there is ambiguity in some studies reporting neurodevelopment outcomes that seem to depend on confounding variables; b) the risk of neurotoxicity due to low doses of thimerosal is plausible at least for susceptible infants; c) there is a need to address these issues in less developed countries still using TCV in pregnant mothers, newborns, and young children.

CONCLUSIONS:

Since the use of TCV is still inevitable in many countries, this increases the need to protect vulnerable infants and promote actions that strengthen neurodevelopment. Developing countries should intensify campaigns that include breastfeeding among efforts to help prime the central nervous system to tolerate exposure to neurotoxic substances, especially thimerosal-Hg.

“Since the use of thimerosal-containing vaccines is still inevitable in many countries, this increases the need to protect vulnerable infants ...”

“The neurotoxic effects of both mercurials are interwoven with their modulatory actions on GABA(A) and NMDA receptors, which most likely involve binding to these macromolecules.”

Journal Of Physiological Pharmacology • December 2010

Intermingled modulatory and neurotoxic effects of thimerosal and mercuric ions on electrophysiological responses to GABA and NMDA in hippocampal neurons

Author information

Wyrembek P1, Szczuraszek K, Majewska MD, Mozrzymas JW.

Laboratory of Neuroscience, Department of Biophysics
Wroclaw Medical University, Wroclaw, Poland
paulina_wyrembek@op.pl

Abstract

The organomercurial, thimerosal, is at the center of medical controversy as a suspected factor contributing to neurodevelopmental disorders in children. Many neurotoxic effects of thimerosal have been described, but its interaction with principal excitatory and inhibitory neurotransmitter systems is not known. We examined, using electrophysiological recordings, thimerosal effects on GABA and NMDA-evoked currents in cultured hippocampal neurons. After brief (3 to 10 min) exposure to thimerosal at concentrations up to 100 μ M, there was no significant effect on GABA or NMDA-evoked currents. However, following exposure for 60-90 min to 1 or 10 μ M thimerosal, there was a significant decrease in NMDA-induced currents ($p < 0.05$) and GABAergic currents ($p < 0.05$). Thimerosal was also neurotoxic, damaging a significant proportion of neurons after 60-90 min exposure; recordings were always conducted in the healthiest looking neurons. Mercuric chloride, at concentrations 1 μ M and above, was even more toxic, killing a large proportion of cells after just a few minutes of exposure. Recordings from a few sturdy cells revealed that micromolar mercuric chloride markedly potentiated the GABAergic currents ($p < 0.05$), but reduced NMDA-evoked currents ($p < 0.05$). The results reveal complex interactions of thimerosal and mercuric ions with the GABA(A) and NMDA receptors. Mercuric chloride act rapidly, decreasing electrophysiological responses to NMDA but enhancing responses to GABA, while thimerosal works slowly, reducing both NMDA and GABA responses. The neurotoxic effects of both mercurials are interwoven with their modulatory actions on GABA(A) and NMDA receptors, which most likely involve binding to these macromolecules.

<http://www.ncbi.nlm.nih.gov/pubmed/21224507>

“... results show an association between the apparent level of mercury toxicity as measured by recognized urinary porphyrin biomarkers of mercury toxicity and the magnitude of the specific hallmark features of autism ...”

Biometals • December 2010

A biomarker of mercury body-burden correlated with diagnostic domain specific clinical symptoms of autism spectrum disorder

Author information

Kern JK1, Geier DA, Adams JB, Geier MR.
Autism Treatment Center, Dallas, TX, USA
jkern@dfwair.net

Abstract

The study purpose was to compare the quantitative results from tests for urinary porphyrins, where some of these porphyrins are known biomarkers of heavy metal toxicity, to the independent assessments from a recognized quantitative measurement, the Autism Treatment Evaluation Checklist (ATEC), of specific domains of autistic disorders symptoms (Speech/Language, Sociability, Sensory/Cognitive Awareness, and Health/Physical/Behavior) in a group of children having a clinical diagnosis of autism spectrum disorder (ASD). After a Childhood Autism Rating Scale (CARS) evaluation to assess the development of each child in this study and aid in confirming their classification, and an ATEC was completed by a parent, a urinary porphyrin profile sample was collected and sent out for blinded analysis. Urinary porphyrins from twenty-four children, 2-13 years of age, diagnosed with autism or PDD-NOS were compared to their ATEC scores as well as their scores in the specific domains (Speech/Language, Sociability, Sensory/Cognitive Awareness, and Health/Physical/Behavior) assessed by ATEC. Their urinary porphyrin samples were evaluated at Laboratoire Philippe Auguste (which is an ISO-approved clinical laboratory). The results of the study indicated that the participants' overall ATEC scores and their scores on each of the ATEC subscales (Speech/Language, Sociability, Sensory/Cognitive Awareness, and Health/Physical/Behavior) were linearly related to urinary porphyrins associated with mercury toxicity. The results show an association between the apparent level of mercury toxicity as measured by recognized urinary porphyrin biomarkers of mercury toxicity and the magnitude of the specific hallmark features of autism as assessed by ATEC.

<http://www.ncbi.nlm.nih.gov/pubmed/20532957>

“... there has been a great deal of information
... that repetitive mercury exposure during pregnancy, through thimerosal,
dental amalgam, and fish consumption, and after birth, through thimerosal-containing vaccinations ...
is one potential factor in autism.”

Education and Training in Autism and Developmental Disabilities • 2010

Mercury and Autism: A Review

Jie Zhang John J. Wheeler

The College at Brockport, SUNY Tennessee Technological University

Abstract

The prevalence of autism has increased approximately four times in children in nearly one decade (California Health and Human Services Agency, 2003). It has been reported that explanations such as immigration, shifts in the interpretation of diagnostic criteria, improved identification, or diagnostic accuracies cannot explain the observed increase (Geier & Geier, 2005). One potential cause that has alarmed many has been the presence of thimerosal, the mercury-based preservative found among immunizations. Although many refute this, concern has been leveled by many families and professionals concerning the potential impact of mercury poisoning as a causal factor. Researchers have proposed that autism may be in part caused by mercury, because there was cumulative mercury exposure through dental amalgam, fish consumption, environment pollution, and additionally, through increased thimerosal-containing vaccines for both mothers and newborns (Mutter, Naumann, Schneider, Walach, & Haley, 2005). The purpose of this study is to review the information from studies concerning the relationship between mercury exposure and autism.

Conclusion

To sum up, there has been a great deal of information from different studies that seems to indicate that repetitive mercury exposure during pregnancy, through thimerosal, dental amalgam, and fish consumption, and after birth, through thimerosal-containing vaccinations and pollution, in genetically susceptible individuals is one potential factor in autism. Certainly this question continues to stir debate among professionals across the medical and behavioral sciences. It serves as a grey area for many families as they seek to quell their anxiety invoked by this debate by discovering the facts. The purpose of this article was to synthesize the findings relative to this question to hopefully serve as a resource to educators as we seek to become more well-informed on this timely issue. As the prevalence rate for autism in children continues to rise, more research is needed to better understand causal factors. It is also crucial that quality reviews be conducted to synthesize a body of knowledge pertaining to these questions if the puzzle is to be solved pertaining to the link between mercury exposure and autism.

Age-dependent lower or higher levels of hair mercury in autistic children than in healthy controls

Author information

Majewska MD1, Urbanowicz E, Rok-Bujko P,
Namyslowska I, Mierzejewski P.

¹Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology, Warsaw, Poland
majewska@ipin.edu.pl

Abstract

An association between autism and early life exposure to mercury is a hotly debated issue. In this study, 91 autistic Polish children, male and female, 3-4 and 7-9 years old, were compared to 75 age- and sex-matched healthy children with respect to: demographic, perinatal, clinical and developmental measures, parental age, birth order, morphometric measures, vaccination history, and hair mercury content. In demographic and perinatal measures there were no consistent differences between the autistic and control groups. Autistic children had a significantly greater prevalence of adverse reactions after vaccinations and abnormal development than controls. Between 45 and 80% of autistic children experienced developmental regress. Autistic children significantly differed from healthy peers in the concentrations of mercury in hair: younger autistics had lower levels, while older - higher levels than their respective controls. The results suggest that autistic children differ from healthy children in metabolism of mercury, which seems to change with age.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20628443>

“The results suggest
that autistic children
differ from healthy children
in metabolism of mercury,
which seems to change with age.”

Sorting out the spinning of autism: heavy metals and the question of incidence

Author information

Desoto MC1, Hitlan RT.

1Department of Psychology
University of Northern Iowa
Cedar Falls, Iowa, USA
cathy.desoto@uni.edu

Abstract

The reasons for the rise in autism prevalence are a subject of heated professional debate. Featuring a critical appraisal of some research used to question whether rising levels of autism are related to environmental exposure to toxins (Soden et al. 2007, Barbaresi et al. 2009, Thompson et al. 2007) we aim to evaluate the actual state of scientific knowledge. In addition, we surveyed the empirical research on the topic of autism and heavy metal toxins. In our opinion empirical investigations are finding support for a link with heavy metal toxins. The various causes that have led to the increase in autism diagnosis are likely multi-faceted, and understanding the causes is one of the most important health topics today. We argue that scientific research does not support rejecting the link between the neurodevelopmental disorder of autism and toxic exposures.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20628440>

“In our opinion empirical investigations are finding support for a link with heavy metal toxins. We argue that scientific research does not support rejecting the link between the neurodevelopmental disorder of autism and toxic exposures.”

Delayed acquisition
of neonatal reflexes in newborn primates
receiving a thimerosal-containing hepatitis B vaccine:
influence of gestational age and birth weight

Author information

Hewitson L1, Houser LA, Stott C, Sackett G,
Tomko JL, Atwood D, Blue L, White ER.

Department of Obstetrics and Gynecology
University of Pittsburgh School of Medicine
Pittsburgh, Pennsylvania, USA
lch1@pitt.edu

Abstract

This study examined whether acquisition of neonatal reflexes in newborn rhesus macaques was influenced by receipt of a single neonatal dose of hepatitis B vaccine containing the preservative thimerosal (Th). Hepatitis B vaccine containing a weight-adjusted Th dose was administered to male macaques within 24 h of birth (n = 13). Unexposed animals received saline placebo (n = 4) or no injection (n = 3). Infants were tested daily for acquisition of nine survival, motor, and sensorimotor reflexes. In exposed animals there was a significant delay in the acquisition of root, snout, and suck reflexes, compared with unexposed animals. No neonatal responses were significantly delayed in unexposed animals. Gestational age (GA) and birth weight (BW) were not significantly correlated. Cox regression models were used to evaluate main effects and interactions of exposure with BW and GA as independent predictors and time-invariant covariates. Significant main effects remained for exposure on root and suck when controlling for GA and BW, such that exposed animals were relatively delayed in time-to-criterion. Interaction models indicated there were various interactions between exposure, GA, and BW and that inclusion of the relevant interaction terms significantly improved model fit. This, in turn, indicated that lower BW and/or lower GA exacerbated the adverse effects following vaccine exposure. This primate model provides a possible means of assessing adverse neurodevelopmental outcomes from neonatal Th-containing hepatitis B vaccine exposure, particularly in infants of lower GA or BW. The mechanisms underlying these effects and the requirements for Th requires further study.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20711932>

“This primate model
provides a possible means of assessing
adverse neurodevelopmental outcomes from
neonatal Thimerosal-containing hepatitis B vaccine
exposure, particularly in infants ...”

Blood mercury levels in autism spectrum disorder: Is there a threshold level?

Author information

Geier DA1, Audhya T, Kern JK, Geier MR.
Institute of Chronic Illnesses, Inc.
Silver Spring, MD, USA

Abstract

Mercury (Hg) may significantly impact the pathogenesis of autism spectrum disorders (ASDs). Lab results generated by Vitamin Diagnostics (CLIA-approved) from 2003-2007, were examined among subjects diagnosed with an ASD (n=83) in comparison to neurotypical controls (n=89). Blood Hg levels were determined by analyzing Hg content in red blood cells (RBC) using cold vapor analysis, and consistent Hg measurements were observed between Vitamin Diagnostics and the University of Rochester. Adjusted (age, gender, and date of collection) mean Hg levels were 1.9-fold significantly ($P < .0001$) increased among subjects diagnosed with an ASD (21.4 microg/L) in comparison to controls (11.4 microg/L). Further, an adjusted significant ($P < .0005$) threshold effect >15 microg/L was observed for Hg levels on the risk of a subject being diagnosed with an ASD in comparison to controls (odds ratio=6.4). The weight of scientific evidence supports Hg as a causal factor in subjects diagnosed with an ASD.

Full Report: <http://www.ncbi.nlm.nih.gov/pubmed/20628441>

“The weight of scientific evidence supports ethyl mercury as a causal factor in subjects diagnosed with an Autistic Spectrum Disorder”

“These findings document neurotoxic effects of thimerosal,
at doses equivalent to those used in infant vaccines ...”

Folia Neuropathology • 2010

Lasting neuropathological changes in rat brain after intermittent neonatal administration of thimerosal

Author information

Olczak M1, Duszczyk M, Mierzejewski P, Wierzba-Bobrowicz T, Majewska MD.

Department of Pharmacology and Physiology of the Nervous System,
Institute of Psychiatry and Neurology, ul. Sobieskiego 9, Warsaw, Poland

Abstract

Thimerosal, an organomercurial added as a preservative to some vaccines, is a suspected iatrogenic factor, possibly contributing to paediatric neurodevelopmental disorders including autism. We examined the effects of early postnatal administration of thimerosal (four i.m. injections, 12 or 240 µg THIM-Hg/kg, on postnatal days 7, 9, 11 and 15) on brain pathology in Wistar rats. Numerous neuropathological changes were observed in young adult rats which were treated postnatally with thimerosal. They included: ischaemic degeneration of neurons and “dark” neurons in the prefrontal and temporal cortex, the hippocampus and the cerebellum, pathological changes of the blood vessels in the temporal cortex, diminished synaptophysin reaction in the hippocampus, atrophy of astroglia in the hippocampus and cerebellum, and positive caspase-3 reaction in Bergmann astroglia. These findings document neurotoxic effects of thimerosal, at doses equivalent to those used in infant vaccines or higher, in developing rat brain, suggesting likely involvement of this mercurial in neurodevelopmental disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21225508>

“... investigators have long recognized that Hg is a neurodevelopmental poison;
it can cause problems in neuronal cell migration and division,
and can ultimately cause cell degeneration and death.”

Acta Neurobiologia Experimentalis • 2010

The biological basis of autism spectrum disorders: Understanding causation and treatment by clinical geneticists

Author information

Geier DA1, Kern JK, Geier MR.
The Institute of Chronic Illnesses, Inc., Silver Spring, Maryland, USA

Abstract

Autism spectrum disorders (ASDs) also known as pervasive developmental disorders (PDD) are a behaviorally defined group of neurodevelopmental disorders that are usually diagnosed in early childhood. ASDs disproportionately affect male children. Mercury (Hg) a heavy metal, is widespread and persistent in the environment. Mercury is a ubiquitous source of danger in fish, drugs, fungicides/herbicides, dental fillings, thermometers, and many other products. Elevated Hg concentrations may remain in the brain from several years to decades following exposure. This is important because investigators have long recognized that Hg is a neurodevelopmental poison; it can cause problems in neuronal cell migration and division, and can ultimately cause cell degeneration and death. Case-reports of patients have described developmental regressions with ASD symptoms following fetal and/or early childhood Hg exposure, and epidemiological studies have linked exposure to Hg with an elevated risk of a patient being diagnosed with an ASD. Immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with ASDs were reported following Hg intoxication with similarities extending to neuroanatomy, neurotransmitters, and biochemistry. The sexual dimorphism of ASDs may result from synergistic neurotoxicity caused by the interaction of testosterone and Hg; in contrast, estrogen is protective, mitigating the toxicity of Hg. Mercury exposure may significantly increase androgen levels, and as a result, patients diagnosed with an ASD may significantly benefit from anti-androgen therapy. Finally, the clinical geneticist has a wealth of biomarkers to evaluate and treat patients diagnosed with an ASD.

Access to full report: <http://www.ncbi.nlm.nih.gov/pubmed/20628444>

Correlations Between Gene Expression and Mercury Levels in Blood of Boys With and Without Autism

Boryana Stamova,^{1,9,10} Peter G. Green,² Yingfang Tian,^{1,9,10} Irva Hertz-Picciotto,^{3,9,10} Isaac N. Pes-
sah,^{4,9,10} Robin Hansen,^{5,9,10} Xiaowei Yang,³ Jennifer Teng,¹ Jeffrey P. Gregg,^{6,9,10} Paul Ashwood,^{7,9,10}
Judy Van de Water,^{8,9,10} and Frank R. Sharp^{1,9,10}

1. Department of Neurology, University of California at Davis Medical Center, Sacramento, CA 95817 USA
2. Department of Civil and Environmental Engineering, University of California at Davis, Sacramento, CA USA
3. Department of Public Health Sciences, University of California at Davis Medical Center, Sacramento, CA USA
4. Department of VM: Molecular Biosciences, University of California at Davis Medical Center, Sacramento, CA USA
5. Department of Pediatrics, University of California at Davis Medical Center, Sacramento, CA USA
6. Department of Pathology, University of California at Davis Medical Center, Sacramento, CA USA
7. Department of Medical Microbiology and Immunology, University of California at Davis Medical Center, Sacramento, CA USA
8. Division of Rheumatology, Allergy and Clinical Immunology, University of California at Davis Medical Center, Sacramento, CA
9. The MIND Institute, University of California at Davis Medical Center, 2805 50th Street, Room 2434, Sacramento, CA USA
10. UC Davis Center for Children's Environmental Health and Disease Prevention, Sacramento, CA USA

Abstract

Gene expression in blood was correlated with mercury levels in blood of 2- to 5-year-old boys with autism (AU) compared to age-matched typically developing (TD) control boys. This was done to address the possibility that the two groups might metabolize toxicants, such as mercury, differently. RNA was isolated from blood and gene expression assessed on whole genome Affymetrix Human U133 expression microarrays. Mercury levels were measured using an inductively coupled plasma mass spectrometer. Analysis of covariance (ANCOVA) was performed and partial correlations between gene expression and mercury levels were calculated, after correcting for age and batch effects. To reduce false positives, only genes shared by the ANCOVA models were analyzed. Of the 26 genes that correlated with mercury levels in both AU and TD boys, 11 were significantly different between the groups ($P(\text{Diagnosis} \times \text{Mercury}) \leq 0.05$). The expression of a large number of genes ($n = 316$) correlated with mercury levels in TD but not in AU boys ($P \leq 0.05$), the most represented biological functions being cell death and cell morphology. Expression of 189 genes correlated with mercury levels in AU but not in TD boys ($P \leq 0.05$), the most represented biological functions being cell morphology, amino acid metabolism, and antigen presentation. These data and those in our companion study on correlation of gene expression and lead levels show that AU and TD children display different correlations between transcript levels and low levels of mercury and lead. These findings might suggest different genetic transcriptional programs associated with mercury in AU compared to TD children.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3006666/>

“These data and those in our companion study on correlation of gene expression and lead levels show that Autistic and Typically Developing children display different correlations between transcript levels and low levels of mercury and lead. These findings might suggest different genetic transcriptional programs associated with mercury in Autistic compared to Typically Developing children.”

Is dental amalgam safe for humans? The opinion of the scientific committee of the European Commission

Author information

Mutter J.

Department of Environmental and integrative medicine
Lohnerhofstraße 2, 78467 Constance/Germany
jm@zahnklinik.de.

Abstract

It was claimed by the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) in a report to the EU-Commission that “.... no risks of adverse systemic effects exist and the current use of dental amalgam does not pose a risk of systemic disease...” [1, available from: http://ec.europa.eu/health/ph_risk/committees/04_scenihhr/docs/scenihhr_o_016.pdf]. SCENIHR disregarded the toxicology of mercury and did not include most important scientific studies in their review. But the real scientific data show that: (a) Dental amalgam is by far the main source of human total mercury body burden. This is proven by autopsy studies which found 2-12 times more mercury in body tissues of individuals with dental amalgam. Autopsy studies are the most valuable and most important studies for examining the amalgam-caused mercury body burden. (b) These autopsy studies have shown consistently that many individuals with amalgam have toxic levels of mercury in their brains or kidneys. (c) There is no correlation between mercury levels in blood or urine, and the levels in body tissues or the severity of clinical symptoms. SCENIHR only relied on levels in urine or blood. (d) The half-life of mercury in the brain can last from several years to decades, thus mercury accumulates over time of amalgam exposure in body tissues to toxic levels. However, SCENIHR state that the half-life of mercury in the body is only “20-90 days”. (e) Mercury vapor is about ten times more toxic than lead on human neurons and with synergistic toxicity to other metals. (f) Most studies cited by SCENIHR which conclude that amalgam fillings are safe have severe methodical flaws.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3025977/>

“The half-life of mercury in the brain can last from several years to decades, thus mercury accumulates over time of amalgam exposure in body tissues to toxic levels. However, SCENIHR state that the half-life of mercury in the body is only “20-90 days”. Mercury vapor is about ten times more toxic than lead on human neurons and with synergistic toxicity to other metals. Most studies cited by SCENIHR which conclude that amalgam fillings are safe have severe methodical flaws.”

Toxicity biomarkers among US children compared to a similar cohort in France: a blinded study measuring urinary porphyrins

Author information

Kern JK1, Geier DA2, Ayzac F3, Adams JB4, Mehta JA5, Geier MR6.

1. Genetic Consultants of Dallas, 408 North Allen Drive, Allen, TX
Autism Treatment Center, 10503 Metric Drive, Dallas, TX
University of Texas Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard, Dallas, TX
2. CoMeD, Inc. and Institute of Chronic Illnesses, Inc.
14 Redgate Court, Silver Spring, MD 20905
3. Autism Research Institute, 4182 Adams Avenue, San Diego, CA 92116
4. Department of Chemical and Materials Engineering, Arizona State University
7001 East Williams Field Road, Mesa, AZ 85212
5. Department of Communication Sciences and Disorders, Texas Woman's University
304 Administration Drive, Denton, Texas 76204, USA
6. Autism Spectrum Disorder Centers, LLC
14 Redgate Court, Silver Spring, MD 20905, USA

Abstract

The purpose of this blinded study was to evaluate potential environmental toxicity in a cohort of neurotypical children (n = 28) living in a suburban area of north-central Texas in the United States (US) with a comparable age- and gender-matched cohort of neurotypical children (n = 28) living in a suburban area of southeastern France using urinary porphyrin testing: uroporphyrin (uP), heptacarboxyporphyrin (7cxP), hexacarboxyporphyrin (6cxP), pentacarboxyporphyrin (5cxP), precoproporphyrin (preP), and coproporphyrin (cP). Results showed significantly elevated 6cxP, preP (an atypical, mercury-specific porphyrin), and cP levels, and increasing trends in 5cxP levels, among neurotypical children in the USA compared to children in France. Data suggest that in US neurotypical children, there is a significantly increased body-burden of mercury (Hg) compared to the body-burden of Hg in the matched neurotypical children in France. The presence of lead contributing to the higher levels of cP also needs to be considered. Further, other factors including genetics can not be completely ruled out.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3898545/>

“Data suggest that in US neurotypical children, there is a significantly increased body-burden of mercury compared to the body-burden of mercury in the matched neurotypical children in France.”

A significant relationship
between mercury exposure from dental amalgams and
urinary porphyrins: a further assessment of the
Casa Pia children's dental amalgam trial

Author information

Geier DA1, Carmody T, Kern JK, King PG, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA
mgeier@comcast.net

Abstract

Previous studies noted specific changes in urinary porphyrin excretion patterns associated with exposure to mercury (Hg) in animals and humans. In our study, urinary porphyrin concentrations were examined in normal children 8-18 years-old from a reanalysis of data provided from a randomized, prospective clinical trial that was designed to evaluate the potential health consequences of prolonged exposure to Hg from dental amalgam fillings (the parent study). Our analysis examined dose-dependent correlations between increasing Hg exposure from dental amalgams and urinary porphyrins utilizing statistical models with adjustments for the baseline level (i.e. study year 1) of the following variables: urinary Hg, each urinary porphyrin measure, gender, race, and the level of lead (Pb) in each subject's blood. Significant dose-dependent correlations between cumulative exposure to Hg from dental amalgams and urinary porphyrins associated with Hg body-burden (pentacarboxyporphyrin, precoproporphyrin, and coproporphyrin) were observed. Overall, 5-10% increases in Hg-associated porphyrins for subjects receiving an average number of dental amalgam fillings in comparison to subjects receiving only composite fillings were observed over the 8-year course of the study. In contrast, no significant correlations were observed between cumulative exposure to Hg from dental amalgams and urinary porphyrins not associated with Hg body-burden (uroporphyrin, heptacarboxyporphyrin, and hexacarboxyporphyrin). In conclusion, our study, in contrast to the no-effect results published from the parent study, further establishes the sensitivity and specificity of specific urinary porphyrins as a biomarker for low-level Hg body-burden, and also reveals that dental amalgams are a significant chronic contributor to Hg body-burden.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21053054>

“In conclusion, our study, in contrast to the no-effect results published from the parent study, further establishes the sensitivity and specificity of specific urinary porphyrins as a biomarker for low-level mercury body-burden, and also reveals that dental amalgams are a significant chronic contributor to mercury body-burden.”

“Recent studies suggest that children diagnosed with an autism spectrum disorder have significantly increased levels of urinary porphyrins associated with mercury (Hg) toxicity ...”

Pediatrics International • April 2011

Toxicity biomarkers in autism spectrum disorder: a blinded study of urinary porphyrins

Author information

Kern JK1, Geier DA, Adams JB, Mehta JA, Grannemann BD, Geier MR.
Research Department, Genetics Consultants of Dallas/ASD Centers, LLC.,
408 N. Allen Dr, Allen, TX 75013, USA
jkern@dfwair.net

Abstract

BACKGROUND

Recent studies suggest that children diagnosed with an autism spectrum disorder (ASD) have significantly increased levels of urinary porphyrins associated with mercury (Hg) toxicity, including pentacarboxyporphyrin (5cxP), precoproporphyrin (prcP), and coproporphyrin (cP), compared to typically developing controls. However, these initial studies were criticized because the controls were not age- and gender-matched to the children diagnosed with an ASD.

METHODS

Urinary porphyrin biomarkers in a group of children (2-13 years of age) diagnosed with an ASD (n= 20) were compared to matched (age, gender, race, location, and year tested) group of typically developing controls (n= 20).

RESULTS

Participants diagnosed with an ASD had significantly increased levels of 5cxP, prcP, and cP in comparison to controls. No significant differences were found in non-Hg associated urinary porphyrins (uroporphyrins, hexacarboxyporphyrin, and heptacarboxyporphyrin). There was a significantly increased odds ratio for an ASD diagnosis relative to controls among study participants with precoproporphyrin (odds ratio = 15.5, $P < 0.01$) and coproporphyrin (odds ratio = 15.5, $P < 0.01$) levels in the second through fourth quartiles in comparison to the first quartile.

CONCLUSION

These results suggest that the levels of Hg-toxicity-associated porphyrins are higher in children with an ASD diagnosis than controls. Although the pattern seen (increased 5cxP, prcP, and cP) is characteristic of Hg toxicity, the influence of other factors, such as genetics and other metals cannot be completely ruled out.

“Mercury (Hg) is recognized as a ubiquitous environmental neurotoxin and there is mounting evidence linking it to neurodevelopmental disorders, including autism.”

Toxicology And Environmental Chemistry • May 2011

The plausibility of a role for mercury in the etiology of autism: a cellular perspective

Matthew Garrecht and David W. Austin

Swinburne Autism Bio-Research Initiative
Faculty of Life and Social Sciences
Swinburne University of Technology
Hawthorn, Victoria 3122, Australia

Abstract

Autism is defined by a behavioral set of stereotypic and repetitious behavioral patterns in combination with social and communication deficits. There is emerging evidence supporting the hypothesis that autism may result from a combination of genetic susceptibility and exposure to environmental toxins at critical moments in development. Mercury (Hg) is recognized as a ubiquitous environmental neurotoxin and there is mounting evidence linking it to neurodevelopmental disorders, including autism. Of course, the evidence is not derived from experimental trials with humans but rather from methods focusing on biomarkers of Hg damage, measurements of Hg exposure, epidemiological data, and animal studies. For ethical reasons, controlled Hg exposure in humans will never be conducted. Therefore, to properly evaluate the Hg-autism etiological hypothesis, it is essential to first establish the biological plausibility of the hypothesis. This review examines the plausibility of Hg as the primary etiological agent driving the cellular mechanisms by which Hg-induced neurotoxicity may result in the physiological attributes of autism. Key areas of focus include: (1) route and cellular mechanisms of Hg exposure in autism; (2) current research and examples of possible genetic variables that are linked to both Hg sensitivity and autism; (3) the role Hg may play as an environmental toxin fueling the oxidative stress found in autism; (4) role of mitochondrial dysfunction; and (5) possible role of Hg in abnormal neuroexcitatory and excitotoxicity that may play a role in the immune dysregulation found in autism. Future research directions that would assist in addressing the gaps in our knowledge are proposed.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3173748/>

Integrating experimental (in vitro and in vivo) neurotoxicity studies of low-dose thimerosal relevant to vaccines

Author information

Dórea JG.

Faculty of Health Sciences
Universidade de Brasília
CP 04322, 70919-970, Brasília, DF, Brazil
dorea@rudah.com.br

Abstract

There is a need to interpret neurotoxic studies to help deal with uncertainties surrounding pregnant mothers, newborns and young children who must receive repeated doses of Thimerosal-containing vaccines (TCVs). This review integrates information derived from emerging experimental studies (in vitro and in vivo) of low-dose Thimerosal (sodium ethyl mercury thiosalicylate). Major databases (PubMed and Web-of-science) were searched for in vitro and in vivo experimental studies that addressed the effects of low-dose Thimerosal (or ethylmercury) on neural tissues and animal behaviour. Information extracted from studies indicates that: (a) activity of low doses of Thimerosal against isolated human and animal brain cells was found in all studies and is consistent with Hg neurotoxicity; (b) the neurotoxic effect of ethylmercury has not been studied with co-occurring adjuvant-Al in TCVs; (c) animal studies have shown that exposure to Thimerosal-Hg can lead to accumulation of inorganic Hg in brain, and that (d) doses relevant to TCV exposure possess the potential to affect human neuro-development. Thimerosal at concentrations relevant for infants' exposure (in vaccines) is toxic to cultured human-brain cells and to laboratory animals. The persisting use of TCV (in developing countries) is counterintuitive to global efforts to lower Hg exposure and to ban Hg in medical products; its continued use in TCV requires evaluation of a sufficiently nontoxic level of ethylmercury compatible with repeated exposure (co-occurring with adjuvant-Al) during early life.

<http://www.ncbi.nlm.nih.gov/pubmed/21350943>

“... activity of low doses of Thimerosal against isolated human and animal brain cells was found in all studies and is consistent with mercury neurotoxicity ... animal studies have shown that exposure to Thimerosal-Hg can lead to accumulation of inorganic mercury in brain, and that doses relevant to Thimerosal-containing vaccine exposure possess the potential to affect human neuro-development.”

Automated speciation of mercury
in the hair of breastfed infants exposed to ethylmercury
from thimerosal-containing vaccines

Author information

Dórea JG1, Wimer W, Marques RC, Shade C.

Universidade de Brasília, C.P.04322, 70919-970
Brasília, Federal District, Brasil
dorea@rudah.com.br

Abstract

A simplified thiourea-based chromatography method, originally developed for methyl and inorganic mercury, was adapted to separate methylmercury (MeHg), ethylmercury (EtHg), and inorganic mercury (Hg(II)) in infants' hair. Samples were weighed and leached with an acidic thiourea solution. Leachates were concentrated on a polymeric resin prior to analysis by Hg-thiourea liquid chromatography/cold vapor atomic fluorescence spectrometry. All but one sample showed small amounts of EtHg, and four of the six analyzed samples had proportionally higher Hg(II) as a percent of total Hg. Breastfed infants from riverine Amazonian communities are exposed to mercury in breast milk (from high levels of maternal sources that include both fish consumption and dental amalgam) and to EtHg in vaccines (from thimerosal). The method proved sensitive enough to detect and quantify acute EtHg exposure after shots of thimerosal-containing vaccines. Based on work with MeHg and Hg(II), estimated detection limits for this method are 0.050, 0.10, and 0.10 ng g⁻¹ for MeHg, Hg(II), and EtHg, respectively, for a 20-mg sample. Specific limits depend on the amount of sample extracted and the amount of extract injected.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20419397>

“The method proved sensitive enough to detect and quantify acute Ethyl Mercury exposure after shots of thimerosal-containing vaccines.”

“... significant elevation in the concentration of copper, lead and mercury ...”

Biological Trace Element Research • August 2011

Level of trace elements (copper, zinc, magnesium and selenium) and toxic elements (lead and mercury) in the hair and nail of children with autism

Author information

Lakshmi Priya MD1, Geetha A.

Department of Biochemistry, Bharathi Women's College
Chennai, 600 108 Tamil Nadu, India

Abstract

Autism is a multi-factorial pathology observed in children with altered levels of essential and elevated levels of toxic elements. There are also studies reporting a decrease in nutritional trace elements in the hair and nail of autistic children with healthy controls; moreover, bioelements have been shown to play an important role in the central nervous system. Therefore, the purpose of the present study was to assess the levels of trace elements like copper (Cu), zinc (Zn), magnesium (Mg), and selenium (Se) and toxic elements like mercury (Hg), and lead (Pb) in the hair and nail samples of autistic children and to evaluate whether the level of these elements could be correlated with the severity of autism. The subjects of the study were 45 autistic children with different grades of severity (low (LFA), medium (MFA), and high (HFA) functioning autism) according to Childhood Autism Rating Scale, n = 15 children in each group and 50 healthy children (age and sex matched). The boys and girls ratio involved in this study was 4:1, and they were 4-12 years of age. The study observed a valid indication of Cu body burden in the autistic children. The children with different grades of autism showed high significance ($p < 0.001$) in the level of copper in their hair and nail samples when compared to healthy controls. The level of Cu in the autistic children could be correlated with their degree of severity (more the Cu burden severe is autism). The study showed a significant elevation ($p < 0.001$) in the levels of toxic metals Pb and Hg in both hair and nail samples of autistic children when compared to healthy control group. The elevation was much pronounced in LFA group subjects when compared among autistic groups MFA and HFA. The levels of trace elements Mg and Se were significantly decreased ($p < 0.001$) in autistic children when compared to control. The trace element Zn showed significant variation in both hair and nails of LFA group children when compared to control group and other study groups. The significant elevation in the concentration of Cu, Pb, and Hg and significant decrease in the concentration of Mg and Se observed in the hair and nail samples of autistic subjects could be well correlated with their degrees of severity.

<http://www.ncbi.nlm.nih.gov/pubmed/20625937>

Mercury exposure and risks from dental amalgam in the US population post-2000

Author information

Richardson GM1, Wilson R,
Allard D, Purtil C, Douma S, Gravière J.

SNC-Lavalin Environment, Suite 110
20 Colonnade Road, Ottawa, ON Canada
mark.richardson@snclavalin.com

Abstract

Dental amalgam is 50% metallic mercury (Hg) by weight and Hg vapour continuously evolves from in-place dental amalgam, causing increased Hg content with increasing amalgam load in urine, faeces, exhaled breath, saliva, blood, and various organs and tissues including the kidney, pituitary gland, liver, and brain. The Hg content also increases with maternal amalgam load in amniotic fluid, placenta, cord blood, meconium, various foetal tissues including liver, kidney and brain, in colostrum and breast milk. Based on 2001 to 2004 population statistics, 181.1 million Americans carry a grand total of 1.46 billion restored teeth. Children as young as 26 months were recorded as having restored teeth. Past dental practice and recently available data indicate that the majority of these restorations are composed of dental amalgam. Employing recent US population-based statistics on body weight and the frequency of dentally restored tooth surfaces, and recent research on the incremental increase in urinary Hg concentration per amalgam-filled tooth surface, estimates of Hg exposure from amalgam fillings were determined for 5 age groups of the US population. Three specific exposure scenarios were considered, each scenario incrementally reducing the number of tooth surfaces assumed to be restored with amalgam. Based on the least conservative of the scenarios evaluated, it was estimated that some 67.2 million Americans would exceed the Hg dose associated with the reference exposure level (REL) of 0.3 $\mu\text{g}/\text{m}^3$ established by the US Environmental Protection Agency; and 122.3 million Americans would exceed the dose associated with the REL of 0.03 $\mu\text{g}/\text{m}^3$ established by the California Environmental Protection Agency. Exposure estimates are consistent with previous estimates presented by Health Canada in 1995, and amount to 0.2 to 0.4 $\mu\text{g}/\text{day}$ per amalgam-filled tooth surface, or 0.5 to 1 $\mu\text{g}/\text{day}/\text{amalgam-filled tooth}$, depending on age and other factors.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21782213>

“Based on the least conservative of the scenarios evaluated, it was estimated that some 67.2 million Americans would exceed the mercury dose associated with the reference exposure level (REL) of 0.3 $\mu\text{g}/\text{m}^3$ established by the US Environmental Protection Agency; and 122.3 million Americans would exceed the dose associated with the REL of 0.03 $\mu\text{g}/\text{m}^3$ established by the California Environmental Protection Agency.”

“These data document that early postnatal Thimerosal administration causes lasting neurobehavioral impairments and neurochemical alterations in the brain ...”

Behavioral Brain Research • September 2011

**Persistent behavioral impairments
and alterations of brain dopamine system
after early postnatal administration of thimerosal in rats**

Author information

Olczak M1, Duszczyk M, Mierzejewski P, Meyza K, Majewska MD.

Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology, 02-957 Warsaw, Poland

Abstract

The neurotoxic organomercurial thimerosal (THIM), used for decades as vaccine preservative, is a suspected factor in the pathogenesis of some neurodevelopmental disorders. Previously we showed that neonatal administration of THIM at doses equivalent to those used in infant vaccines or higher, causes lasting alterations in the brain opioid system in rats. Here we investigated neonatal treatment with THIM (at doses 12, 240, 1440 and 3000 μg Hg/kg) on behaviors, which are characteristically altered in autism, such as locomotor activity, anxiety, social interactions, spatial learning, and on the brain dopaminergic system in Wistar rats of both sexes. Adult male and female rats, which were exposed to the entire range of THIM doses during the early postnatal life, manifested impairments of locomotor activity and increased anxiety/neophobia in the open field test. In animals of both sexes treated with the highest THIM dose, the frequency of prosocial interactions was reduced, while the frequency of asocial/antisocial interactions was increased in males, but decreased in females. Neonatal THIM treatment did not significantly affect spatial learning and memory. THIM-exposed rats also manifested reduced haloperidol-induced catalepsy, accompanied by a marked decline in the density of striatal D2 receptors, measured by immunohistochemical staining, suggesting alterations to the brain dopaminergic system. Males were more sensitive than females to some neurodisruptive/neurotoxic actions of THIM. These data document that early postnatal THIM administration causes lasting neurobehavioral impairments and neurochemical alterations in the brain, dependent on dose and sex. If similar changes occur in THIM/mercurial-exposed children, they could contribute to neurodevelopmental disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21549155>

Chronic inorganic mercury exposure induces sex-specific changes in central TNF expression: importance in autism?

Author information

Thomas Curtis J1, Chen Y, Buck DJ, Davis RL.

Department of Pharmacology/Physiology
Oklahoma State University Center for Health Sciences
1111 West 17th Street, Tulsa, OK 74107, United States

Abstract

Mercury is neurotoxic and increasing evidence suggests that environmental exposure to mercury may contribute to neuropathologies including Alzheimer's disease and autism spectrum disorders. Mercury is known to disrupt immunocompetence in the periphery, however, little is known about the effects of mercury on neuroimmune signaling. Mercury-induced effects on central immune function are potentially very important given that mercury exposure and neuroinflammation both are implicated in certain neuropathologies (i.e., autism). Furthermore, mounting evidence points to the involvement of glial activation in autism. Therefore, we utilized an *in vivo* model to assess the effects of mercury exposure on neuroimmune signaling. In prairie voles, 10 week mercury exposure (60ppm HgCl₂ in drinking water) resulted in a male-specific increase in TNF protein expression in the cerebellum and hippocampus. These findings are consistent with our previously reported male-specific mercury-induced deficits in social behavior and further support a role for heavy metals exposure in neuropathologies such as autism. Subsequent studies should further evaluate the mechanism of action and biological consequences of heavy metals exposure. Additionally, these observations highlight the potential of neuroimmune markers in male voles as biomarkers of environmental mercury toxicity.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3443965/>

“These findings are consistent with our previously reported male-specific mercury-induced deficits in social behavior and further support a role for heavy metals exposure in neuropathologies such as autism.”

“... statistically significant differences in the mean urine levels of aluminum, barium, cerium, mercury ...”

Maedica Bucharest • October 2011

Heavy metals and trace elements in hair and urine of a sample of arab children with autistic spectrum disorder

Author information

Blaurock-Busch E1, Amin OR, Rabah T.

Lecturer and Advisor

International Board of Clinical Metal Toxicology & German Medical Association of Clinical Metal Toxicology

Abstract

General information: Autism is a severe developmental disorder which involves social withdrawal, communication deficits, and stereotypic/repetitive behavior. The pathophysiological etiologies which precipitate autism symptoms remain elusive and controversial in many cases, but both genetic and environmental factors (and their interactions) have been implicated. While autism is considered multicausal, environmental factors have received significant attention. International discussion has focused on neurotoxins such as mercury and lead, suggesting that these and other toxic metals contribute to the development of the disorder. An epidemiological study released in 2006 (Palmer et al.) linking Toxic Release Inventory (TRI) data on mercury to special education data in Texas reported a 61% increase in autism prevalence rates (or 17% adjusted) per 1000 pounds of mercury released into the environment (1). We attempted to further evaluate whether exposure to variable environmental contributes to the genesis of autistic spectrum disorder, and thus is a factor increasing the risk for developing autism symptoms in utero or in early childhood.

PURPOSE

The purpose of this study is to examine possible environmental risk factors and sources of exposure to mercury and other heavy metals in children with autism spectrum disorder versus controls. Through laboratory diagnostics we are able to distinguish between present and past exposure (i.e. hair analysis measurements reflect past exposure), urinary excretion levels of unprovoked urine represent immediate exposure. By assessing a spectrum of trace elements and heavy metals in hair and urine of both autistic and control groups, we focused on the participants' past and present exposure.

METHODOLOGY

The participants were 25 Autistic Spectrum Disorder (ASD) children (22 boys and 3 girls) between the age of 3 and 9 years. They were either diagnosed previously by other psychiatrist, psychologist, and developmental pediatrician or suspected by their parents as being autistic. All children were attendants to the Child Psychiatric Clinic in Erfan Psychiatric

Hospital in Jeddah, KSA. Samples were collected during the period of June 2006 to March 2008. A control group of 25 children without any psychiatric or medical disorders was age-matched and sex-matched. All parents signed informed consent forms. All autistic children were subjected to a full clinical child psychiatric sheet for the diagnosis of autism spectrum disorder and exclusion of other psychiatric disorders according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM IV). The severity of autistic symptomatology was measured by the Childhood Autism Rating Scale (CARS) and Autism Behavior Checklist (ABC) using the Arabic versions. Both groups were subjected to the Questionnaire on Exposure to Heavy Metals, Physical Symptoms, and Child Development. Hair and baseline urine samples (i.e. unprovoked urine) were taken from both groups and sent to the German clinical and environmental laboratory Micro Trace Minerals GmbH, for the detection of heavy metals and trace elements levels where metal testing was performed via ICP-MS spectroscopy utilizing cell technique.

RESULTS

By comparing the ASD Group to the Control Group, we found a statistically significant difference in the mean hair levels of arsenic, cadmium, barium, cerium and lead ($p=0.01$, 0.03 , 0.003 , 0.003 , and 0.03 respectively), and in the mean hair levels of magnesium and zinc ($p=0.001$ and 0.003 respectively). There were also statistically significant differences in the mean urine levels of aluminum, barium, cerium, mercury, and lead ($p=0.004$, 0.002 , 0.014 , 0.006 and 0.004 respectively), and in the mean urine levels of copper and germanium ($p=0.049$ and 0.02 respectively). An agreement was found in both specimen (hair and urine) for barium and lead. The statistically significant differences in mean hair levels of arsenic, cadmium, and cerium were not supported by urine baseline levels. Also, the statistically significant magnesium and zinc levels of hair were not supported by urine levels. A disagreement was also found with copper and germanium concentrations.

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3391939/>

Toxicity of volatile methylated species of bismuth, arsenic, tin, and mercury in Mammalian cells in vitro

Author information

Dopp E1, von Recklinghausen U, Hippler J,
Diaz-Bone RA, Richard J, Zimmermann U,
Rettenmeier AW, Hirner AV.

Institute of Hygiene and Occupational Medicine
University of Duisburg-Essen, Hufelandstraße 55
45122 Essen, Germany

Abstract

The biochemical transformation of mercury, tin, arsenic and bismuth through formation of volatile alkylated species performs a fundamental role in determining the environmental processing of these elements. While the toxicity of inorganic forms of most of these compounds are well documented (e.g., arsenic, mercury) and some of them are of relatively low toxicity (e.g., tin, bismuth), the more lipid-soluble organometals can be highly toxic. In the present study we investigated the cyto- and genotoxicity of five volatile metal(loid) compounds: trimethylbismuth, dimethylarsenic iodide, trimethylarsine, tetramethyltin, and dimethylmercury. As far as we know, this is the first study investigating the toxicity of volatile metal(loid) compounds in vitro. Our results showed that dimethylmercury was most toxic to all three used cell lines (CHO-9 cells, CaCo, Hep-G2) followed by dimethylarsenic iodide. Tetramethyltin was the least toxic compound; however, the toxicity was also dependend upon the cell type. Human colon cells (CaCo) were most susceptible to the toxicity of the volatile compounds compared to the other cell lines. We conclude from our study that volatile metal(loid) compounds can be toxic to mammalian cells already at very low concentrations but the toxicity depends upon the metal(loid) species and the exposed cell type.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3189616/>

“We conclude from our study
that volatile metal(loid) compounds
can be toxic to mammalian cells already
at very low concentrations but the toxicity
depends upon the metal(loid) species
and the exposed cell type.”

Ancestry of pink disease (infantile acrodynia) identified as a risk factor for autism spectrum disorders

Author information

Shandley K1, Austin DW.

Swinburne Autism Bio-Research Initiative (SABRI)
Brain and Psychological Sciences Research Centre
Swinburne University of Technology
Hawthorn, Victoria, Australia

Abstract

Pink disease (infantile acrodynia) was especially prevalent in the first half of the 20th century. Primarily attributed to exposure to mercury (Hg) commonly found in teething powders, the condition was developed by approximately 1 in 500 exposed children. The differential risk factor was identified as an idiosyncratic sensitivity to Hg. Autism spectrum disorders (ASD) have also been postulated to be produced by Hg. Analogous to the pink disease experience, Hg exposure is widespread yet only a fraction of exposed children develop an ASD, suggesting sensitivity to Hg may also be present in children with an ASD. The objective of this study was to test the hypothesis that individuals with a known hypersensitivity to Hg (pink disease survivors) may be more likely to have descendants with an ASD. Five hundred and twenty-two participants who had previously been diagnosed with pink disease completed a survey on the health outcomes of their descendants. The prevalence rates of ASD and a variety of other clinical conditions diagnosed in childhood (attention deficit hyperactivity disorder, epilepsy, Fragile X syndrome, and Down syndrome) were compared to well-established general population prevalence rates. The results showed the prevalence rate of ASD among the grandchildren of pink disease survivors (1 in 22) to be significantly higher than the comparable general population prevalence rate (1 in 160). The results support the hypothesis that Hg sensitivity may be a heritable/genetic risk factor for ASD.

<http://www.ncbi.nlm.nih.gov/pubmed/21797771>

“Pink disease was especially prevalent in the first half of the 20th century. Primarily attributed to exposure to mercury commonly found in teething powders, the condition was developed by approximately 1 in 500 exposed children.”

A positive association found between autism prevalence and childhood vaccination uptake across the U.S. population

Author information

DeLong G.

Department of Economics and Finance
Baruch College/City University of New York
New York, New York, USA
gayle.delong@baruch.cuny.edu

Abstract

The reason for the rapid rise of autism in the United States that began in the 1990s is a mystery. Although individuals probably have a genetic predisposition to develop autism, researchers suspect that one or more environmental triggers are also needed. One of those triggers might be the battery of vaccinations that young children receive. Using regression analysis and controlling for family income and ethnicity, the relationship between the proportion of children who received the recommended vaccines by age 2 years and the prevalence of autism (AUT) or speech or language impairment (SLI) in each U.S. state from 2001 and 2007 was determined. A positive and statistically significant relationship was found: The higher the proportion of children receiving recommended vaccinations, the higher was the prevalence of AUT or SLI. A 1% increase in vaccination was associated with an additional 680 children having AUT or SLI. Neither parental behavior nor access to care affected the results, since vaccination proportions were not significantly related (statistically) to any other disability or to the number of pediatricians in a U.S. state. The results suggest that although mercury has been removed from many vaccines, other culprits may link vaccines to autism. Further study into the relationship between vaccines and autism is warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/21623535>

“The results suggest
that although mercury has been
removed from many vaccines, other
culprits may link vaccines to autism.”

“Our data supports the historic evidence that heavy metals play a role in the development of Autistic Spectrum Disorder.”

Maedica Bucharest • January 2012

Toxic Metals and Essential Elements in Hair and Severity of Symptoms among Children with Autism

Author information

Blaurock-Busch E1, Amin OR, Dessoki HH, Rabah T.

Lecturer and Advisor
International Board of Clinical Metal Toxicology and
German Medical Association of Clinical Metal Toxicology Hersbruck, Germany

Abstract

OBJECTIVE

The objective of this study was to assess the levels of ten toxic metals and essential elements in hair samples of children with autism, and to correlate the level of these elements with the severity of autism.

METHOD

The participants were 44 children, age 3 to 9 years, with Autistic Spectrum Disorder (ASD) according to Diagnostic and Statistical Manual of Mental Disorders 4th Edition, (DSM-IV). The severity of autistic symptomatology was measured by the Childhood Autism Rating Scale (CARS). Hair analysis was performed to evaluate the long term metal exposure and mineral level.

RESULTS

By comparing hair concentration of autistic vs nonautistic children, elevated hair concentrations were noted for aluminum, arsenic, cadmium, mercury, antimony, nickel, lead, and vanadium. Hair levels of calcium, iron, iodine, magnesium, manganese, molybdenum, zinc, and selenium were considered deficient. There was a significant positive correlation between lead & verbal communication ($p = 0.020$) and general impression ($p = 0.008$). In addition, there was a significant negative correlation between zinc & fear and nervousness ($p = 0.022$).

CONCLUSION

Our data supports the historic evidence that heavy metals play a role in the development of ASD. In combination with an inadequate nutritional status the toxic effect of metals increase along with the severity of symptoms.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484795/>

Administration of thimerosal to infant rats increases overflow of glutamate and aspartate in the prefrontal cortex: protective role of dehydroepiandrosterone sulfate

Author information

Duszczyk-Budhathoki M1, Olczak M, Lehner M, Majewska MD.

Marie Curie Chairs Program
Department of Pharmacology and Physiology of Nervous System
Institute of Psychiatry and Neurology, 02-957, Warsaw, Poland

Abstract

Thimerosal, a mercury-containing vaccine preservative, is a suspected factor in the etiology of neurodevelopmental disorders. We previously showed that its administration to infant rats causes behavioral, neurochemical and neuropathological abnormalities similar to those present in autism. Here we examined, using microdialysis, the effect of thimerosal on extracellular levels of neuroactive amino acids in the rat prefrontal cortex (PFC). Thimerosal administration (4 injections, i.m., 240 µg Hg/kg on postnatal days 7, 9, 11, 15) induced lasting changes in amino acid overflow: an increase of glutamate and aspartate accompanied by a decrease of glycine and alanine; measured 10-14 weeks after the injections. Four injections of thimerosal at a dose of 12.5 µg Hg/kg did not alter glutamate and aspartate concentrations at microdialysis time (but based on thimerosal pharmacokinetics, could have been effective soon after its injection). Application of thimerosal to the PFC in perfusion fluid evoked a rapid increase of glutamate overflow. Coadministration of the neurosteroid, dehydroepiandrosterone sulfate (DHEAS; 80 mg/kg; i.p.) prevented the thimerosal effect on glutamate and aspartate; the steroid alone had no influence on these amino acids. Coapplication of DHEAS with thimerosal in perfusion fluid also blocked the acute action of thimerosal on glutamate. In contrast, DHEAS alone reduced overflow of glycine and alanine, somewhat potentiating the thimerosal effect on these amino acids. Since excessive accumulation of extracellular glutamate is linked with excitotoxicity, our data imply that neonatal exposure to thimerosal-containing vaccines might induce excitotoxic brain injuries, leading to neurodevelopmental disorders. DHEAS may partially protect against mercurials-induced neurotoxicity.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/?term=22015977>

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3264864/>

“Since excessive accumulation of extracellular glutamate is linked with excitotoxicity, our data imply that neonatal exposure to thimerosal-containing vaccines might induce excitotoxic brain injuries, leading to neurodevelopmental disorders.”

Thimerosal-induced apoptosis in mouse C2C12 myoblast cells occurs through suppression of the PI3K/Akt/survivin pathway

Author information

Li WX1, Chen SF, Chen LP,
Yang GY, Li JT, Liu HZ, Zhu W.

Department of Toxicology
Guangzhou Center for Disease Control and Prevention
Guangzhou, China

Abstract

BACKGROUND

Thimerosal, a mercury-containing preservative, is one of the most widely used preservatives and found in a variety of biological products. Concerns over its possible toxicity have reemerged recently due to its use in vaccines. Thimerosal has also been reported to be markedly cytotoxic to neural tissue. However, little is known regarding thimerosal-induced toxicity in muscle tissue. Therefore, we investigated the cytotoxic effect of thimerosal and its possible mechanisms on mouse C2C12 myoblast cells.

METHODOLOGY/PRINCIPAL FINDINGS

The study showed that C2C12 myoblast cells underwent inhibition of proliferation and apoptosis after exposure to thimerosal (125-500 nM) for 24, 48 and 72 h. Thimerosal caused S phase arrest and induced apoptosis as assessed by flow cytometric analysis, Hoechst staining and immunoblotting. The data revealed that thimerosal could trigger the leakage of cytochrome c from mitochondria, followed by cleavage of caspase-9 and caspase-3, and that an inhibitor of caspase could suppress thimerosal-induced apoptosis. Thimerosal inhibited the phosphorylation of Akt(ser473) and survivin expression. Wortmannin, a PI3K inhibitor, inhibited Akt activity and decreased survivin expression, resulting in increased thimerosal-induced apoptosis in C2C12 cells, while the activation of PI3K/Akt pathway by mIGF-I (50 ng/ml) increased the expression of survivin and attenuated apoptosis. Furthermore, the inhibition of survivin expression by siRNA enhanced thimerosal-induced cell apoptosis, while overexpression of survivin prevented thimerosal-induced apoptosis. Taken together, the data show that the PI3K/Akt/survivin pathway plays an important role in the thimerosal-induced apoptosis in C2C12 cells.

CONCLUSIONS/SIGNIFICANCE

Our results suggest that in C2C12 myoblast cells, thimerosal induces S phase arrest and finally causes apoptosis via inhibition of PI3K/Akt/survivin signaling followed by activation of the mitochondrial apoptotic pathway.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3492179/>

“Our results suggest that in C2C12 myoblast cells, thimerosal induces S phase arrest and finally causes apoptosis via inhibition of PI3K/Akt/survivin signaling followed by activation of the mitochondrial apoptotic pathway.”

A Link Between mercury exposure, Autism Spectrum Disorder, and other neurodevelopmental Disorders? Implications for thimerosal-containing Vaccines

Lucija Tomljenovic,¹ José G. Dórea,²
Christopher A. Shaw,¹

1. Department of Ophthalmology and Visual Sciences
University of British Columbia, Vancouver, BC
2. Faculty of Health Sciences
Universidade de Brasilia, Brasilia, Brazil

Abstract

Autism is a multisystem developmental disorder characterized by dysfunctional immunity and impaired brain function. Although autism is partly determined by genetic susceptibility factors, reported dramatic increases in the prevalence of autism in developed countries have intensified scientific focus on environmental exposures. Pre and perinatal immunotoxic insults are now strongly suspected as contributors to this increase. Mercury (Hg) is both a neuro and an immuno toxin and continues to be used in some pediatric vaccines in the form of the preservative thimerosal. Although currently there are no direct human studies on the risks of Hg exposure from thimerosal-containing vaccines (TCVs), animal studies show that doses relevant to human TCV exposure can result in adverse neurodevelopmental outcomes. To date, TCVs continue to be administered on a regular basis to potentially the most vulnerable populations: pregnant women and children. In light of existing experimental evidence, the rationale for using this known immunotoxic and neurotoxic substance in human vaccines should be reconsidered.

Given the dramatic and rapidly-growing reported prevalence of autism spectrum disorder (ASD) (Newschaffer, Falb, & Gurney, 2005), a clear answer to the etiology of this apparent epidemic would serve parents as well as the medical community entrusted with the health of all children. The focus of this commentary is on the possible involvement of thimerosal (49% ethylmercury (EtHg)) in neurodevelopmental disorders. In the past, thimerosal was used worldwide as a preservative in vaccines. Although this practice has largely been discontinued due to safety concerns (Offit & Jew, 2003), thimerosal continues to be used in less-developed and developing countries (Dórea, Marques, & Brandao, 2009)), as well as in the preservation of multi-dose vaccine vials in Canada and the United States (Centers for Disease Control and Prevention, 2011; Public Health Agency of Canada, 2011). The use of thimerosal-containing vaccines (TCVs) continues to be a highly contentious issue. The fact that a causal link between thimerosal exposure and neurodevelopmental disorders in children is not supported by many studies (Andrews et al., 2004; Hviid, Stellfeld, Wohlfahrd, & Melbye, 2003; Parker, Schwartz, Todd, & Pickering, 2004; Verstraeten et al., 2003) fails to put this issue at rest.

“Given the dramatic and rapidly-growing reported prevalence of autism spectrum disorder (ASD) (Newschaffer, Falb, & Gurney, 2005), a clear answer to the etiology of this apparent epidemic would serve parents as well as the medical community entrusted with the health of all children. The fact that a causal link between thimerosal exposure and neurodevelopmental disorders in children is not supported by many studies fails to put this issue at rest.”

Environmental Sources Of Mercury

Mercury Concentration	Form	Biological Significance
0.4ppb	MetHg	Median chronic intake of contaminated fish (0.4ug/kg body weight) causes delayed speech and autistic-like symptoms in male children (Corbett & Poor, 2008)
1.6ppb	MetHg	Provisional Tolerable Weekly Intake (PTWI) based on body weight for infants and pregnant women (1.6ug/kg; Food & Agricultural Association/World Health Organization 2006)
2.0ppb	Inorganic Mercury	US EPA limit for drinking water (US EPA, 2011)
200ppb	Various Types Of Mercury	Level in liquid that the US EPA classifies as hazardous waste based on toxicity characteristics (US EPA, 2010)
600ppb	EtHg	Concentration of mercury in vaccines containing trace amounts of thimerosal (0.3ug/0.5 ml. dose, or 600ug/L;Halsey, 1999)
25,000-50,000ppb	EtHg	Concentration in Thimerosal containing multi-dose influenza, meningococcal pneumococcal polysaccharide and diphtheria-tetanus vaccines (Offit & Jew, 2003)

**Thimerosal-Derived Ethylmercury
Is a Mitochondrial Toxin in Human Astrocytes:
Possible Role of Fenton Chemistry
in the Oxidation and Breakage of mtDNA**

Martyn A. Sharpe, * Andrew D. Livingston, and David S. Baskin

Department of Neurosurgery, The Methodist Hospital
6565 Fannin Street, Houston, TX 77030, USA

Abstract

Thimerosal generates ethylmercury in aqueous solution and is widely used as preservative. We have investigated the toxicology of Thimerosal in normal human astrocytes, paying particular attention to mitochondrial function and the generation of specific oxidants. We find that ethylmercury not only inhibits mitochondrial respiration leading to a drop in the steady state membrane potential, but also concurrent with these phenomena increases the formation of superoxide, hydrogen peroxide, and Fenton/Haber-Weiss generated hydroxyl radical. These oxidants increase the levels of cellular aldehyde/ketones. Additionally, we find a five-fold increase in the levels of oxidant damaged mitochondrial DNA bases and increases in the levels of mtDNA nicks and blunt-ended breaks. Highly damaged mitochondria are characterized by having very low membrane potentials, increased superoxide/hydrogen peroxide production, and extensively damaged mtDNA and proteins. These mitochondria appear to have undergone a permeability transition, an observation supported by the five-fold increase in Caspase-3 activity observed after Thimerosal treatment.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3395253/>

“We find that ethylmercury not only inhibits mitochondrial respiration leading to a drop in the steady state membrane potential, but also concurrent with these phenomena increases the formation of superoxide, hydrogen peroxide, and Fenton/Haber-Weiss generated hydroxyl radical. These oxidants increase the levels of cellular aldehyde/ketones. Additionally, we find a five-fold increase in the levels of oxidant damaged mitochondrial DNA bases and increases in the levels of mtDNA nicks and blunt-ended breaks.”

Maternal thimerosal exposure
results in aberrant cerebellar oxidative stress,
thyroid hormone metabolism, and motor behavior
in rat pups; sex- and strain-dependent effects

Author information

Sulkowski ZL1, Chen T, Midha S,
Zavacki AM, Sajdel-Sulkowska EM.

Department of Psychiatry
Harvard Medical School and Brigham and Women's Hospital
Boston, MA, USA

Abstract

Methylmercury (Met-Hg) and ethylmercury (Et-Hg) are powerful toxicants with a range of harmful neurological effects in humans and animals. While Met-Hg is a recognized trigger of oxidative stress and an endocrine disruptor impacting neurodevelopment, the developmental neurotoxicity of Et-Hg, a metabolite of thimerosal (TM), has not been explored. We hypothesized that TM exposure during the perinatal period impairs central nervous system development, and specifically the cerebellum, by the mechanism involving oxidative stress. To test this, spontaneously hypertensive rats (SHR) or Sprague-Dawley (SD) rat dams were exposed to TM (200 µg/kg body weight) during pregnancy (G10-G15) and lactation (P5-P10). Male and female neonates were evaluated for auditory and motor function; cerebella were analyzed for oxidative stress and thyroid metabolism. TM exposure resulted in a delayed startle response in SD neonates and decreased motor learning in SHR male (22.6%), in SD male (29.8%), and in SD female (55.0%) neonates. TM exposure also resulted in a significant increase in cerebellar levels of the oxidative stress marker 3-nitrotyrosine in SHR female (35.1%) and SD male (14.0%) neonates. The activity of cerebellar type 2 deiodinase, responsible for local intra-brain conversion of thyroxine to the active hormone, 3',3,5-triiodothyronine (T3), was significantly decreased in TM-exposed SHR male (60.9%) pups. This coincided with an increased (47.0%) expression of a gene negatively regulated by T3, *Odf4* suggesting local intracerebellar T3 deficiency. Our data thus demonstrate a negative neurodevelopmental impact of perinatal TM exposure which appears to be both strain- and sex-dependent.

<http://www.ncbi.nlm.nih.gov/pubmed/22015705>

“Our data thus demonstrate
a negative neurodevelopmental impact
of perinatal Thimerosal exposure which appears
to be both strain- and sex-dependent.”

Toxic effects of mercury on the cardiovascular and central nervous systems

Author information

Fernandes Azevedo B1, Barros Furieri L, Peçanha FM,
Wiggers GA, Frizera Vassallo P, Ronacher Simões M, Fiorim J,
Rossi de Batista P, Fiorese M, Rossoni L, Stefanon I, Alonso MJ,
Salaices M, Valentim Vassallo D.

Programa de Pós-Graduação em Ciências Fisiológicas
Universidade Federal do Espírito Santo
29042-755 Vitória, ES, Brazil

Abstract

Environmental contamination has exposed humans to various metal agents, including mercury. This exposure is more common than expected, and the health consequences of such exposure remain unclear. For many years, mercury was used in a wide variety of human activities, and now, exposure to this metal from both natural and artificial sources is significantly increasing. Many studies show that high exposure to mercury induces changes in the central nervous system, potentially resulting in irritability, fatigue, behavioral changes, tremors, headaches, hearing and cognitive loss, dysarthria, incoordination, hallucinations, and death. In the cardiovascular system, mercury induces hypertension in humans and animals that has wide-ranging consequences, including alterations in endothelial function. The results described in this paper indicate that mercury exposure, even at low doses, affects endothelial and cardiovascular function. As a result, the reference values defining the limits for the absence of danger should be reduced.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3395437/>

“The results described
in this paper indicate
that mercury exposure,
even at low doses,
affects endothelial and
cardiovascular function.”

Mercury Toxicity

João B. T. Rocha, Michael Aschner, José G. Dórea,
Sandra Ceccatelli, Marcelo Farina and Luiz Carlos L. Silveira

Abstract

Mercury (Hg) is one of the most toxic elements in the periodic table. Although Hg is present in nature, it has also been released into the environment for centuries as a result of anthropogenic activities. Nowadays, there are efforts to reduce its anthropogenic use; however, its environmental presence is significant and will persist. We are pleased to present this special issue on mercury toxicity. The objective of collecting research findings in a single issue devoted to the toxicology of mercury was to compile reports on the latest findings on Hg's toxicity from renowned research groups across the world. This special issue affords the opportunity to bring together a wide range of review and research papers devoted both to basic and applied toxicity associated with various exposure scenarios and Hg species (dental material, iatrogenic ethylmercury, fish-methylmercury) along with comprehensive description on experimental models. While human studies demonstrated the noxious effects of these forms of Hg, experimental studies have assisted in defining mechanistic pathways central to Hg's toxicity in various tissues and organ systems.

The volume is dedicated in part to articles that provide new insights on important considerations of subtle effects of exposure to multiple forms of organic mercury (ethylmercury in thimerosal-containing vaccines and methylmercury (MeHg) derived from maternal fish consumption) and neurological outcomes in infants (J. G. Dórea et al.). In addition, hypersensitivity to low-dose Hg exposure from dental amalgam fillings is detailed, showing exquisite sensitivity to amalgam-derived Hg in sensitized individuals (H. McParland and S. Warnakulasuriya). Local effects of amalgam and Hg dental restoration represent the most important nonoccupational exposure to inorganic mercury, while fish consumption represents the most common source of MeHg exposure.

The impacts of exposure to fish-derived MeHg at levels below those considered to pose neurological risk (hair level: 50 µg/g) were explored by Japanese researchers in subjects of the Niigata mercury poisoning (K. Maruyama et al.). Experimental research papers from this issue confirmed and extended observations that exposure of immature rodents to different chemical forms of Hg is associated with differential bodily distribution Hg (M. Blanuša et al.; C.-F. Huang et al.). C.-F. Huang et al. demonstrated that exposure of developing rats to cinnabar (HgS) caused long-lasting neurobehavioral and neurochemical toxic effect, indicating that the use of this millenary component of traditional Chinese medicine continues to represent a toxicological concern. Using an important, yet little explored experimental mouse model, J. P. Bourdineaud and colleagues demonstrated that the ingestion of MeHg-adulterated fish led to higher neurotoxicity in comparison to the

ingestion of the “free salt” of methylmercury chloride (MeHgCl). The scarcity of studies on this subject highlights the need for future studies to address these persistent toxicological issues.

The molecular, subcellular, cellular, and systemic toxicity of Hg was also addressed here in this volume. The cardiovascular toxicity of Hg in humans and rodents was reviewed by B. F. Azevedo et al. The impact of Hg exposure on endothelial cell physiology is well established; however, the limit of dietary-derived Hg needed to trigger cardiotoxic effects is still debatable. The negative impact of oral exposure to Hg(II) on reproductive performance of male rats was demonstrated by J. C. Heath and collaborators, highlighting the need for detailed studies to determine the nonobservable adverse effect level (NOAEL) of Hg(II) in the male reproductive system, as well as Hg deposition in target tissues. The comparative renal and hepatic toxicity of Hg(II) and MeHg in fish was addressed by V. Branco et al., demonstrating that both forms of mercury targeted the antioxidant selenoenzyme thioredoxin-reductase (TrxR) and reinforcing the central role of disrupted selenoprotein function in mercurial toxicity. The *in vitro* and *in vivo* targeting of the critical sulfhydryl-containing enzyme, Na⁺, K⁺-ATPase was reviewed by I. Kade and addressed by T. S. Huang et al., noting divergent effects *in vitro* and *in vivo*. The role of mitochondria and calcium in the neurotoxicity of MeHg was reviewed by D. Roos et al., providing evidence that Ca²⁺, glutamate, oxidative stress, and mitochondria play a central role in its neurotoxicity. The efficacy of the marine n-3 fatty acids, eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) in attenuating MeHg-induced toxicity was studied in fish and mammalian cell cultures. O. J. Nøstbakken et al. demonstrated that DHA decreased MeHg uptake into mammalian cells but increased MeHg-induced apoptosis in fish cells.

We hope that the new findings on the subtle effects of combined exposure to iatrogenic ethylmercury (from thimerosal-containing vaccines) and maternal MeHg (from fish consumption), as well as the results of experimental studies and the critical reviews presented herein can shed novel information on mercury's absorption, distribution, metabolism, and excretion, as well as its ill effects at the cellular, molecular, and organismal levels. Understanding of these facets of research is required for derivation on environmental and health policies as well as guidance for the most promising future research venues. Finally, we would like to thank all the reviewers that have contributed their time and insight to this special issue as well as the journal's personnel (particularly Doaa Hassan) for their support and making possible the publication of this special issue.

Neonatal exposure to Thimerosal from vaccines and child development in the first 3 years of life

Author information

Mrozek-Budzyn D1, Majewska R, Kieltyka A, Augustyniak M.

Epidemiology and Preventive Medicine
Jagiellonian University Medical College, Krakow, Poland
dorota.mrozek-budzyn@uj.edu.pl

Abstract

BACKGROUND:

Despite the common use of Thimerosal as a preservative in childhood vaccines since the 1930s, there are not many studies on ethylmercury toxicokinetics and toxicodynamics in infants. The knowledge of ethylmercury's potential adverse effects is derived mostly from parallel methylmercury research or from animal and theoretical models.

AIM OF THE STUDY:

This study was designed to examine the relationship between neonatal exposure to Thimerosal-containing vaccine (TCV) and child development.

MATERIAL AND METHODS:

The study sample consisted of 196 infants born between January 2001 and March 2003 to mothers attending ambulatory prenatal clinics in the first and second trimesters of pregnancy in Krakow. Vaccination history (date and the type of the vaccine) was extracted from physicians' records. Child development was assessed using the Bayley Scales of Infant Development (BSID-II) measured in one-year intervals over 3 years. General Linear Model (GLM) and Generalized Estimating Equation (GEE) models adjusted for potential confounders were used to assess the association.

RESULTS:

An adverse effect of neonatal TCV exposure was observed for the psychomotor development index (PDI) only in the 12th and 24th months of life ($\beta=-6.44$, $p<0.001$ and $\beta=-5.89$, $p<0.001$). No significant effect of neonatal TCV exposure was found in the 36th month. The overall deficit in the PDI attributable to neonatal TCV exposure measured over the course of the three-year follow-up (GEE) was significantly higher in TCV group ($\beta=-4.42$, $p=0.001$). MDI scores did not show the adverse association with neonatal TCV exposure.

“Despite the common use of Thimerosal as a preservative in childhood vaccines since the 1930s, there are not many studies on ethylmercury toxicokinetics and toxicodynamics in infants. An adverse effect of neonatal TCV exposure was observed for the psychomotor development index ...”

Re: “Prenatal Exposure to Mercury and Infant Neurodevelopment in a Multicenter Cohort in Spain: Study of Potential Modifiers”

Author Information

José G. Dórea

Department of Nutrition, Faculty of Health Sciences
Universidade de Brasilia, 70919-970 Brasilia, DF, Brazil
dorea@rudah.com.br

Abstract

In an interesting study, Llop et al. (1) addressed the vulnerability of the central nervous system to mercury during early development. Their findings suggested a negative association between total cord blood mercury levels and psychomotor development at approximately 14 months of age only in girls. Although I welcome these interesting findings, I would like to raise the issue of a source of organic mercury exposure during the perinatal period, namely ethylmercury in vaccines that contain Thimerosal (Noah Technologies Corporation, San Antonio, Texas). During recruitment of mothers (in November 2003) and infants born in 2004 in the study by Llop et al., Thimerosal-containing vaccines (TCVs) were still used in some European Union countries and probably in Spain (2). Therefore, it is reasonable to assume that additional mercury exposure could have occurred, at least for some of the sampled subjects. According to Spain's vaccination schedule, some children could be exposed to TCV ethylmercury (mainly in diphtheria-tetanus-pertussis and hepatitis B vaccines); furthermore, during pregnancy, some mothers were also likely to be exposed to TCVs. Neither infant vaccines nor maternal exposure to TCVs, anti- Rho(D) immune globulin (to Rh-negative participants), or dental amalgams during pregnancy were mentioned in the otherwise assiduous study of Llop et al.

Assuming that there was a gradual discontinuation of TCVs in Spain, readers familiar with the changes occurring in vaccine type used in European Union countries during the early 2000s could benefit from a post hoc discussion of this confounding mercury source. The pertinence of this discussion is further justified by the recent reports that a subtle but significant association with psychomotor development can be shown in young children as a result of exposure to TCVs in Poland (3), Korea (4), and Brazil (5). Indeed, ecologic and epidemiologic studies in the United States, United Kingdom, and

Italy (6) that addressed children's neurodevelopment associated with ethylmercury exposure in TCVs indicated collectively that “a) there is ambiguity in some studies reporting neurodevelopment outcomes that seem to depend on confounding variables; b) the risk of neurotoxicity due to low doses of Thimerosal is plausible at least for susceptible infants” (6, p. 1580). Furthermore, recent findings have shown that neurologic responses in animals (mice, rats, and rhesus monkeys) exposed to ethylmercury from the hepatitis B vaccine in the early postnatal life presented statistically significant differences when compared with controls (7); there is also strong in vitro evidence of Thimerosal neurotoxicity in small doses relevant to TCVs (7).

Ethylmercury has a shorter half-life than does methylmercury; therefore, it is unlikely that it could contribute to total mercury levels in cord blood measured by Llop et al. (1). Nevertheless, ethylmercury exposure can be ascertained from vaccination cards (3–5). Information on the association of neurodevelopment and coexposure to multiple forms of mercury is limited, and despite the current widespread use of TCVs (in most countries), it is even scarcer for specific exposure to small amounts of ethylmercury (8). Therefore, only studies like that of Llop et al. (1) can offer the opportunity to explore possible cumulative insults resulting from maternal environmental (methylmercury) exposure and additional infant ethylmercury exposure due to differential (TCV) immunization. Although I do not question the statistical model, results, or interpretation of the study by Llop et al. (1), I hope to provoke a post hoc discussion highlighting possible ethylmercury exposure during pregnancy and postnatal periods via TCVs. Without proper testing, we will never discover whether additional TCV-related mercury exposure in early life can affect neurodevelopment tests.

“... a subtle but significant association with psychomotor development can be shown in young children as a result of exposure to Thimerosal containing vaccines in Poland, Korea, and Brazil ... there is also strong in vitro evidence of Thimerosal neurotoxicity in small doses relevant to Thimerosal containing vaccines.”

Prenatal exposure to organomercury, thimerosal,
persistently impairs the serotonergic and dopaminergic
systems in the rat brain: implications for
association with developmental disorders

Author information

Ida-Eto M1, Oyabu A, Ohkawara T,
Tashiro Y, Narita N, Narita M.

Department of Anatomy II
Mie University Graduate School of Medicine
Tsu, Mie 514-8507, Japan
etom@doc.medic.mie-u.ac.jp

Abstract

Thimerosal, an organomercury compound, has been widely used as a preservative. Therefore, concerns have been raised about its neurotoxicity. We recently demonstrated perturbation of early serotonergic development by prenatal exposure to thimerosal (Ida-Eto et al. (2011) [11]). Here, we investigated whether prenatal thimerosal exposure causes persistent impairment after birth. Analysis on postnatal day 50 showed significant increase in hippocampal serotonin following thimerosal administration on embryonic day 9. Furthermore, not only serotonin, striatal dopamine was significantly increased. These results indicate that embryonic exposure to thimerosal produces lasting impairment of brain monoaminergic system, and thus every effort should be made to avoid the use of thimerosal.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22658806>

“These results indicate that
embryonic exposure to thimerosal
produces lasting impairment of brain
monoaminergic system, and thus every effort
should be made to avoid the use of thimerosal.”

“... dental amalgams contribute to ongoing kidney damage ... in a dose-dependent fashion.”

Human Experiments In Toxicology • April 2013

A significant dose-dependent relationship between mercury exposure from dental amalgams and kidney integrity biomarkers:
a further assessment of the Casa Pia children's dental amalgam trial

Author information

Geier DA1, Carmody T, Kern JK, King PG, Geier MR.
Institute of Chronic Illnesses, Inc., Silver Spring, USA

Abstract

Dental amalgams are a commonly used dental restorative material. Amalgams are about 50% mercury (Hg), and Hg is known to significantly accumulate in the kidney. It was hypothesized that because Hg accumulates in the proximal tubules (PTs), glutathione-S-transferases (GST)-a (suggestive of kidney damage at the level of PT) would be expected to be more related to Hg exposure than GST- π (suggestive of kidney damage at the level of the distal tubules). Urinary biomarkers of kidney integrity were examined in children of 8-18 years old, with and without dental amalgam fillings, from a completed clinical trial (parent study). Our study determined whether there was a significant dose-dependent correlation between increasing Hg exposure from dental amalgams and GST-a and GST- π as biomarkers of kidney integrity. Overall, the present study, using a different and more sensitive statistical model than the parent study, revealed a statistically significant dose-dependent correlation between cumulative exposure to Hg from dental amalgams and urinary levels of GST-a, after covariate adjustment; whereas, a nonsignificant relationship was observed with urinary levels of GST- π . Furthermore, it was observed that urinary GST-a levels increased by about 10% over the 8-year course of the study among individuals with an average exposure to amalgams among the study subjects from the amalgam group, in comparison with study subjects with no exposure to dental amalgams. The results of our study suggest that dental amalgams contribute to ongoing kidney damage at the level of the PTs in a dose-dependent fashion.

<http://www.ncbi.nlm.nih.gov/pubmed/22893351>

“This suggests certain individuals with a mild mitochondrial defect may be highly susceptible to mitochondrial specific toxins like the vaccine preservative thimerosal.”

Journal Of Toxicology • June 2013

**B-lymphocytes from a population of children
with autism spectrum disorder and their unaffected siblings
exhibit hypersensitivity to thimerosal**

Author information

Sharpe MA1, Gist TL, Baskin DS.

Department of Neurosurgery, The Methodist Neurological Institute
6560 Fannin Street, Scurlock Tower No. 944, Houston, TX 77030, USA

Abstract

The role of thimerosal containing vaccines in the development of autism spectrum disorder (ASD) has been an area of intense debate, as has the presence of mercury dental amalgams and fish ingestion by pregnant mothers. We studied the effects of thimerosal on cell proliferation and mitochondrial function from B-lymphocytes taken from individuals with autism, their nonautistic twins, and their nontwin siblings. Eleven families were examined and compared to matched controls. B-cells were grown with increasing levels of thimerosal, and various assays (LDH, XTT, DCFH, etc.) were performed to examine the effects on cellular proliferation and mitochondrial function. A subpopulation of eight individuals (4 ASD, 2 twins, and 2 siblings) from four of the families showed thimerosal hypersensitivity, whereas none of the control individuals displayed this response. The thimerosal concentration required to inhibit cell proliferation in these individuals was only 40% of controls. Cells hypersensitive to thimerosal also had higher levels of oxidative stress markers, protein carbonyls, and oxidant generation. This suggests certain individuals with a mild mitochondrial defect may be highly susceptible to mitochondrial specific toxins like the vaccine preservative thimerosal.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23843785>

“... decreased glutathione reserve capacity in children with an Autistic Spectrum Disorder could make them more susceptible to the toxic effects of Thimerosal routinely administered as part of mandated childhood immunization schedules.”

International Journal Of Environmental Research And Public Health • August 2013

Thimerosal exposure and the role of sulfation chemistry and thiol availability in autism

Author information

Kern JK1, Haley BE, Geier DA, Sykes LK, King PG, Geier MR.

Institute of Chronic Illnesses, Inc., Silver Spring, MD 20905, USA
jKern@dfwair.net

Abstract

Autism spectrum disorder (ASD) is a neurological disorder in which a significant number of the children experience a developmental regression characterized by a loss of previously acquired skills and abilities. Typically reported are losses of verbal, nonverbal, and social abilities. Several recent studies suggest that children diagnosed with an ASD have abnormal sulfation chemistry, limited thiol availability, and decreased glutathione (GSH) reserve capacity, resulting in a compromised oxidation/reduction (redox) and detoxification capacity. Research indicates that the availability of thiols, particularly GSH, can influence the effects of thimerosal (TM) and other mercury (Hg) compounds. TM is an organomercurial compound (49.55% Hg by weight) that has been, and continues to be, used as a preservative in many childhood vaccines, particularly in developing countries. Thiol-modulating mechanisms affecting the cytotoxicity of TM have been identified. Importantly, the emergence of ASD symptoms post-6 months of age temporally follows the administration of many childhood vaccines. The purpose of the present critical review is provide mechanistic insight regarding how limited thiol availability, abnormal sulfation chemistry, and decreased GSH reserve capacity in children with an ASD could make them more susceptible to the toxic effects of TM routinely administered as part of mandated childhood immunization schedules.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3774468/>

Toxicity of ethylmercury (and Thimerosal): a comparison with methylmercury

José G. Dórea^{1,*}, Marcelo Farina² and João B. T. Rocha³

Department of Nutrition, Faculty of Health Sciences
Universidade de Brasília, Brasília, DF, Brazil
Departamento de Bioquímica, Centro de Ciências Biológicas
Universidade Federal de Santa Catarina, Florianópolis, SC, Brazil
Departamento de Química, Centro de Ciências Naturais e Exatas
Universidade Federal de Santa Maria, Santa Maria, RS, Brazil

Abstract

Ethylmercury (etHg) is derived from the metabolism of thimerosal (o-carboxy-phenyl-thio-ethyl-sodium salt), which is the most widely used form of organic mercury. Because of its application as a vaccine preservative, almost every human and animal (domestic and farmed) that has been immunized with thimerosal-containing vaccines has been exposed to etHg. Although methylmercury (meHg) is considered a hazardous substance that is to be avoided even at small levels when consumed in foods such as seafood and rice (in Asia), the World Health Organization considers small doses of thimerosal safe regardless of multiple/repetitive exposures to vaccines that are predominantly taken during pregnancy or infancy. We have reviewed *in vitro* and *in vivo* studies that compare the toxicological parameters among etHg and other forms of mercury (predominantly meHg) to assess their relative toxicities and potential to cause cumulative insults. *In vitro* studies comparing etHg with meHg demonstrate equivalent measured outcomes for cardiovascular, neural and immune cells. However, under *in vivo* conditions, evidence indicates a distinct toxicokinetic profile between meHg and etHg, favoring a shorter blood half-life, attendant compartment distribution and the elimination of etHg compared with meHg. EtHg's toxicity profile is different from that of meHg, leading to different exposure and toxicity risks. Therefore, in real-life scenarios, a simultaneous exposure to both etHg and meHg might result in enhanced neurotoxic effects in developing mammals. However, our knowledge on this subject is still incomplete, and studies are required to address the predictability of the additive or synergic toxicological effects of etHg and meHg (or other neurotoxicants).

<http://www.ncbi.nlm.nih.gov/pubmed/23401210>

“the World Health Organization considers small doses of thimerosal safe regardless of multiple/repetitive exposures to vaccines that are predominantly taken during pregnancy or infancy ... in real-life scenarios, a simultaneous exposure to both etHg and meHg might result in enhanced neurotoxic effects in developing mammals. However, our knowledge on this subject is still incomplete, and studies are required to address the predictability of the additive or synergic toxicological effects of etHg and meHg (or other neurotoxicants).”

“Ethylmercury (EtHg) ... has received significant toxicological attention due to its presence in thimerosal-containing vaccines.”

Neuro Toxicology • September 2013

Comparative study on methyl- and ethylmercury-induced toxicity in C6 glioma cells and the potential role of LAT-1 in mediating mercurial-thiol complexes uptake

Luciana T. Zimmermann, Danúbia B. Santosa, Aline A. Naimea, Rodrigo B. Leala, José G. Dórea, Fernando Barbosa Jr.c, Michael Aschnerd, João Batista T. Rochae, Marcelo Farinaa

- a. Departamento de Bioquímica, Centro de Ciências Biológicas, Universidade Federal de Santa Catarina, Florianópolis, Santa Catarina, Brazil
- b. Departamento de Nutrição, Faculdade de Ciências da Saúde, Faculdade de Medicina, Universidade de Brasília, Brasília, Brazil
- c. Laboratório de Toxicologia e Essencialidade de Metais, Faculdade de Ciências, Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil
- d. Department of Pediatrics, Vanderbilt University Medical Center, Nashville, TN 37232, USA
- e. Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, Rio Grande do Sul, Brazil

Abstract

Various forms of mercury possess different rates of absorption, metabolism and excretion, and consequently, toxicity. Methylmercury (MeHg) is a highly neurotoxic organic mercurial. Human exposure is mostly due to ingestion of contaminated fish. Ethylmercury (EtHg), another organic mercury compound, has received significant toxicological attention due to its presence in thimerosal-containing vaccines. This study was designed to compare the toxicities induced by MeHg and EtHg, as well as by their complexes with cysteine (MeHg-S-Cys and EtHg-S-Cys) in the C6 rat glioma cell line. MeHg and EtHg caused significant ($p < 0.0001$) decreases in cellular viability when cells were treated during 30 min with each mercurial following by a washing period of 24 h (EC50 values of 4.83 and 5.05 μM , respectively). Significant cytotoxicity ($p < 0.0001$) was also observed when cells were treated under the same conditions with MeHg-S-Cys and EtHg-S-Cys, but the respective EC50 values were significantly increased (11.2 and 9.37 μM). l-Methionine, a substrate for the l-type neutral amino acid carrier transport (LAT) system, significantly protected against the toxicities induced by both complexes (MeHg-S-Cys and EtHg-S-Cys). However, no protective effects of l-methionine were observed against MeHg and EtHg toxicities. Corroborating these findings, l-methionine significantly decreased mercurial uptake when cells were exposed to MeHg-S-Cys ($p = 0.028$) and EtHg-S-Cys ($p = 0.023$), but not to MeHg and EtHg. These results indicate that the uptake of MeHg-S-Cys and EtHg-S-Cys into C6 cells is mediated, at least in part, through the LAT system, but MeHg and EtHg enter C6 cells by mechanisms other than LAT system.

<http://www.sciencedirect.com/science/article/pii/S0161813X13000922>

Mercury transfer during pregnancy and breastfeeding: hair mercury concentrations as biomarker

Author information

Marques RC1, Bernardi JV, Dórea JG, Leão RS, Malm O.

Universidade Federal do Rio de Janeiro
Campus Macaé, Rio de Janeiro, RJ, Brazil

Abstract

Hair mercury (HHg) concentration is a biomarker of exposure that is widely used to assess environmental contamination by fish methylmercury and neurodevelopment in children. In the Rio Madeira basin (Brazilian Amazon), total HHg concentrations in 649 mother-infant pairs were measured at birth (prenatal exposure) and after 6 months of exclusive breastfeeding; these mother-infant pairs were from high fish-eating communities (urban, $n = 232$; rural, $n = 35$; and Riverine, $n = 262$) and low fish-eating tin-miner settlers ($n = 120$). Differences in kinetics were seen between Hg exposure from fish consumption and environmental exposure to a tin-ore mining environment. Overall maternal HHg concentrations (at childbirth and after 6 months of lactation) were higher than those of infant HHg. However, the relative change in HHg after 6 months of lactation showed that mothers decreased HHg while infants increased HHg. The relative change showed a consistently higher increase for girls than boys with a statistical significance only in high fish-eating mothers. The correlation coefficients between maternal and newborn hair were high and statistically significant for mothers living in urban ($r = 0.66$, $p < 0.001$), rural ($r = 0.89$, $p < 0.001$), and Riverine ($r = 0.89$, $p < 0.001$) communities not for tin miner settlers ($r = 0.07$, $p = 0.427$). After 6 months of exclusive breastfeeding, correlation coefficients showed high correlation coefficients and statistical significance for all groups (urban, $r = 0.73$, $p < 0.001$; rural, $r = 0.88$, $p < 0.001$; Riverine, $r = 0.91$, $p < 0.001$) except for Tin miners ($r = -0.07$, $p = 0.428$). A linear model analysis was used to assess the longitudinal associations of maternal total HHg and total HHg at birth (0 days) and 6 months of age in exclusively breastfed infants. Regression analysis significantly predicted HHg in newborn from maternal HHg for high fish-eating maternal-infant pairs.

CONCLUSION:

The concentration of mercury accumulated in newborn tissues (in utero and during breastfeeding) relevant to both, maternal sources and infant exposure, can be reliably assessed from maternal hair.

<http://www.ncbi.nlm.nih.gov/pubmed/23836367>

“The concentration of mercury accumulated in newborn tissues (in utero and during breastfeeding) relevant to both, maternal sources and infant exposure, can be reliably assessed from maternal hair.”

Thimerosal in childhood vaccines contributes to accumulating mercury toxicity in the kidney

Maria Fernanda Hornos Carneiro,
Christudas Morais, Fernando Barbosa Jr, Glenda C Gobe

Abstract

Mercury (Hg) is a hazardous chemical that accumulates in many cells and tissues, thereby producing toxicity. The kidney is a key target organ for Hg accumulation and toxicity. The contributing factors to Hg accumulation in humans include: (1) elemental and inorganic Hg exposure, often occurring by inhalation of Hg vapors; (2) exposure to methyl Hg (meHg), for example, through contaminated seafood; and (3) exposure to ethyl mercury (etHg) via thimerosal-containing vaccines. Systematic investigations on the toxic effects of etHg/thimerosal on the nervous system were carried out, and etHg/thimerosal emerged as a possible risk factor for autism and other neurodevelopmental disorders. There is, however, little known about the mechanisms and molecular interactions underlying toxicity of etHg/thimerosal in the kidney, which is the focus of the current review. Susceptible populations such as infants, pregnant women, and the elderly are exposed to etHg through thimerosal-containing vaccines, and in-depth study of the potential adverse effects on the kidney is needed. In general, toxicity occurring in association with different forms of Hg is related to: intracellular thiol metabolism and oxidative stress reactions; mitochondrial function; intracellular distribution and build-up of calcium; apoptosis; expression of stress proteins; and also interaction with the cytoskeleton. Available evidence for the etHg-induced toxicity in the kidney was examined, and the main mechanisms and molecular interactions of cytotoxicity of etHg/thimerosal exposure in kidney described. Such accumulating knowledge may help to indicate molecular pathways that, if modulated, may better handle Hg-mediated toxicity.

“Systematic investigations on the toxic effects of ethyl mercury/thimerosal on the nervous system were carried out, and ethyl mercury/thimerosal emerged as a possible risk factor for autism and other neurodevelopmental disorders.”

The kinetic signature of toxicity of four heavy metals and their mixtures on MCF7 breast cancer cell line

Author information

Egiebor E1, Tulu A, Abou-Zeid N, Aighewi IT, Ishaque A.

Abstract

This study evaluated the kinetic signature of toxicity of four heavy metals known to cause severe health and environmental issues--cadmium (Cd), mercury (Hg) lead (Pb) arsenic (As)--and the mixture of all four metals (Mix) on MCF7 cancer cells, in the presence and absence of the antioxidant glutathione (GSH). The study was carried out using real time cell electronic sensing (RT-CES). RT-CES monitors in real time the electrical impedance changes at the electrode/culture medium interface due to the number of adhered cells, which is used as an index of cell viability. Cells were seeded for 24 h before exposure to the metals and their mixtures. The results showed that in the presence and absence of cellular glutathione, arsenic was the most cytotoxic of all five treatments, inducing cell death after 5 h of exposure. Lead was the least cytotoxic in both scenarios. In the presence of cellular GSH, the cytotoxic trend was As > Cd > MIX > Hg > Pb, while in the absence of GSH, the cytotoxic trend was As > Hg > MIX > Cd > Pb. The findings from this study indicate the significance of glutathione-mediated toxicity of the metals examined--particularly for mercury--and may be clinically relevant for disorders such as autism spectrum disorder where decreased glutathione-based detoxification capacity is associated with increased mercury intoxication.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3822392/>

“The findings from this study indicate the significance of glutathione-mediated toxicity of the metals examined—particularly for mercury—and may be clinically relevant for disorders such as autism spectrum disorder where decreased glutathione-based detoxification capacity is associated with increased mercury intoxication.”

Effect of thimerosal on the neurodevelopment of premature rats

Author information

Chen YN1, Wang J, Zhang J, Li SJ, He L, Shao DD, Du HY.

The Key Laboratory of Biomedical Information Engineering of Ministry of Education and Institute of Biomedical Engineering School of Life Science and Technology Xi'an Jiaotong University, Xi'an, 710049, China

Abstract

BACKGROUND

This study was undertaken to determine the effect of thimerosal on the neurodevelopment of premature rats.

METHODS

Thimerosal was injected into premature SD rats at a dose of 32.8, 65.6, 98.4 or 131.2 µg/kg on postnatal day 1. Expression of dopamine D4 receptor (DRD4) and serotonin 2A receptor (5-HT2AR), apoptosis in the prefrontal cortex on post-injection day 49, and learning and memory function were studied and compared with those in a control group injected with saline.

RESULTS

Expression of DRD4 and 5-HT2AR and learning function decreased, and apoptosis increased significantly in the 131.2 µg/kg group ($P < 0.001$). Memory function was significantly impaired by 65.6 ($P < 0.05$), 98.4 and 131.2 µg/kg ($P < 0.001$).

CONCLUSIONS

The negative adverse consequences on neurodevelopment observed in the present study are consistent with previous studies; this study raised serious concerns about adverse neurodevelopmental disorder such as autism in humans following the ongoing worldwide routine administration of thimerosal-containing vaccines to infants.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24235069>

“The negative adverse consequences on neurodevelopment observed in the present study are consistent with previous studies; this study raised serious concerns about adverse neurodevelopmental disorder such as autism in humans following the ongoing worldwide routine administration of thimerosal containing vaccines to infants.”

Proposed toxic and hypoxic impairment of a brainstem locus in autism

Author information

McGinnis WR1, Audhya T, Edelson SM.
Autism Research Institute, 4182 Adams Avenue, San Diego, CA 92116, USA
woody.mcginis@gmail.com

Abstract

Electrophysiological findings implicate site-specific impairment of the nucleus tractus solitarius (NTS) in autism. This invites hypothetical consideration of a large role for this small brainstem structure as the basis for seemingly disjointed behavioral and somatic features of autism. The NTS is the brain's point of entry for visceral afference, its relay for vagal reflexes, and its integration center for autonomic control of circulatory, immunological, gastrointestinal, and laryngeal function. The NTS facilitates normal cerebrovascular perfusion, and is the seminal point for an ascending noradrenergic system that modulates many complex behaviors. Microvascular configuration predisposes the NTS to focal hypoxia. A subregion--the "pNTS"--permits exposure to all blood-borne neurotoxins, including those that do not readily transit the blood-brain barrier. Impairment of acetylcholinesterase (mercury and cadmium cations, nitrates/nitrites, organophosphates, monosodium glutamate), competition for hemoglobin (carbon monoxide, nitrates/nitrites), and higher blood viscosity (net systemic oxidative stress) are suggested to potentiate microcirculatory insufficiency of the NTS, and thus autism.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3881151/>

“A subregion—the “pNTS”—permits exposure to all blood-borne neurotoxins, including those that do not readily transit the blood-brain barrier. Impairment of acetylcholinesterase (mercury and cadmium cations, nitrates/nitrites, organophosphates, monosodium glutamate), competition for hemoglobin (carbon monoxide, nitrates/nitrites), and higher blood viscosity (net systemic oxidative stress) are suggested to potentiate microcirculatory insufficiency of the NTS, and thus autism.”

“... the present study provides new epidemiological evidence supporting an association between increasing organic-mercury exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an Autistic Spectrum Disorder diagnosis.”

Translational Neurodegeneration • December 2013

A two-phase study evaluating the relationship between Thimerosal-containing vaccine administration and the risk for an autism spectrum disorder diagnosis in the United States

Author information

Geier DA, Hooker BS, Kern JK, King PG, Sykes LK, Geier MR1.
The Institute of Chronic Illnesses Inc, 14 Redgate Ct, Silver Spring, MD, USA
mgeier@comcast.net

Abstract

BACKGROUND

Autism spectrum disorder (ASD) is defined by standardized criteria of qualitative impairments in social interaction, qualitative impairments in communication, and restricted and stereotyped patterns of behavior, interests, and activities. A significant number of children diagnosed with ASD suffer a loss of previously-acquired skills, which is suggestive of neurodegeneration or a type of progressive encephalopathy with an etiological pathogenic basis occurring after birth. To date, the etiology of ASD remains under debate, however, many studies suggest toxicity, especially from mercury (Hg), in individuals diagnosed with an ASD. The present study evaluated concerns about the toxic effects of organic-Hg exposure from Thimerosal (49.55% Hg by weight) in childhood vaccines by conducting a two-phased (hypothesis generating/hypothesis testing) study with documented exposure to varying levels of Thimerosal from vaccinations.

METHODS

A hypothesis generating cohort study was undertaken to evaluate the relationship between exposure to organic-Hg from a Thimerosal-containing Diphtheria-Tetanus-acellular-Pertussis (DTaP) vaccine in comparison to a Thimerosal-free DTaP vaccine administered, from 1998 through 2000, for the risk of ASD as reported in the Vaccine Adverse Event Reporting System (VAERS) database (phase I). A hypothesis testing case-control study was undertaken to evaluate the relationship between organic-Hg exposure from

Thimerosal-containing hepatitis B vaccines administered at specific intervals in the first six months of life among cases diagnosed with an ASD and controls born between 1991 through 1999 in the Vaccine Safety Datalink (VSD) database (phase II).

RESULTS

In phase I, it was observed that there was a significantly increased risk ratio for the incidence of ASD reported following the Thimerosal-containing DTaP vaccine in comparison to the Thimerosal-free DTaP vaccine. In phase II, it was observed that cases diagnosed with an ASD were significantly more likely than controls to receive increased organic-Hg from Thimerosal-containing hepatitis B vaccine administered within the first, second, and sixth month of life.

CONCLUSIONS

Routine childhood vaccination is an important public health tool to reduce the morbidity and mortality associated with infectious diseases, but the present study provides new epidemiological evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD diagnosis.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3878266/>

Low-dose mercury exposure in early life: relevance of thimerosal to fetuses, newborns and infants

Author information

Dórea JG.

Faculty of Health Sciences
Universidade de Brasília
70919-970 Brasília, DF, Brazil
jg.dorea@gmail.com

Abstract

This review explores the different aspects of constitutional factors in early life that modulate toxicokinetics and toxicodynamics of low-dose mercury resulting from acute ethylmercury (etHg) exposure in Thimerosal-containing vaccines (TCV). Major databases were searched for human and experimental studies that addressed issues related to early life exposure to TCV. It can be concluded that: a) mercury load in fetuses, neonates, and infants resulting from TCVs remains in blood of neonates and infants at sufficient concentration and for enough time to penetrate the brain and to exert a neurologic impact and a probable influence on neurodevelopment of susceptible infants; b) etHg metabolism related to neurodevelopmental delays has been demonstrated experimentally and observed in population studies; c) unlike chronic Hg exposure during pregnancy, neurodevelopmental effects caused by acute (repeated/cumulative) early life exposure to TCV-etHg remain unrecognized; and d) the uncertainty surrounding low-dose toxicity of etHg is challenging but recent evidence indicates that avoiding cumulative insults by alkyl-mercury forms (which include Thimerosal) is warranted. It is important to a) maintain trust in vaccines while reinforcing current public health policies to abate mercury exposure in infancy; b) generally support WHO policies that recommend vaccination to prevent and control existing and impending infectious diseases; and c) not confuse the 'need' to use a specific 'product' (TCV) by accepting as 'innocuous' (or without consequences) the presence of a proven 'toxic alkyl-mercury' (etHg) at levels that have not been proven to be toxicologically safe.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23992327>

“... mercury load in fetuses, neonates, and infants resulting from TCVs remains in blood of neonates and infants at sufficient concentration and for enough time to penetrate the brain and to exert a neurologic impact and a probable influence on neurodevelopment of susceptible infants ...”

The retention time of inorganic mercury in the brain a systematic review of the evidence

Author information

Rooney JP.

Academic Unit of Neurology
Trinity Biomedical Sciences Institute
Trinity College, 152-160 Pearse Street
Dublin 2, Ireland
jrooney@rcsi.ie

Abstract

Reports from human case studies indicate a half-life for inorganic mercury in the brain in the order of years-contradicting older radioisotope studies that estimated half-lives in the order of weeks to months in duration. This study systematically reviews available evidence on the retention time of inorganic mercury in humans and primates to better understand this conflicting evidence. A broad search strategy was used to capture 16,539 abstracts on the Pubmed database. Abstracts were screened to include only study types containing relevant information. 131 studies of interest were identified. Only 1 primate study made a numeric estimate for the half-life of inorganic mercury (227-540 days). Eighteen human mercury poisoning cases were followed up long term including autopsy. Brain inorganic mercury concentrations at death were consistent with a half-life of several years or longer. 5 radionucleotide studies were found, one of which estimated head half-life (21 days). This estimate has sometimes been misinterpreted to be equivalent to brain half-life-which ignores several confounding factors including limited radioactive half-life and radioactive decay from surrounding tissues including circulating blood. No autopsy cohort study estimated a half-life for inorganic mercury, although some noted bioaccumulation of brain mercury with age. Modelling studies provided some extreme estimates (69 days vs 22 years). Estimates from modelling studies appear sensitive to model assumptions, however predications based on a long half-life (27.4 years) are consistent with autopsy findings. In summary, shorter estimates of half-life are not supported by evidence from animal studies, human case studies, or modelling studies based on appropriate assumptions. Evidence from such studies point to a half-life of inorganic mercury in human brains of several years to several decades. This finding carries important implications for pharmacokinetic modelling of mercury and potentially for the regulatory toxicology of mercury.

<http://www.ncbi.nlm.nih.gov/pubmed/24368178>

“Evidence from such studies point to a half-life of inorganic mercury in human brains of several years to several decades. This finding carries important implications for pharmacokinetic modelling of mercury and potentially for the regulatory toxicology of mercury.”

“These and other studies suggest that susceptibility to mercury toxicity differs among individuals based on multiple genes, not all of which have been identified. These studies further suggest that the levels of exposure to mercury vapor from dental amalgams may be unsafe for certain subpopulations.”

Biometals • February 2014

New science challenges old notion that mercury dental amalgam is safe

Author information

Homme KG1, Kern JK, Haley BE, Geier DA, King PG, Sykes LK, Geier MR.

International Academy of Oral Medicine and Toxicology
Champions Gate, FL, 33896, USA
khomme@sbcglobal.net

Abstract

Mercury dental amalgam has a long history of ostensibly safe use despite its continuous release of mercury vapor. Two key studies known as the Children’s Amalgam Trials are widely cited as evidence of safety. However, four recent reanalyses of one of these trials now suggest harm, particularly to boys with common genetic variants. These and other studies suggest that susceptibility to mercury toxicity differs among individuals based on multiple genes, not all of which have been identified. These studies further suggest that the levels of exposure to mercury vapor from dental amalgams may be unsafe for certain subpopulations. Moreover, a simple comparison of typical exposures versus regulatory safety standards suggests that many people receive unsafe exposures. Chronic mercury toxicity is especially insidious because symptoms are variable and nonspecific, diagnostic tests are often misunderstood, and treatments are speculative at best. Throughout the world, efforts are underway to phase down or eliminate the use of mercury dental amalgam.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3905169/>

Redox Regulation and the Autistic Spectrum: Role of Tryptophan Catabolites, Immuno-inflammation, Autoimmunity and the Amygdala

Author information

Anderson G1, Maes M2.

1. CRC, Rm:30, 57 Laurel Street, Glasgow, Scotland
2. Department of Psychiatry, Chulalongkorn University, Bangkok, Thailand
Department of Psychiatry, Deakin University, Geelong, Australia

Abstract

The autistic spectrum disorders (ASD) form a set of multi-faceted disorders with significant genetic, epigenetic and environmental determinants. Oxidative and nitrosative stress (O&NS), immuno-inflammatory pathways, mitochondrial dysfunction and dysregulation of the tryptophan catabolite (TRYCATs) pathway play significant interactive roles in driving the early developmental etiology and course of ASD. O&NS interactions with immuno-inflammatory pathways mediate their effects centrally via the regulation of astrocyte and microglia responses, including regional variations in TRYCATs produced. Here we review the nature of these interactions and propose an early developmental model whereby different ASD genetic susceptibilities interact with environmental and epigenetic processes, resulting in glia biasing the patterning of central interarea interactions. A role for decreased local melatonin and N-acetylserotonin production by immune and glia cells may be a significant treatment target.

Perinatal Mercury

Maternal prenatal mercury levels have sharply increased in recent decades, with foetal cord blood levels being significantly increased versus maternal levels [61,62]. This suggests that prenatal mercury, which can induce many of the changes evident in ASD, including increased O&NS and immuno-inflammation, as well as decreased endogenous anti-oxidants and mitochondrial functioning, may play a significant role in the etiology of ASD. As to whether mercury interacts with the consequences of prenatal infection in the offspring is unknown, although not unlikely given that mercury significantly modulates murine viral immune response [63,64] and viral infection increases brain mercury levels [65]. SNPs in genes involved in mercury regulation associate with ASD [66]. It also requires testing as to whether mercury has any impact on the development of foetal gamma-delta ($\gamma\delta$) T cells and prenatal epigenetic regulation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24669209>

“Maternal prenatal mercury levels have sharply increased in recent decades, with foetal cord blood levels being significantly increased versus maternal levels. This suggests that prenatal mercury, which can induce many of the changes evident in Autistic Spectrum Disorder, including increased O&NS and immuno-inflammation, as well as decreased endogenous anti-oxidants and mitochondrial functioning, may play a significant role in the etiology of Autistic Spectrum Disorder.”

Suppression by Thimerosal of Ex-Vivo CD4+ T Cell Response to Influenza Vaccine and Induction of Apoptosis in Primary Memory T Cells

Emily Loison,¹ Béatrice Poirier-Beaudouin,¹ Valérie Seffer,¹
Audrey Paoletti,² Vered Abitbol,³ Eric Tartour,⁴ Odile
Launay,⁵ and Marie-Lise Gougeon^{1,*}

Jon C.D. Houtman, Editor

1. Antiviral Immunity Biotherapy and Vaccine Unit, Institut Pasteur, Paris, France
2. Inserm U1030, Institut Gustave Roussy, Villejuif, France
3. Gastroenterology Department, Hôpital Cochin, AP-HP, Paris, France
4. Inserm U970, Université Paris Descartes, PARCC/HEGP, Paris, France
5. Centre d'Investigation Clinique BT-505, Hôpital Cochin, AP-HP, Paris, France
University of Iowa, United States of America

Competing Interests

CrossJect provided the academic research/private research partnership to fund a CIFRE fellowship used in this study. There are no patents, products in development or marketed products to declare. This does not alter the authors' adherence to all the PLOS ONE policies on sharing data and materials.

Abstract

Thimerosal is a preservative used widely in vaccine formulations to prevent bacterial and fungal contamination in multidose vials of vaccine. Thimerosal was included in the multidose non-adjuvanted pandemic 2009 H1N1 vaccine Panenza. In the context of the analysis of the ex-vivo T cell responses directed against influenza vaccine, we discovered the in vitro toxicity Panenza, due to its content in thimerosal. Because thimerosal may skew the immune response to vaccines, we investigated in detail the ex-vivo effects of thimerosal on the fate and functions of T cells in response to TCR ligation. We report that ex-vivo exposure of quiescent or TCR-activated primary human T cells to thimerosal induced a dose-dependent apoptotic cell death associated with depolarization of mitochondrial membrane, generation of reactive oxygen species, cytochrome c release from the mitochondria and caspase-3 activation. Moreover, exposure to non-toxic concentrations of thimerosal induced cell cycle arrest in G0/G1 phase of TCR-activated T cells, and inhibition of the release of proinflammatory cytokines such as IFN gamma, IL-1 beta, TNF alpha, IL-2, as well as the chemokine MCP1. No shift towards Th2 or Th17 cells was detected. Overall these results underline the proapoptotic effect of thimerosal on primary human lymphocytes at concentrations 100 times less to those contained in the multidose vaccine, and they reveal the inhibitory effect of this preservative on T-cell proliferation and functions at nanomolar concentrations.

“Overall these results underline the proapoptotic effect of thimerosal on primary human lymphocytes at concentrations 100 times less to those contained in the multidose vaccine, and they reveal the inhibitory effect of this preservative on T-cell proliferation and functions at nanomolar concentrations.”

Ecogenetics of mercury:
from genetic polymorphisms and epigenetics
to risk assessment and decision-making

Author information

Basu N1, Goodrich JM, Head J.

Department of Environmental Health Sciences
University of Michigan School of Public Health
Ann Arbor, Michigan, USA
Faculty of Agricultural and Environmental Sciences
McGill University, Montreal, Quebec, Canada

Abstract

The risk assessment of mercury (Hg), in both humans and wildlife, is made challenging by great variability in exposure and health effects. Although disease risk arises following complex interactions between genetic (“nature”) and environmental (“nurture”) factors, most Hg studies thus far have focused solely on environmental factors. In recent years, ecogenetic-based studies have emerged and have started to document genetic and epigenetic factors that may indeed influence the toxicokinetics or toxicodynamics of Hg. The present study reviews these studies and discusses their utility in terms of Hg risk assessment, management, and policy and offers perspectives on fruitful areas for future research. In brief, epidemiological studies on populations exposed to inorganic Hg (e.g., dentists and miners) or methylmercury (e.g., fish consumers) are showing that polymorphisms in a number of environmentally responsive genes can explain variations in Hg biomarker values and health outcomes. Studies on mammals (wildlife, humans, rodents) are showing Hg exposures to be related to epigenetic marks such as DNA methylation. Such findings are beginning to increase understanding of the mechanisms of action of Hg, and in doing so they may help identify candidate biomarkers and pinpoint susceptible groups or life stages. Furthermore, they may help refine uncertainty factors and thus lead to more accurate risk assessments and improved decision-making.

<http://www.ncbi.nlm.nih.gov/pubmed/24038486>

“In recent years,
ecogenetic-based studies
have emerged and have started
to document genetic and epigenetic
factors that may indeed influence the
toxicokinetics or toxicodynamics of mercury.”

Thimerosal compromises human dendritic cell maturation, IL-12 production, chemokine release, and T-helper polarization

by Emily Loison & Marie-Lise Gougeon

Abstract

In conclusion, our study indicates that ex-vivo exposure of human immature dendritic cells to very low nontoxic concentrations of thimerosal alters the LPS-induced maturation process and dampens their proinflammatory response, in particular the production of the T-helper polarizing cytokine IL-12. Moreover, thimerosal exposure of DCs corrupts their interaction with naïve CD4+ T cells, leading to a decreased production of IFN- γ , IP10 and GM-CSF and increased levels of IL-8, IL-9, and MIP-1 α . Today, except for some flu vaccines in multi-dose vials, no recommended childhood vaccines contain thimerosal as a preservative. It must be stressed that the toxicity and immunomodulatory effects of thimerosal that we report ex-vivo on human monocyte-derived DCs may occur in vivo and induce an alteration of the immune response to the vaccine. These observations highlight the need to use this preservative with caution and avoid it if possible.

Full Report

<https://app.box.com/s/0dg5ksp3f377qes3m5qsp16rl1gxws8l>

“These observations highlight the need to use this preservative with caution and avoid it if possible.”

“Our results indicate that higher dose of neonatal thimerosal-mercury is capable of inducing long-lasting substantial dysregulation of neurodevelopment, synaptic function, and endocrine system, which could be the causal involvements of autistic-like behavior in mice.”

Toxicology Science • June 2014

Transcriptomic analyses of neurotoxic effects in mouse brain after intermittent neonatal administration of thimerosal

Author information

Li X1, Qu F, Xie W, Wang F, Liu H, Song S,
Chen T, Zhang Y, Zhu S, Wang Y, Guo C, Tang TS.

State Key Laboratory of Biomembrane and Membrane Biotechnology
Institute of Zoology, Chinese Academy of Sciences, Beijing 100101, China

Abstract

Thimerosal is a vaccine antimicrobial preservative which has long been suspected an iatrogenic factor possibly contributing to neurodevelopmental disorders including autism. The association between infant vaccine thimerosal exposure and autism remains an open question. Although thimerosal has been removed from mandatory childhood vaccines in the United States, thimerosal-preserved vaccines are still widely used outside of the United States especially in developing countries. Notably, thimerosal-containing vaccines are being given to the newborns within the first 12-24 h after birth in some countries. To examine the possible neurotoxic effects of early neonatal exposure to a higher level of thimerosal, FVB mice were subcutaneously injected with thimerosal-mercury at a dose which is 20× higher than that used for regular Chinese infant immunization during the first 4 months of life. Thimerosal-treated mice exhibited neural development delay, social interaction deficiency, and inclination of depression. Apparent neuropathological changes were also observed in adult mice neonatally treated with thimerosal. High-throughput RNA sequencing of autistic-behaved mice brains revealed the alternation of a number of canonical pathways involving neuronal development, neuronal synaptic function, and the dysregulation of endocrine system. Intriguingly, the elevation of anterior pituitary secreting hormones occurred exclusively in male but not in female thimerosal-treated mice, demonstrating for the first time the gender bias of thimerosal-mercury toxicity with regard to endocrine system. Our results indicate that higher dose of neonatal thimerosal-mercury (20× higher than that used in human) is capable of inducing long-lasting substantial dysregulation of neurodevelopment, synaptic function, and endocrine system, which could be the causal involvements of autistic-like behavior in mice.

<http://www.ncbi.nlm.nih.gov/pubmed/24675092>

Ecogenetics of mercury: From genetic polymorphisms and epigenetics to risk assessment and decision-making

Author Information

Niladri Basu, Jaclyn M. Goodrich and Jessica Head

Cooperative Institute for Limnology and Ecosystems Research
School of Natural Resources and Environment, University of Michigan
Ann Arbor, Michigan, USA

Abstract

The risk assessment of mercury (Hg), in both humans and wildlife, is made challenging by great variability in exposure and health effects. Although disease risk arises following complex interactions between genetic (“nature”) and environmental (“nurture”) factors, most Hg studies thus far have focused solely on environmental factors. In recent years, ecogenetic-based studies have emerged and have started to document genetic and epigenetic factors that may indeed influence the toxicokinetics or toxicodynamics of Hg. The present study reviews these studies and discusses their utility in terms of Hg risk assessment, management, and policy and offers perspectives on fruitful areas for future research. In brief, epidemiological studies on populations exposed to inorganic Hg (e.g., dentists and miners) or methylmercury (e.g., fish consumers) are showing that polymorphisms in a number of environmentally responsive genes can explain variations in Hg biomarker values and health outcomes. Studies on mammals (wildlife, humans, rodents) are showing Hg exposures to be related to epigenetic marks such as DNA methylation. Such findings are beginning to increase understanding of the mechanisms of action of Hg, and in doing so they may help identify candidate biomarkers and pinpoint susceptible groups or life stages. Furthermore, they may help refine uncertainty factors and thus lead to more accurate risk assessments and improved decision-making.

<http://onlinelibrary.wiley.com/doi/10.1002/etc.2375/abstract>

“In brief, epidemiological studies on populations exposed to inorganic mercury (e.g., dentists and miners) or methylmercury (e.g., fish consumers) are showing that polymorphisms in a number of environmentally responsive genes can explain variations in mercury biomarker values and health outcomes.”

[polymorphisms explain why some individuals injected with an aluminum containing vaccine will become autistic and others will not. Polymorphism is the genetic variant]

Effect of low-level prenatal mercury exposure on neonate neurobehavioral development in China

Author information

Wu J1, Ying T2, Shen Z2, Wang H2.

Zhoushan Women's & Children's Health Hospital
Zhoushan, Zhejiang, China

Abstract

BACKGROUND:

This study aimed to assess the effects of low-level prenatal mercury exposure on neonate neurobehavioral development in China.

METHODS:

In total, 418 mother-neonate pairs were included in the study. Maternal urine, hair, and blood samples and cord blood samples were used to document prenatal exposure to mercury. The Neonatal Behavioral Neurological Assessment was used to estimate neurobehavioral development in the neonates at 3 days of age.

RESULTS:

Total mercury level was significantly higher in cord blood than that in maternal blood. A strong correlation was found between total mercury levels in maternal blood and those in cord blood ($r = 0.7431$; $P < 0.0001$). Trend analysis revealed that mothers who consumed more fish had higher blood and cord blood mercury levels (all $P < 0.0001$). Significant differences were also found between male and female cord blood mercury levels among groups with different fish consumption frequencies (all $P < 0.0001$). Cord blood mercury level was significantly associated with total Neonatal Behavioral Neurological Assessment scores ($\beta = 0.03$; standard error = 0.01; $P = 0.0409$), passive muscle tone (odds ratio = 1.07; 95% confidence interval = 1.12-1.13; $P = 0.0071$), and active muscle tone (odds ratio = 1.06; 95% confidence interval = 1.01-1.11; $P = 0.0170$) scores after adjustment, respectively.

CONCLUSIONS:

Neonatal neurodevelopment was associated with prenatal exposure to mercury. Women with high mercury levels should avoid intake seafood excessively during pregnancy. Long-term effects of exposure to mercury on childhood development need to be further explored.

Full Report

[http://www.pedneur.com/article/S0887-8994\(14\)00195-7/fulltext](http://www.pedneur.com/article/S0887-8994(14)00195-7/fulltext)

“Neonatal neurodevelopment was associated with prenatal exposure to mercury. Women with high mercury levels should avoid intake seafood excessively during pregnancy.”

A Dose-Response Relationship between Organic Mercury Exposure from Thimerosal-Containing Vaccines and Neurodevelopmental Disorders

David A. Geier,¹ Brian S. Hooker,²
Janet K. Kern,^{1,3} Paul G. King,⁴
Lisa K. Sykes,⁴ and Mark R. Geier¹

1. Institute of Chronic Illnesses, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA
2. Department of Biology, Simpson University, 2211 College View Dr., Redding, CA 96003, USA
3. Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas
5353 Harry Hine Blvd., Dallas, TX 75390, USA
4. CoMeD, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA

Abstract

A hypothesis testing case-control study evaluated concerns about the toxic effects of organic-mercury (Hg) exposure from thimerosal-containing (49.55% Hg by weight) vaccines on the risk of neurodevelopmental disorders (NDs). Automated medical records were examined to identify cases and controls enrolled from their date-of-birth (1991–2000) in the Vaccine Safety Datalink (VSD) project. ND cases were diagnosed with pervasive developmental disorder (PDD), specific developmental delay, tic disorder or hyperkinetic syndrome of childhood. In addition, putative non-thimerosal-related outcomes of febrile seizure, failure to thrive and cerebral degenerations were examined. The cumulative total dose of Hg exposure from thimerosal-containing hepatitis B vaccine (T-HBV) administered within the first six months of life was calculated. On a per microgram of organic-Hg basis, PDD (odds ratio (OR) = 1.054), specific developmental delay (OR = 1.035), tic disorder (OR = 1.034) and hyperkinetic syndrome of childhood (OR = 1.05) cases were significantly more likely than controls to receive increased organic-Hg exposure. By contrast, none of the non-thimerosal related outcomes were significantly more likely than the controls to have received increased organic-Hg exposure. Routine childhood vaccination may be an important public health tool to reduce infectious disease-associated morbidity/mortality, but the present study significantly associates organic-Hg exposure from T-HBV with an increased risk of an ND diagnosis.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4199012/>

“Routine childhood vaccination may be an important public health tool to reduce infectious disease-associated morbidity/mortality, but the present study significantly associates organic-mercury exposure from thimerosal-containing hepatitis B vaccine with an increased risk of an neurodevelopmental disorder diagnosis.”

“... the present study supports an association between increasing organic-mercury exposure from Thimerosal-containing childhood vaccines and the subsequent risk of specific delays in development ...”

North American Journal Of Medical Science • October 2014

Thimerosal-containing hepatitis B vaccination and the risk for diagnosed specific delays in development in the United States: a case-control study in the vaccine safety datalink

Author information

Geier DA1, Kern JK2, Hooker BS3, King PG4, Sykes LK4, Geier MR1.

1. Institute of Chronic Illnesses, Inc, Silver Spring, Maryland, USA
2. Institute of Chronic Illnesses, Inc, Silver Spring, Maryland, USA
Department of Psychiatry, University of Texas Southwestern Medical Center, Dallas, Texas, USA
3. Biology Department, Simpson University, Redding, California, USA
4. CoMeD, Inc, Silver Spring, Maryland, USA

Abstract

BACKGROUND

Within the first 3 years of life, the brain develops rapidly. Its development is characterized by critical developmental periods for speech, vision, hearing, language, balance, etc.; and alteration in any of the processes occurring in those critical periods can lead to specific delays in development.

AIMS

The present study evaluated the potential toxic effects of organic-mercury exposure from Thimerosal (49.55% mercury by weight) in childhood vaccines and its hypothesized possible relationship with specific delays in development.

MATERIALS AND METHODS

A hypothesis testing case-control study was undertaken to evaluate the relationship between exposure to Thimerosal-containing hepatitis B vaccines administered at specific intervals in the first 6 months among cases diagnosed with specific delays in development and controls born between 1991-2000, utilizing data in the Vaccine Safety Datalink database.

RESULTS

Cases were significantly more likely than controls to have received increased organic-mercury from Thimerosal-containing hepatitis B vaccine administered in the first, second, and sixth month of life.

CONCLUSION

Though routine childhood vaccination may be an important public health tool to reduce the morbidity and mortality associated with infectious diseases, the present study supports an association between increasing organic-mercury exposure from Thimerosal-containing childhood vaccines and the subsequent risk of specific delays in development among males and females.

Thimerosal as discrimination: vaccine disparity in the UN Minamata Convention on mercury

Author information

Sykes LK1, Geier DA2, King PG1, Kern JK3, Haley BE1,
Chaigneau CG1, Megson MN4, Love JM5, Reeves RE1, Geier MR2.

1. CoMeD, Inc, Silver Spring, MD USA
2. CoMeD, Inc, Silver Spring, MD; Institute of Chronic Illnesses, Inc, Silver Spring, MD USA
3. Institute of Chronic Illnesses, Inc, Silver Spring, MD USA
4. Pediatric and Adolescent Ability Center, Richmond, VA USA
5. CoMeD, Inc, Silver Spring, MD USA

Abstract

When addressing toxins, one unmistakable parallel exists between biology and politics: developing children and developing nations are those most vulnerable to toxic exposures. This disturbing parallel is the subject of this critical review, which examines the use and distribution of the mercury (Hg)-based compound, thimerosal, in vaccines. Developed in 1927, thimerosal is 49.55% Hg by weight and breaks down in the body into ethyl-Hg chloride, ethyl-Hg hydroxide and sodium thiosalicylate. Since the early 1930s, there has been evidence indicating that thimerosal poses a hazard to the health of human beings and is ineffective as an antimicrobial agent. While children in the developed and predominantly western nations receive doses of mostly no-thimerosal and reduced-thimerosal vaccines, children in the developing nations receive many doses of several unreduced thimerosal-containing vaccines (TCVs). Thus, thimerosal has continued to be a part of the global vaccine supply and its acceptability as a component of vaccine formulations remained unchallenged until 2010, when the United Nations (UN), through the UN Environment Programme, began negotiations to write the global, legally binding Minamata Convention on Hg. During the negotiations, TCVs were dropped from the list of Hg-containing products to be regulated. Consequently, a double standard in vaccine safety, which previously existed due to ignorance and economic reasons, has now been institutionalised as global policy. Ultimately, the Minamata Convention on Hg has sanctioned the inequitable distribution of thimerosal by specifically exempting TCVs from regulation, condoning a two-tier standard of vaccine safety: a predominantly no-thimerosal and reduced-thimerosal standard for developed nations and a predominantly thimerosal-containing one for developing nations. This disparity must now be evaluated urgently as a potential form of institutionalised discrimination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25101548>

“While children in the developed and predominantly western nations receive doses of mostly no-thimerosal and reduced-thimerosal vaccines, children in the developing nations receive many doses of several unreduced thimerosal-containing vaccines (TCVs).”

“... the preponderance of evidence suggests that mercury exposure from dental amalgams may cause or contribute to many chronic conditions.”

Neuro Endocrinology Letters • 2014

Evidence supporting a link between dental amalgams and chronic illness, fatigue, depression, anxiety, and suicide

Author information

Kern JK1, Geier DA1, Bjørklund G2, King PG3, Homme KG4, Haley BE5, Sykes LK3, Geier MR1.

1. Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA
2. Council for Nutritional and Environmental Medicine, Mo i Rana, Norway
3. CoMeD, Inc., Silver Spring, MD, USA
4. International Academy of Oral Medicine and Toxicology, ChampionsGate, FL, USA
5. University of Kentucky, Lexington, KY, USA

Abstract

The purpose of this review is to examine the evidence for a relationship between mercury (Hg) exposure from dental amalgams and certain idiopathic chronic illnesses--chronic fatigue syndrome (CFS), fibromyalgia (FM), depression, anxiety, and suicide. Dental amalgam is a commonly used dental restorative material that contains approximately 50% elemental mercury (Hg⁰) by weight and releases Hg⁰ vapor. Studies have shown that chronic Hg exposure from various sources including dental amalgams is associated with numerous health complaints, including fatigue, anxiety, and depression--and these are among the main symptoms that are associated with CFS and FM. In addition, several studies have shown that the removal of amalgams is associated with improvement in these symptoms. Although the issue of amalgam safety is still under debate, the preponderance of evidence suggests that Hg exposure from dental amalgams may cause or contribute to many chronic conditions. Thus, consideration of Hg toxicity may be central to the effective clinical investigation of many chronic illnesses, particularly those involving fatigue and depression.

<http://www.ncbi.nlm.nih.gov/pubmed/25617876>

Mercury toxicity and neurodegenerative effects

Author information

Carocci A1, Rovito N, Sinicropi MS, Genchi G.

Dipartimento di Farmacia-Scienze del Farmaco
Università degli Studi di Bari "A. Moro"
Bari, 70125, Italia

Abstract

Mercury is among the most toxic heavy metals and has no known physiological role in humans. Three forms of mercury exist: elemental, inorganic and organic. Mercury has been used by man since ancient times. Among the earliest were the Chinese and Romans, who employed cinnabar (mercury sulfide) as a red dye in ink (Clarkson et al. 2007). Mercury has also been used to purify gold and silver minerals by forming amalgams. This is a hazardous practice, but is still widespread in Brazil's Amazon basin, in Laos and in Venezuela, where tens of thousands of miners are engaged in local mining activities to find and purify gold or silver. Mercury compounds were long used to treat syphilis and the element is still used as an antiseptic, as a medicinal preservative and as a fungicide. Dental amalgams, which contain about 50% mercury, have been used to repair dental caries in the U.S. since 1856. Mercury still exists in many common household products around the world. Examples are: thermometers, barometers, batteries, and light bulbs (Swain et al. 2007). In small amounts, some organo mercury-compounds (e.g., ethylmercury thiosalicylate (thimerosal) and phenylmercury nitrate) are used as preservatives in some medicines and vaccines (Ballet et al. 2001). Each mercury form has its own toxicity profile. Exposure to Hg⁰ vapor and MeHg produce symptoms in CNS, whereas, the kidney is the target organ when exposures to the mono- and di-valent salts of mercury (Hg⁺ and Hg⁺⁺, respectively) occur. Chronic exposure to inorganic mercury produces stomatitis, erethism and tremors. Chronic MeHg exposure induced symptoms similar to those observed in ALS, such as the early onset of hind limb weakness (Johnson and Atchison 2009). Among the organic mercury compounds, MeHg is the most biologically available and toxic (Scheuhammer et al. 2007). MeHg is neurotoxic, reaching high levels of accumulation in the CNS; it can impair physiological function by disrupting endocrine glands (Tan et al. 2009). The most important mechanism by which mercury causes toxicity appears to be mitochondrial damage via depletion of GSH (Nicole et al. 1998), coupled with binding to thiol groups (-SH), which generates free radicals. Mercury has a high affinity for thiol groups (-SH) and seleno groups (-SeH) that are present in amino acids as cysteine and N-acetyl cysteine, lipoic acid, proteins, and enzymes. N-acetylcysteine and cysteine are precursors for the biosynthesis of GSH, which is among the most powerful intracellular antioxidants available to protect against oxidative stress and inflammation. Mercury and methylmercury induce mitochondrial dysfunction, which reduces ATP synthesis and increases lipid, protein and DNA peroxidation. The content of metallothioneines, GSH, selenium and fish high in omega-3 fatty acids appear to be strongly related with degree of inorganic and organic mercury toxicity, and with the protective detoxifying mechanisms in humans. In conclusion, depletion of GSH, breakage of mitochondria, increased lipid peroxidation, and oxidation of proteins and DNA in the brain, induced by mercury and his salts, appear to be important factors in conditions such as ALS and AD (Bains and Shaw 1997; Nicole et al. 1998; Spencer et al. 1998; Alberti et al. 1999).

“In conclusion,
depletion of GSH,
breakage of mitochondria,
increased lipid peroxidation,
and oxidation of proteins and DNA in the brain,
induced by mercury and his salts,
appear to be important factors in
conditions such as Amyotrophic Lateral Sclerosis
and Alzheimers Disease ...”

“These findings suggest that the epidemiological link between environmental mercury exposure and an increased risk of developing autism may be mediated through mitochondrial dysfunction ...”

Journal of Toxicology • January 2015

Increased Susceptibility to Ethylmercury-Induced Mitochondrial Dysfunction in a Subset of Autism Lymphoblastoid Cell Lines

Shannon Rose, Rebecca Wynne, Richard E. Frye, Stepan Melnyk, and S. Jill James

Department of Pediatrics, University of Arkansas for Medical Sciences
Arkansas Children's Hospital Research Institute
13 Children's Way, Slot 512-41B
Little Rock, AR 72202, USA

Abstract

The association of autism spectrum disorders with oxidative stress, redox imbalance, and mitochondrial dysfunction has become increasingly recognized. In this study, extracellular flux analysis was used to compare mitochondrial respiration in lymphoblastoid cell lines (LCLs) from individuals with autism and unaffected controls exposed to ethylmercury, an environmental toxin known to deplete glutathione and induce oxidative stress and mitochondrial dysfunction. We also tested whether pretreating the autism LCLs with N-acetyl cysteine (NAC) to increase glutathione concentrations conferred protection from ethylmercury. Examination of 16 autism/control LCL pairs revealed that a subgroup (31%) of autism LCLs exhibited a greater reduction in ATP-linked respiration, maximal respiratory capacity, and reserve capacity when exposed to ethylmercury, compared to control LCLs. These respiratory parameters were significantly elevated at baseline in the ethylmercury-sensitive autism subgroup as compared to control LCLs. NAC pretreatment of the sensitive subgroup reduced (normalized) baseline respiratory parameters and blunted the exaggerated ethylmercury-induced reserve capacity depletion. These findings suggest that the epidemiological link between environmental mercury exposure and an increased risk of developing autism may be mediated through mitochondrial dysfunction and support the notion that a subset of individuals with autism may be vulnerable to environmental influences with detrimental effects on development through mitochondrial dysfunction.

<http://www.hindawi.com/journals/jt/2015/573701/>

“... the present study provides new epidemiological evidence of a significant relationship between increasing organic ethyl mercury exposure from Thimerosal-containing vaccines and the subsequent risk of pervasive developmental disorder diagnosis ...”

Biological Trace Element Research • February 2015

**A case-control study
evaluating the relationship between thimerosal-containing haemophilus influenzae type b vaccine administration
and the risk for a pervasive developmental disorder diagnosis in the United States**

Author information

Geier DA1, Kern JK, King PG, Sykes LK, Geier MR.

The Institute of Chronic Illnesses, Inc, 14 Redgate Ct, Silver Spring, MD, 20905, USA

Abstract

Thimerosal is an organic mercury (Hg)-containing compound (49.55 % Hg by weight) historically added to many multi-dose vials of vaccine as a preservative. A hypothesis testing case-control study evaluated automated medical records in the Vaccine Safety Datalink (VSD) for organic Hg exposure from Thimerosal in Haemophilus influenzae type b (Hib)-containing vaccines administered at specific times within the first 15 months of life among subjects diagnosed with pervasive developmental disorder (PDD) (n=534) in comparison to controls. The generally accepted biologically non-plausible linkage between Thimerosal exposure and subsequent diagnosis of febrile seizure (n=5886) was examined as a control outcome. Cases diagnosed with PDD received significantly more organic Hg within the first 6 months of life (odds ratio (OR)=1.97, $p<0.001$) and first 15 months of life (OR=3.94, $p<0.0001$) than controls, whereas cases diagnosed with febrile seizure were no more likely than controls to have received increased organic Hg. On a per microgram of organic Hg basis, cases diagnosed with a PDD in comparison to controls were at significantly greater odds (OR=1.0197, $p<0.0001$) of receiving increasing organic Hg exposure within the first 15 months of life, whereas cases diagnosed febrile seizure were no more likely than controls (OR=0.999, $p>0.20$) to have received increasing organic Hg exposure within the first 15 months of life. Routine childhood vaccination is an important public health tool to reduce the morbidity and mortality associated with infectious diseases, but the present study provides new epidemiological evidence of a significant relationship between increasing organic Hg exposure from Thimerosal-containing vaccines and the subsequent risk of PDD diagnosis in males and females.

<http://www.ncbi.nlm.nih.gov/pubmed/25382662>

Thimerosal: clinical, epidemiologic and biochemical studies

Author information

Geier DA1, King PG2, Hooker BS3, Dórea JG4, Kern JK5, Sykes LK6, Geier MR7.

1. Institute of Chronic Illnesses, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA
2. CoMeD, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA
3. Biology Department, Simpson University, 2211 College View Drive, Redding, CA 96001, USA
4. Health Sciences, Universidade de Brasilia, 70919-970 Brasilia, DF, Brazil. Electronic address: jg.dorea@gmail.com.
5. Institute of Chronic Illnesses, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA. Electronic address: jkern@dfwair.net.
6. CoMeD, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA. Electronic address: syklone5@verizon.net.
7. Institute of Chronic Illnesses, Inc., 14 Redgate Ct., Silver Spring, MD 20905, USA. Electronic address: mgeier@comcast.net

Abstract

INTRODUCTION

Thimerosal (or Thiomersal) is a trade name for an organomercurial compound (sodium ethyl-mercury (Hg) thio-salicylate) that is 49.55% Hg by weight, which rapidly decomposes in aqueous saline solutions into ethyl-Hg hydroxide and ethyl-Hg chloride. Developed in 1927, it has been and is still being used as a preservative in some cosmetics, topical pharmaceuticals, and biological drug products, including vaccines. Concerns have been voiced about its use because it is toxic to human cells. Although it is banned in several countries, it continues to be added to some vaccines in the United States and many vaccines in the developing world.

DISCUSSION

This critical review focuses on the clinical, epidemiological, and biochemical studies of adverse effects from Thimerosal in developing humans. This review will include research that examines fetal, infant, and childhood death; birth defects; neurodevelopmental testing deficits in children; and neurodevelopmental disorders (attention deficit/hyperactivity disorder, autism spectrum disorder, tic disorder, and specific developmental delays). The review will also look at the research that examined the outcomes of acute accidental ethyl-Hg poisoning in humans. The studies that examine the underlying biochemical insights into the neuronal cellular damage will also be explored.

CONCLUSION

The culmination of the research that examines the effects of Thimerosal in humans indicates that it is a poison at minute levels with a plethora of deleterious consequences, even at the levels currently administered in vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25708367>

“The culmination of the research that examines the effects of Thimerosal in humans indicates that it is a poison at minute levels with a plethora of deleterious consequences, even at the levels currently administered in vaccines.”

“During the decade in which Thimerosal-containing hepatitis B vaccines were routinely recommended and administered to US infants, an estimated 0.5-1 million additional US children were diagnosed with specific delays in development as a consequence of 25µg or 37.5µg organic mercury from Thimerosal-containing hepatitis B vaccines ...

The resulting lifetime costs to the United States may exceed \$1 trillion.”

Journal Of Epidemiology And Global Health • July 2015

A longitudinal cohort study of the relationship between Thimerosal-containing hepatitis B vaccination and specific delays in development in the United States: Assessment of attributable risk and lifetime care costs

Author information

Geier DA1, Kern JK2, Hooker BS3, King PG4, Sykes LK4, Geier MR1.

1. Institute of Chronic Illnesses, Inc, Silver Spring, MD, USA.

2. Institute of Chronic Illnesses, Inc, Silver Spring, MD, USA. Electronic address: jkern@dfwair.net.

3 .Biology Department, Simpson University, Redding, CA, USA.

4. CoMeD, Inc, Silver Spring, MD, USA.

Abstract

Epidemiological evidence suggests a link between mercury (Hg) exposure from Thimerosal-containing vaccines and specific delays in development. A hypothesis-testing longitudinal cohort study (n=49,835) using medical records in the Vaccine Safety Datalink (VSD) was undertaken to evaluate the relationship between exposure to Hg from Thimerosal-containing hepatitis B vaccines (T-HBVs) administered at specific intervals in the first 6 months of life and specific delays in development [International Classification of Disease, 9th revision (ICD-9): 315.xx] among children born between 1991 and 1994 and continuously enrolled from birth for at least 5.81 years. Infants receiving increased Hg doses from T-HBVs administered within the first month, the first 2 months, and the first 6 months of life were significantly more likely to be diagnosed with specific delays in development than infants receiving no Hg doses from T-HBVs. During the decade in which T-HBVs were routinely recommended and administered to US infants (1991-2001), an estimated 0.5-1 million additional US children were diagnosed with specific delays in development as a consequence of 25µg or 37.5µg organic Hg from T-HBVs administered within the first 6 months of life. The resulting lifetime costs to the United States may exceed \$1 trillion.

Full Report

<http://www.sciencedirect.com/science/article/pii/S2210600615000647>

[an epidemic with a multi-trillion-dollar cost]

Systematic Assessment of Research on Autism Spectrum Disorder and Mercury Reveals Conflicts of Interest and the Need for Transparency in Autism Research

Author information

Kern JK1, Geier DA2, Deth RC3, Sykes LK4,
Hooker BS5, Love JM6, Bjørklund G7, Chaigneau CG8,
Haley BE9, Geier MR10.

1. Institute of Chronic Illnesses, Inc., 14 Redgate Court, Silver Spring, MD, 20905
2. Institute of Chronic Illnesses, Inc., 14 Redgate Court, Silver Spring, MD, 20905
3. Nova Southeastern University, Fort Lauderdale, FL, USA. rdeth@nova.edu.
4. CoMeD, Inc., Silver Spring, MD, USA. syklone5@verizon.net.
5. Simpson University, Redding, CA, USA. bhooker@simpsonu.edu.
6. CoMeD, Inc., Silver Spring, MD, USA. jlove@titushillis.com.
7. Council for Nutritional and Environmental Medicine, Mo i Rana, Norway. bjorklund@conem.org.
8. CoMeD, Inc., Silver Spring, MD, USA. mamadelchinito@gmail.com.
9. University of Kentucky, Lexington, KY, USA. behaley@ctiscience.com.
10. Institute of Chronic Illnesses, Inc., 14 Redgate Court, Silver Spring, MD, 20905
mgeier@comcast.net

Abstract

Historically, entities with a vested interest in a product that critics have suggested is harmful have consistently used research to back their claims that the product is safe. Prominent examples are: tobacco, lead, bisphenol A, and atrazine. Research literature indicates that about 80-90 % of studies with industry affiliation found no harm from the product, while only about 10-20 % of studies without industry affiliation found no harm. In parallel to other historical debates, recent studies examining a possible relationship between mercury (Hg) exposure and autism spectrum disorder (ASD) show a similar dichotomy. Studies sponsored and supported by industry or entities with an apparent conflict of interest have most often shown no evidence of harm or no “consistent” evidence of harm, while studies without such affiliations report positive evidence of a Hg/autism association. The potentially causal relationship between Hg exposure and ASD differs from other toxic products since there is a broad coalition of entities for whom a conflict of interest arises. These include influential governmental public health entities, the pharmaceutical industry, and even the coal burning industry. This review includes a systematic literature search of original studies on the potential relationship between Hg and ASD from 1999 to date, finding that of the studies with public health and/or industry affiliation, 86 % reported no relationship between Hg and ASD. However, among studies without public health and/or industry affiliation, only 19 % find no relationship between Hg and ASD. The discrepancy in these results suggests a bias indicative of a conflict of interest.

<http://www.ncbi.nlm.nih.gov/pubmed/26507205>

This review includes a systematic literature search of original studies on the potential relationship between Hg [ethyl mercury] and ASD [Autistic Spectrum Disorder] from 1999 to date, finding that of the studies with public health and/or industry affiliation, 86% reported no relationship between Hg [ethyl mercury] and ASD [Autistic Spectrum Disorder]. However, among studies without public health and/or industry affiliation, only 19% find no relationship between Hg [ethyl mercury] and ASD [Autistic Spectrum Disorder]. The discrepancy in these results suggests a bias indicative of a conflict of interest.”

Increased Susceptibility to Ethylmercury-Induced Mitochondrial Dysfunction in a Subset of Autism Lymphoblastoid Cell Lines

Shannon Rose, Rebecca Wynne,
Richard E. Frye, Stepan Melnyk, and S. Jill James

Department of Pediatrics
University of Arkansas for Medical Sciences
Arkansas Children's Hospital Research Institute
13 Children's Way, Slot 512-41B, Little Rock, AR 72202, USA

Abstract

The association of autism spectrum disorders with oxidative stress, redox imbalance, and mitochondrial dysfunction has become increasingly recognized. In this study, extracellular flux analysis was used to compare mitochondrial respiration in lymphoblastoid cell lines (LCLs) from individuals with autism and unaffected controls exposed to ethylmercury, an environmental toxin known to deplete glutathione and induce oxidative stress and mitochondrial dysfunction. We also tested whether pretreating the autism LCLs with N-acetyl cysteine (NAC) to increase glutathione concentrations conferred protection from ethylmercury. Examination of 16 autism/control LCL pairs revealed that a subgroup (31%) of autism LCLs exhibited a greater reduction in ATP-linked respiration, maximal respiratory capacity, and reserve capacity when exposed to ethylmercury, compared to control LCLs. These respiratory parameters were significantly elevated at baseline in the ethylmercury-sensitive autism subgroup as compared to control LCLs. NAC pretreatment of the sensitive subgroup reduced (normalized) baseline respiratory parameters and blunted the exaggerated ethylmercury-induced reserve capacity depletion. These findings suggest that the epidemiological link between environmental mercury exposure and an increased risk of developing autism may be mediated through mitochondrial dysfunction and support the notion that a subset of individuals with autism may be vulnerable to environmental influences with detrimental effects on development through mitochondrial dysfunction.

<http://www.hindawi.com/journals/jt/2015/573701/>

“These findings suggest that the epidemiological link between environmental mercury exposure and an increased risk of developing autism may be mediated through mitochondrial dysfunction and support the notion that a subset of individuals with autism may be vulnerable to environmental influences with detrimental effects on development through mitochondrial dysfunction.”

Eli Lilly And The History of Thimerosal

The following is a summary of the history of thimerosal. It is not a complete list, as there is much more information out there but we hit the high points and we give a good frame of reference for where the discussion of the safety of this product and its relationship to autism and neurodevelopmental disorders should begin.

Invented in the 1920's by Eli Lilly, thimerosal is 49.6% ethylmercury by weight, a neurotoxin known to be more than a hundreds times more lethal to tissue than lead.

Eli Lilly's safety testing of the product consists of a 1930 study of 22 patients dieing from meningococcal meningitis in an Indiana hospital. Patients are injected with the solutions and followed until their death, which is within days. Because the patients die of meningitis, they are declared to show no adverse reaction to thimerosal and the product is declared safe for use. Thimerosal is subsequently introduced for use in vaccines and in over the counter remedies as a preservative to kill bacteria in the product.

When the FDA is created, Thimerosal is grandfathered in and is not subjected to any additional safety testing. The 1930 study remains the only safety testing done on the substance even after being in use for over 75 years.

Through FOIA requests and documents acquired as a part of discovery process in lawsuits against Lilly, it is clear that they have been warned about, and have been aware of the dangers of the product since at least 1947.

The use of thimerosal in teething powders for infants leads to a fatal out break of Acrodynia, or "Pink's Disease", a form of mercury poisoning. This illness has many symptoms in common with Autism. The link to mercury powders was found in the 1940's and by the 1950's Pink's disease was disappearing.

In 1963 Eli Lilly was forwarded an article that read in part: "There is another point of practical significance: does the parenteral injection of thimerosal - containing fluids cause disturbances in thimerosal-sensitive patients?" "It is known that persons that are contact sensitive to a drug may tolerate the same medications internally, but it seems advisable to use a preservative other than thimerosal for injections in thimerosal-sensitive people."

On August 17, 1967 the Medical/Science department requests that the claim "non-toxic" on thimerosal labels be deleted in next printing run. Two weeks later the label is changed to "non-irritating to body tissues," and the phrase non-toxic omitted.

In 1972 The British Medical Journal reports case of skin burns resulting from the chemical interaction of thimerosal and aluminum. "Mercury is known to act as a catalyst and to cause aluminum to oxidize rapidly, with the production of heat." The manufacturers who supply us with thimerosal have been informed." [Thimerosal is being used in vaccines which also contain aluminum].

In the 1970's six newborns at one hospital die as a result of having a thimerosal containing antiseptic wiped on their wounds.

In 1982 the FDA reviews the use of thimerosal. Their statement reads in part: "At the cellular level, thimerosal has been found to be more toxic for human epithelial cells in vitro than mercuric chloride, mercuric nitrate, and merbromim (mercurichrom). "It was found to be 35.3 times more toxic for embryonic chick heart tissue than for staphylococcus aureus." [a pathogen that the thimerosal is intended to kill]. A 1950 study showed that thimerosal was no better than water in protecting mice from potential fatal streptococcal infection." "The Panel concludes that thimerosal is not safe for over the counter topical use because of its potential for cell damage if applied to broken skin and its allergy potential. It is not effective as a topical antimicrobial because its bacteriastatic action can be reversed." Additional language added to some Lilly labels: "As with any drug, if you are pregnant or nurs-

ing a baby, seek the advice of a health professional before using this product." The FDA orders the withdrawal of over the counter thimerosal containing products within a 6 month period. It does not order removal from vaccines, but recommends that the issue be studied and that the incidence of neurological problems in unvaccinated populations like the Amish be compared to the vaccinated population. [22 years later no such study has yet been done. On July 19, 2005 Dr. Julie Gerberding, head of the CDC says that such a study would be difficult to undertake because of genetic confounders. This seems contrary to the scientific process because if indeed such a study is done and it is found that the Amish have a lower incidence of neurodevelopmental disorders, the next step would be to undertake genetic studies to see if their genes differ dramatically from the general population and if their differences can help us locate the genetic component of autism. In addition studies designed to see if the small number of vaccinated Amish differ in their risk for NDDs to the larger Amish population would offer information about increased risk from thimerosal.]

In the 1930's the average child only received three vaccines in their young life. Many vaccines are added to the schedule over the years, with an increase in the 1980's and with 3 vaccines added to the schedule in 1991 alone. The current vaccine schedule calls for 31 vaccines in the first 18 months of life, 48 with full flu vaccination by 72 months of life.

A Merck internal memo is obtained during discovery discloses that in 1991 a Merck researcher added up the amount of mercury that is in the new vaccine schedule and sounded an alarm at the company that children who are vaccinated according to it would receive amounts of mercury far and above that considered to be safe by the EPA. Merck takes no action in regard to the information.

During the 1990's, autism rates begin to rise dramatically. Parents complain to the health authorities that they believe that their children's developmental disorders are related to their vaccines.

In 1998, a researcher at the CDC does the same math that Merck did 7 years previously. She finds that children are getting as much as 125 times the EPA limit of mercury for their weight. The EPA limit is based on the ingestion of methylmercury in food by a healthy adult. Because 90% of ingested mercury is excreted in the digestive track and never enters the blood stream, so even the EPA limit may be drastically lacking considering that thimerosal is injected directly into the blood stream and is not subject to the bodies natural defenses against toxic poisoning.

In 1999, the CDC and the American Association of Pediatrics issue a joint statement saying that although they find no "evidence of harm" from the mercury exposure that children are getting in their vaccines, they are calling on vaccine manufacturers to remove it from vaccines on a voluntary basis as a precautionary measure because "some children may" get more than the EPA limit for mercury at their 6 month visits. Manufactures begin the process in 1999, but do not remove it from all vaccines.

No legal ban on thimerosal is issued.

No recall of the mercury laden vaccines is issued and companies continue to sell lots already manufactured. Some of these vaccines containing full doses of thimerosal have been found in doctors' offices by parents who request to read package inserts with expiration dates as late as 2007.

No independent or government testing of vaccines is done to confirm that thimerosal has been removed. FDA denies parents request that they set up a system to verify manufacturers claims of low dose or thimerosal free vaccines. No statement is issued to pediatricians to alert them to the symptoms of mercury poisoning. No recommendation is made to pediatricians to screen children who suffered the onset of neurological impairment after vaccination for mercury toxicity.

Vaccines with 25mcg of thimerosal are still shipped to developing countries. Most flu shots still contain a full dose

of thimerosal. The EPA estimates that a person must weigh 550 lbs. to safely tolerate this amount of mercury.

In November of 1999, the CDC commissions one of its new employees, a Belgian named Thomas Verstraten, to study the Vaccine Safety Datalink to find the risk of autism and other NDDs in relation to thimerosal exposure. Verstraten's first draft of the study finds a relative risk above 7 for children who receive the highest dose of thimerosal to develop autism. In simple terms, such children have more than a 600% higher chance of developing autism than children who don't receive any thimerosal. A relative risk of 2 is sufficient proof in U.S. courts to find for vaccine injury. Verstraten and other scientists at the CDC spend 4 years trying to change the study so that the relationship between the preservative and NDD's is significantly reduced or eliminated. The Center for Disease Control will later describe these changes to the study as "improvements". When the study is published in 2003, it concludes that "no consistent significant associations are found between thimerosal containing vaccines and neurodevelopmental outcomes." By this time Thomas Verstraten, who is listed as a CDC employee on the study, has been an employee of GlaxoSmithKlein (a defendant in thimerosal law suits) for more than 2 years.

In November of 2000, despite being born almost two months prematurely and despite the assurance of my pediatrician that thimerosal had been removed from vaccines, my son Webster is injected with a DTaP vaccine that was 74.5 times the EPA limit for mercury exposure for his weight, just two weeks past his due date. He will go on to develop verbal apraxia and sensory integration disorder.

In 2001 Bernard et. al. publish their hypothesis: Autism: A Novel Form of Mercury Poisoning. It reads in part: "Exposure to mercury can cause immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with autism, and the similarities extend to neuroanatomy, neurotransmitters, and biochemistry. Thimerosal, a preservative added to many vaccines, has become a major source of mercury in children who, within their first two years, may have received a quantity of mercury that exceeds safety guidelines. A review of medical literature and US government data suggests that: (i) many cases of idiopathic autism are induced by early mercury exposure from thimerosal; (ii) this type of autism represents an unrecognized mercurial syndrome; and (iii) genetic and non-genetic factors establish a predisposition whereby thimerosal's adverse effects occur only in some children."

In 2001 the Institute of Medicine is commissioned by the CDC to undertake a comprehensive review of all research into the thimerosal/autism connection. At their first meeting, Dr Stratton, head of the commission, when discussing what the process and product of the working group would be states that, "We said this before you got here, and I think we said this yesterday, the point of no return, the line we will not cross in public policy is to pull the vaccine, change the schedule. We could say it is time to revisit this, but we would never recommend that level. Even recommending research is recommendations for policy. We wouldn't say compensate, we wouldn't say pull the vaccine, we wouldn't say stop the program". When the transcript of the meeting is made public through a FOIA request, many interpret this to mean that no matter what they find, they will not publicly say that there is any link between the thimerosal and autism. Dr. Harvey Fineberg, head of the IOM, states that this is an incorrect interpretation of the comments, but will not offer any alternate interpretation of what else they could mean.

In 2001 Verstraten presents a version of his study to the IOM. He begins his presentation by telling the panel that as of 8 am that morning, he had become an employee of Glaxo Smith Klein. Despite the conflict of interest and the drastic changes made over the course of the study, the IOM will rely heavily on the study in making their determination. Dr. Verstraten returns to Belgium and except for a letter published in Pediatrics, little is heard from him again.

In March of 2002 my son Chandler, who was born one month early, is injected with Hepatitis B vaccine containing a "trace amount" of thimerosal (currently still on the schedule), despite the fact that he has no risk factors for Hepatitis B, and he is still two weeks from reaching his due date. Within days he develops fevers and uncontrollable crying that lasts for three months and bowel problems that persist for two years until he is placed on the

GFCF diet. He will go on to be diagnosed with both Autism and mercury poisoning at age 2. I later discover that the "trace amount" of thimerosal is still just over the EPA limit of mercury for his weight.

In 2003 the Verstraten Study is published in Pediatrics with no mention of the conflict of interest of the lead researcher. Later a private contractor would testify before congress that he was ordered to destroy the original data sets used in the 1999 version of the study that found the dramatic link between thimerosal and autism in the interest of "patient confidentiality". The entire Vaccine Safety Datalink is eventually moved to an offshore private company and can no longer be accessed by FOIA request.

In February of 2004, the IOM rushes to hold public hearings where researchers on both sides of the issues present their studies. The meeting is considered to be a "draw" between the two sides by many of those in attendance. A link is neither proved nor disproved, but new research in to the mechanism of how mercury can trigger autism and NDDs in a genetically vulnerable sub population is presented, along with case studies of successful treatment of autistic symptoms based on the new research.

In May of the same year, the IOM issues their final conclusion on the link between Thimerosal and NDDs. They state that, "the body of epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism. The committee further finds that potential biological mechanisms for vaccine-induced autism that have been generated to date are theoretical only." They then go on to take the unusual step of recommending that research into a link between the two be abandoned and funds be spent on other lines of inquiry. The conclusion relies heavily on Verstraten and several other epidemiological studies that are considered to implement fatally flawed methods and to be riddled with conflict of interest by members of the autism community. Parent groups are enraged. The IOM panel disbands.

Later that year, Thomas Verstraten publishes a letter in Pediatrics in response to those who criticize his study and his conflict of interest. His letter does not address the substance of the charges made against the study and the changes that were made to it over its 4 year evolution, but instead says that continuing to debate the validity of the 1999 study would be a "waste of scientific energy and not to the benefit of the safety of US children or of all the children world wide that have the privilege of being vaccinated." He goes on to say that any suggestion of impropriety on the part of himself, the CDC or GSK is an insult and accuses his critics of having "pitiable attitudes".

In July of 2005, in the face of continuing criticism of the IOM findings, the head of the IOM, Dr. Harvey Fineberg, issues a letter stating that Dr. Stratton's 2001 comments that they would not say "pull the vaccine" or "change the schedule" were taken out of context and did not suggest that the IOM decision was compromised. Dr. Fineberg has not, despite requests, offered an alternative interpretation of what her comments meant in context.

In March of 2005, Author David Kirby released his book, "Evidence of Harm - Mercury in Vaccines and the Autism Epidemic: A Medical Controversy" detailing the history of thimerosal in vaccines and its relationship to autism. In April of 2005 the CDC posts a notice on their web site stating that they were in the process of reviewing "Evidence of Harm" and would be responding to the book.

In June of 2005 Robert F. Kennedy Jr. echoed the information found in the book and charged the CDC and Eli Lilly of malfeasance in covering up evidence of a causal effect between thimerosal and autism in an article published in Rolling Stone and Salon.com. It is entitled "Deadly Immunity: Robert F. Kennedy Jr. investigates the government cover-up of a mercury/autism scandal".

July 19, 2005. The CDC holds a press conference to: "communicate the importance of infants and children receiving their recommended vaccinations on time, and reassure parents that vaccines are safe. The renewed attention to the potential causal link between thimerosal, a vaccine preservative, and autism will also be addressed during the press conference." Vaccine safety groups are not informed of the press conference nor invited. The conference

presents no new information and does not answer important questions raised in Evidence of Harm or Deadly Immunity about the conduct of the CDC the IOM or the reliability of the research that continues to be used to show no link between thimerosal and autism.

In June of 2007 the first vaccinated v. unvaccinated study is finally done ... by parents. Generation Rescue funded a survey using the CDC's techniques for determining incidence of a disorder and found that vaccinated children are two and a half times more likely to have a neurodevelopmental disorder. CDC spokesman Curtis Allen said, "We look forward to learning more about the survey."

On June 25, 2007 Congresswoman Carolyn Maloney (D-NY) introduced the "Comprehensive Comparative Study of Vaccinated and Unvaccinated Populations Act of 2007" (H.R. 2832), legislation that would require the National Institutes of Health (NIH) to conduct a comprehensive comparative study of vaccinated and unvaccinated populations. Her stated purpose is to resolve the controversy about the possible link between autism and mercury or other vaccine components. The study is never done.

Today, January 2016, autism, ADHD and learning disabilities are at truly epidemic levels with one in six children presenting. The government and the pharmaceutical companies will claim that mercury has not been used in the manufacture of most vaccines for some time now, is used only in influenza vaccines and appears only in trace amounts in others. In the next chapter you'll read about aluminum which is even more deadly than mercury.

Chapter Three
Aluminum • Alum
1911 - 2015

Aluminum rescued Big Pharma from the mercury-autism connection. Not only does aluminum cause the symptoms found on the autistic spectrum, it also causes nearly 100 more disorders. Big Pharma can rest easy. Vaccines no longer contain mercury and the autism epidemic continues to grow. Obviously it couldn't have been the mercury ...

JAMA • September 2, 1911

Some Objections To The Use Of Alum Baking Powder

by William J. Gies, Ph.D.

Abstract

During a period of about seven years I have occasionally conducted experiments on the effects of aluminum salts. These studies have convinced me that the use in food of alum or any other aluminum compound is a dangerous practice. That the aluminum ion is very toxic is well known. That "aluminized" food yields soluble aluminum compounds to gastric juice (and stomach contents) has been demonstrated. That such soluble aluminum is in part absorbed and carried to all parts of the body by the blood can no longer be doubted. That the organism can "tolerate" such treatment without suffering harmful consequences has not been shown. It is believed that the facts in this paper will give emphasis to my conviction that aluminum should be excluded from food.

<http://jama.jamanetwork.com/article.aspx?articleid=448038>

"That the aluminum ion is very toxic is well known.

That "aluminized" food yields soluble aluminum compounds to gastric juice (and stomach contents) has been demonstrated.

That such soluble aluminum is in part absorbed and carried to all parts of the body by the blood can no longer be doubted.

That the organism can "tolerate" such treatment without suffering harmful consequences has not been shown."

“I was recently called to see a man ...”

The Lancet • June 18, 1921

Case Of Aluminum Poisoning

by Dr. John Spofforth

L.R.C.P.EDIN., Membership At The Royal College Of Surgeons, England

Abstract

I was recently called to see a man, aged 46, who was then employed at a firm of metalworkers. He was in a state of great exhaustion and suffering from very severe and persistent vomiting. The pulse was slow and irregular. I suspected metallic poisoning and later sent a specimen of his urine to ..., analytical chemists, who reported that it contained a large amount of aluminium, also of phosphates. The patient said he had been dipping red-hot metal articles, contained in an aluminium holder, into concentrated nitric acid. Aluminium produces a rather slow intoxication. In this case it caused loss of memory, tremor, jerking movements and impaired co-ordination. There was also a chronic constipation and incontinence of urine.

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(01\)24927-7/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(01)24927-7/abstract)

JAMA • February 17, 1945

Early immunization against Pertussis with Alum precipitated vaccine

by Wallace Sako, MD., Ph.D., W. L. Treuting, MD., MPH.,
David B. Witt, Samuel J. Nichamin

Abstract

According to the recent mortality records the majority of deaths from pertussis occur in infants. Between 1938 and 1940 inclusive almost 67 per cent of the 10,730 deaths from whooping cough reported in the United States occurred during the first year of life and 47 per cent of these deaths were in infants under 7 months of age (table 1 and fig. 1). The exceptionally high mortality which pertussis exacts in the first half year of life calls for thorough investigation of the possibility of increasing the resistance of young infants to the disease by immunizing them shortly after birth. This procedure has been objected to chiefly because of the belief that young infants do not possess the ability to develop active immunity. No extensive study has been carried out, however, to establish the earliest age at which immunity to pertussis can be acquired.

<http://jama.jamanetwork.com/article.aspx?articleid=272944&resultClick=3>

“This procedure has been objected to chiefly because of the belief that young infants do not possess the ability to develop active immunity. No extensive study has been carried out, however, to establish the earliest age at which immunity to pertussis can be acquired.”

“Aluminium intoxication ... is associated with periorbital bleeding, lethargy, anorexia, and death. It is recommended that aluminium salts should be withdrawn from use in patients with renal failure and their use restricted in normal persons pending clarification of the issue.”

The Lancet • Volume 299, No. 7750, p564–568 • March 1972

Aluminium Toxicity In Rats

G.M. Berlyne, J. Ben Ari, E. Knopf, R.
Yagil, G. Weinberger, G.M. Danovitch

Department of Nephrology
Negev Central Hospital and Division of Life Sciences
Negev Arid Zone Research Institute and Faculty of Natural Science
University of Negev, Beer Sheva, Israel

Abstract

Aluminium intoxication has been demonstrated in the uræmic and non-uræmic rat after modest doses of oral and parenteral aluminium salts. The clinical syndrome is associated with periorbital bleeding, lethargy, anorexia, and death. Plasma-levels of aluminium were greatly raised, as were tissue levels in liver, heart, striated muscle, brain, and bone. Histological changes were found in the cornea. Liver oxygen consumption was reduced by giving the animals aluminium salts before death or by adding aluminium in vitro to normal liver homogenates. It is recommended that aluminium salts should be withdrawn from use in patients with renal failure and their use restricted in normal persons pending clarification of the issue.

<http://www.ncbi.nlm.nih.gov/pubmed/4110051>

Science • May 1973

**Brain aluminum distribution
in Alzheimer's disease and
experimental neurofibrillary degeneration**

Crapper DR, Krishnan SS, Dalton AJ.

Abstract

Neurofibrillary degeneration is an important pathological finding in senile and presenile dementia of the Alzheimer type. Experimentally, aluminum induces neurofibrillary degeneration in neurons of higher mammals. Aluminum concentrations approaching those used experimentally have been found in some regions of the brains of patients with Alzheimer's disease.

<http://www.ncbi.nlm.nih.gov/pubmed/4735595>

“Experimentally,
aluminum induces neurofibrillary degeneration
in neurons of higher mammals.”

Alterations in short-term retention,
conditioned avoidance response acquisition and
motivation following aluminum induced
neurofibrillary degeneration

D.R. Crapper

Departments of Physiology and Medicine
Faculty of Medicine, University of Toronto
Toronto, Canada

A.J. Dalton
Department of Psychology
Mental Retardation Centre, Toronto, Canada

Abstract

Aluminum chloride induced neurofibrillary degeneration may provide a useful model for the study of a human dementia process. This possibility was assessed in cats trained to perform on a delayed-response task, a conditioned avoidance task, visual and temporal discrimination tasks and a motivational task involving rewarding intracranial electrical stimulation. After an initial asymptomatic period short term retention and acquisition of a conditioned avoidance response were selectively impaired. The associated ultrastructural abnormalities plausibly implicate the cytoplasmic streaming mechanism in the cellular substrate for some retention and acquisition phenomena.

<http://www.sciencedirect.com/science/article/pii/0031938473900632>

“Aluminum chloride induced
neurofibrillary degeneration
may provide a useful model for the
study of a human dementia process.”

“... exerted selective and differential effects on the transport systems of neurotransmitter substances in the synaptosomal membrane.”

Journal of Inorganic Biochemistry • 1981

Selective inhibition of L-glutamate and gammaaminobutyrate transport in nerve ending particles by aluminium, manganese, and cadmium chloride

Patrick C.L. Wong, James C.K. Lai, Louis Lim, Alan N. Davison

Abstract

AlCl₃, MnCl₂, and CdCl₂ inhibited the rates of accumulation of [¹⁴C] L-glutamate and [³H] gammaaminobutyrate (GABA) in purified rat forebrain nerve-ending particles in a dose-dependent fashion. The concentrations that would give 50% inhibition (IC₅₀) of GABA transport were 316 μM, 7.4 mM, and 1.4 mM, respectively. Ca²⁺ (1 mM) enhanced the inhibitory effect of Al³⁺ (IC₅₀ decreased to 149 μM) but antagonized that of Mn²⁺ (IC₅₀ = 10 mM) and Cd²⁺ (IC₅₀ = 2.1 mM). For glutamate transport 1 mM Ca²⁺ changed the IC₅₀ values from 299 to 224 μM for Al³⁺, 7.1 to 10 mM for Mn²⁺, and 2 to 3 mM for Cd²⁺. In contrast, the rates of accumulation of [¹⁴C] 2-deoxy-glucose and [³H] L-phenylalanine were mostly unaffected by these metal ions. The results indicate that Al³⁺, Mn²⁺, and Cd²⁺ exerted selective and differential effects on the transport systems of neurotransmitter substances in the synaptosomal membrane.

<http://www.sciencedirect.com/science/article/pii/S0162013400800057>

Inhibition of brain glycolysis by aluminum

Lai JC, Blass JP.

Abstract

Aluminum inhibited both the cytosolic and mitochondrial hexokinase activities in rat brain. The IC₅₀ values were between 4 and 9 microM. Aluminum was effective at mildly acidic (pH 6.8) or slightly alkaline (pH 7.2-7.5) pH, in the presence of a physiological level of magnesium (0.5 mM). However, saturating (8 mM) magnesium antagonized the effect of aluminum on both forms of hexokinase activity. Other enzymes examined were considerably less sensitive to inhibition by aluminum. The IC₅₀ of aluminum for phosphofructokinase was 1.8 mM and for lactate dehydrogenase 0.4 mM. At 10-600 microM, aluminum actually stimulated pyruvate kinase. Aluminum also inhibited lactate production by rat brain extracts: this effect was much more marked with glucose as substrate than with glucose-6-phosphate. However, the IC₅₀ for inhibiting lactate production using glucose as substrate was 280 microM, higher than that required to inhibit hexokinase. This concentration of aluminum is comparable to those reportedly found in the brains of patients who had died with dialysis dementia and in the brains of some of the patients who had died with Alzheimer disease. Inhibition of carbohydrate utilization may be one of the mechanisms by which aluminum can act as a neurotoxin.

<http://www.ncbi.nlm.nih.gov/pubmed/6229606>

“This concentration of aluminum is comparable to those reportedly found in the brains of patients who had died with dialysis dementia and in the brains of some of the patients who had died with Alzheimer disease. Inhibition of carbohydrate utilization may be one of the mechanisms by which aluminum can act as a neurotoxin.”

**Experimental aluminium encephalopathy:
quantitative EEG analysis of aluminium bioavailability**

Cutrufo C, Caroli S, Delle Femmine P, Ortolani E,
Palazzesi S, Violante N, Zapponi GA, Loizzo A.

Abstract

Single oral doses of aluminium hydroxide (50 to 200 mg/kg) were found to induce in mice a dose-dependent diminution of the power of the 7.5 to 12 Hz frequency band, with a parallel dose-dependent increase of aluminium content in the brain, as early as 45 min after administration, and indicated that aluminium hydroxide is readily absorbed through an empty stomach or duodenum and is able to induce alterations of background EEG rhythms at doses equivalent to the ones used in human therapy. These data suggest that the EEG disturbances of the background type, (which are observed during the early stage of dialysis encephalopathy in man), may be partly due to a pharmacological and therefore reversible effect induced by an increase in aluminium level in the brain.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1027694/>

“Single oral doses of aluminium hydroxide were found to induce in mice a dose-dependent diminution of the power of the 7.5 to 12 Hz frequency band, with a parallel dose-dependent increase of aluminium content in the brain, as early as 45 min after administration, and indicated that aluminium hydroxide is readily absorbed through an empty stomach or duodenum and is able to induce alterations of background EEG rhythms at doses equivalent to the ones used in human therapy.”

Histochemical localization of aluminum in the rabbit Central Nervous System

Wen GY, Wisniewski HM.

Abstract

Aluminum was observed in the nucleolus, interchromatin granules, rough endoplasmic reticulum, free ribosomes, euchromatin, and the heterochromatin of the neuron. The association of aluminum with the first four r-RNA-containing cellular components and with the last two DNA-containing chromatins suggests the association of aluminum with the nucleic acids. The aluminum may interfere with the normal mechanism of the protein synthesis of r-RNA and of the transcription or gene modulation of DNA. Aluminum was also observed in the astrocytic process and in the nuclei of endothelial cells, pericytes, and the muscle cells of the blood vessels. The detection of aluminum in the pyramidal cells of the cerebral cortex and hippocampus and in the spinal cord neurons, was observed 1 h after i.v. injection, indicating a rapid entry of aluminum from the injection site through the blood-brain barrier (BBB) to the neurons. Using Morin stain, pyramidal neurons of the cerebral cortex and hippocampus, motoneurons of spinal cord, ganglion cells, and bipolar cells of retina and Purkinje cells of cerebellum, exhibited yellow fluorescence, with peak intensity at 560 nm. Tangles were observed in these six types of neurons. The granule cells of hippocampus and cerebellum and the photoreceptors of the retina exhibited green fluorescence with the peak intensity at 490-500 nm. Tangles were not observed in these three types of neurons.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=2417440>

“The detection of aluminum in the pyramidal cells of the cerebral cortex and hippocampus and in the spinal cord neurons, was observed 1-hour after i.v. injection, indicating a rapid entry of aluminum from the injection site through the blood-brain barrier (BBB) to the neurons.”

Metabolism and possible health effects of aluminum

by P. O. Ganrot

Abstract

Literature regarding the biochemistry of aluminum and eight similar ions is reviewed. Close and hitherto unknown similarities were found. A hypothetical model is presented for the metabolism, based on documented direct observations of Al^{3+} and analogies from other ions. Main characteristics are low intestinal absorption, rapid urinary excretion, and slow tissue uptake, mostly in skeleton and reticuloendothelial cells. Intracellular Al^{3+} is probably first confined in the lysosomes but then slowly accumulates in the cell nucleus and chromatin. Large, long-lived cells, e.g., neurons, may be the most liable to this accumulation. In heterochromatin, Al^{3+} levels can be found comparable to those used in leather tanning. It is proposed that an accumulation may take place at a subcellular level without any significant increase in the corresponding tissue concentration. The possible effects of this accumulation are discussed. As Al^{3+} is neurotoxic, the brain metabolism is most interesting. The normal and the lethally toxic brain levels of Al^{3+} are well documented and differ only by a factor of 3-10. The normal brain uptake of Al^{3+} is estimated from data on intestinal uptake of Al^{3+} and brain uptake of radionuclides of similar ions administered intravenously. The uptake is very slow, 1 mg in 36 years, and is consistent with an assumption that Al^{3+} taken up by the brain cannot be eliminated and is therefore accumulated. The possibility that Al^{3+} may cause or contribute to some specific diseases, most of them related to aging, is discussed with the proposed metabolic picture in mind.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1474689/>

“The uptake is very slow,
1 mg in 36 years, and is
consistent with an assumption
that Al^{3+} taken up by the brain
cannot be eliminated and is
therefore accumulated.”

Maternal and Developmental Toxicity of Chronic Aluminum Exposure in Mice

Author Information

Mari S. Golub*, M. Eric Gershwin*,
James M. Donald*, Scott Negri, Carl L. Keen*

*Department of Internal Medicine, University of California Davis, California 95616
a Department of Nutrition, University of California Davis, California 95616

Abstract

The present study demonstrated aluminum-induced neurotoxicity in mouse dams and developmental retardation in their offspring following oral exposure to several dose levels during gestation and lactation. Female mice fed aluminum lactate (AL) at levels of 500 or 1000 ppm in their diet from Day 0 gestation to Day 21 postpartum were compared to mice which received a 100 ppm aluminum diet either ad libitum or pair-fed to the 1000 ppm AL group. Dams receiving the 500 and 1000 ppm AL diets showed signs of neurotoxicity beginning at Days 12–15 postpartum and showed significant weight loss. Offspring showed dose-dependent decreases in body weight ($F = 6.47, p < 0.001$), crown-rump length ($F = 1.11, p < 0.0001$), and ponderal index ($F = 6.90, p < 0.0002$), at birth and preweaning. Absolute and relative liver and spleen weights were lower in pups from the high AL groups compared to controls ($F = 3.34, p < 0.025$ and $F = 15.54, p < 0.001$, respectively). Neurobehavioral development was somewhat delayed in aluminum-treated pups, but not in their pair-fed controls ($F = 5.52, p < 0.005$). In addition to showing oral toxicity of excess AL during development dose-dependent toxic effects of parenteral aluminum exposure were demonstrated in pregnant mice which were injected subcutaneously with aluminum lactate solution at 10, 20, or 40 mg Al/kg body wt on Days 3, 5, 7, 9, 12, 13, and 15 of gestation. Maternal spleen and liver weights were significantly increased in aluminum treated animals ($p < 0.001$ and $p < 0.05$, respectively). Fetal crown-rump lengths were significantly reduced in the 20 mg/kg aluminum group ($F = 9.79, p < 0.001$).

“The present study demonstrated aluminum-induced neurotoxicity in mouse dams and developmental retardation in their offspring following oral exposure to several dose levels during gestation and lactation.”

Neuropathologic, neurochemical and immunocytochemical characteristics of aluminum-induced neurofilamentous degeneration

Author information

Pendlebury WW1, Beal MF,
Kowall NW, Solomon PR.

Department of Pathology
University of Vermont College of Medicine, Burlington

Abstract

Inoculation of aluminum salts or metallic aluminum into the central nervous system of rabbits produces an encephalomyelopathy accompanied by widespread neurofibrillary degeneration (NFD) affecting restricted neuronal populations. Some investigators have suggested that this preparation may serve as an animal model for human neurodegenerative disorders, such as Alzheimer's disease (AD), in which neurofibrillary tangle (NFT) formation is a prominent histopathologic finding. However, neurochemical, immunocytochemical and behavioral features of the model are largely unknown and its neuropathology only partially described. We have undertaken a series of experiments designed to further characterize these aspects of the model. We have used an intraventricular route of injection of aluminum chloride and found that the distribution of NFD in rabbit brain is similar to the distribution of NFT formation in AD. Immunocytochemical probes demonstrate that phosphorylated neurofilaments accumulate in neuronal perikarya containing NFD, and double labelling techniques suggest that NFD affects primarily projection type neurons. The neurochemical profile of aluminum intoxicated rabbits shows both similarities and discrepancies to that of AD. Finally, as reported in a companion article in this issue of Neurotoxicology (Solomon and Pendlebury, 1988), aluminum-exposed rabbits develop learning and memory deficits which are strongly correlated with the degree of whole brain NFD but not with motor, sensory or motivational factors. We conclude that aluminum-induced NFD may have relevance for understanding NFT formation in AD and other neurodegenerative disorders in which abnormalities of the neuronal cytoskeletal architecture are present.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=3200512>

“... aluminum-induced neurofibrillary degeneration may have relevance for understanding neurofibrillary tangle formation in Alzheimer's disease and other neurodegenerative disorders ...”

**Aluminum-induced neurotoxicity:
alterations in membrane function
at the blood-brain barrier**

Author information

Banks WA1, Kastin AJ.

1Veterans Administration Medical Center
New Orleans, LA

Abstract

Aluminum is established as a neurotoxin, although the basis for its toxicity is unknown. It recently has been shown to alter the function of the blood-brain barrier (BBB), which regulates exchanges between the central nervous system (CNS) and peripheral circulation. The BBB owes its unique properties to the integrity of the cell membranes that comprise it. Aluminum affects some of the membrane-like functions of the BBB. It increases the rate of transmembrane diffusion and selectively changes saturable transport systems without disrupting the integrity of the membranes or altering CNS hemodynamics. Such alterations in the access to the brain of nutrients, hormones, toxins, and drugs could be the basis of CNS dysfunction. Aluminum is capable of altering membrane function at the BBB; many of its effects on the CNS as well as peripheral tissues can be explained by its actions as a membrane toxin.

<http://www.ncbi.nlm.nih.gov/pubmed/2671833>

“Aluminum is established as a neurotoxin ...
Aluminum affects some of the membrane-like
functions of the BBB ... many of its effects on
the CNS as well as peripheral tissues can be
explained by its actions as a membrane toxin.”

Micromolar aluminum levels
reduce 3H-thymidine incorporation
by cell line UMR 106-01

Author information

Blair HC1, Finch JL, Avioli R,
Crouch EC, Slatopolsky E, Teitelbaum SL.

Department of Pathology and Laboratory Medicine
Jewish Hospital, Washington University Medical Center
St. Louis, Missouri

Abstract

Aluminum-induced osteomalacia is a frequent complication observed in patients on maintenance hemodialysis. However, it is not known whether there are direct effects of aluminum on osteoblasts, or alternatively, whether the observed changes are due to changes in PTH or other factors. We sought to determine the effect of micromolar levels of aluminum on osteoblasts using a well-defined cell line derived from a 32P induced osteosarcoma of rat, UMR 106-01, which is alkaline-phosphatase positive, responds to PTH, and synthesizes type I collagen. Aluminum exposure was controlled using tissue culture media with [Al] less than 1 microgram/liter (40 nM), produced by precipitation of aluminum salts at pH 8.5. The effect of defined [Al], from 20 to 800 micrograms/liter (0.7 to 30 microM), was then determined by adding back aluminum while measuring DNA and protein synthesis. We found that aluminum depressed DNA synthesis, as determined by 3H-thymidine incorporation, by 60%, with half maximal effect at 20 micrograms/liter (740 nM) in cells at a density of 20,000/cm². Alternatively, protein synthesis, as determined by 3H-leucine incorporation, did not decline, and in some cases increased. However, qualitative analysis of matrix proteins produced with and without 800 micrograms/liter (30 mM) [Al] showed no differences. Direct measurements of cell number and protein synthesis confirmed these findings. Al does not alter the PTH-induced cAMP response of these cells. Thus, aluminum has a direct effect on cell division, and probably on protein synthesis, in this osteoblast-like cell line. These effects occur at levels of aluminum below those commonly contaminating tissue culture media, and thus are seen reproducibly only in media of defined [Al].

“... aluminum has a direct effect
on cell division, and probably on protein synthesis ...”

Effect of aluminium on superoxide dismutase

Author information

Shainkin-Kestenbaum R1,
Adler AJ, Berlyne GM, Caruso C.

Nephrology Section
Brooklyn VA Medical Center
New York 11209

Abstract

1. The effect of Al³⁺ on superoxide dismutase in vitro was studied, since in uraemia there is excessive superoxide production and frequently an elevated serum Al³⁺ level. Thus, the protective role of superoxide dismutase is particularly important.
2. Al³⁺ in concentrations similar to those found in the serum of uraemic patients inhibits superoxide dismutase activity. The degree of inhibition is directly proportional to the Al³⁺ level.
3. The combination of excessive oxygen free radical production with an increased Al³⁺ level may contribute to a variety of complications, including aluminium dementia or initiation and promotion of carcinogenic processes, which are known to be more common in uraemic patients.

<http://www.ncbi.nlm.nih.gov/pubmed/2582719>

“The combination of excessive oxygen free radical production with an increased aluminum level may contribute to a variety of complications, including aluminium dementia or initiation and promotion of carcinogenic processes ...”

Aluminum neurotoxicity in mammals

Author information

Wisniewski HM1, Moretz RC,
Sturman JA, Wen GY, Shek JW.

Institute for Basic Research in Developmental Disabilities
Departments of Pathological and Neurobiology
New York State Office of Mental Retardation and Developmental Disabilities, USA

Abstract

Although aluminum comprises a large percentage of the Earth's crust, it is excluded from body tissues, and especially from the central nervous system. When aluminum is experimentally introduced to the central nervous system, several neurotoxic effects are observed: i.e. neurofibrillary changes, behavioral and cognitive deficits and enzymatic and neurotransmitter changes, as well as certain types of epileptic seizures. The localization of relatively high levels of aluminum in Alzheimer disease, Guamanian amyotrophic lateral sclerosis and Parkinsonism-dementia has led to the implication of aluminum as a pathogenic factor in these diseases. Recent studies have shown that microtubule-associated proteins are part of the paired helical filaments which make up the intraneuronal neurofibrillary tangle. Other studies have identified the protein making the vascular and neuritic (senile) plaque amyloid and located the gene responsible for this protein to chromosome 21. Our electron microprobe analysis studies have not found the levels of aluminum or silicon in either the neurofibrillary tangles or amyloid cores reported elsewhere, nor have the levels of aluminum been elevated in approximately one half of the tangles and plaque cores examined to date.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24202577>

“When aluminum is experimentally introduced to the central nervous system, several neurotoxic effects are observed: i.e. neurofibrillary changes, behavioral and cognitive deficits and enzymatic and neurotransmitter changes, as well as certain types of epileptic seizures.”

Biofactors • July 1990

Aluminum, a neurotoxin which affects diverse metabolic reactions

Author information

Joshi JG.

Department of Biochemistry
University of Tennessee
Knoxville 37996-0840

Abstract

Experimental evidence is summarized to support the hypothesis that chronic exposure to low levels of aluminum may lead to neurological disorders. These disorders result from defective phosphorylation--dephosphorylation reactions, reduced glucose utilization and site-specific damage inflicted by free radicals produced by altered iron metabolism. The brain is a highly compartmentalized organ. Therefore, a co-localization of critical mass of metabolic errors rather than a single event may be essential to precipitate a neural disease. Aluminum appears to participate in formulating this critical mass. Patients with dialysis dementia get partial relief by desferroxamine which chelates aluminum. However, it also chelates iron and therefore limits its applicability. While the specific chelator for aluminum is yet to be made available, exercising a caution in aluminum intake appears prudent.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=2198876>

“Experimental evidence is summarized
to support the hypothesis that chronic exposure
to low levels of aluminum may lead to
neurological disorders.”

Mechanism of aluminum-induced inhibition of hepatic glycolysis: inactivation of phosphofructokinase

Author information

Xu ZX1, Fox L, Melethil S, Winberg L, Badr M.

School of Pharmacy
University of Missouri-Kansas City

Abstract

Aluminum, an abundant element in the earth's crust, has been implicated in various pathological disorders and low concentrations of this element have recently been shown to inhibit brain glycolysis. However, despite the fact that aluminum accumulates in high concentrations in the liver, potential effects of this metal on hepatic intermediary metabolism have not been explored. In perfused livers from untreated rats, maximal rates of production of lactate plus pyruvate (glycolysis) were 93 ± 15 $\mu\text{mols/g/hr}$. Glycolysis was severely inhibited in livers from aluminum-treated rats (0.5 mg/kg, 6 hr before experiment) with maximal rates of only 23 ± 4 $\mu\text{mols/g/hr}$. In contrast, glucose production (glycogenolysis) and hepatic oxygen uptake were not altered significantly by prior treatment with aluminum. In livers from fasted rats, pretreatment with aluminum did not influence gluconeogenesis or production of lactate and pyruvate from fructose (5 mM). This finding indicates that pyruvate kinase is not inhibited by aluminum and implicates phosphofructokinase, hexokinase and/or glucokinase as sites for the inhibitory effect of aluminum on glycolysis. In liver homogenates from untreated rats, increasing concentrations of aluminum did not show any appreciable effect on hexokinase or glucokinase activity but did cause progressive decreases in phosphofructokinase activity. Therefore, aluminum-induced inhibition of liver phosphofructokinase, an important control site in the glycolytic pathway, is most likely responsible for aluminum-induced inhibition of hepatic glycolysis.

<http://www.ncbi.nlm.nih.gov/pubmed/2142221>

“Aluminum, an abundant element in the earth's crust, has been implicated in various pathological disorders and low concentrations of this element have recently been shown to inhibit brain glycolysis.”

“These studies clearly demonstrate the philosophy that chronic rather than acute experimental models of toxicity are necessary in order to enhance our understanding of human neurodegenerative disorders with long-latency and slow progression.”

Neurotoxicology • Fall 1991

Pacific paradigms of environmentally-induced neurological disorders: clinical, epidemiological and molecular perspectives

Author information

Garruto RM

Laboratory of Central Nervous System Studies
National Institutes of Health, Bethesda, Maryland 20892

Abstract

During the past quarter century biomedical scientists have begun to recognize the unique opportunities for studying disease etiology and mechanisms of pathogenesis in non-Western anthropological populations with focal, endemic diseases. Such natural experiments as they are called, are important paradigms for solving etiological and epidemiological problems of widespread medical significance, with an ultimate goal towards treatment and prevention. The systematic search for etiological factors and mechanisms of pathogenesis of neurodegenerative disorders is perhaps nowhere better exemplified than in the western Pacific. During the past three decades, the opportunistic and multidisciplinary study of hyperendemic foci of amyotrophic lateral sclerosis and parkinsonism-dementia which occur in different cultures, in different ecological zones and among genetically divergent populations have served as natural models that have had a major impact on our thinking and enhanced our understanding of these and other neurodegenerative disorders such as Alzheimer disease and the process of early neuronal aging. Our cross-disciplinary approach to these intriguing neurobiological problems and the accumulated epidemiological, genetic, cellular and molecular evidence strongly implicates environmental factors in their causation, specifically the role of aluminum and its interaction with calcium in neuronal degeneration. As a direct consequence of our studies in these Pacific populations, we have undertaken the long-term development of experimental models of neuronal degeneration, in an attempt to understand the cellular and molecular mechanisms by which these toxicants affect the central nervous system. Our experimental studies have resulted in the establishment of an aluminum-induced chronic myelopathy in rabbits and the development of neurofilamentous lesions after low-dose aluminum administration in cell culture. These studies clearly demonstrate the philosophy that chronic rather than acute experimental models of toxicity are necessary in order to enhance our understanding of human neurodegenerative disorders with long-latency and slow progression. Finally, the ultimate significance of these Pacific paradigms may well depend on our ability to comprehensively evaluate and synthesize the growing body of relevant scientific data from other human disorders and from widely divergent academic fields, as well as our ability to recognize emerging new models in nature.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1745428>

Selective accumulation of aluminum and iron
in the neurofibrillary tangles of Alzheimer's disease:
a laser microprobe (LAMMA) study

Author information

Good PF1, Perl DP, Bierer LM, Schmeidler J.

Department of Pathology
Mount Sinai School of Medicine
New York, NY 10029

Abstract

We report the results of an examination of the elemental content of neurofibrillary tangle-bearing and neurofibrillary tangle-free neurons identified within the hippocampus of 10 subjects with Alzheimer's disease and 4 neuropathologically intact age-matched control subjects. The study employed laser microprobe mass analysis (LAMMA), a technique that provides extremely sensitive multielement detection in plastic-embedded, semithin-sectioned tissues. Evidence for the selective accumulation of aluminum within the neurofibrillary tangle-bearing neurons was obtained in all 10 subjects with Alzheimer's disease. The site of aluminum deposition within these cells was the neurofibrillary tangle itself, and not the "nuclear region," as we previously reported. Iron accumulation was also detected within neurofibrillary tangles. Evaluation for the accumulation of other elements within the tangle-bearing neurons failed to reveal any other metallic element as being consistently present. In addition, probe sites directed to neurons identified in snap-frozen cryostat sections from 2 subjects with Alzheimer's disease revealed similar spectra with prominent aluminum-related peaks, confirming that our findings are not related to exogenous contamination through fixation, embedding, or other procedures prior to analysis. This study further confirms the association of aluminum and neurofibrillary tangle formation in Alzheimer's disease.

<http://www.ncbi.nlm.nih.gov/pubmed/1637136>

"This study further confirms
the association of aluminum
and neurofibrillary tangle formation
in Alzheimer's disease."

Pharmacology And Toxicology • April 1992

Aluminium-adjuvanted vaccines transiently increase aluminium levels in murine brain tissue

Author information

Redhead K1, Quinlan GJ, Das RG, Gutteridge JM.

Division of Bacteriology
National Institute for Biological Standards and Control
Herts., UK

Abstract

Aluminium is widely used as an adjuvant in human vaccines, and children can often receive up to 3.75 mg of parenteral aluminium during the first six months of life. We show that intraperitoneal injection of aluminium adsorbed vaccines into mice causes a transient rise in brain tissue aluminium levels peaking around the second and third day after injection. This rise is not seen in the saline control group of animals or with vaccine not containing aluminium. It is likely that aluminium is transported to the brain by the iron-binding protein transferrin and enters the brain via specific transferrin receptors.

<http://www.ncbi.nlm.nih.gov/pubmed/1608913>

“... children can often receive up to 3.75 mg of parenteral aluminium during the first six months of life. We show that intraperitoneal injection of aluminium adsorbed vaccines into mice causes a transient rise in brain tissue aluminium levels peaking around the second and third day after injection.”

Life Sciences • June 1992

Long-term effects of aluminium on the fetal mouse brain

Author information

Clayton RM1, Sedowofia SK, Rankin JM, Manning A.

Division of Biological Sciences
University of Edinburgh

Abstract

Potentially noxious substances may act as fetal teratogens at levels far lower than those required to produce detectable effects in adults, and behavioural teratogenicity may occur at levels lower than those which produce morphological teratogenesis. Aluminium (Al) is a potential neurotoxin in adults. Since pregnant women may be exposed to untoward levels of Al compounds under certain conditions, we have examined the long-term effects of treating the pregnant mouse with intraperitoneal or oral aluminium sulphate on brain biochemistry and behaviour of the offspring. The cholinergic system, as evaluated by the activity of choline acetyltransferase (ChAT), was affected differentially in different regions of the brain, and still showed significant effects in the adult. Differences between the intraperitoneal and oral series in the magnitude of effect seen in the regions of the brain probably reflect differences in the effective level of exposure. Growth rate and psychomotor maturation in the pre-weaning mouse were affected in the intraperitoneal series only, showing a marked post-natal maternal effect.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1453876>

“Potentially noxious substances may act as fetal teratogens at levels far lower than those required to produce detectable effects in adults, and behavioural teratogenicity may occur at levels lower than those which produce morphological teratogenesis.”

Aluminum inhibits glutamate release from transverse rat hippocampal slices: role of G proteins, Ca channels and protein kinase C

Author information

Provan SD1, Yokel RA.

College of Pharmacy
University of Kentucky
Lexington 40536-0082

Abstract

Aluminum (Al) has been shown to produce deficits in learning and memory. The present experiments tested the hypothesis that Al-induced inhibition of learning may be due to its effect on glutamate release secondary to changes in calcium channel function and/or intracellular events triggering glutamate release. Calcium-dependent potassium (K)-evoked [¹⁴C]-glutamate release from 400 microns transverse rat hippocampal slices was inhibited by Al in a concentration dependent manner (IC₅₀ = 40 microM). Aluminum (30, 100 microM) noncompetitively inhibited Bay K 8644-evoked glutamate release. 4-Aminopyridine (30, 1000 microM) noncompetitively attenuated the Al inhibition of glutamate release, suggesting an Al-induced alteration of Ca channel function. Activation of the Gi protein by R(-)-phenylisopropyladenosine (PIA; 1 microM) reduced K-evoked glutamate release 69%, whereas 300 microM Al produced an 84% reduction. These effects were prevented by the Gi protein inhibitor N-ethylmaleimide (NEM; 100 microM), suggesting an effect of Al on the Gi protein to inhibit glutamate release. Phorbol myristate acetate (0.16 microM)-induced glutamate release was inhibited by 300 microM Al and 80 microM polymyxin B, suggesting an Al modulation of protein kinase C (PKC)-evoked glutamate release. These results demonstrate an Al inhibition of glutamate release that may be mediated by multiple, but interconnected mechanisms (e.g., via interactions with Ca systems), providing multiple targets for an Al-induced alteration of neuronal function.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1359483>

“Aluminum (Al) has been shown to produce deficits in learning and memory.”

The cellular toxicity of aluminium

Author information

Exley C, Birchall JD.

Institute of Aquaculture
University of Stirling
Scotland, UK

Abstract

Aluminium is a serious environmental toxicant and is inimical to biota. Omnipresent, it is linked with a number of disorders in man including Alzheimer's disease, Parkinson's dementia and osteomalacia. Evidence supporting aluminium as an aetiological agent in such disorders is not conclusive and suffers principally from a lack of consensus with respect to aluminium's toxic mode of action. Obligatory to the elucidation of toxic mechanisms is an understanding of the biological availability of aluminium. This describes the fate of and response to aluminium in any biological system and is thus an important influence of the toxicity of aluminium. A general theme in much aluminium toxicity is an accelerated cell death. Herein mechanisms are described to account for cell death from both acute and chronic aluminium challenges. Aluminium associations with both extracellular surfaces and intracellular ligands are implicated. The cellular response to aluminium is found to be biphasic having both stimulatory and inhibitory components. In either case the disruption of second messenger systems is observed and GTPase cycles are potential target sites. Specific ligands for aluminium at these sites are unknown though are likely to be proteins upon which oxygen-based functional groups are orientated to give exceptionally strong binding with the free aluminium ion.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1291812>

“A general theme in much aluminium toxicity
is an accelerated cell death.”

Toxicology • 1992

**Role of aluminium
in skin reactions after
diphtheria-tetanus-pertussis-poliomyelitis vaccination:
an experimental study in rabbits**

Author information

Pineau A1, Durand C, Guillard O, Bureau B, Stalder JF.

Laboratoire de Toxicologie et d'Hygiène Industrielle
Faculté de Pharmacie, Centre Hospitalier Régional Universitaire
Nantes, France

Abstract

The occurrence of subcutaneous nodules at the injection site is one of the complications of diphtheria-tetanus-pertussis-poliomyelitis vaccination, but the causes and mechanisms involved are still poorly understood. An experimental study in the New Zealand rabbit enabled us to determine the frequency of occurrence of these nodules, how long they persist and the histopathologic features of the cells involved. Aluminium (Al) assays by electrothermal atomic absorption spectrometry allowed us to study concentrations both in nodules and the organism (serum, normal skin). The results show an absence of Al diffusion outside nodules, a correlation between infiltrate intensity and Al concentration in nodules and modifications in the histological constituents of nodule cells. The histological picture indicates a foreign body reaction to Al. All these data underscore the role of Al in the formation of early postvaccinal nodules at the injection site.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1589878>

“All these data

underscore the role of Aluminum
in the formation of early postvaccinal
nodules at the injection site.”

[this is one of the earliest examples of “nodules at the
injection site” mentioned in the medical literature. As
you’ll see, eventually this phenomenon leads to a new
disorder, Macrophagic Myofasciitis and the coining of
the term “ASIA,” a wide variety of nearly 100 recognized
autoimmune and inflammatory disorders induced by the
Aluminum adjuvant in vaccines]

“Generally, the intake of aluminium from foods is less than 1% of that consumed by individuals using aluminium-containing pharmaceuticals.

Currently the real scientific question is not the amount of aluminium in foods but the availability of the aluminium in foods and the sensitivity of some population groups to aluminium.”

Ciba Foundation Symposium • 1992

Dietary and other sources of aluminium intake

Author information

Greger JL.

Department of Nutritional Sciences
University of Wisconsin, Madison 53706

Abstract

Aluminium in the food supply comes from natural sources including water, food additives, and contamination by aluminium utensils and containers. Most unprocessed foods, except for certain herbs and tea leaves, contain low (< 5 micrograms Al/g) levels of aluminium. Thus most adults consume 1-10 mg aluminium daily from natural sources. Cooking in aluminium containers often results in statistically significant, but not practically important, increases in the aluminium content of foods. Intake of aluminium from food additives varies greatly (0 to 95 mg Al daily) among residents in North America, with the median intake for adults being about 24 mg daily. Generally, the intake of aluminium from foods is less than 1% of that consumed by individuals using aluminium-containing pharmaceuticals. Currently the real scientific question is not the amount of aluminium in foods but the availability of the aluminium in foods and the sensitivity of some population groups to aluminium. Several dietary factors, including citrate, may affect the absorption of aluminium. Aluminium contamination of soy-based formulae when fed to premature infants with impaired kidney function and aluminium contamination of components of parenteral solutions (i.e. albumin, calcium and phosphorus salts) are of concern.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1490425>

Neurotoxic effect of enteral aluminium

Author information

Bilkei-Gorzó A.

Pharmacological Department
Chinoin Pharmaceutical and Chemical Works Co. Ltd
Budapest, Hungary

Abstract

Long Evans rats were treated for 90 days with water-soluble, insoluble or chelated aluminium compounds. The daily treatments given were as follows: controls, NaCl (100 mg/kg body weight) plus citric acid (30 mg/kg); AlCl₃ (30 or 100 mg/kg); Al(OH)₃ (100 mg/kg) plus citric acid (30 mg/kg); Al(OH)₃ (300 mg/kg). Their learning ability was determined in the labyrinth test at day 90, and the choline-acetyltransferase, acetylcholinesterase activity and aluminium content of the brains were measured. Soluble and chelated aluminium compounds seriously worsened the learning ability, and the aluminium content of the brain was elevated. Acetylcholinesterase activity increased and choline-acetyltransferase activity decreased, resulting in a diminished cholinergic activity, which is a characteristic of Alzheimer's disease.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8505021>

“... resulting in a diminished
cholinergic activity, which is a
characteristic of Alzheimer's disease.”

Vaccine • 1993

Adjuvants—
a balance between
toxicity and adjuvanticity

Author information

Gupta RK1, Relyveld EH, Lindblad EB,
Bizzini B, Ben-Efraim S, Gupta CK.

Massachusetts Public Health Biologic Laboratories
Boston 02130

Abstract

Adjuvants have been used to augment the immune response in experimental immunology as well as in practical vaccination for more than 60 years. The chemical nature of adjuvants, their mode of action and the profile of their side effects are highly variable. Some of the side effects can be ascribed to an unintentional stimulation of different mechanisms of the immune system whereas others may reflect general adverse pharmacological reactions. The most common adjuvants for human use today are still aluminium hydroxide, aluminium phosphate and calcium phosphate although oil emulsions, products from bacteria and their synthetic derivatives as well as liposomes have also been tested or used in humans. In recent years monophosphoryl lipid A, ISCOMs with Quil-A and Syntex adjuvant formulation (SAF) containing the threonyl derivative of muramyl dipeptide have been under consideration for use as adjuvants in humans. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side effects.

<http://www.ncbi.nlm.nih.gov/pubmed/8447157>

“At present the choice of adjuvants
for human vaccination reflects a compromise
between a requirement for adjuvanticity
and an acceptable low level of side effects.”

[today those “Side Effects” are at epidemic proportions]

“Vaccines adsorbed onto aluminium salts
are a more frequent cause of local post-vaccinal reactions than plain vaccines.”

Roczniki Państwowego Zakładu Higieny • 1993

Aluminum as an adjuvant in vaccines and post-vaccine reactions

Author information

Fiejka M1, Aleksandrowicz J.

Zakładu Badania Surowic
Warszawie

Abstract

Aluminium compounds have been widely used as adjuvants in prophylactic and therapeutic vaccines. Adjuvants are able to stimulate the immune system in a nonspecific manner, i.e. high antibody level can be obtained with minimal dose of the antigen and with reduced number of inoculations. Adjuvants use has been mostly empirically determined by such factors as efficacy and safety. The mechanism of action of the aluminium adjuvants is not completely understood and is very complex. The basic factors of the mode of action: 1) the complex of antigen and aluminium gel is more immunogenic in structure than free antigen, 2) effect “depot”--The antigen stimulus last longer, 3) the production of local granulomas. Vaccines adsorbed onto aluminium salts are a more frequent cause of local post-vaccinal reactions than plain vaccines. 5-10% those vaccinated can develop a nodule lasting several weeks at the injection site. In some rare cases the nodules may become inflammatory and even turn into an aseptic abscess. The nodules persisting more than 6 weeks may indicate development of aluminium hypersensitivity. Finally aluminium adjuvant immunogens induce the production of IgE antibodies.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8235346>

Annali dell'istituto Superiore di Sanita • 1993

Behavioural effects of gestational exposure to aluminium

Author information

Rankin JI, Sedowofia K, Clayton R, Manning A.

Institute of Cell, Animal and Population Biology
Edinburgh, UK

Abstract

The involvement of aluminium in the aetiology of a number of human pathological diseases has altered its status from being a non-toxic, nonabsorbable, harmless element. This maybe of particular concern to the developing foetus which is more susceptible to agents and at lower levels than the adult. Little attention has been given to aluminium's potential reproductive toxicity until recently and further research is required for a full evaluation of its toxicity. Our preliminary results demonstrate behavioural and neurochemical alterations in the offspring of mice exposed to aluminium during gestation. Further, the effects of such exposure are also present in the adult animal suggesting persistent changes in behaviour following prenatal exposure.

<http://www.ncbi.nlm.nih.gov/pubmed/8129261>

“Our preliminary results demonstrate behavioural and neurochemical alterations in the offspring of mice exposed to aluminium during gestation. Further, the effects of such exposure are also present in the adult animal suggesting persistent changes in behaviour following prenatal exposure.”

Vaccine • 1993

Studies on the toxicities
of aluminium hydroxide and calcium phosphate
as immunological adjuvants for vaccines

Author information

Goto N1, Kato H,
Maeyama J, Eto K, Yoshihara S.

Department of Safety Research on Biologics
National Institute of Health, Tokyo, Japan

Abstract

Aluminium hydroxide (Al) and calcium phosphate (Ca) have been used for many years as immunological adjuvants for biologicals. We investigated the toxic effects of both adjuvants with different physical properties. Al-gel elicited vascular permeability-increasing and toxic effects to macrophages (M phi), while its haemolytic effect was weak. Ca-gel elicited a significantly stronger haemolytic effect, but no other toxic effect. Incubation of M phi or polymorphonuclear leucocytes with Al-suspension resulted in the largest release of lactate dehydrogenase. Ca-suspension caused haemolysis of about 50% of that caused by Ca-gel.

<http://www.ncbi.nlm.nih.gov/pubmed/8212836>

“Aluminum-gel elicited vascular
permeability-increasing and toxic
effects to macrophages ...”

Effects of aluminum on the mechanical and electrical activity of the Langendorff-perfused rat heart

Author information

Gomes MG1, Moreira CA, Mill JG,
Massaroni L, Oliveira EM, Stefanon I, Vassallo DV.

Departamento de Ciências Fisiológicas
Universidade Federal do Espírito Santo
Vitória, Brasil

Abstract

The effect of aluminum (Al³⁺) chloride (1, 5, 10, 50 and 100 microM) on myocardial electromechanical activity was studied in 10 Langendorff-perfused hearts from adult female Wistar rats. Al³⁺ decreased the development of isovolumic systolic pressure from 34.3 +/- 2.95 mmHg under control conditions to 11.8 +/- 1.53 mmHg at 100 microM AlCl₃ (P < 0.01) (diastolic pressure = 0 mmHg). The atrial and ventricular rates also decreased, but only with AlCl₃ concentrations greater than 1 microM (from 180 +/- 5 to 94 +/- 11 bpm for atrial rate and from 180 +/- 5 to 78 +/- 7 bpm for ventricular rate). Reduction of coronary flow was also observed, reaching 60% at 100 microM Al³⁺. A delay in atrioventricular conduction occurred at 10 microM Al³⁺, increasing progressively up to 100 microM (62.3 +/- 4 ms in the Al(3+)-free solution to 143 +/- 34 ms in the presence of 100 microM Al³⁺, P < 0.01, ANOVA). QRS duration did not change as a function of increasing Al³⁺ concentrations (37.1 +/- 1.7 ms in the Al(3+)-free solution vs 32.1 +/- 1.6 ms in the presence of 100 microM Al³⁺). No qualitative changes in ECG were observed. These data show that the toxic effects of Al³⁺ on the myocardium are reflected in reduced systolic pressure development and coronary flow and increased PR interval. These effects are discussed in terms of the inhibition of nucleotide hydrolysis by Al³⁺.

<http://www.ncbi.nlm.nih.gov/pubmed/8173535>

“These data show that
the toxic effects of aluminum chloride
on the myocardium are reflected in reduced
systolic pressure development and
coronary flow and increased PR interval.”

Estimates of dietary exposure to aluminium

Author information

Pennington JA1, Schoen SA.

Food and Drug Administration
Center for Food Safety and Applied Nutrition
Washington, DC 20204, USA

Abstract

Daily intakes of aluminium were estimated for 14 age-sex groups based on the Food and Drug Administration's (FDA) Total Diet Study dietary exposure model. The aluminium content of the core foods of the FDA Total Diet Study were determined by analyses, recipe calculation, or literature values and coupled with information on food consumption from the 1987-88 US Department of Agriculture Nationwide Food Consumption Survey. Estimates of aluminium intakes ranged from 0.7 mg/day for 6-11-month-old infants to 11.5 mg/day for 14-16-year-old males. Average intakes for adult men and women were 8-9 and 7 mg/day, respectively. The major contributors to daily intake of aluminium were foods with aluminium-containing food additives, e.g. grain products and processed cheese.

<http://www.ncbi.nlm.nih.gov/pubmed/7758626>

“Estimates of aluminium intakes ranged from 0.7 mg/day for 6-11-month-old infants to 11.5 mg/day for 14-16-year-old males. Average intakes for adult men and women were 8-9 and 7 mg/day, respectively.”

“Although aluminum (Al) contributes to a variety of cognitive dysfunctions and mental diseases, the underlying mechanisms of Al interactions with the nervous system are still unknown.”

Experimental Neurology • July 1995

Aluminum impairs hippocampal long-term potentiation in rats in vitro and in vivo

Author information

Platt B1, Carpenter DO, Büsselberg D, Reymann KG, Riedel G.

New York State Department of Health
Wadsworth Center for Laboratories and Research, Albany 12201, USA

Abstract

Although aluminum (Al) contributes to a variety of cognitive dysfunctions and mental diseases, the underlying mechanisms of Al interactions with the nervous system are still unknown. We have studied the action of Al on synaptic transmission and long-term potentiation (LTP) by performing electrophysiological recordings both in vivo, using freely moving animals, and in vitro, using hippocampal slices. In vivo recordings of the population spikes (PSs) of dentate gyrus granule cells in response to medial perforant path stimulation were performed on both acutely and chronically (Al each day for 5 days) intraventricularly injected animals. Acute Al-infusion (calculated brain concentrations of 0.27, 0.68, and 2.7 micrograms/ml) had no influence on baseline values. Al at 0.27 microgram/ml did not alter the induction and maintenance of LTP, but 0.68 and especially 2.7 micrograms/ml Al lead to a reduction in LTP, and the potentiation declined to baseline within 2 h. In chronic animals their neuronal responsiveness was reduced and in 30% of the rats the PS was completely lost. High-frequency tetanization failed to induce LTP. In slices, field potentials were evoked stimulating Schaffer collaterals and recording pyramidal cells of the CA1 region. Bath application of 0.68 microgram/ml Al increased the baseline amplitude of the PS slightly, whereas 2.7 micrograms/ml decreased the amplitude and concentrations > 5.4 micrograms/ml blocked the PS completely. Induction of LTP in the presence of 0.68 microgram/ml Al led to a smaller increase of the PS amplitude compared to controls, but the duration of LTP was not affected. In the presence of 2.7 micrograms/ml Al LTP was further reduced and declined to baseline levels within 60 min. Given that LTP is a form of synaptic plasticity underlying some forms of learning, our data suggest that both preparations are suitable models for investigating actions of Al-induced neurotoxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=7672040>

Reproductive and developmental toxicity of aluminum: a review

Author information

Domingo JL1.

Laboratory of Toxicology and Biochemistry
School of Medicine, Rovira i Virgili University, Reus, Spain

Abstract

It is well known that aluminum is a developmental toxicant when administered parenterally. However, until recently, there was little concern about embryo/fetal consequences of aluminum ingestion because bioavailability was considered low. The importance of the route of exposure and the chemical form of the aluminum compound on the developmental toxicity of this element are now well established. Although no evidence of maternal and embryo/fetal toxicity was observed when high doses of aluminum hydroxide were given orally to pregnant rats and mice during organogenesis, signs of maternal and developmental toxicity were found in mice when aluminum hydroxide was given concurrently with citric or lactic acids. On the other hand, studies in rabbits have shown that aluminum-induced behavioral toxicity is greater in adult and aged animals than in young adults. However, maternal dietary exposure to excess Al during gestation and lactation which did not produce maternal toxicity would be capable of causing permanent neurobehavioral deficits in weanling mice and rats. Adverse effects of parenteral aluminum administration on the mouse male reproductive system have also been reported. The embryo/fetal toxicity of aluminum administration, the potential reproductive toxicology of aluminum exposure, and the neurodevelopmental effects of aluminum are here reviewed.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=7565498>

“The embryo/fetal toxicity of aluminum administration, the potential reproductive toxicology of aluminum exposure, and the neurodevelopmental effects of aluminum are here reviewed.”

Adjuvants for human vaccines— current status, problems and future prospects

Author information

Gupta RK1, Siber GR.

Massachusetts Public Health Biologic Laboratories
State Laboratory Institute, Boston 02130, USA

Abstract

Adjuvants help antigen to elicit an early, high and long-lasting immune response with less antigen, thus saving on vaccine production costs. In recent years, adjuvants received much attention because of the development of purified, subunit and synthetic vaccines which are poor immunogens and require adjuvants to evoke the immune response. With the use of adjuvants immune response can be selectively modulated to major histocompatibility complex (MHC) class I or MHC class II and Th1 or Th2 type, which is very important for protection against diseases caused by intracellular pathogens such as viruses, parasites and bacteria (*Mycobacterium*). A number of problems are encountered in the development and use of adjuvants for human vaccines. The biggest issue with the use of adjuvants for human vaccines, particularly routine childhood vaccines, is the toxicity and adverse side-effects of most of the adjuvant formulations. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side-effects. Other problems with the development of adjuvants include restricted adjuvanticity of certain formulations to a few antigens, use of aluminum adjuvants as reference adjuvant preparations under suboptimal conditions, non-availability of reliable animal models, use of non-standard assays and biological differences between animal models and humans leading to the failure of promising formulations to show adjuvanticity in clinical trials. The most common adjuvants for human use today are still aluminum hydroxide and aluminum phosphate, although calcium phosphate and oil emulsions also have some use in human vaccinations. During the last 15 years much progress has been made on development, isolation and chemical synthesis of alternative adjuvants such as derivatives of muramyl dipeptide, monophosphoryl lipid A, liposomes, QS21, MF-59 and immunostimulating complexes (ISCOMS). Other areas in adjuvant research which have received much attention are the controlled release of vaccine antigens using biodegradable polymer microspheres and reciprocal enhanced immunogenicity of protein-polysaccharide conjugates. Biodegradable polymer microspheres are being evaluated for targeting antigens on mucosal surfaces and for controlled release of vaccines with an aim to reduce the number of doses required for primary immunization. Reciprocal enhanced immunogenicity of protein-polysaccharide conjugates will be useful for the development of combination vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/8585280>

“Adjuvants help antigen
to elicit an early, high and long-lasting
immune response with less antigen, thus
saving on vaccine production costs.

Spectroscopic study of the interaction of aluminum ions with human transferrin

Author information

Tang S1, MacColl R, Parsons PJ.

Department of Environmental Health and Toxicology
School of Public Health, State University of New York at Albany, USA

Abstract

Transferrin is the plasma protein responsible for transporting Fe³⁺ from the absorption to the utilization site. Interactions of apo- and holo-transferrin with Al³⁺ were studied by circular dichroism (CD), UV-visible, and fluorescence spectrometry. Binding of Al³⁺ to both metal-ion binding sites of apo-transferrin was confirmed by fluorescence studies. No interaction of Al³⁺ with holo-transferrin was observed, indicating that Al³⁺ cannot displace Fe³⁺ under the experimental conditions employed. An increase in tryptophan fluorescence (lambda max at 330 nm) by excitation at either 280 or 295 nm was observed after Al³⁺ interaction with apo-transferrin. There was no shift in wavelength of the fluorescence band of apo-transferrin after interaction with Al³⁺, but the intensity did increase. Since excitation at 295 nm is specific for tryptophan residues, tryptophan but not tyrosine must be responsible for the change in fluorescence intensity. Decreased fluorescence is the result of Fe³⁺ binding to apo-transferrin. The CD spectrum of apo-transferrin was slightly affected in the far UV by Al³⁺ binding, but a salient change was noted in the near UV at approximately 288 nm where tyrosine and tryptophan absorb. It is concluded that a small conformational change in the protein was induced by Al³⁺ binding to apo-transferrin.

<http://www.ncbi.nlm.nih.gov/pubmed/8586971>

“It is concluded that a small conformational change in the protein was induced by Al³⁺ binding to apo-transferrin.”

Altered calcium homeostasis:
a possible mechanisms of
aluminium-induced neurotoxicity

Author information

Julka D1, Gill KD.

Department of Biochemistry
Postgraduate Institute of Medical Education and Research
Chandigarh, India

Abstract

The effect of aluminium, Al(3+) (10 mg/kg body weight/day i.p.) for a period of 4 weeks was examined on the calcium homeostatic mechanisms in rat central nervous system. Incubation of synaptosomes prepared from rat brain, with aluminium in vitro had a detrimental effect on the activity of Ca²⁺ ATPase which could be reversed completely on exogenous addition of desferrioxamine (10 microM) and partially with glutathione (1 mM). In vivo administration also revealed a similar observation. A marked increase in the levels of intracellular calcium was observed after aluminium treatment. Concomitant to the increased levels of intracellular calcium, there was an increase in the levels of lipid peroxidation and a consequent decrease in fluidity of synaptic plasma membranes. In addition, aluminium also had an inhibitory effect on the depolarization-induced calcium uptake which was found to be of a competitive type. The biological activity of calcium regulatory proteins calmodulin and protein kinase C was considerably affected by aluminium. The results suggest that aluminium exerts its toxic effects by modification of the intracellular calcium messenger system with detrimental consequences on neuronal functioning.

<http://www.ncbi.nlm.nih.gov/pubmed/8611646>

“The results suggest
that aluminium exerts its toxic effects
by modification of the intracellular calcium
messenger system with detrimental
consequences on neuronal functioning.”

“Macrophages at the base of human gut associated lymphoid tissue (GALT),
become loaded early in life with dark granular pigment that is rich in aluminium ...”

Gut • March 1996

Characterisation of inorganic microparticles in pigment cells of human gut associated lymphoid tissue

Author information

Powell JJ1, Ainley CC, Harvey RS, Mason IM,
Kendall MD, Sankey EA, Dhillon AP, Thompson RP.

Gastrointestinal Laboratory, Rayne Institute
St Thomas' Hospital, London

Abstract

Macrophages at the base of human gut associated lymphoid tissue (GALT), become loaded early in life with dark granular pigment that is rich in aluminium, silicon, and titanium. The molecular characteristics, intracellular distribution, and source of this pigment is described. Laser scanning and electron microscopy showed that pigmented macrophages were often closely related to collagen fibres and plasma cells in GALT of both small and large intestine and contained numerous phagolysosomes, previously described as granules, that are rich in electron dense submicron sized particles. Morphological assessment, x ray microanalysis, and image electron energy loss spectroscopy showed three distinct types of microparticle: type I - spheres of titanium dioxide, 100-200 nm diameter, characterised as the synthetic food-additive polymorph anatase; type II - aluminosilicates, < 100-400 nm in length, generally of flaky appearance, often with adsorbed surface iron, and mostly characteristic of the natural clay mineral kaolinite; and type III - mixed environmental silicates without aluminium, 100-700 nm in length and of variable morphology. Thus, this cellular pigment that is partly derived from food additives and partly from the environment is composed of inert inorganic microparticles and loaded into phagolysosomes of macrophages within the GALT of all human subjects. These observations suggest that the pathogenicity of this pigment should be further investigated since, in susceptible individuals, the same intracellular distribution of these three types of submicron particle causes chronic latent granulomatous inflammation.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1383068/>

“... the mechanisms of Aluminum neurotoxicity are reviewed ...”

Journal Of Toxicology And Environmental Health • August 1996

Can the mechanisms of aluminum neurotoxicity be integrated into a unified scheme?

Author information

Strong MJ1, Garruto RM, Joshi JG, Mundy WR, Shafer TJ.

Department of Clinical Neurological Sciences
University of Western Ontario, London, Canada
mstrong@julian.uwo.ca

Abstract

Regardless of the host, the route of administration, or the speciation, aluminum is a potent neurotoxicant. In the young adult or developmentally mature host, the neuronal response to Al exposure can be dichotomized on morphological grounds. In one, intraneuronal neurofilamentous aggregates are formed, whereas in the other, significant neurochemical and neurophysiological perturbations are induced without neurofilamentous aggregate formation. Evidence is presented that the induction of neurofilamentous aggregates is a consequence of alterations in the posttranslational processing of neurofilament (NF), particularly with regard to phosphorylation state. Although Al has been reported to impact on gene expression, this does not appear to be critical to the induction of cytoskeletal pathology. In hosts responding to Al exposure without the induction of cytoskeletal pathology, impairments in glucose utilization, agonist-stimulated inositol phosphate accumulation, free radical-mediated cytotoxicity, lipid peroxidation, reduced cholinergic function, and altered protein phosphorylation have been described. The extent to which these neurochemical modifications correlate with the induction of a characteristic neurobehavioral state is unknown. In addition to these paradigms, Al is toxic in the immediate postnatal interval. Whether unique mechanisms of toxicity are involved during development remains to be determined. In this article, the mechanisms of Al neurotoxicity are reviewed and recommendations are put forth with regard to future research. Primary among these is the determination of the molecular site of Al toxicity, and whether this is based on Al substitution for divalent metals in a number of biological processes. Encompassed within this is the need to further understand the genesis of host- and developmental-specific responses.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8772801>

Speciation of aluminum in biological systems

Author information

Harris WR1, Berthon G, Day JP, Exley C,
Flaten TP, Forbes WF, Kiss T, Orvig C, Zatta PF.

Department of Chemistry
University of Missouri-St. Louis 63121 USA

Abstract

As a “hard”, trivalent metal ion, Al³⁺ binds strongly to oxygen-donor ligands such as citrate and phosphate. The aqueous coordination chemistry of Al is complicated by the tendency of many Al complexes to hydrolyze and form polynuclear species, many of which are sparingly soluble. Thus there is considerable variation among the Al stability constants reported for several important ligands. The complexity in the aqueous chemistry of Al has also affected Al toxicity studies, which have often utilized poorly characterized Al stock solutions. Serum fractionation studies show that most Al is protein bound, primarily to the serum iron transport protein transferrin. Albumin appears to play little, if any, role in serum transport. There is little agreement as to the speciation of the remaining low-molecular mass fraction of serum Al. The lability of the Al³⁺-ion precludes the simple separation and identification of individual Al complexes. Computational methods are available for detailed computer calculations of the Al speciation in serum, but efforts in this area have been severely hampered by the uncertainties regarding the stability constants of the low molecular mass Al complexes with citrate, phosphate, and hydroxide. Specific recommendations for further research on Al speciation include: (1) Determine more accurate Al stability constants with critical low molecular mass ligands such as citrate and phosphate; (2) supplement traditional potentiometric studies on Al complexes with data from other techniques such as ²⁷Al-NMR and accelerator mass spectrometry with ²⁶Al; (3) develop new methods for generating reliable linear free energy relationships for Al complexation; (4) determine equilibrium and rate constants for Al binding to transferrin at 37 degrees C; (5) confirm the possible formation of low-molecular-mass Al-protein complexes following desferrioxamine therapy; (6) continue research efforts to incorporate kinetic considerations into the present equilibrium speciation calculations; (7) improve methods for preparing chemically well-defined stock solutions for toxicological studies; (8) incorporate more detailed speciation data into studies on Al toxicity and pharmacokinetics; and (9) incorporate more detailed speciation data into future epidemiological studies on the relationship between Al toxicity and various water quality parameters.

[this report explains why determining the fate of aluminum in the human body is so difficult]

What we know and what we need to know about developmental aluminum toxicity

Author information

Golub MS1, Domingo JL.

Department of Internal Medicine
University of California, Davis 95616, USA

Abstract

Information concerning developmental aluminum (Al) toxicity is available from clinical studies and from animal testing. An Al toxicity syndrome including encephalopathy, osteomalacia, and anemia has been reported in uremic children receiving dialysis. In addition, some components of the syndrome, particularly osteomalacia, have been reported in non-dialyzed uremic children receiving Al-based phosphate binders, nonuremic infants receiving parenteral nutrition with Al-containing fluids, and nonuremic infants given high doses of Al antacids. The number of children in clinical populations that are at risk of Al toxicity is not known and needs to be determined. Work in animal models (rats, mice, and rabbits) demonstrates that Al is distributed transplacentally and is present in milk. Oral Al administration during pregnancy produces a syndrome including growth retardation, delayed ossification, and malformations at doses that also lead to reduced maternal weight gain. The severity of the effects is highly dependent on the form of Al administered. In the postnatal period, reduced pup weight gain and effects on neuromotor development have been described as a result of developmental exposures. The significance of these findings for human health requires better understanding of the amount and bioavailability of Al in food, drinking water, and medications and from sources unique to infants and children such as breast milk, soil ingestion, and medications used specifically by pregnant women and children. We also need a better understanding of the unique biological actions of Al that may occur during developmental periods, and unique aspects of the developing organism that make it more or less susceptible to Al toxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8772800>

“The number of children in clinical populations that are at risk of Al toxicity is not known and needs to be determined.

Work in animal models demonstrates that Aluminum is distributed transplacentally and is present in milk.”

Aluminum toxicokinetics

Author information

Exley C1, Burgess E, Day JP, Jeffery EH, Melethil S, Yokel RA.

Department of Chemistry, Keele University, Staffordshire
United Kingdom
cha38@keele.ac.uk

Abstract

In this study of the toxicokinetics of aluminum we have examined some of the fundamental issues that currently define our understanding of the toxicology of aluminum in humans. There is a vast literature on this subject, and it was not our aim to review this literature but to use it to develop our understanding of the toxicokinetics of aluminum and to identify critical and unresolved issues related to its toxicity. In undertaking this task we have chosen to define the term toxicokinetics to encompass those factors that influence both the lability of aluminum in a body and the sites at which aluminum is known to accumulate, with or without consequent biological effect. We have approached our objective from the classical pharmacological approach of ADME: the absorption, distribution, metabolism, and excretion of aluminum. This approach was successful in identifying several key deficits in our understanding of aluminum toxicokinetics. For example, we need to determine the mechanisms by which aluminum crosses epithelia, such as those of the gastrointestinal tract and the central nervous system, and how these mechanisms influence both the subsequent transport and fate of the absorbed aluminum and the concomitant nature and severity of the biological response to the accumulation of aluminum. Our hope in highlighting these unresolved issues (summarized in Table 1) is that they will be addressed in future research.

<http://www.ncbi.nlm.nih.gov/pubmed/8772799>

“... we need to determine the mechanisms by which aluminum crosses epithelia, such as those of the gastrointestinal tract and the central nervous system, and how these mechanisms influence both the subsequent transport and fate of the absorbed aluminum and the concomitant nature and severity of the biological response to the accumulation of aluminum.”

“Subtle neurocognitive and psychomotor effects and electroencephalograph (EEG) abnormalities have been reported at plasma Aluminum levels as low as 50 micrograms/L. Infants could be particularly susceptible to Al accumulation and toxicity ...”

Journal Of Toxicology And Environmental Health • August 1996

Status and future concerns of clinical and environmental aluminum toxicology

Author information

Flaten TP1, Alfrey AC, Birchall JD, Savory J, Yokel RA.

Department of Chemistry, Norwegian University of Science and Technology
Trondheim, Norway
trond.flaten@avh.unit.no

Abstract

A wide range of toxic effects of aluminum (Al) have been demonstrated in plants and aquatic animals in nature, in experimental animals by several routes of exposure, and under different clinical conditions in humans. Aluminum toxicity is a major problem in agriculture, affecting perhaps as much as 40% of arable soils in the world. In fresh waters acidified by acid rain, Al toxicity has led to fish extinction. Aluminum is a very potent neurotoxicant. In humans with chronic renal failure on dialysis, Al causes encephalopathy, osteomalacia, and anemia. There are also reports of such effects in certain patient groups without renal failure. Subtle neurocognitive and psychomotor effects and electroencephalograph (EEG) abnormalities have been reported at plasma Al levels as low as 50 micrograms/L. Infants could be particularly susceptible to Al accumulation and toxicity, reduced renal function being one contributory cause. Recent reports clearly show that Al accumulation occurs in the tissues of workers with long-term occupational exposure to Al dusts or fumes, and also indicate that such exposure may cause subtle neurological effects. Increased efforts should be directed toward defining the full range of potentially harmful effects in humans. To this end, multidisciplinary collaborative research efforts are encouraged, involving scientists from many different specialties. Emphasis should be placed on increasing our understanding of the chemistry of Al in biological systems, and on determining the cellular and molecular mechanisms of Al toxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8772797>

Aluminum Neurotoxicity in Preterm Infants Receiving Intravenous-Feeding Solutions

Nicholas J. Bishop, M.D., Ruth Morley, M.B., B.Chir., J. Philip Day, Ph.D., and Alan Lucas, M.D.

BACKGROUND

Aluminum, a contaminant of commercial intravenous-feeding solutions, is potentially neurotoxic. We investigated the effect of perinatal exposure to intravenous aluminum on the neurologic development of infants born prematurely.

METHODS

We randomly assigned 227 premature infants with gestational ages of less than 34 weeks and birth weights of less than 1850 g who required intravenous feeding before they could begin enteral feeding to receive either standard or specially constituted, aluminum-depleted intravenous-feeding solutions. The neurologic development of the 182 surviving infants who could be tested was assessed by using the Bayley Scales of Infant Development at 18 months of age.

RESULTS

The 90 infants who received the standard feeding solutions had a mean (\pm SD) Bayley Mental Development Index of 95 ± 22 , as compared with 98 ± 20 for the 92 infants who received the aluminum-depleted solutions ($P = 0.39$). In a planned subgroup analysis of infants in whom the duration of intravenous feeding exceeded the median and who did not have neuromotor impairment, the mean values for the Bayley Mental Development Index for the 39 infants who received the standard solutions and the 41 infants who received the aluminum-depleted solutions were 92 ± 20 and 102 ± 17 , respectively ($P = 0.02$). The former were significantly more likely (39 percent, vs. 17 percent of the latter group; $P = 0.03$) to have a Mental Development Index of less than 85, increasing their risk of subsequent educational problems. For all 157 infants without neuromotor impairment, increasing aluminum exposure was associated with a reduction in the Mental Development Index ($P = 0.03$), with an adjusted loss of one point per day of intravenous feeding for infants receiving the standard solutions.

CONCLUSIONS

In preterm infants, prolonged intravenous feeding with solutions containing aluminum is associated with impaired neurologic development.

“In preterm infants, prolonged intravenous feeding with solutions containing aluminum is associated with impaired neurologic development.”

Aluminum potentiates
glutamate-induced calcium accumulation
and iron-induced oxygen free radical formation
in primary neuronal cultures

Author information

Mundy WR1, Freudenrich TM, Kodavanti PR.

Neurotoxicology Division
US Environmental Protection Agency
Research Triangle Park, NC 27711, USA

Abstract

Aluminum is a neurotoxic metal that may be involved in the progression of neurodegenerative diseases, including Alzheimer disease and amyotrophic lateral sclerosis (ALS). Although the mechanism of action is not known, aluminum has been shown to alter Ca²⁺ flux and homeostasis, and facilitate peroxidation of membrane lipids. Since abnormal increases of intracellular Ca²⁺ and oxygen free radicals have both been implicated in pathways leading to neurodegeneration, we examined the effect of aluminum on these parameters in vitro using primary cultures of cerebellar granule cells. Exposure to glutamate (1-300 microM) caused a concentration-dependent uptake of ⁴⁵Ca in granule cells to a maximum of 280% of basal. Pretreatment with AlCl₃ (1-1000 microM) had no effect on ⁴⁵Ca accumulation, but increased the uptake induced by glutamate. Similarly, AlCl₃ had no effect on intracellular free Ca²⁺ levels measured using fluorescent probe fura-2, but potentiated the increase induced by glutamate. The production of reactive oxygen species (ROS) was examined using the fluorescent probe dichlorofluorescein. By itself, AlCl₃ had little effect on ROS production. However, AlCl₃ pretreatment potentiated the ROS production induced by 50 microM Fe²⁺. These results suggest that aluminum may facilitate increases in intracellular Ca²⁺ and ROS, and potentially contribute to neurotoxicity induced by other neurotoxicants.

<http://www.ncbi.nlm.nih.gov/pubmed/9437657>

“Aluminum is a neurotoxic metal that may be involved in the progression of neurodegenerative diseases, including Alzheimer disease and amyotrophic lateral sclerosis ... aluminum may facilitate increases in intracellular Ca²⁺ and ROS, and potentially contribute to neurotoxicity induced by other neurotoxicants.”

“Although the mechanisms of aluminum absorption have not been elucidated, both passive and active transcellular processes and paracellular transport are believed to occur.”

Critical Reviews In Clinical Laboratory Science • 1997

Aluminum exposure and metabolism

Author information

Greger JL1, Sutherland JE.

Department of Nutritional Sciences
University of Wisconsin, Madison 53706, USA

Abstract

Aluminum (Al) is a nonessential, toxic metal to which humans are frequently exposed. Oral exposure to aluminum occurs through ingestion of aluminum-containing pharmaceuticals and to a lesser extent foods and water. Parenteral exposure to aluminum can occur via contaminated total parenteral nutrition (TPN), intravenous (i.v.) solutions, or contaminated dialysates. Inhalation exposure may be important in some occupational settings. The gut is the most effective organ in preventing tissue aluminum accumulation after oral exposure. Typically gastrointestinal absorption of aluminum from diets is < 1%. Although the mechanisms of aluminum absorption have not been elucidated, both passive and active transcellular processes and paracellular transport are believed to occur. Aluminum and calcium may share some absorptive pathways. Aluminum absorption is also affected by the speciation of aluminum and a variety of other substances, including citrate, in the gut milieu. Not all absorbed or parenterally delivered aluminum is excreted in urine. Low glomerular filtration of aluminum reflects that most aluminum in plasma is nonfiltrable because of complexation to proteins, predominantly transferrin. The importance of biliary secretion of aluminum is debatable and the mechanism(s) is poorly understood and appears to be saturable by fairly low oral doses of aluminum.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9405895>

“Metal ions are believed to participate in many neurodegenerative conditions.”

Metal-Based Drugs • 1997

Metal Ions in Neuroscience

C. Ian Ragan

Department of Biochemistry and Molecular Biology
Neuroscience Research Centre, Merck Sharp and Dohme Research Laboratories
Terlings Park, Harlow CM20 2QR, UK

Abstract

Metal ions are believed to participate in many neurodegenerative conditions. In excitotoxic cell death there is convincing evidence for the participation of Ca^{2+} and Zn^{2+} ions although the exact molecular mechanisms by which these metals exert their effects are unclear. Only in one instance has the metal binding site of metalloenzymes been exploited for therapeutic purposes and this is the use of Li^+ in the treatment of bipolar affective disorder. Again the exact molecular target is not clear but is likely to involve a Mg^{2+} -dependent enzyme of an intracellular signalling pathway. In Parkinson's disease, the selective loss of dopaminergic neurones in the substantia nigra may be caused by radical-mediated damage and there is good evidence to suggest that Fe^{2+} or 3^+ is important in promoting formation of radical species. The evidence that free radicals are important in mediating other neurodegenerative conditions is less strong but still substantial enough to suggest that removal of reactive oxygen species or preventing their formation may be a valid approach to therapy.

Full Report

<http://www.hindawi.com/archive/1997/532916/abs/>

Neurobehavioral alteration in rodents following developmental exposure to aluminum

Author information

Alleva E1, Rankin J, Santucci D.

Behavioural Pathophysiology Section
Istituto Superiore di Sanità, Roma, Italy
alleva@iss.it

Abstract

Aluminum (Al) is one of the most abundant metals in the earth's crust, and humans can be exposed to it from several sources. It is present in food, water, pharmaceutical compounds, and in the environment, e.g., as a result of acid rain leaching it from the soil. Exposure to Al has recently been implicated in a number of human pathologies, but it has not yet been definitely proved that it plays a major causal role in any of them. In this paper we review the effects of developmental exposure of laboratory animals to Al salts as a model for human pathological conditions. The data presented show behavioral and neurochemical changes in the offspring of AL-exposed mouse dams during gestation, which include alterations in the pattern of ultrasonic vocalizations and a marked reduction in central nervous system (CNS) choline acetyltransferase activity. Prenatal Al also affects CNS cholinergic functions under Nerve Growth Factor (NGF) control, as shown by increased central NGF levels and impaired performances in a maze learning task in young-adult mice. The need for more detailed studies to evaluate the risks for humans associated with developmental exposure to Al, as well as the importance of using more than one strain of laboratory animal in the experimental design, is emphasized.

<http://www.ncbi.nlm.nih.gov/pubmed/9460176>

“The data presented show behavioral and neurochemical changes in the offspring of Aluminum-exposed mouse dams during gestation, which include alterations in the pattern of ultrasonic vocalizations and a marked reduction in central nervous system choline acetyltransferase activity. Prenatal Al also affects central nervous system cholinergic functions under Nerve Growth Factor (NGF) control, as shown by increased central NGF levels and impaired performances in a maze learning task in young-adult mice.”

The precipitation of mucin by aluminium

Author information

Christopher Exley

Birchall Centre for Inorganic Chemistry and Materials Science
Department of Chemistry, Keele University, Staffordshire, UK
cha38@keele.ac.uk

Abstract

The interactions of Al with a mucin glycopeptide have been studied. A number of specific reactions were identified the nature of which were dependent upon the Al chemistry in the hydration environment. In particular, Al was observed to precipitate mucin and it is suggested that this proceeded via the intercalation of the hydroxide within the hydrated macroreticular network of the mucin biopolymer. This precipitation of mucin was visible by eye and abolished the viscosity of native mucin. Viscometry indicated that Al was bound by mucin at low pH. At pH > 3 Al formed a low molecular weight complex with mucin which was hydrolytically stable and was not precipitated at pH up to 8. In an additional and competitive reaction Al was bound by mucin and the resultant mucin-Al complex was suggested to be the precursor to self-assembled mucin-Al spheres identified in solution, by photon correlation spectroscopy, and in precipitate using selective histochemistry. The majority of these spherical structures were of sub-micron diameter and, through their interaction with each other, were probably responsible for the observed pH-dependent peaks of mucin solution viscosity. The larger spheres, between 20 and 80 microns in diameter, were only identified in isolated mucin/Al precipitates and, being comparatively rare, were unlikely to have influenced solution viscosities. These large spheres were observed to act as possible nucleation sites for the flocculation of mucin/Al precipitate. Al at concentrations as low as 0.015 mM induced changes in the rheological properties of mucin. Considering the ubiquitous nature of mucin and the degree to which it is conserved within biota the interactions of Al with mucin may have wide ranging implications for biological systems.

<http://www.ncbi.nlm.nih.gov/pubmed/9720305>

“Aluminum at concentrations as low as 0.015 mM induced changes in the rheological properties of mucin. Considering the ubiquitous nature of mucin and the degree to which it is conserved within biota the interactions of Aluminum with mucin may have wide ranging implications for biological systems.”

Influence of alum on intestinal flora in mice

Author information

Yan M1, Song H, Zhang L,
Wang Y, Wu Y, Zhou Z.

Institute of Chinese Materia Medica
China Academy of Traditional Chinese Medicine
Beijing 100700

Abstract

OBJECTIVE

To observe the influence of alum
on the intestinal microecological balance
in normal microorganisms.

METHOD

The mice were administered orally with alum of a small dosage(0.25/
kg) and a large dosage(1 g/kg) for half a month, two months and
three months, and a micro flora analysis of the mice was carried out
at intervals of the above mentioned administrations.

RESULT

The intestinal flora in the animals administered with alum was im-
balanced. The counts of bifidobacteria and lactobacilli closely re-
lated to human physiological activities were decreased. The counts
of pathogenic E. Coli significantly increased; and the longer the
animals were treated with alum, the stronger the microecological
balance was influenced.

CONCLUSION

Alum could induce imbalance
of the normal intestinal flora in mice.

<http://www.ncbi.nlm.nih.gov/pubmed/12242827>

“The counts of pathogenic E. Coli
significantly increased; and the longer
the animals were treated with alum, the
stronger the microecological balance was influenced.”

“Aluminum toxicity is well documented and contamination of milk formulas has been implicated as the source of accumulation in bone and brain tissues.”

Journal Of Pediatric Gastroenterology And Nutrition • March 1999

Aluminum contents of human milk, cow's milk, and infant formulas

Author information

Fernandez-Lorenzo JR1, Cocho JA, Rey-Goldar ML, Couce M, Fraga JM.

Service of Neonatology and Metabolic and Nutritional Laboratory
Hospital Xeral de Galicia, Santiago de Compostela, Spain

Abstract

BACKGROUND

Aluminum toxicity is well documented and contamination of milk formulas has been implicated as the source of accumulation in bone and brain tissues. The purpose of the current study was to evaluate the aluminum contents of human milk, cow's milk, and infant formulas.

METHODS

Aluminum contents were determined by atomic absorption spectrometry in samples of human milk in the colostrum, intermediate, and mature stages; infant formulas from eight manufacturers; and various types and brands of commercially available cow's milk.

RESULTS

Mean aluminum concentration was lowest in human milk (23.4 +/- 9.6 microg/l), and did not differ significantly between colostrum, intermediate-stage and mature-stage milk. Mean aluminum concentration was 70 microg/l in cow's milk, and 226 microg/l in reconstituted infant formulas. Aluminum concentrations in infant formulas differed markedly among manufacturers; concentration in milk from one of the manufacturers was particularly high (mean, 551 microg/l; range, 302-1149 microg/l). These values are for milk reconstituted with aluminum-free water under laboratory conditions; formulas prepared with tap water in the University Hospital's infant-feeding unit had even higher aluminum content. Experiments showed that aluminum concentration in the high-aluminum milk could be reduced by more than 70% at the manufacturing stage, by using low aluminum components.

CONCLUSIONS

The results of the present study support the recommendations for infant formula manufacturers to strive to reduce aluminum concentration in their products.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10067727>

Influence of aluminum adjuvant to experimental rabies vaccine

Author information

Lin H1, Perrin P.

National Institute for the Control of Pharmaceutical and Biological Products
Beijing 100050

Abstract

OBJECTIVE

To study whether the rabies vaccine for human use should contain aluminum adjuvant.

METHODS

Testing vaccine antibodies and efficacy (ED50), comparing the effect between aluminum adjuvant contained and non-aluminum adjuvant contained vaccines in a new animal model which accords with the rabies field practice.

RESULTS

At fourth and seventh day after immunization, the neutralizing antibody titres of the rabies vaccine containing aluminium adjuvant were much lower than that of the vaccine not containing aluminum adjuvant. In the NIH efficacy test the ED50 of the vaccine containing aluminum adjuvant was 93-132 ng while the ED50 of the vaccine not containing aluminum adjuvant was 221 ng, but the NIH test does not accord with the rabies field practice. In that new animal model, aluminum adjuvant to rabies vaccine had not any promoting effect for preventing and treating rabies.

CONCLUSION

Aluminum adjuvant to rabies vaccine has no advantages, this paper suggests that the vaccines containing and not-containing aluminium adjuvant had better compare in human bodies. If the results are the same as our experiments, the aluminum adjuvant should be eliminated from rabies vaccine for human use.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12569779>

“Aluminum adjuvant to rabies vaccine has no advantages, this paper suggests that the vaccines containing and not-containing aluminium adjuvant had better compare in human bodies. If the results are the same as our experiments, the aluminum adjuvant should be eliminated from rabies vaccine for human use.”

Particulate adjuvants can induce macrophage survival,
DNA synthesis, and a synergistic proliferative response
to GM-CSF and CSF-1

Author information

Hamilton JA1, Byrne R, Whitty G.

Inflammation Research Centre, University of Melbourne
Department of Medicine, The Royal Melbourne Hospital
Parkville, Victoria, Australia
j.hamilton@medicine.unimelb.edu.au

Abstract

The mode of action of immunological adjuvants is not yet completely understood. Many are particulate. Certain antigen-presenting (dendritic) cell populations belong to the monocyte/macrophage lineage and, like other members of the lineage, in some tissues appear to be short-lived. We report that many poorly degradable, particulate adjuvants, for example, aluminum hydroxide, oil-in-water emulsions, calcium phosphate, and silica, enhance murine bone marrow-derived macrophage survival; induction of DNA synthesis was even observed. No evidence could be found for a requirement for endogenous granulocyte-macrophage colony-stimulating factor (GM-CSF) or macrophage-CSF (M-CSF or CSF-1). Synergy for the proliferative effects was noted in the presence of added GM-CSF or CSF-1. It is suggested from these in vitro findings that one function of certain particulate adjuvants may be to increase by enhanced survival or even proliferation the number of cells available for subsequent antigen presentation and cytokine production.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10670584>

“The mode of action
of immunological adjuvants
is not yet completely understood.”

Macrophagic myofasciitis
Study and Research Group
on Acquired and Dysimmunity-related muscular diseases
(GERMMAD)

Author information

Chérin P1, Laforêt P, Ghérardi RK, Authier FJ, Maisonobe T, Coquet M,
Mussini JM, Pellissier JF, Eymard B, Herson S.

Service de Médecine Interne
Groupe Hospitalier Pitié-Salpêtrière, Paris
patrick.cherin@psl.ap-hop-paris.fr

Abstract

Macrophagic Myofasciitis

A most unusual inflammatory myopathy, first described by Germmad had been reported with increasing frequency since 1993 in the leading French myopathology centers. We present our experience with this new disease: macrophagic myofasciitis.

CLINICAL FEATURES

By November 1999, 70 cases of macrophagic myofasciitis had been recorded since our first description. The first 22 patients (sex ratio M/F = 1:3) referred with the presumptive diagnosis of polymyositis (n = 11), polymyalgia rheumatica (n = 5), mitochondrial cytopathy (n = 4), and congenital myopathy or muscle dystrophy (n = 1 each). Symptoms included myalgia (91%), anthralgia (68%), marked asthenia (55%), muscle weakness (45%), and fever (32%).

LABORATORY FINDINGS

Abnormal laboratory findings included elevated CK levels (50%), markedly increased erythrocyte sedimentation rate (37%), and myopathic EMG (35%). Muscle biopsy showed a unique myopathological pattern characterized by: i) centripetal infiltration of epimysium, perimysium and perifascicular endomysium by sheets of large cells of the monocyte/macrophage lineage (CD68+, CD1a-, S100-, with a PAS-positive content; ii) absence of necrosis, of both epithelioid and giant cells, and of mitotic figures; iii) presence of occasional CD8+ T-cells; iv) inconspicuous muscle fiber damage. The picture was easily distinguishable from sarcoid myopathy and fasciitis-panniculitis syndromes. The infectious diseases known to be associated with reactive histiocytes, including Whipple's disease, Mycobacterium avium intracellulare infection and malakoplakia, could not be documented. Patients improved under corticosteroid therapy and/or immunomodulatory therapeutic.

CONCLUSION

A new inflammatory muscle disorder, characterized by a distinctive pathological pattern of macrophagic myofasciitis is emerging in France.

<http://www.ncbi.nlm.nih.gov/pubmed/10705901>

“A most unusual inflammatory myopathy,
first described by Germmad had been reported
with increasing frequency since 1993 in the
leading French myopathology centers. We present
our experience with this new disease:
macrophagic myofasciitis.”

Effects of various aluminium compounds given orally to mice on Al tissue distribution and tissue concentrations of essential elements

Author information

Dsugaszek M1, Fiejka MA, Graczyk A, Aleksandrowicz JC, Slowikowska M.

Institute of Optoelectronics
Military University of Technology
Warsaw, Poland

Abstract

To evaluate the risk of gastrointestinal long-term aluminium (Al) exposure, aluminium distribution and the levels of the following essential elements: Ca, Mg, Zn, Cu, and Fe in tissue were studied. Aluminium was administered in drinking water as aluminium chloride, dihydroxyaluminium sodium carbonate or aluminium hydroxide. Mice (strain Pzh:SFIS) were exposed to a total dose of 700 mg Al in long-term treatment (for each Al compound $n = 15$). Concentrations of Al, Ca, Mg, Zn, Cu, and Fe in stomach, kidneys, bone and liver were analyzed by atomic absorption spectrometry. After $AlCl_3$ treatment, aluminium was found to accumulate in all tested tissues. A significant decrease in Fe concentration in liver and Zn in kidneys was observed in comparison to concentrations of these elements in the control group. In the $Al(OH)_3$ -treated group, accumulation of aluminium was observed in bone only and decline of Fe concentration in stomach and Cu in liver and kidney. In the $NaAl(OH)_2CO_3$ -treated group the increase in Al concentration was significant in bone; there was no change in concentration of essential elements in the examined tissues. The observed aluminium accumulation was not accompanied by changes in Ca and Mg concentration except for bone. This study showed that oral administration as a route of Al exposure can result in diverging accumulation of aluminium in tissues, the concentration depending on the chemical form.

Full Report

<http://onlinelibrary.wiley.com/doi/10.1034/j.1600-0773.2000.pto860308.x/epdf>

“This study showed that oral administration as a route of Aluminum exposure can result in diverging accumulation of aluminium in tissues ...”

“Complaints about ... a mysterious muscle ailment
have prompted researchers to take a fresh look at the use of aluminum adjuvants ... This month,
as some 70 scientists gathered here for 2 days of often vigorous discussion of the findings about the muscle ailment,
a larger question hung over the gathering: Will aluminum be the next battleground in the vaccine wars?”

Science • May 2000

Public health: Aluminum is put on trial as a vaccine booster

Malakoff D.

SAN JUAN, PUERTO RICO—Complaints about vaccine safety and debate over a mysterious muscle ailment have prompted researchers to take a fresh look at the use of aluminum adjuvants, which are used to cause the immune system to react earlier, more potently, and more persistently to the antigen contained in the vaccine. This month, as some 70 scientists gathered here for 2 days of often vigorous discussion of the findings about the muscle ailment, a larger question hung over the gathering: Will aluminum be the next battleground in the vaccine wars?

<http://www.sciencemag.org/content/288/5470/1323.summary?sid=82b7933f-c912-48c2-b2cf-40874fa78e61>

Aluminium-induced granulomas after inaccurate intradermal hyposensitization injections of aluminium-adsorbed depot preparations

Author information

Vogelbruch M1, Nuss B, Körner M, Kapp A, Kiehl P, Bohm W.

Department of Dermatology and Allergology
Hannover Medical University, Germany

Abstract

BACKGROUND

The development of persistent subcutaneous nodules at the injection sites of aluminium-adsorbed hyposensitization solutions is rare. These nodules have been interpreted as a delayed, granulomatous hypersensitivity reaction to aluminium. We report for the first time a case of persistent intradermal granulomas that developed at the sites of inaccurate intradermal, instead of subcutaneous, hyposensitization injections.

METHODS

An intradermal nodule was excised and processed for histopathology, scanning electron microscopy, and X-ray microanalysis. Intradermal and patch tests with aluminium hydroxide were performed.

RESULTS

Histologically, the nodule presented a pattern of granulomatous inflammatory reaction surrounding foci of necrotic tissue. Scanning electron microscopy and X-ray microanalysis revealed deposits of aluminium within the granulomas. Patch tests with aluminium hydroxide were negative, and intradermal tests caused persistent intradermal granulomas. Subsequent hyposensitization therapy in our department with the usual subcutaneous injections of aluminium-adsorbed allergen extracts was well tolerated by the patient.

CONCLUSIONS

Local toxic effects of aluminium may be crucial in the development of persistent intradermal injection-site granulomas. Such intradermal nodules may develop even if the subcutaneous route is well tolerated. We conclude that inaccurate intradermal injections of aluminium-containing solutions have to be strictly avoided.

Full Report

<http://onlinelibrary.wiley.com/doi/10.1034/j.1398-9995.2000.00501.x/full>

“We report for the first time a case of persistent intradermal granulomas that developed at the sites of inaccurate intradermal, instead of subcutaneous, hyposensitization injections.”

Aluminum Compounds

Prepared for Scott Masten, Ph.D., National Institute of Environmental Health Sciences P.O. Box 12233
Research Triangle Park, North Carolina 27709 Contract No. N01-ES-65402

Submitted by Bonnie L. Carson, M.S.
Integrated Laboratory Systems, P.O. Box 13501, Research Triangle Park, North Carolina 27709

EXECUTIVE SUMMARY

Human Toxicity

The effects of aluminum on humans have been extensively reviewed. Overall, there is little indication that aluminum is acutely toxic for the general population; few cases of acute aluminum toxicity during alum therapy (i.e., alum bladder irrigation) have been reported. Prolonged exposure to aluminum, however, can cause systemic toxicity, mainly affecting the gastrointestinal tract and causing neurological and skeletal effects.

Aluminum is a potent neurotoxic agent in humans. The association between aluminum and characteristics of Alzheimer's disease have prompted numerous studies of all sources of intake of aluminum. Epidemiological and case control studies have examined the potential link between oral exposure to aluminum via drinking water and the disease. The causal role of aluminum, however, remains controversial. Some studies have found a significant relationship between the exposure to aluminum in water and an increased risk of Alzheimer's disease, while other studies have not. There is ... convincing evidence that aluminum is the causative agent in dialysis dementia, which is seen in patients undergoing long-term hemodialysis.

Developmental effects such as encephalopathy, bone disease, microcytic anemia, and rickets have occurred in premature infants with reduced or failed renal function receiving aluminum-containing treatment (e.g., dialysate or aluminum-based phosphate binders) and in nonuremic infants receiving parenteral nutrition with aluminum-containing fluids or high doses of aluminum antacids. There are no adequate studies of the long-term effects of aluminum exposure on brain development and skeletal maturation.

No immunotoxicity studies are available. Few cases, however, report of hypersensitivity to aluminum following dermal application or parenteral administration. There have also been no reports of genetic or reproductive effects in humans.

In mice, oral administration of aluminum as aluminum ammonium sulfate decreased dopamine, dihydroxyphenylacetic acid, and homovanillic acid levels in the hypothalamus, and aluminum lactate increased the 2-thiobarbituric acid reactive substances (TBARS) in the brain but decreased brain stem weight.

In rats, oral administration of aluminum as the sulfate, nitrate, chloride, hydroxide, citrate, and lactate resulted in aluminum accumulation in bone, brain, spleen, liver, heart, gastrointestinal tract, and spleen. Significant decreases occurred in body weight, water consumption, urine volume, plasma glutamic-pyruvic transaminase, serum triglycerides, serum iron concentration, and alkaline phosphatase, ATP, ADP, and AMP, as well as in motor activity. Additional health effects include changes in the cytological and enzymatic content of the lavage fluid, inhibition of colony-forming units-erythroid (CFU-E), and neurobehavioral effects.

Subcutaneous (s.c.) injections of aluminum produced a significant decrease in iron levels in plasma and the striatum. Significant aluminum accumulation was induced in the striatum, hippocampus, and cortex, and in the hippocampus, TBARS production was increased.

Reproductive and Teratological Effects

Reproductive toxicity and teratogenicity from aluminum compounds has been reported in a number of papers. Reproductive effects observed in male mice, rats, or dogs given aluminum compounds orally or s.c. included repressed sexual behavior, decreased spermatogenesis, or other effects on the testes, sperm duct, and/or epididymis. Reproductive effects from oral administration to female rats included irregularity of the estrus cycle of female offspring or effects on the ovaries or fallopian tubes in treated adults. Maternal toxicity was observed in several studies in which pregnant mice, rats, or rabbits were administered aluminum compounds orally, i.p., or s.c. during gestation. Developmental toxicity from oral, i.p., or s.c. aluminum compound administration was also noted in some rat and mouse studies. Teratogenic effects induced by oral, i.p., or s.c. administration of aluminum compounds included skeletal or musculoskeletal variations, cleft palate or other craniofacial malformations, cardiovascular system abnormalities, and other unspecified physical effects. Injection of aluminum compounds into the yolk sac of fertilized chicken eggs induced similar developmental malformations. Neurotoxic effects were observed when aluminum compounds were given orally to mice, rats, or rabbits. A number of studies were also found that reported no reproductive, maternal, developmental toxicity or teratogenicity from oral, inhalation, i.p., or s.c. administration of aluminum compounds.

Genotoxicity

In one acellular assay, aluminum was found to bind to DNA through chelation. It was also found to reduce 3H-thymidine incorporation in a transformed cell line, indicating that aluminum compounds may impede cell cycle progression. Aluminum compounds were not mutagenic in the preponderance of Salmonella typhimurium and Escherichia coli studies. Only one study reported a positive mutagenic response, in which aluminum acetylacetonate was tested on S. typhimurium strain TA104 in the absence of metabolic activation. Effects induced in vitro by aluminum compounds included crosslinking of chromosomal proteins in rat ascites hepatoma cells, anaphasic changes in BALB/c mouse 3T3 cells, and formation of DNA-protein crosslinks, micronuclei, sister chromatid exchanges (SCEs), and chromosomal aberrations in cultured human lymphocytes. Effects induced in vivo included SCEs in mice and sheep, delayed mitosis in mice and sheep, and formation of micronucleated polychromatic lymphocytes in mice, and chromosomal aberrations in rats and mice.

Neurotoxicity

Dementia in dialysis patients and encephalopathy in infants undergoing parenteral nutrition are well known examples of aluminum intoxication in humans. Numerous in vitro studies and epidemiological studies have examined the possible role of aluminum in Alzheimer's disease, other dementias, and cognitive dysfunction.

Numerous animal studies, particularly orally studies in mice and rats, show that aluminum compounds are neurotoxic, but species variation exist. The toxicity is characterized by progressive neurological impairment leading to death associated with repeated seizures. Morphologically, the progressive encephalopathy, associated with neurofibrillary pathology in neurons mostly in the spinal cord, brain stem, and the hippocampus and cingulate gyrus of the cortex, has been induced by aluminum in susceptible animals such as the rabbit, cat, guinea pig, and ferret when given as intrathecal, intracerebral, and subcutaneous injections. For example, in cats and rabbits intracerebral injections of soluble aluminum compounds resulted in impairment in learning and memory, and in rabbits repeated subcutaneous injections affected classical conditioning, while single or repeated intracisternal injection of metallic aluminum altered motor function. Oral administration of aluminum compounds, however, produced no encephalopathy or epilepsy but resulted in behavioral impairment.

Differential toxicity of aluminum salts in human cell lines of neural origin: implications for neurodegeneration

Author information

Campbell AI, Hamai D, Bondy SC.

Department of Community and Environmental Medicine
Center for Occupational and Environmental Health
University of California, Irvine 92697-1820, USA

Abstract

Aluminum is highly oxophilic and its minerals are usually found surrounded by six oxygen atoms. A role for the metal has been established in dialysis encephalopathy and Al-induced osteomalacia. The metal has been implicated in Alzheimer's disease but the issue is at present controversial. Human cell lines of neural origin were utilized to study the effect of lipophilic aluminum acetylacetonate and non-lipophilic aluminum sulfate on cell proliferation and viability. Although analysis of Al species in the cell culture media demonstrated that there are positively charged Al species present in solutions prepared with both Al salts, only the aluminum acetylacetonate salt caused changes in cell proliferation and viability. Therefore, the lipophilic nature of the organic Al salt is a critical determinant of toxicity. The effect of aluminum acetylacetonate was dose-dependent and time-dependent. Neuroblastoma (SK-N-SH) cells were more susceptible to decreased cell proliferation although the lipophilic Al salt was more toxic to the glioblastoma (T98G) cells. While the toxicity of aluminum acetylacetonate was inhibited in the T98G cells by the addition of phosphate, the same treatment did not reverse cell death in the SK-N-SH cells. Thus, the mechanism of Al toxicity appears to be different in the two cell lines. It is possible that the principal neurotoxic target of the metal is glial and when these cells are in a compromised state, this may secondarily impact the neuronal population and thus eventually lead to neurodegeneration.

<http://www.ncbi.nlm.nih.gov/pubmed/11307852>

“It is possible
that the principal neurotoxic target
of the metal is glial and when these cells
are in a compromised state, this may
secondarily impact the neuronal
population and thus eventually
lead to neurodegeneration.”

“Aluminum is a nonessential metal to which humans are frequently exposed.”

Regulatory Toxicology And Pharmacology • February 2001

Safety evaluation of dietary aluminum

Author information

Soni MG1, White SM, Flamm WG, Burdock GA.

Burdock and Associates, Inc.
622 Beachland Boulevard
Suite B, Vero Beach, Florida 32963, USA

Abstract

Aluminum is a nonessential metal to which humans are frequently exposed. Aluminum in the food supply comes from natural sources, water used in food preparation, food ingredients, and utensils used during food preparations. The amount of aluminum in the diet is small, compared with the amount of aluminum in antacids and some buffered analgesics. The healthy human body has effective barriers (skin, lungs, gastrointestinal tract) to reduce the systemic absorption of aluminum ingested from water, foods, drugs, and air. The small amount of aluminum (<1%) that is systemically absorbed is excreted principally in the urine and, to a lesser extent, in the feces. No reports of dietary aluminum toxicity to healthy individuals exist in the literature. Aluminum can be neurotoxic, when injected directly into the brains of animals and when accidentally introduced into human brains (by dialysis or shrapnel). A study from Canada reports cognitive and other neurological deficits among groups of workers occupationally exposed to dust containing high levels of aluminum. While the precise pathogenic role of aluminum in Alzheimer's disease (AD) remains to be defined, present data do not support a causative role for aluminum in AD. High intake of aluminum from antacid for gastrointestinal ailments has not been reported to cause any adverse effects and has not been correlated with neurotoxicity or AD. Foods and food ingredients are generally the major dietary sources of aluminum in the United States. Cooking in aluminum utensils often results in statistically significant, but relatively small, increases in aluminum content of food. Common aluminum-containing food ingredients are used mainly as preservatives, coloring agents, leavening agents, anticaking agents, etc. Safety evaluation and approval of these ingredients by the Food and Drug Administration indicate that these aluminum-containing compounds are safe for use in foods.

<http://www.ncbi.nlm.nih.gov/pubmed/11259180>

Aluminium toxicokinetics: an updated minireview

Author information

Yokel RA1, McNamara PJ.

College of Pharmacy and Graduate Center for Toxicology
University of Kentucky Medical Center
Lexington 40536-0082, USA
ryokell@pop.uky.edu

Abstract

This MiniReview updates and expands the MiniReview of aluminium toxicokinetics by Wilhelm et al. published by this journal in 1990. The use of ²⁶Al, analyzed by accelerator mass spectrometry, now enables determination of Al toxicokinetics under physiological conditions. There is concern about aluminium in drinking water. The common sources of aluminium for man are reviewed. Oral Al bioavailability from water appears to be about 0.3%. Food is the primary common source. Al bioavailability from food has not been adequately determined. Industrial and medicinal exposure, and perhaps antiperspirant use, can significantly increase absorbed aluminium. Inhalation bioavailability of airborne soluble Al appears to be about 1.5% in the industrial environment. Al may distribute to the brain from the nasal cavity, but the significance of this exposure route is unknown. Systemic Al bioavailability after single underarm antiperspirant application may be up to 0.012%. All intramuscularly injected Al, e.g. from vaccines, may eventually be absorbed. Al distributes unequally to all tissues. Distribution and renal excretion appear to be enhanced by citrate. Brain uptake of Al may be mediated by Al transferrin and Al citrate complexes. There appears to be carrier-mediated efflux of Al citrate from the brain. Elimination half-lives of years have been reported in man, probably reflecting release from bone. Al elimination is primarily renal with < or = 2% excreted in bile. The contribution of food to absorbed Al needs to be determined to advance our understanding of the major components of Al toxicokinetics.

<http://www.ncbi.nlm.nih.gov/pubmed/11322172>

“All intramuscularly injected Aluminum,
e.g. from vaccines, may eventually be absorbed.”

Aluminium toxicity in the rat brain: histochemical and immunocytochemical evidence

Author information

Platt B1, Fiddler G, Riedel G, Henderson Z.

Biomedical Sciences, Aberdeen University
Scotland, Aberdeen, UK.
b.platt@abdn.ac.uk

Abstract

Although the neurotoxic actions of aluminium (Al) have been well documented, its contribution to neurodegenerative diseases such as Alzheimer's disease remains controversial. In the present study, we applied histochemical techniques to identify changes induced by intracerebroventricular Al injections (5.4 microg in 5.5 microl, daily over a period of 5 successive days) in the adult rat brain after survival periods of either 1 or 6 weeks. For both Al- and saline-infused controls, no major signs of gross histological changes were evident in cresyl violet-stained sections. Al (as indicated by the fluorescent Morin staining) was concentrated in white matter of the medial striatum, corpus callosum, and cingulate bundle. Immunoreactivity of astrocytes and phagocytic microglia based on glial fibrillary acidic protein and ED1 markers, respectively, revealed a greater inflammatory response in Al-injected animals compared to controls. Damage of the cingulate bundle in Al-treated animals led to a severe anterograde degeneration of cholinergic terminals in cortex and hippocampus, as indicated by acetylcholinesterase labelling. Our data suggest that the enhancement of inflammation and the interference with cholinergic projections may be the modes of action through which Al may cause learning and memory deficits, and contribute to pathological processes in Alzheimer's disease.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11470325>

“Our data suggest that the enhancement of inflammation and the interference with cholinergic projections may be the modes of action through which Aluminum may cause learning and memory deficits, and contribute to pathological processes in Alzheimer's disease.”

“... these results firmly establish that aluminium hydroxide-containing vaccines represent the direct cause of the Macrophagic myofasciitis (MMF) lesion.”

Brain • September 2001

Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle

Author information

Gherardi RK1, Coquet M, Cherin P, Belec L,
Moretto P, Dreyfus PA, Pellissier JF, Chariot P, Authier FJ.

Equipe mixte INSERM
E 0011/Université Paris XII, France
romain.gherardi@hmn.ap-hop-paris.fr

Abstract

Macrophagic myofasciitis (MMF) is an emerging condition of unknown cause, detected in patients with diffuse arthromyalgias and fatigue, and characterized by muscle infiltration by granular periodic acid-Schiff's reagent-positive macrophages and lymphocytes. Intracytoplasmic inclusions have been observed in macrophages of some patients. To assess their significance, electron microscopy was performed in 40 consecutive cases and chemical analysis was done by microanalysis and atomic absorption spectrometry. Inclusions were constantly detected and corresponded to aluminium hydroxide, an immunostimulatory compound frequently used as a vaccine adjuvant. A lymphocytic component was constantly observed in MMF lesions. Serological tests were compatible with exposure to aluminium hydroxide-containing vaccines. History analysis revealed that 50 out of 50 patients had received vaccines against hepatitis B virus (86%), hepatitis A virus (19%) or tetanus toxoid (58%), 3-96 months (median 36 months) before biopsy. Diffuse myalgias were more frequent in patients with than without an MMF lesion at deltoid muscle biopsy ($P < 0.0001$). Myalgia onset was subsequent to the vaccination (median 11 months) in 94% of patients. MMF lesion was experimentally reproduced in rats. We conclude that the MMF lesion is secondary to intramuscular injection of aluminium hydroxide-containing vaccines, shows both long-term persistence of aluminium hydroxide and an ongoing local immune reaction, and is detected in patients with systemic symptoms which appeared subsequently to vaccination.

Full Report

<http://brain.oxfordjournals.org/content/124/9/1821>

Aluminum phagocytosis
in quadriceps muscle following vaccination in children:
relationship to macrophagic myofasciitis

Author information

Lacson AG1, D’Cruz CA,
Gilbert-Barnes E, Sharer L, Jacinto S, Cuenca R.

Departments of Pediatrics and Pathology
University of South Florida at All Children’s Hospital
801 Sixth Street South 7020, St. Petersburg, FL 33731, USA

Abstract

Macrophagic myofasciitis (MMF) is a rare, seemingly emerging entity among adult patients in France. We encountered two children with the first two cases of MMF in North America. A 5-year-old male with chronic intestinal pseudo-obstruction required nighttime parenteral nutrition. Abnormal pupillary reflexes and urinary retention suggested a diffuse dysautonomia, which prompted a neurological diagnostic work-up. A 3-year-old child had developmental delay and hypotonia. Both children received age-appropriate immunizations. Quadriceps muscle biopsy from each child showed the typical patchy, cohesive centripetal infiltration of alpha-1-antitrypsin+, alpha-1-antichymotrypsin+, CD68+, PAS+, CD1a-, S-100-, factor XIII- granular macrophages with adjacent myofiber atrophy, dilated blood vessels, and mild endomysial and perimysial fibrosis. No myonecrosis was observed and no discrete granulomas were seen. A single aluminum peak was demonstrated on energy dispersive X-ray microanalysis. The etiology of the clinical symptoms in these cases and in cases reported as MMF remains intriguing. Despite numerous stains to demonstrate organisms, most infectious causes leading to macrophage activation were ruled out. These cases are being reported to increase awareness of this condition and to encourage a systematic epidemiologic and clinicopathologic study in North America.

<http://www.ncbi.nlm.nih.gov/pubmed/11910509>

“Macrophagic myofasciitis (MMF)
is a rare, seemingly emerging entity
among adult patients in France. We
encountered two children with the
first two cases of MMF in North America.”

Mechanisms of stimulation of the immune response by aluminum adjuvants

Author information

HogenEsch H.

Department of Veterinary Pathobiology
Purdue University, West Lafayette
IN 47907-1243, USA
hogenesch@purdue.edu

Abstract

Aluminum adjuvants are widely used in human and veterinary vaccines. They are appropriate adjuvants for vaccines that confer protection by inducing antibodies via the induction of a type 2 immune response, but they do not induce cytotoxic T cell and cell-mediated immunity. The mechanisms by which aluminum adjuvants selectively enhance the immune response are poorly understood. Following exposure to interstitial fluid *in vitro* and *in vivo*, most antigens are rapidly desorbed from aluminum adjuvants, suggesting that sustained release of antigen from a depot does not significantly contribute to the adjuvant effect of aluminum compounds. However, the adsorption of antigens onto aluminum salts may result in a high local concentration of antigen at the injection site and enhance the uptake by antigen-presenting cells. Aluminum compounds can further enhance the immune response by direct or indirect stimulation of dendritic cells, activation of complement and by inducing the release of chemokines. The relative importance of these mechanisms remains to be determined.

<http://www.ncbi.nlm.nih.gov/pubmed/12184362>

“Aluminum compounds
can further enhance the immune response
by direct or indirect stimulation of dendritic
cells, activation of complement and by inducing
the release of chemokines. The relative
importance of these mechanisms
remains to be determined.”

“Dr. Gherardi believes that Macrophagic Myofasciitis, a syndrome of ascending myalgias, fatigue and diffuse musculoskeletal pain, may be related to a chronic immune response to aluminum granulomas persisting at the sites of prior immunization with aluminum adjuvated vaccines.”

Vaccine • May 2002

**Macrophagic myofasciitis:
a summary of Dr. Gherardi's presentations**

Author information

Brenner A1.
Rheumatological Services, Inc.
Framington, MA 01702, USA
alanrsi@aol.com

Abstract

Dr. R.K. Gherardi presented two papers at the symposium, detailing his researches into a proposed new clinical entity which he has entitled Macrophagic Myofasciitis (MMF). In his first paper he described the histopathologic and immunologic characteristics of the condition, and in the second, the clinical and serologic features. Dr. Gherardi believes that MMF, a syndrome of ascending myalgias, fatigue and diffuse musculoskeletal pain, may be related to a chronic immune response to aluminum granulomas persisting at the sites of prior immunization with aluminum adjuvated vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12184366>

“there is no known physiological role for aluminum within the body ...”

Environmental Research • June 2002

Aluminum: impacts and disease

Author information

Nayak P.

Department of Physiology
Sikkim Manipal Institute of Medical Sciences
5th Mile, Tadong, Gangtok, 737102, Sikkim, India

Abstract

Aluminum is the most widely distributed metal in the environment and is extensively used in modern daily life. Aluminum enters into the body from the environment and from diet and medication. However, there is no known physiological role for aluminum within the body and hence this metal may produce adverse physiological effects. The impact of aluminum on neural tissues is well reported but studies on extraneural tissues are not well summarized. In this review, the impacts of aluminum on humans and its impact on major physiological systems are summarized and discussed. The neuropathologies associated with high brain aluminum levels, including structural, biochemical, and neurobehavioral changes, have been summarized. In addition, the impact of aluminum on the musculoskeletal system, respiratory system, cardiovascular system, hepatobiliary system, endocrine system, urinary system, and reproductive system are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12123643>

“The exact mechanism of aluminum toxicity is not known but accumulating evidence suggests that the metal can potentiate oxidative and inflammatory events, eventually leading to tissue damage.”

Toxicology And Industrial Health • August 2002

Aluminum as a toxicant

Author information

Becaria A1, Campbell A, Bondy SC.

Department of Community and Environmental Medicine
Center for Occupational and Environmental Health Sciences
Irvine, CA 92697-1820, USA
abecaria@uci.edu

Abstract

Although aluminum is the most abundant metal in nature, it has no known biological function. However, it is known that there is a causal role for aluminum in dialysis encephalopathy, microcytic anemia, and osteomalacia. Aluminum has also been proposed to play a role in the pathogenesis of Alzheimer's disease (AD) even though this issue is controversial. The exact mechanism of aluminum toxicity is not known but accumulating evidence suggests that the metal can potentiate oxidative and inflammatory events, eventually leading to tissue damage. This review encompasses the general toxicology of aluminum with emphasis on the potential mechanisms by which it may accelerate the progression of chronic age-related neurodegenerative disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15068131>

“... even intermittent or low-dose use of aluminium-based phosphate binders adds to the total load of this toxin in the bone; thus, aluminium use is inadvisable, even for a ‘rescue indication’.”

Nephrology, Dialysis, Transplantation • 2002

Aluminium and bone disease in chronic renal failure

Author information

Malluche HH

University of Kentucky, Division of Nephrology
Bone and Mineral Metabolism
Lexington, 40536-1052, USA
hhmall@uky.edu

Abstract

Aluminium is absorbed by the intestines and is rapidly transported into bone, where it disrupts mineralization and bone cell growth and activity. Its toxicities result in or exacerbate painful forms of renal osteodystrophy, most notably adynamic bone disease and osteomalacia, but also other forms of the disease. Because aluminium is sequestered in bone for long periods, its toxic effects are cumulative. As a result, even intermittent or low-dose use of aluminium-based phosphate binders adds to the total load of this toxin in the bone; thus, aluminium use is inadvisable, even for a ‘rescue indication’. Aluminium blood levels are not a reliable marker of aluminium absorption or organ load in dialysis patients: only stainable aluminium at the mineralization front reflects the histopathological changes observed in bone. Therefore, bone biopsies remain the only approach for definitive diagnosis of aluminium-related bone disease. Most importantly, lack of correlation between overall organ concentrations of a toxin, such as aluminium, and pathological changes does not rule out toxicity. Thus, the specific localization of the toxin is more important than overall organ concentration. What has been observed with aluminium during 25 years of research might be reproduced with other metals that are absorbed, transported and accumulated in bone. What we have learned about the toxicity of aluminium should inform our interpretation of data from studies of other metal-based therapeutics for renal patients. This calls for careful evaluation of any newly introduced therapeutic agents for bone disease in patients lacking excretory kidney function.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11904354>

Workshop Summary Aluminum In Vaccines

Conference report

Theodore C. Eickhoff

Division of Infectious Disease University of Colorado Health Sciences
4200 East 9th Avenue Denver, CO 80262, USA

Martin Myers

National Vaccine Program Office
1600 Clifton Road MS 0-66, Atlanta, GA 30333

Abstract

On May 11–12 in San Juan, Puerto Rico the National Vaccine Program Office (NVPO) sponsored a workshop on aluminum in vaccines. The meeting was attended by a diverse group of vaccinologists, immunologists, experts on metals, pathologists, rheumatologists, and other interested parties. The objectives of this meeting were to: (1) establish a better understanding of the role and need of aluminum as an adjuvant in vaccines; (2) explore the possibility of adverse events due to the use of aluminum in vaccines; and (3) develop a research agenda to expand existing knowledge of the impact of aluminum on the human body. From the Metal Ions in Biology and Medicine International Symposium held immediately prior to the aluminum workshop, we learned about “pervasive uncertainty”, a phrase used in this workshop to denote missing data on pharmacokinetics and toxicities of aluminum injected into humans. Even with identification of areas needing further study, it was apparent that aluminum which has been used as a vaccine adjuvant for more than 70 years, has an established safety record with low incidence of reported adverse events.

The first session of the workshop was devoted to important background about immunologic adjuvants in general and aluminum adjuvants in particular. Dr. Robert Hunter, University of Texas, provided a broad overview of the history and development of adjuvants, and the conventional views of their mechanism of action and uses. Aluminum adjuvants have been thought to form a repository of antigen in tissue, to produce particulate antigen for presentation to immune cells, and perhaps to activate complement and other immune enhancers. The immune response to some, but not all, protein antigens is enhanced by aluminum salts, however, these salts have little effect on peptide and polysaccharide antigens. Aluminum adjuvants enhance the primary immunization series, reducing the amount of antigen needed per dose and the number of required doses. They increase the proportion of responders, however, there appears to be little effect of adjuvant in subsequent booster doses.

Dr. Norman Baylor, US Food and Drug Administration, provided a detailed analysis of aluminum adjuvants, as well as regulatory perspectives. The three general types of

aluminum-containing adjuvants are: (1) aluminum hydroxide, (2) aluminum phosphate, and (3) alum, or potassium aluminum sulfate. Each of these types of formulations has different isoelectric points, and properties; they are not simply interchangeable. The efficacy of each salt as an adjuvant depends also on the characteristics of the antigens in the vaccine. FDA regulations limit the aluminum content of an individual dose of a vaccine to 0.85 mg. of elemental aluminum. This is equivalent to 15 mg. of alum per dose.

The immunologic advantage conferred by these adjuvants has been well documented, although most of this documentation is found in studies published before 1970. In general, these studies showed that aluminum-adjuvanted vaccines resulted in higher and more prolonged antibody responses than did comparable aqueous vaccines. This advantage was most apparent during primary immunization; there seemed to be little advantage to incorporating adjuvant in booster doses.

The US licensed products that contain aluminum adjuvants include DTP, DTaP, some but not all HIB vaccines, hepatitis B vaccine, and all combination DTaP, HIB, or HB vaccines. Others containing aluminum include hepatitis A vaccine, lyme disease vaccine, anthrax vaccine, and rabies vaccine. Inactivated vaccines that do not contain aluminum salts include IPV and influenza vaccines. Of interest was the fact that there are substantial differences among manufacturers both in the specific aluminum adjuvant used, as well as the amount of that adjuvant, in vaccines such as DTaP and in combination vaccines made by several manufacturers. Dr. Baylor also pointed out that any alteration of a vaccine, such as removal of aluminum in booster doses, would necessitate treating the altered vaccine as a new product requiring the collection of additional clinical data.

Adverse reactions that have been reported with aluminum-containing vaccines are generally local reactions including sterile abscesses, erythema, subcutaneous (SC) nodules, granulomatous inflammation, and contact hypersensitivity. None of these reactions, however, has been sufficiently frequent to arouse concern.

A biogeochemical cycle for aluminium?

Author information

Exley C1.

Birchall Centre for Inorganic Chemistry and Materials Science
Keele University, Staffordshire ST5 5BG, UK
c.exley@chem.keele.ac.uk

Abstract

The elaboration of biogeochemical cycles for elements which are known to be essential for life has enabled a broad appreciation of the homeostatic mechanisms which underlie element essentiality. In particular they can be used effectively to identify any part played by human activities in element cycling and to predict how such activities might impact upon the lithospheric and biospheric availability of an element in the future. The same criteria were the driving force behind the construction of a biogeochemical cycle for aluminium, a non-essential element which is a known ecotoxicant and a suspected health risk in humans. The purpose of this exercise was to examine the concept of a biogeochemical cycle for aluminium and not to review the biogeochemistry of this element. The cycle as presented is rudimentary and qualitative though, even in this nascent form, it is informative and predictive and, for these reasons alone, it is deserving of future quantification. A fully fledged biogeochemical cycle for aluminium should explain the biospheric abundance of this element and whether we should expect its (continued) active involvement in biochemical evolution.

“a non-essential element
which is a known ecotoxicant and a
suspected health risk in humans.”

Vaccine • December 2003

Unexpectedly high incidence
of persistent itching nodules and delayed hypersensitivity
to aluminium in children after the use of adsorbed vaccines
from a single manufacturer

Author information

Bergfors E1, Trollfors B, Inerot A.

Department of Primary Health Care, Göteborg University
Box 454, S-40530 Göteborg, Sweden
elisabet.bergfors@allmed.gu.se

Abstract

During trials of aluminium adsorbed diphtheria-tetanus/acellular pertussis vaccines from a single producer, persistent itching nodules at the vaccination site were observed in an unexpectedly high frequency. The afflicted children were followed in a longitudinal observational study, and the presence of aluminium sensitization was investigated in the children with itching nodules and their symptomless siblings by patch tests. Itching nodules were found in 645 children out of about 76,000 vaccinees (0.8%) after both subcutaneous (s.c.) and intramuscular (i.m.) injection. The itching was intense and long-lasting. So far, 75% still have symptoms after a median duration of 4 years. Contact hypersensitivity to aluminium was demonstrated in 77% of the children with itching nodules and in 8% of the symptomless siblings who had received the same vaccines ($P < 0.001$). Children with persistent itching nodules and/or aluminium sensitization should be warned about aluminium containing products (e.g. vaccines and antiperspirants). The reason for the high incidence of itching nodules after SSI vaccines is unknown and should be further investigated.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14604572>

“Itching nodules were found in 645 children out of about 76,000 vaccinees after both subcutaneous and intramuscular injection. The itching was intense and long-lasting. So far, 75% still have symptoms after a median duration of 4 years.”

Chronic exposure to aluminum in drinking water increases inflammatory parameters selectively in the brain

Author information

Campbell A1, Becaria A, Lahiri DK, Sharman K, Bondy SC.

Department of Community and Environmental Medicine
Center for Occupational and Environmental Health Sciences
Irvine, California 92697, USA

Abstract

A link between aluminum (Al) exposure and age-related neurological disorders has long been proposed. Although the exact mechanism by which the metal may influence disease processes is unknown, there is evidence that exposure to Al causes an increase in both oxidative stress and inflammatory events. These processes have also been suggested to play a role in Alzheimer's disease (AD), and exposure to the metal may contribute to the disorder by potentiating these events. Al lactate (0.01, 0.1, and 1 mM) in drinking water for 10 weeks increased inflammatory processes in the brains of mice. The lowest of these levels is in the range found to increase the prevalence of AD in regions where the concentrations of the metal are elevated in residential drinking water (Flaten [2001] Brain Res. Bull. 55:187-196). Nuclear factor-kappaB as well as tumor necrosis factor-alpha (TNF-alpha) and interleukin 1alpha (IL-1alpha) levels were increased in the brains of treated animals. The mRNA for TNF-alpha was also up-regulated following treatment. Enhancement of glial fibrillary acidic protein levels and reactive microglia was seen in the striatum of Al-treated animals. The level of amyloid beta (Abeta40) was not significantly altered in the brains of exposed animals. Insofar as no parallel changes were observed in the serum or liver of treated animals, the proinflammatory effects of the metal may be selective to the brain. Al exposure may not be sufficient to cause abnormal production of the principal component of senile plaques directly but does exacerbate underlying events associated with brain aging and thus could contribute to progression of neurodegeneration.

<http://www.ncbi.nlm.nih.gov/pubmed/14743440>

“Although the exact mechanism by which the metal may influence disease processes is unknown, there is evidence that exposure to Al causes an increase in both oxidative stress and inflammatory events. Insofar as no parallel changes were observed in the serum or liver of treated animals, the proinflammatory effects of the metal may be selective to the brain.”

“... the more detailed mode of action of these adjuvants is still not completely understood.”

Vaccine • September 2004

Aluminium adjuvants—in retrospect and prospect

Author information

Lindblad EB.

Adjuvant Dept. Brenntag Biosector
DK-3600 Frederikssund, Denmark

Abstract

Aluminium compounds have been used as adjuvants in practical vaccination for more than 60 years to induce an early, an efficient and a long lasting protective immunity and are at present the most widely used adjuvants in both veterinary and human vaccines. Although the last two decades of systematic research into the nature of these adjuvants has contributed significantly to understanding their nature and their limitations as Th2 stimulators the more detailed mode of action of these adjuvants is still not completely understood. We have a comprehensive record of their behaviour and performance in practical vaccination, but an empirical approach to optimising their use in new vaccine formulations is still to some extent a necessity. The aim of the present review is to put the recent findings into a broader perspective to facilitate the application of these adjuvants in general and experimental vaccinology.

<http://www.ncbi.nlm.nih.gov/pubmed/15315845>

Mitochondrial viability and apoptosis induced by aluminum, mercuric mercury and methylmercury in cell lines of neural origin

Author information

Toimela T1, Tähti H.

Medical School, Cell Research Center
University of Tampere
33014 University of Tampere, Finland
Tarja.Toimela@uta.fi

Abstract

Mercury and aluminum are considered to be neurotoxic metals, and they are often connected with the onset of neurodegenerative diseases. In this study, mercuric mercury, methylmercury and aluminum were studied in three different cell lines of neural origin. To evaluate the effects, mitochondrial cytotoxicity and apoptosis induced by the metals were measured after various incubation times. SH-SY5Y neuroblastoma, U 373MG glioblastoma, and RPE D407 retinal pigment epithelial cells were subcultured to appropriate cell culture plates and 0.01-1,000 microM concentrations of methylmercury, mercuric and aluminum chloride were added into the growth medium. In the assay measuring the mitochondrial dehydrogenase activity, WST-1, the cultures were exposed for 15 min, 24 or 48 h before measurement. Cells were allowed to recover from the exposure in part of the study. Apoptosis induced by the metals was measured after 6-, 24- and 48-h exposure times with the determination of activated caspase 3 enzyme. Mitochondrial assays showed a clear dose-response and exposure time-response to the metals. The most toxic was methylmercury (EC50 ~0.8 microM, 48 h), and the most sensitive cell line was the neuroblastoma cell line SH-SY5Y. Furthermore, there was marked mitochondrial activation, especially in connection with aluminum and methylmercury at low concentrations. This activation may be important during the initiation of cellular processes. All the metals tested induced apoptosis, but with a different time-course and cell-line specificity. In microscopic photographs, glioblastoma cells formed fibrillary tangles, and neuroblastoma cells settled along the fibrilles in cocultures of glial and neuronal cell lines during aluminum exposure. The study emphasized the toxicity of methylmercury to neural cells and showed that aluminum alters various cellular activities.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15150681>

“Mercury and aluminum are considered to be neurotoxic metals, and they are often connected with the onset of neurodegenerative diseases. The study emphasized the toxicity of methylmercury to neural cells and showed that aluminum alters various cellular activities.”

Nanomolar aluminum induces pro-inflammatory and pro-apoptotic gene expression in human brain cells in primary culture

Author information

Lukiw WJ1, Percy ME, Kruck TP.

Neuroscience Center of Excellence and Department of Ophthalmology
Louisiana State University Health Sciences Center
2020 Gravier Street, Suite 8B8, New Orleans, LA 70112-2272, USA
wlukiw@lsuhsc.edu

Abstract

Aluminum, the most abundant neurotoxic metal in our biosphere, has been implicated in the etiology of several neurodegenerative disorders including Alzheimer's disease (AD). To further understand aluminum's influence on gene expression, we examined total messenger RNA levels in untransformed human neural cells exposed to 100 nanomolar aluminum sulfate using high density DNA microarrays that interrogate the expression of every human gene. Preliminary data indicate that of the most altered gene expression levels, 17/24 (70.8%) of aluminum-affected genes, and 7/8 (87.5%) of aluminum-induced genes exhibit expression patterns similar to those observed in AD. The seven genes found to be significantly up-regulated by aluminum encode pro-inflammatory or pro-apoptotic signaling elements, including NF-kappaB subunits, interleukin-1beta precursor, cytosolic phospholipase A2, cyclooxygenase-2, beta-amyloid precursor protein and DAXX, a regulatory protein known to induce apoptosis and repress transcription. The promoters of genes up-regulated by aluminum are enriched in binding sites for the stress-inducible transcription factors HIF-1 and NF-kappaB, suggesting a role for aluminum, HIF-1 and NF-kappaB in driving atypical, pro-inflammatory and pro-apoptotic gene expression. The effect of aluminum on specific stress-related gene expression patterns in human brain cells clearly warrant further investigation.

<http://www.ncbi.nlm.nih.gov/pubmed/15961160>

“The effect of aluminum on specific stress-related gene expression patterns in human brain cells clearly warrant further investigation.”

Synergistic effects
of iron and aluminum
on stress-related gene expression
in primary human neural cells

Author information

Alexandrov PN1, Zhao Y, Pogue AI,
Tarr MA, Kruck TP, Percy ME, Cui JG, Lukiw WJ.

Russian Academy of Medical Sciences
Moscow 113152, Russia

Abstract

Disturbances in metal-ion transport, homeostasis, overload and metal ion-mediated catalysis are implicated in neurodegenerative conditions such as Alzheimer's disease (AD). The mechanisms of metal-ion induced disruption of genetic function, termed genotoxicity, are not well understood. In these experiments we examined the effects of non-apoptotic concentrations of magnesium-, iron- and aluminum-sulfate on gene expression patterns in untransformed human neural (HN) cells in primary culture using high density DNA array profiling and Western immunoassay. Two week old HN cells were exposed to low micromolar magnesium, iron, or aluminum for 7 days, representing trace metal exposure over one-third of their lifespan. While total RNA yield and abundance were not significantly altered, both iron and aluminum were found to induce HSP27, COX-2, betaAPP and DAXX gene expression. Similarly up-regulated gene expression for these stress-sensing, pro-inflammatory and pro-apoptotic elements have been observed in AD brain. The combination of iron and aluminum together was found to be particularly effective in up-regulating these genes, and was preceded by the evolution of reactive oxygen intermediates as measured by 2',7'-dichlorofluorescein diacetate assay. These data indicate that physiologically relevant amounts of iron and aluminum are capable of inducing Fenton chemistry-triggered gene expression programs that may support downstream pathogenic responses and brain cell dysfunction.

<http://www.ncbi.nlm.nih.gov/pubmed/16308480>

“These data indicate that physiologically relevant amounts of iron and aluminum are capable of inducing Fenton chemistry-triggered gene expression programs that may support downstream pathogenic responses and brain cell dysfunction.”

Aluminium content of some foods and food products in the USA, with aluminium food additives

Author information

Saiyed SM1, Yokel RA.

College of Pharmacy
University of Kentucky Medical Center
Lexington, KY, USA

Abstract

The primary objective was to determine the aluminium (Al) content of selected foods and food products in the USA which contain Al as an approved food additive. Intake of Al from the labeled serving size of each food product was calculated. The samples were acid or base digested and analysed for Al using electrothermal atomic absorption spectrometry. Quality control (QC) samples, with matrices matching the samples, were generated and used to verify the Al determinations. Food product Al content ranged from <math><1-27,000 \text{ mg kg}^{-1}</math>. Cheese in a serving of frozen pizzas had up to 14 mg of Al, from basic sodium aluminium phosphate; whereas the same amount of cheese in a ready-to-eat restaurant pizza provided 0.03-0.09 mg. Many single serving packets of non-dairy creamer had approximately 50-600 mg Al kg^{-1} as sodium aluminosilicate, providing up to 1.5 mg Al per serving. Many single serving packets of salt also had sodium aluminosilicate as an additive, but the Al content was less than in single-serving non-dairy creamer packets. Acidic sodium aluminium phosphate was present in many food products, pancakes and waffles. Baking powder, some pancake/waffle mixes and frozen products, and ready-to-eat pancakes provided the most Al of the foods tested; up to 180 mg/serving. Many products provide a significant amount of Al compared to the typical intake of 3-12 mg/day reported from dietary Al studies conducted in many countries.

<http://www.ncbi.nlm.nih.gov/pubmed/16019791>

“The primary objective was to determine the aluminium (Al) content of selected foods and food products in the USA which contain Al as an approved food additive. Intake of Al from the labeled serving size of each food product was calculated.”

“Aluminum has been associated with several neurodegenerative diseases, such as dialysis encephalopathy, amyotrophic lateral sclerosis and Parkinsonism dementia in the Kii peninsula and Guam, and in particular, Alzheimer’s disease.”

Journal Of Alzheimers Disease • November 2005

Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases

Author information

Kawahara M.

Department of Analytical Chemistry
School of Pharmaceutical Sciences
Kyushu University of Health and Welfare
Nobeoka-city, Miyazaki, 882-8508, Japan

Abstract

Aluminum is environmentally abundant, but not an essential element. Aluminum has been associated with several neurodegenerative diseases, such as dialysis encephalopathy, amyotrophic lateral sclerosis and Parkinsonism dementia in the Kii peninsula and Guam, and in particular, Alzheimer’s disease. Although this association remains controversial, there is increasing evidence which suggests the implication of metal homeostasis in the pathogenesis of Alzheimer’s disease. Aluminum, zinc, copper, and iron cause the conformational changes of Alzheimer’s amyloid-beta protein. Al causes the accumulation of tau protein and amyloid-beta protein in experimental animals. Aluminum induces neuronal apoptosis in vivo as well as in vitro. Furthermore, a relationship between aluminum and the iron-homeostasis or calcium-homeostasis has been suggested. Based on these findings, the characteristics of aluminum neurotoxicity are reviewed, and the potential link between aluminum and neurodegenerative diseases is reconsidered.

<http://www.ncbi.nlm.nih.gov/pubmed/16308486>

(How) do aluminium adjuvants work?

Author information

Brewer JM.

Division of Immunology
Infection and Inflammation
University of Glasgow, Western Infirmary
Glasgow G11 6NT, UK
j.m.brewer@clinmed.gla.ac.uk

Abstract

The aluminium compounds, originally identified as adjuvants over 70 years ago, remain unique in their widespread application to human vaccines. Given this history, it is surprising that the physicochemical interactions between aluminium compounds and antigens are relatively poorly understood. This has clearly been a contributing factor to vaccine failures, for example, through inappropriate selection of aluminium species or buffers. Similarly, the mechanism(s) of action of aluminium adjuvants are relatively unstudied, although it appears that these agents fail to fit within the current principles underlying activation of the immune response. This review aims to examine recent developments in our understanding of the physicochemical and biological aspects of research into aluminium adjuvants.

<http://www.ncbi.nlm.nih.gov/pubmed/16188325?dopt=Abstract>

“The aluminium compounds, originally identified as adjuvants over 70 years ago, remain unique in their widespread application to human vaccines. Given this history, it is surprising that the physicochemical interactions between aluminium compounds and antigens are relatively poorly understood.”

Al(OH)₃-adjuvanted vaccine-induced macrophagic myofasciitis in rats is influenced by the genetic background

Author information

Authier FJ1, Sauvat S, Christov C, Chariot P,
Raisbeck G, Poron MF, Yiou F, Gherardi R.

Centre de Référence Pour Maladies Neuromusculaires
CHU Henri Mondor, AP-HP, Créteil, France
francois-jerome.authier@hmn.aphp.fr

Abstract

Macrophagic myofasciitis (MMF) is a specific histopathologic lesion involved in the persistence for years of aluminum hydroxide [Al(OH)₃] at the site of previous intramuscular (i.m.) injection. In order to study mechanisms involved persistence of MMF lesions, we set up an experimental model of MMF-lesion in Sprague-Dawley and Lewis rat, by i.m. injections of 10 microL of an Al(OH)₃-adjuvanted vaccine. An evaluation carried out over a 12-month period disclosed significant shrinkage of MMF lesions with time. A radioisotopic study did not show significant aluminium uptake by Al(OH)₃-loaded macrophages. A morphometric approach showed that Lewis rats with Th1-biased immunity had significantly smaller lesions than Sprague-Dawley rats with balanced Th1/Th2 immunity. Concluding, our results indicate that genetic determinatives of cytotoxic T-cell responses could interfere with the clearance process and condition the persistence of vaccine-induced MMF-lesions.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16616846>

“Macrophagic myofasciitis (MMF) is ... involved in the persistence for years of aluminum hydroxide at the site of previous intramuscular injection. Concluding, our results indicate that genetic determinatives of cytotoxic T-cell responses could interfere with the clearance process and condition the persistence of vaccine-induced MMF-lesions.”

Blood-brain barrier flux of
aluminum, manganese, iron and other metals
suspected to contribute to
metal-induced
neurodegeneration

Author information

Yokel RA.

College of Pharmacy and Graduate Center for Toxicology
University of Kentucky Medical Center
Lexington, KY 40536-0082, USA
ryokel@email.uky.edu

Abstract

The etiology of many neurodegenerative diseases has been only partly attributed to acquired traits, suggesting environmental factors may also contribute. Metal dyshomeostasis causes or has been implicated in many neurodegenerative diseases. Metal flux across the blood-brain barrier (the primary route of brain metal uptake) and the choroid plexuses as well as sensory nerve metal uptake from the nasal cavity are reviewed. Transporters that have been described at the blood-brain barrier are listed to illustrate the extensive possibilities for moving substances into and out of the brain. The controversial role of aluminum in Alzheimer's disease, evidence suggesting brain aluminum uptake by transferrin-receptor mediated endocytosis and of aluminum citrate by system Xc;{-} and an organic anion transporter, and results suggesting transporter-mediated aluminum brain efflux are reviewed. The ability of manganese to produce a parkinsonism-like syndrome, evidence suggesting manganese uptake by transferrin- and non-transferrin-dependent mechanisms which may include store-operated calcium channels, and the lack of transporter-mediated manganese brain efflux, are discussed. The evidence for transferrin-dependent and independent mechanisms of brain iron uptake is presented. The copper transporters, ATP7A and ATP7B, and their roles in Menkes and Wilson's diseases, are summarized. Brain zinc uptake is facilitated by L- and D-histidine, but a transporter, if involved, has not been identified. Brain lead uptake may involve a non-energy-dependent process, store-operated calcium channels, and/or an ATP-dependent calcium pump. Methyl mercury can form a complex with L-cysteine that mimics methionine, enabling its transport by the L system. The putative roles of zinc transporters, ZnT and Zip, in regulating brain zinc are discussed. Although brain uptake mechanisms for some metals have been identified, metal efflux from the brain has received little attention, preventing integration of all processes that contribute to brain metal concentrations.

<http://www.ncbi.nlm.nih.gov/pubmed/17119290>

“Although brain uptake mechanisms for some metals have been identified, metal efflux from the brain has received little attention, preventing integration of all processes that contribute to brain metal concentrations.”

The effects of low dose aluminum on hemorheological and hematological parameters in rats

Author information

Turgut S1, Bor-Kucukatay M,
Emmungil G, Atsak P, Turgut G.

Department of Physiology
Medical Faculty, Pamukkale University
20020 Denizli, Turkey
sturgut@pamukkale.edu.tr

Abstract

Aluminum (Al) is a nonessential element and humans are constantly exposed to Al as a result of an increase in industrialization and improving technology practices. Al toxicity can induce several clinical disorders such as neurotoxicity, gastrointestinal toxicity, hepatotoxicity, bone diseases, and anemia. This study aimed at evaluating the possible effects of short term and low dose Al exposure on hemorheological and hematological parameters in rats. Fourteen young, male Wistar albino rats were divided into two groups: 1 mg/200 g body weight of aluminum sulfate (Al₂(SO₄)₃) was injected intraperitoneally to the first group for two weeks, three times a week. The animals of the control group received only physiological saline solution during this period. At the end of the experimental period, anticoagulated blood samples were collected and hematological parameters were determined using an electronic hematology analyzer. Red blood cell (RBC) deformability and aggregation were measured using an ektacytometer (LORCA) and plasma and whole blood viscosities were determined with a Wells-Brookfield cone-plate rotational viscometer. Significant decreases in mean corpuscular volume (MCV), red blood cell (RBC) deformability at low shear stress levels, the aggregation half time (t_{1/2}) and the amplitude (AMP) of aggregation and significant increments in whole blood viscosity (WBV) at native and 40% hematocrit (Hct) of Al-treated rats have been observed. In conclusion, low dose Al₂(SO₄)₃ exposure for a short-time may be responsible for alterations in either rheological properties of blood or hemorheological properties through a remarkable effect on RBC membrane mechanical properties. These alterations may also play an important role in the development of anemia in the Al-treated animals.

“In conclusion, low dose Aluminum exposure for a short-time may be responsible for alterations in either rheological properties of blood or hemorheological properties through a remarkable effect on RBC membrane mechanical properties.”

“It is hypothesized, in the present review, that Aluminum is a potential factor for induction or maintaining the inflammation in Crohn’s Disease ...”

Annals Of The New York Academy Of Science • June 2007

Aluminum is a potential environmental factor for Crohn’s disease induction: extended hypothesis

Author information

Lerner A.

Pediatric Gastroenterology and Nutrition Unit
Carmel Medical Center, Pappaport School of Medicine
Technion-Israel Institute of Technology, Haifa, Israel
lerner_aaron@clalit.org.il

Abstract

Aluminum (Al) is a common environmental compound with immune-adjuvant activity and granulomatous inflammation inducer. Al exposure in food, additives, air, pharmaceuticals, and water pollution is ubiquitous in Western culture. Crohn’s disease (CD) is a chronic relapsing intestinal inflammation in genetically susceptible individuals and is influenced by yet unidentified environmental factors. It is hypothesized, in the present review, that Al is a potential factor for induction or maintaining the inflammation in CD. Epidemiologically, CD incidence is higher in urban areas, where microparticle pollution is prevalent. Al immune activities share many characteristics with the immune pathology of CD: increased antigen presentation and APCs activation, many luminal bacterial or dietary compounds can be adsorbed to the metal and induce Th1 profile activity, promotion of humoral and cellular immune responses, proinflammatory, apoptotic, oxidative activity, and stress-related molecule expression enhancement, affecting intestinal bacterial composition and virulence, granuloma formation, colitis induction in an animal model of CD, and terminal ileum uptake. The Al-bacterial interaction, the microparticles homing the intestine together with the extensive immune activity, put Al as a potential environmental candidate for CD induction and maintenance.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17804561>

Effect of alternative aluminum adjuvants on the absorption and immunogenicity of HPV16 L1 VLPs in mice

Author information

Caulfield MJ1, Shi L, Wang S, Wang B,
Tobery TW, Mach H, Ahl PL, Cannon JL,
Cook JC, Heinrichs JH, Sitrin RD.

Vaccine & Biologics Research
Merck Research Laboratories
West Point, Pennsylvania USA
michael_caulfield@merck.com

Abstract

Aluminum adjuvants are commonly used in prophylactic vaccines to enhance antigen immunogenicity through induction of high-titer antibody responses. Three major forms of aluminum adjuvants with substantially different physical and chemical properties have been described: aluminum phosphate (AlPO₄), aluminum hydroxide (Al(OH)₃) and amorphous aluminum hydroxyphosphate sulfate (AAHS). Here we describe the effect of these different aluminum adjuvants on the formulation and subsequent immunogenicity in mice of virus-like particles (VLPs) consisting of the L1 protein of Human Papillomavirus (HPV) Type 16. Electron microscopy demonstrated that the physical appearance of the phosphate-containing aluminum adjuvants was markedly different from that of aluminum hydroxide. All three aluminum adjuvants were found to display unique surface charge profiles over a range of pH, while AAHS demonstrated the greatest inherent capacity for adsorption of L1 VLPs. These differences were associated with differences in immunogenicity: anti-HPV L1 VLP responses from mice immunized with AAHS-formulated HPV16 vaccine were substantially greater than those produced by mice immunized with the same antigen formulated with aluminum hydroxide. In addition, HPV L1 VLPs formulated on AAHS also induced a substantial interferon-gamma secreting T cell response to L1 peptides indicating the potential for an enhanced memory response to this antigen. These results indicate that the chemical composition of aluminum adjuvants can have a profound influence on the magnitude and quality of the immune response to HPV VLP vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/17581283>

“These results indicate that the chemical composition of aluminum adjuvants can have a profound influence on the magnitude and quality of the immune response to HPV VLP vaccines.”

Aluminum: a potential pro-oxidant in sunscreens/sunblocks?

Nicholson S, Exley C.

Scientists at Keele University in Staffordshire have questioned the safety of aluminium added to sunscreens and sunblocks

The researchers, Scott Nicholson, BSc, and Dr Christopher Exley, PhD, Birchall Centre for Inorganic Chemistry and Materials Science at Keele, measured the aluminium content of sunscreens/sunblocks, which either include or do not include an aluminium salt (for example, aluminium hydroxide, aluminium oxide, aluminium silicate, aluminium stearate, aluminium starch octenylsuccinate) as an ingredient.

Aluminium was present in all seven products tested and its content was of particular significance in three products, each of which listed it as an ingredient. Following numerous enquiries the manufacturers were not forthcoming as to the role of aluminium in their product, except one manufacturer, who confirmed that aluminium hydroxide was added to their product to coat the surface and thereby prevent the agglomeration of another ingredient, titanium dioxide particles.

World Health Organisation guidelines recommend a single application of at least 35mL of a sunscreen/sunblock to achieve the stated sun protection factor. For three of the sunscreens/sunblocks investigated a single application of product would result in 200 mg of aluminium being applied to the skin surface. In addition, WHO guidelines suggest re-application of product every two hours which, for example, for an average day on the beach, would result in up to 1g of aluminium being applied to the skin surface.

Skin is permeable to aluminium salts when, for example, they are topically applied as antiperspirant formulations. It will accumulate in the skin and be transported to sites throughout the body. It is highly likely that the everyday use of sunscreens/sunblocks is an hitherto unrecognised contributor of aluminium to the human body burden of this non-essential metal. Perhaps of immediate significance is the potential for aluminium in the skin to act as a pro-oxidant.

Recent research in the journal *Free Radical Biology and Medicine* has shown that UV filters in sunscreens promote the formation of reactive oxygen species (ROS) in the nucleated epidermis of the skin. The authors speculate upon the role which might be played by anti-oxidants, either already in the skin or included in sunscreen formulations, in counteracting the pro-oxidant activities of UV filters though they did not consider how the presence of additional pro-oxidants might exacerbate such effects.

Aluminium is one such pro-oxidant and could significantly increase the potential for oxidative damage in the skin. While the relationship between the burgeoning use of sunscreens/sunblocks and the increased incidence of skin cancers and, in particular, melanoma, is highly controversial it has not hitherto been considered that aluminium in these products could be an extremely significant contributing factor. Of course, aluminium is already in the skin surface and may not need to be a component of sunscreens/sunblocks to exacerbate oxidative damage attributed to the application of such products.

A systems biology approach to the blood-aluminium problem: the application and testing of a computational model

Author information

Beardmore J1, Rugg G, Exley C.

Birchall Centre for Inorganic Chemistry and Materials Science
Lennard-Jones Laboratories, Keele University
Staffordshire ST5 5BG, UK

Abstract

Transport and distribution of systemic aluminium are influenced by its interaction with blood. Current understanding is centred upon the role played by the iron transport protein transferrin which has been shown to bind up to 90% of serum total aluminium. We have coined what we have called the blood-aluminium problem which states that the proportion of serum aluminium which, at any one moment in time, is bound by transferrin is more heavily influenced by kinetic constraints than thermodynamic equilibria with the result that the role played by transferrin in the transport and distribution of aluminium is likely to have been over estimated. To begin to solve the blood-aluminium problem and therewith provide a numerical solution to the aforementioned kinetic constraints we have applied and tested a simple computational model of the time-dependency of a putative transferrin ligand (L) binding aluminium to form an Al-L complex with a probability of existence, $K(E)$, between 0% (no complex) and 100% (complex will not dissociate). The model is based upon the principles of a lattice-gas automaton which when ran for $K(E)$ in the range 0.1-98.0% demonstrated the emergence of complex behaviour which could be defined in the terms of a set of parameters (equilibrium value, $E(V)$, equilibrium time, $E(T)$, peak value, $P(V)$, peak time, $P(T)$, area under curve, AUC) the values of which varied in a predictable way with $K(E)$. When $K(E)$ was set to 98% the model predicted that ca. 90% of the total aluminium would be bound by transferrin within ca. 350 simulation timesteps. We have used a systems biology approach to develop a simple model of the time-dependency of the binding of aluminium by transferrin. To use this approach to begin to solve the blood-aluminium problem we shall need to increase the complexity of the model to better reflect the heterogeneity of a biological system such as the blood.

<http://www.ncbi.nlm.nih.gov/pubmed/17629565>

“Aluminum is a metal with known neurotoxic properties
which are linked to encephalopathy and neurodegenerative diseases.”

Neurotoxicology • November 2007

Occupational aluminum exposure: evidence in support of its neurobehavioral impact

Author information

Meyer-Baron M1, Schäper M, Knapp G, van Thriel C.

Leibniz Research Centre for Working Environment and Human Factors
Ardeystr. 67, 44139 Dortmund, Germany
meyerbaron@ifado.de

Abstract

Aluminum is a metal with known neurotoxic properties which are linked to encephalopathy and neurodegenerative diseases. The objectives of the current meta-analysis study were: (1) to summarize neurobehavioral data obtained by epidemiological studies in occupational settings and (2) to analyze confounding within these data. The meta-analysis was based on estimates of effect sizes. Overall effect sizes were obtained by application of a random effects model. The final sample consisted of nine studies examining 449 exposed and 315 control subjects. The mean urinary aluminum concentrations in the exposed groups ranged from 13 to 133 microg/l. Six neuropsychological tests, which yielded 10 performance variables, were analyzed. Nine overall effect sizes indicated an inferior performance for the exposed group. A significant overall effect size ($d(RE)=-0.43$) was obtained for the digit symbol test measuring speed-related components of cognitive and motor performance. Moreover, the individual effect sizes obtained for this test suggested an exposure-response relationship. Results obtained from either raw or adjusted mean scores revealed that confounding in the data could not be excluded. The results were compared to studies not included here due to a shortage of required data. Similarities were discussed in terms of sensitivity of the tests for detecting aluminum-related changes in brain function. There was concurring evidence from different studies that urinary Al concentrations below 135 microg/l have an impact on cognitive performance. The significant effect for the digit symbol might be related to its multifaceted character which requires functioning in different components of cognitive and motor performance. This feature could possibly turn the test into a screening instrument for neurobehavioral effects. However, additional studies are necessary to verify and to differentiate the effect of aluminum on cognitive performance. From a neuropsychological perspective, implicit and explicit memory, visuo-spatial and central odor processing should be examined. A measure of verbal intelligence should be included in order to address the influence of confounding. Internationally standardized exposure measures would enhance the comparability of studies.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17692380>

Aluminum adjuvant linked to Gulf War illness induces motor neuron death in mice

Author information

Petrik MS1, Wong MC,
Tabata RC, Garry RF, Shaw CA.

Department of Ophthalmology and Program in Neuroscience
University of British Columbia, Vancouver
British Columbia, Canada
mspetrik@interchange.ubc.ca

Abstract

Gulf War illness (GWI) affects a significant percentage of veterans of the 1991 conflict, but its origin remains unknown. Associated with some cases of GWI are increased incidences of amyotrophic lateral sclerosis and other neurological disorders. Whereas many environmental factors have been linked to GWI, the role of the anthrax vaccine has come under increasing scrutiny. Among the vaccine's potentially toxic components are the adjuvants aluminum hydroxide and squalene. To examine whether these compounds might contribute to neuronal deficits associated with GWI, an animal model for examining the potential neurological impact of aluminum hydroxide, squalene, or aluminum hydroxide combined with squalene was developed. Young, male colony CD-1 mice were injected with the adjuvants at doses equivalent to those given to US military service personnel. All mice were subjected to a battery of motor and cognitive-behavioral tests over a 6-mo period postinjections. Following sacrifice, central nervous system tissues were examined using immunohistochemistry for evidence of inflammation and cell death. Behavioral testing showed motor deficits in the aluminum treatment group that expressed as a progressive decrease in strength measured by the wire-mesh hang test (final deficit at 24 wk; about 50%). Significant cognitive deficits in water-maze learning were observed in the combined aluminum and squalene group (4.3 errors per trial) compared with the controls (0.2 errors per trial) after 20 wk. Apoptotic neurons were identified in aluminum-injected animals that showed significantly increased activated caspase-3 labeling in lumbar spinal cord (255%) and primary motor cortex (192%) compared with the controls. Aluminum-treated groups also showed significant motor neuron loss (35%) and increased numbers of astrocytes (350%) in the lumbar spinal cord. The findings suggest a possible role for the aluminum adjuvant in some neurological features associated with GWI and possibly an additional role for the combination of adjuvants.

“Among the vaccine’s potentially toxic components are the adjuvants aluminum hydroxide and squalene. The findings suggest a possible role for the aluminum adjuvant in some neurological features associated with Gulf War Illness and possibly an additional role for the combination of adjuvants.”

Human Health Risk Assessment For Aluminum, Aluminum Oxide, And Aluminum Hydroxide

Author Information

Daniel Krewski,1,2 Robert A Yokel,3 Evert Nieboer,4
David Borchelt,5 Joshua Cohen,6 Jean Harry,7 Sam Kacew,2,8 Joan Lindsay,9
Amal M Mahfouz,10 and Virginie Rondeau11

1. Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
2. McLaughlin Centre for Population Health Risk Assessment, Institute of Population Health, University of Ottawa, Ottawa, Ontario, Canada
3. College of Pharmacy and Graduate Center for Toxicology, University of Kentucky Medical Center, Kentucky, USA
4. Department of Biochemistry and Biomedical Sciences, McMaster University Hamilton, Ontario, Canada and Institute of Community Medicine, University of Tromsø, Norway
5. SantaFe Health Alzheimer's Disease Research Center, Department of Neuroscience, McKnight Brain Institute, University of Florida, USA
6. Institute for Clinical Research and Health Policy Studies, Tufts-New England Medical Center, USA
7. National Institute of Environmental Health Sciences, NIH, Research Triangle Park, NC, USA
8. Department of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Ontario, Canada
9. Aging-Related Diseases Section, Surveillance Division, Public Health Agency of Canada, Ottawa, Ontario, Canada
10. United States Environmental Protection Agency, Washington DC, USA
11. INSERM E0338 (Biostatistic), Université Victor Segalen Bordeaux 2, Bordeaux, France

Corresponding Author: Daniel Krewski
Professor and Director, McLaughlin Centre for Population Health Risk Assessment
University of Ottawa, Room 320, One Stewart Street, Ottawa, Ontario
Tel: 613-562-5381, Fax: 613-562-5380

Findings

“This report classified the weight of evidence for each exposure pathway and health effect as strong, modest, limited, or having no clear evidence (see Table 25). We concluded that there is strong evidence that aluminum can cause irritation following exposure via either inhalation or injection. Modest evidence of an effect exists for reproductive toxicity following oral exposure, for neurological toxicity following either oral or injection exposure, and for bone toxicity following injection exposure.”

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2782734/>

“Modest evidence
of an effect exists for
reproductive toxicity following oral exposure,
for neurological toxicity following either oral or
injection exposure, and for bone toxicity
following injection exposure.”

**Alum adjuvant
boosts adaptive immunity
by inducing uric acid and activating
inflammatory dendritic cells**

Kool M1, Soullié T, van Nimwegen M,
Willart MA, Muskens F, Jung S, Hoogsteden HC,
Hammad H, Lambrecht BN.

Department of Pulmonary Medicine
Erasmus University Medical Centre
3015 GD Rotterdam, Netherlands

Abstract

Alum (aluminum hydroxide) is the most widely used adjuvant in human vaccines, but the mechanism of its adjuvanticity remains unknown. In vitro studies showed no stimulatory effects on dendritic cells (DCs). In the absence of adjuvant, Ag was taken up by lymph node (LN)-resident DCs that acquired soluble Ag via afferent lymphatics, whereas after injection of alum, Ag was taken up, processed, and presented by inflammatory monocytes that migrated from the peritoneum, thus becoming inflammatory DCs that induced a persistent Th2 response. The enhancing effects of alum on both cellular and humoral immunity were completely abolished when CD11c(+) monocytes and DCs were conditionally depleted during immunization. Mechanistically, DC-driven responses were abolished in MyD88-deficient mice and after uricase treatment, implying the induction of uric acid. These findings suggest that alum adjuvant is immunogenic by exploiting “nature’s adjuvant,” the inflammatory DC through induction of the endogenous danger signal uric acid.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18362170>

“Alum (aluminum hydroxide)
is the most widely used adjuvant
in human vaccines, but the mechanism
of its adjuvanticity remains unknown.”

Late-onset
vaccination-induced
subcutaneous pseudolymphoma

Author information

Croce S1, Lhermitte B, Tomasetto C,
Guillard O, Bellocq JP, Chenard MP.

Département de Pathologie
CHU de Strasbourg, hôpital de Hautepierre
1 avenue Molière, 67098 Strasbourg cedex, France

Abstract

Persistent subcutaneous nodules arise on rare occasions at sites of injection of aluminium hydroxide-adsorbed vaccine. We report a case following a diphtheria, tetanus and pertussis vaccination. The late onset of the lesion, four years after the injection, led to an uncertain preoperative diagnosis. Histopathologic examination showed features of a subcutaneous pseudolymphoma. The demonstration of aluminium by Morin staining and atomic absorption spectrometry on a paraffin-embedded tissue probe supported the diagnosis of a vaccination-induced pseudolymphoma.

<http://www.ncbi.nlm.nih.gov/pubmed/18675172>

“The late onset of the lesion,
four years after the injection,
led to an uncertain preoperative diagnosis.”

Effects of aluminium sulphate in the mouse liver: similarities to the aging process

Author information

Stacchiotti A1, Lavazza A,
Ferroni M, Sberveglieri G,
Bianchi R, Rezzani R, Rodella LF.

Department of Biomedical Sciences and Biotechnologies
Brescia University, Brescia, Italy
stacchio@med.unibs.it

Abstract

Aluminium (Al) is a ubiquitous metal that is potentially toxic to the brain. Its effects on other fundamental organs are not completely understood. This morphological *in vivo* study sought to compare sublethal hepatotoxic changes and Al deposition in adult mice that orally ingested Al sulphate daily for 10 months, in age matched control mice that drank tap water and in senescent mice (24 months old). Livers were examined for collagen deposition using Sirius red and Masson, for iron accumulation using Perls' stain. Light, electron microscopy and morphometry were used to assess fibrosis and vascular changes. Scanning transmission electron microscopy and EDX microanalysis were used to detect *in situ* elemental Al. Iron deposition, transferrin receptor expression were significantly altered following Al exposure and in the aged liver but were unaffected in age matched control mice. In Al treated mice as in senescent mice, endothelial thickness was increased and porosity was decreased like perisinusoidal actin. Furthermore, Al stimulated the deposition of collagen and laminin, mainly in acinar zones 1 and 3. Pseudocapillarization and periportal laminin in senescent mice were similar to Al treated adult liver. In conclusion, prolonged Al sulphate intake accelerates features of senescence in the adult mice liver.

<http://www.ncbi.nlm.nih.gov/pubmed/18337038>

“Aluminium (Al) is a ubiquitous metal
that is potentially toxic to the brain ... prolonged
Al sulphate intake accelerates features of
senescence in the adult mice liver.”

B-cell pseudolymphoma caused by aluminium hydroxide following hyposensitization therapy

Author information

Hernández I1, Sanmartín O,
Cardá C, Góme S, Alfaro A.

Servicio de Dermatología
Hospital General Básico de la Defensa de Valencia
España

Abstract

Aluminium hydroxide is used as an adjuvant in vaccines. We describe the case of a patient who presented a persistent adverse local reaction to aluminium hydroxide due to hyposensitization therapy to dust mites. Multiple painful and pruriginous subcutaneous nodules were observed in both arms, along with hypertrichosis at the injection site. Histology revealed a pseudolymphomatous B cell reaction predominantly involving cells that were CD20 positive, did not express bcl-2, and did not display the t(14-18) translocation. The cells also exhibited polyclonal rearrangement of the immunoglobulin heavy chains. X-ray spectral microanalysis revealed deposits of inorganic aluminium in the granular histiocytes among the germinal centers. The patient was diagnosed with cutaneous B-cell pseudolymphoma due to aluminium hydroxide as a result of immunotherapy.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18358197>

“The patient was diagnosed with
cutaneous B-cell pseudolymphoma
due to aluminium hydroxide ...”

Alum boosts TH2-type antibody responses to whole-inactivated virus influenza vaccine in mice but does not confer superior protection

Author information

Bungener L1, Geeraedts F, Ter Veer W, Medema J, Wilschut J, Huckriede A.

Department of Medical Microbiology, Molecular Virology Section
University Medical Center Groningen and University of Groningen
Postbus 30.001, 9700 RB Groningen, The Netherlands

Abstract

Clinical trials with pandemic influenza vaccine candidates have focused on aluminium hydroxide as an adjuvant to boost humoral immune responses. In this study we investigated the effect of aluminium hydroxide on the magnitude and type of immune response induced by whole-inactivated virus (WIV) vaccine. Balb/c mice were immunized once with a range of antigen doses (0.04-5 microg) of WIV produced from A/PR/8 virus, either alone or in combination with aluminium hydroxide. The hemagglutination inhibition (HI) titers of mice receiving WIV+aluminium hydroxide were 4-16-fold higher than HI titers in mice receiving the same dose of WIV alone, indicating the boosting effect of aluminium hydroxide. WIV induced a TH1 skewed humoral and cellular immune response, characterized by strong influenza-specific IgG2a responses and a high number of IFN γ -secreting T cells. In contrast, immunization with WIV adsorbed to aluminium hydroxide resulted in skewing of this response to a TH2 phenotype (high IgG1 levels and a low number of IFN γ -producing T cells). To assess the effect of the observed immune response skewing on viral clearance from the lungs mice immunized once with 1 microg WIV without or with aluminium hydroxide were challenged with A/PR/8 virus 4 weeks later. The immunized mice showed a significant decrease in viral lung titers compared to control mice receiving buffer. However, despite higher antibody titers, mice immunized with WIV adsorbed to aluminium hydroxide suffered from more severe weight loss and had significantly higher virus loads in their lung tissue than mice receiving WIV alone. Major difference between these groups of mice was the type of immune response induced, TH2 instead of TH1, indicating that a TH1 response plays a major role in viral clearance.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18400340>

“despite higher antibody titers, mice immunized with whole-inactivated virus adsorbed to aluminium hydroxide suffered from more severe weight loss and had significantly higher virus loads in their lung tissue than mice receiving whole-inactivated virus alone.”

Aluminum bioavailability
from basic sodium aluminum phosphate,
an approved food additive emulsifying agent,
incorporated in cheese

Author information

Yokel RA1, Hicks CL, Florence RL.

Department of Pharmaceutical Sciences
College of Pharmacy
University of Kentucky Academic Medical Center
511C Pharmacy Building, 725 Rose Street
Lexington, KY 40536-0082, USA
ryokel@email.uky.edu

Abstract

Oral aluminum (Al) bioavailability from drinking water has been previously estimated, but there is little information on Al bioavailability from foods. It was suggested that oral Al bioavailability from drinking water is much greater than from foods. The objective was to further test this hypothesis. Oral Al bioavailability was determined in the rat from basic [²⁶Al]-sodium aluminum phosphate (basic SALP) in a process cheese. Consumption of approximately 1g cheese containing 1.5% or 3% basic SALP resulted in oral Al bioavailability (F) of approximately 0.1% and 0.3%, respectively, and time to maximum serum ²⁶Al concentration (T_{max}) of 8-9h. These Al bioavailability results were intermediate to previously reported results from drinking water (F approximately 0.3%) and acidic-SALP incorporated into a biscuit (F approximately 0.1%), using the same methods. Considering the similar oral bioavailability of Al from food vs. water, and their contribution to the typical human's daily Al intake (approximately 95% and 1.5%, respectively), these results suggest food contributes much more Al to systemic circulation, and potential Al body burden, than does drinking water. These results do not support the hypothesis that drinking water provides a disproportionate contribution to total Al absorbed from the gastrointestinal tract.

<http://www.ncbi.nlm.nih.gov/pubmed/18436363>

“these results suggest
food contributes much more Al
to systemic circulation, and
potential Al body burden,
than does drinking water.”

Macrophagic myofasciitis in children is a localized reaction to vaccination

Author information

Lach B1, Cupler EJ.

Department of Pathology and Laboratory Medicine
King Faisal Specialist Hospital and Research Center
Riyadh, Saudi Arabia
boleklach2@hotmail.com

Abstract

Macrophagic myofasciitis is a novel, “inflammatory myopathy” described after a variety of vaccinations, almost exclusively in adults. We examined the relevance of histological findings of this myopathy to the clinical presentation in pediatric patients. Muscle biopsies from 8 children (7 months to 6 years old) with histological features of macrophagic myofasciitis were reviewed and correlated with the clinical manifestations. Patients underwent quadriceps muscle biopsy for suspected mitochondrial disease (4 patients), spinal muscular atrophy (2 patients), myoglobinuria (1 patient), and hypotonia with motor delay (1 patient). All biopsies showed identical granulomas composed of periodic acid-Schiff-positive and CD68-positive macrophages. Characteristic aluminum hydroxide crystals were identified by electron microscopy in 2 cases. The biopsy established diagnoses other than macrophagic myofasciitis in 5 patients: spinal muscular atrophy (2), Duchenne muscular dystrophy (1), phospho-glycerate kinase deficiency (1), and cytochrome c oxidase deficiency (1). Three children with manifestations and/or a family history of mitochondrial disease had otherwise morphologically normal muscle. All children had routine vaccinations between 2 months and 1 year before the biopsy, with up to 11 intramuscular injections, including the biopsy sites. There was no correlation between histological findings of macrophagic myofasciitis in biopsies and the clinical symptoms. We believe that macrophagic myofasciitis represents a localized histological hallmark of previous immunization with the aluminum hydroxide adjuvants contained in vaccines, rather than a primary or distinct inflammatory muscle disease.

<http://www.ncbi.nlm.nih.gov/pubmed/18281624>

“We believe
that macrophagic myofasciitis
represents a localized histological
hallmark of previous immunization
with the aluminum hydroxide adjuvants
contained in vaccines, rather than a primary
or distinct inflammatory muscle disease.”

Impairment of mitochondrial energy metabolism in different regions of rat brain following chronic exposure to aluminium

Author information

Kumar V1, Bal A, Gill KD.

Department of Biochemistry
Postgraduate Institute of Medical Education and Research
Chandigarh, 160 012, India

Abstract

The present study was designed with an aim to evaluate the effects of chronic aluminium exposure (10 mg/kg b.wt, intragastrically for 12 weeks) on mitochondrial energy metabolism in different regions of rat brain in vivo. Mitochondrial preparations from aluminium treated rats revealed significant decrease in the activity of various electron transport complexes viz. cytochrome oxidase, NADH cytochrome c reductase and succinic dehydrogenase as well, in the hippocampus region. The decrease in the activity of these respiratory complexes was also seen in the other two regions viz. corpus striatum and cerebral cortex, but to a lesser extent. This decrease in the activities of electron transport complexes in turn affected the ATP synthesis and ATP levels adversely in the mitochondria isolated from aluminium treated rat brain regions. We also studied the spectral properties of the mitochondrial cytochromes viz. cyt a, cyt b, cyt c1, and cyt c in both control and treated rat brains. The various cytochrome levels were found to be decreased following 12 weeks of aluminium exposure. Further, these impairments in mitochondrial functions may also be responsible for the production of reactive oxygen species and impaired antioxidant defense system as observed in our study. The electron micrographs of neuronal cells depicted morphological changes in mitochondria as well as nucleus only from hippocampus and corpus striatum regions following 12 weeks exposure to aluminium. The present study thus highlights the significance of altered mitochondrial energy metabolism and increased ROS production as a result of chronic aluminium exposure in different regions of the rat brain.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18691561>

“The present study
thus highlights the significance
of altered mitochondrial energy metabolism
and increased ROS production as a result of
chronic aluminium exposure in different
regions of the rat brain.”

“Select human population can be at risk of Aluminum neurotoxicity,
and Aluminum is proposed to be involved in the etiology of neurodegenerative diseases.”

Archives Of Toxicology • November 2008

Aluminium and lead: molecular mechanisms of brain toxicity

Author information

Verstraeten SV1, Aimo L, Oteiza PI.

Department of Biological Chemistry, IIMHNO (UBA) and IQUIFIB (UBA-CONICET)
School of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina

Abstract

The fact that aluminium (Al) and lead (Pb) are both toxic metals to living organisms, including human beings, was discovered a long time ago. Even when Al and Pb can reach and accumulate in almost every organ in the human body, the central nervous system is a particular target of the deleterious effects of both metals. Select human population can be at risk of Al neurotoxicity, and Al is proposed to be involved in the etiology of neurodegenerative diseases. Pb is a widespread environmental hazard, and the neurotoxic effects of Pb are a major public health concern. In spite of the numerous efforts and the accumulating evidence in this area of research, the mechanisms of Al and Pb neurotoxicity are still not completely elucidated. This review will particularly address the involvement of oxidative stress, membrane biophysics alterations, deregulation of cell signaling, and the impairment of neurotransmission as key aspects involved Al and Pb neurotoxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/18668223>

“Aluminium has been implicated in various neurodegenerative diseases
but exact mechanism of action is still not known.”

Toxicology • January 2009

Susceptibility of mitochondrial superoxide dismutase to aluminium induced oxidative damage

Author information

Kumar V1, Bal A, Gill KD.

Department of Biochemistry
Postgraduate Institute of Medical Education and Research
Chandigarh 160012, India

Abstract

Aluminium has been implicated in various neurodegenerative diseases but exact mechanism of action is still not known. Mitochondria being a major site of reactive oxygen species production are considered to be target of oxidative stress and it seems that the oxidative damage to mitochondrial proteins may underlie the pathogenesis of aluminium induced neurodegeneration. Thus, the present study was undertaken to reveal the effects of chronic aluminium exposure (10mg/kg b.wt, intragastrically for 12 weeks) on the oxidative damage to mitochondrial proteins in male albino Wistar rats. Chronic aluminium exposure resulted in decrease in the activity of mitochondrial superoxide dismutase (MnSOD) and aconitase in different regions of rat brain suggesting increased oxidative stress. This decrease in MnSOD activity in turn might be responsible for the increased protein oxidation as observed in our study. All these processes taken together may cause increased oxidative damage to mitochondrial proteins in general. By taking the advantage of recent immunochemical probe for oxidatively modified proteins, we identified MnSOD to be susceptible to oxidative damage in aluminium treated animals. The quantitative RT-PCR analysis for Lon protease, a protease involved in the removal of oxidatively modified proteins from mitochondria, showed decreased mRNA expression suggesting increased oxidative damage and decreased removal of mitochondrial proteins. The identification of specific proteins as targets of oxidative damage may provide new therapeutic measures to reverse the effects of aluminium induced neurodegeneration.

<http://www.ncbi.nlm.nih.gov/pubmed/19010380>

A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome

Author information

Exley C1, Swarbrick L, Gherardi RK, Authier FJ.

Birchall Centre for Inorganic Chemistry and Materials Science
Keele University, Staffordshire ST5 5BG, UK
c.exley@chem.keele.ac.uk

Abstract

Macrophagic myofasciitis and chronic fatigue syndrome are severely disabling conditions which may be caused by adverse reactions to aluminium-containing adjuvants in vaccines. While a little is known of disease aetiology both conditions are characterised by an aberrant immune response, have a number of prominent symptoms in common and are coincident in many individuals. Herein, we have described a case of vaccine-associated chronic fatigue syndrome and macrophagic myofasciitis in an individual demonstrating aluminium overload. This is the first report linking the latter with either of these two conditions and the possibility is considered that the coincident aluminium overload contributed significantly to the severity of these conditions in this individual. This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis.

<http://www.ncbi.nlm.nih.gov/pubmed/19004564>

“This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis.”

Guest editorial
‘The natural history of aluminium:
from non-selection to natural selection’.

Author Information

Christopher Exley

Keele University
Birchall Centre for Inorganic Chemistry and Materials Science
Lennard-Jones Laboratories, Keele
Staffordshire ST5 5BG, UK

Abstract

“Al accumulates in the body with age and particularly so when exposure is high and/or protective gastrointestinal mechanisms are bypassed or renal function is impaired (Kisters et al., 1999). Al toxicity in humans, even at low levels of exposure (Exley, 2009b), is a well-established fact and the brain is a target organ for Al to exert its deleterious effects (Exley et al., 1996; Exley, 1999; Yokel et al., 1999). The molecular mechanisms of Al neurotoxicity are not completely understood: Al has been reported to alter the blood-brain barrier (Zatta et al., 2003) and is deposited in the human brain (Exley and House, 2011). “

“Aluminum toxicity in humans, even at low levels of exposure, is a well-established fact and the brain is a target organ for Aluminum to exert its deleterious effects. The molecular mechanisms of Al neurotoxicity are not completely understood: Aluminum has been reported to alter the blood-brain barrier and is deposited in the human brain ...”

“... our findings indicate that fatty acids common in food increase the paracellular intestinal absorption of Aluminum.”

Chemical-Biological Interactions • October 2009

Fatty acids increase paracellular absorption of aluminium across Caco-2 cell monolayers

Author information

Aspenström-Fagerlund B1, Sundström B,
Tallkvist J, Ilbäck NG, Glynn AW.

Toxicology Division
National Food Administration
Uppsala, Sweden
bfas@slv.se

Abstract

Passive paracellular absorption, regulated by tight junctions (TJs), is the main route for absorption of poorly absorbed hydrophilic substances. Surface active substances, such as fatty acids, may enhance absorption of these substances by affecting the integrity of TJ and increasing the permeability. It has been suggested that aluminium (Al) absorption occurs mainly by the paracellular route. Herein, we investigated if physiologically relevant exposures of fully differentiated Caco-2 cell monolayers to oleic acid and docosahexaenoic acid (DHA), which are fatty acids common in food, increase absorption of Al and the paracellular marker mannitol. In an Al toxicity test, mannitol and Al absorption through Caco-2 cell monolayers were similarly modulated by Al concentrations between 1 and 30mM, suggesting that absorption of the two compounds occurred via the same pathways. Exposure of Caco-2 cell monolayers to non-toxic concentrations of Al (2mM) and (14)C-mannitol in fatty acid emulsions (15 and 30mM oleic acid, 5 and 10mM DHA) caused a decreased transepithelial electrical resistance (TEER). Concomitantly, fractional absorption of Al and mannitol, expressed as percentage of apical Al and mannitol retrieved at the basolateral side, increased with increasing dose of fatty acids. Transmission electron microscopy was applied to assess the effect of oleic acid on the morphology of TJ. It was shown that oleic acid caused a less structured morphology of TJ in Caco-2 cell monolayers. Taken together our findings indicate that fatty acids common in food increase the paracellular intestinal absorption of Al. These findings may influence future risk assessment of human Al exposure.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19576870>

Aluminium neurotoxicity: neurobehavioural and oxidative aspects

Author information

Kumar V1, Gill KD.

Abstract

Aluminium is the most widely distributed metal in the environment and is extensively used in daily life that provides easy exposure to human beings. The exposure to this toxic metal occurs through air, food and water. However, there is no known physiological role for aluminium within the body and hence this metal may produce adverse physiological effects. Chronic exposure of animals to aluminium is associated with behavioural, neuropathological and neurochemical changes. Among them, deficits of learning and behavioural functions are most evident. Some epidemiological studies have shown poor performance in cognitive tests and a higher abundance of neurological symptoms for workers occupationally exposed to aluminium. However, in contrast to well established neurotoxic effects, neurobehavioural studies of aluminium in rodents have generally not produced consistent results. Current researches show that any impairment in mitochondrial functions may play a major role in many human disorders including neurodegenerative disorders. Being involved in the production of reactive oxygen species, aluminium may cause impairments in mitochondrial bioenergetics and may lead to the generation of oxidative stress which may lead to a gradual accumulation of oxidatively modified cellular proteins. In this review, the neuropathologies associated with aluminium exposure in terms of neurobehavioural changes have been discussed. In addition, the impact of aluminium on the mitochondrial functions has also been highlighted.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19568732>

“Aluminium is the most widely distributed metal in the environment and is extensively used in daily life that provides easy exposure to human beings. The exposure to this toxic metal occurs through air, food and water. However, there is no known physiological role for aluminium within the body and hence this metal may produce adverse physiological effects. Chronic exposure of animals to aluminium is associated with behavioural, neuropathological and neurochemical changes. Among them, deficits of learning and behavioural functions are most evident.”

Long-term persistence of vaccine-derived aluminum hydroxide is associated with chronic cognitive dysfunction

Author information

Couette M1, Boisse MF, Maison P, Brugieres P, Cesaro P,
Chevalier X, Gherardi RK, Bachoud-Levi AC, Authier FJ.

INSERM, Unite U955, Team 1, Creteil F-94010, France

Abstract

Macrophagic myofasciitis (MMF) is an emerging condition, characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients mainly complain of arthromyalgias, chronic fatigue, and cognitive difficulties. We designed a comprehensive battery of neuropsychological tests to prospectively delineate MMF-associated cognitive dysfunction (MACD). Compared to control patients with arthritis and chronic pain, MMF patients had pronounced and specific cognitive impairment. MACD mainly affected (i) both visual and verbal memory; (ii) executive functions, including attention, working memory, and planning; and (iii) left ear extinction at dichotic listening test. Cognitive deficits did not correlate with pain, fatigue, depression, or disease duration. Pathophysiological mechanisms underlying MACD remain to be determined. In conclusion, long-term persistence of vaccine-derived aluminum hydroxide within the body assessed by MMF is associated with cognitive dysfunction, not solely due to chronic pain, fatigue and depression.

<http://www.ncbi.nlm.nih.gov/pubmed/19748679>

“In conclusion, long-term persistence
of vaccine-derived aluminum hydroxide
within the body assessed by MMF is associated
with cognitive dysfunction, not solely due to chronic pain,
fatigue and depression.”

Aluminum hydroxide injections ‘ lead to motor deficits and motor neuron degeneration

Author information

Shaw CA1, Petrik MS.

Departments of Ophthalmology and Visual Sciences
University of British Columbia, Vancouver
British Columbia, Canada
cashawlab@gmail.com

Abstract

Gulf War Syndrome is a multi-system disorder afflicting many veterans of Western armies in the 1990-1991 Gulf War. A number of those afflicted may show neurological deficits including various cognitive dysfunctions and motor neuron disease, the latter expression virtually indistinguishable from classical amyotrophic lateral sclerosis (ALS) except for the age of onset. This ALS “cluster” represents the second such ALS cluster described in the literature to date. Possible causes of GWS include several of the adjuvants in the anthrax vaccine and others. The most likely culprit appears to be aluminum hydroxide. In an initial series of experiments, we examined the potential toxicity of aluminum hydroxide in male, outbred CD-1 mice injected subcutaneously in two equivalent-to-human doses. After sacrifice, spinal cord and motor cortex samples were examined by immunohistochemistry. Aluminum-treated mice showed significantly increased apoptosis of motor neurons and increases in reactive astrocytes and microglial proliferation within the spinal cord and cortex. Morin stain detected the presence of aluminum in the cytoplasm of motor neurons with some neurons also testing positive for the presence of hyper-phosphorylated tau protein, a pathological hallmark of various neurological diseases, including Alzheimer’s disease and frontotemporal dementia. A second series of experiments was conducted on mice injected with six doses of aluminum hydroxide. Behavioural analyses in these mice revealed significant impairments in a number of motor functions as well as diminished spatial memory capacity. The demonstrated neurotoxicity of aluminum hydroxide and its relative ubiquity as an adjuvant suggest that greater scrutiny by the scientific community is warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/19740540>

“Possible causes
of Gulf War Syndrome include
several of the adjuvants in the anthrax vaccine
and others. The most likely culprit
appears to be aluminum hydroxide.”

Glia activation induced by peripheral administration of aluminum oxide nanoparticles in rat brains

Author information

Li XB1, Zheng H, Zhang ZR, Li M,
Huang ZY, Schluesener HJ, Li YY, Xu SQ.

MOE Key Lab, Institute of Environmental Medicine
School of Public Health, Tongji Medical College
Huazhong University of Science and Technology
Wuhan, China

Abstract

With the wide application of nanoscaled particles, the risk of human exposure to these particles has been markedly increased. However, knowledge about their safety falls far behind the utility of these nanoparticles. Here we have analyzed the activation of brain microglia and astrocytes, which are sensitive to changes of brain environment after peripheral exposure to nanoscaled aluminum oxide suspension. Sprague-Dawley rats (six rats per treatment) were intraperitoneally injected once every second day for 30 or 60 days with nanoscaled aluminum oxide (NSAO; 1 mg/kg or 50 mg/kg), non-nanoscaled aluminum oxide (nNSAO, 1 mg/kg), or vehicle (saline). After 60 days' exposure the numbers of ED1+, GFAP+, and nestin+ cells in cortex and hippocampus were significantly higher in NSAO-treated rats than nNSAO- or vehicle-treated rats; thus, compared with nNSAO, NSAO has potential effects on the innate immune system of rat brain. This should be considered when evaluating the toxicological effects of nanosized particles.

From The Clinical Editor

Sprague-Dawley rats were intraperitoneally injected with nanosized aluminum oxide, (NSAO); non-nanoscaled aluminum oxide, or vehicle (saline). The numbers of ED1+, GFAP+, and nestin+ cells in cortex and hippocampus were significantly higher in NSAO-treated rats than nNSAO- or vehicle-treated rats; thus, NSAO has potential effects on the innate immune system of rat brain.

<http://www.ncbi.nlm.nih.gov/pubmed/19523415>

“With the wide application of nanoscaled particles, the risk of human exposure to these particles has been markedly increased. However, knowledge about their safety falls far behind the utility of these nanoparticles ... [aluminum] has potential effects on the innate immune system of rat brain.”

Darwin, natural selection and the biological essentiality of aluminium and silicon

by Christopher Exley

The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, UK

Abstract

If one was asked to produce a set of ‘Trump Cards™’ based upon ‘Forces of Nature Defining Life on Earth’ then which card would be ‘Top Trump’? I was recently chastised on the Darwin Today website for suggesting Darwin and ‘natural selection’ rather than, for example, Newton and ‘gravity’. Although there is no denying the significance of gravity, my argument in favour of natural selection is simply that gravity is just one factor that contributes towards an outcome which ultimately is defined by natural selection. Both the beauty and the brilliance of natural selection are reflected in its omnipotence to explain the myriad observations of life and, as I will affirm herein, its explanation of the biological essentiality of aluminium and silicon is no exception.

Together they constitute a form of homeostasis with aluminium being retained both physically and chemically in myriad forms and each form being capable of acting as a sink or source of labile and potentially biologically reactive aluminium. It is always important to emphasise that there is no evolutionarily directed or conserved biology to enable aluminium homeostasis and so this non-essential but highly biologically reactive metal cation is at the whim of the predominant or pre-eminent chemistry of any particular environment [8] [9]. This unpredictability makes biologically available aluminium a concern for all forms of life on Earth [2].

In this year, 200th anniversary of the birth of Charles Darwin and the 150th anniversary of the publication of *On the Origin of Species*, a UK scientist has used Darwin’s seminal work on Natural Selection in helping to define the biological essentiality of the second (silicon) and third (aluminium) most abundant elements of the Earth’s crust.

The lack of any clear or significant biological essentiality for both of these elements is a mystery as all other abundant elements of the Earth’s crust are known to be biologically essential.

Dr Chris Exley, Reader in Bioinorganic Chemistry at Keele University and a world authority on the ways in which aluminium impacts upon life on Earth, says natural selection is often interpreted as ‘survival of the fittest’ but what is often not appreciated is that the selection processes themselves are niche driven, which

means that those characteristics which convey fitness in one environment may not convey fitness in another, perhaps adjacent, environment or niche. This is both the strength and the beauty of natural selection and it can be applied to cellular biochemistry as it is applied to speciation of organisms.

Aluminium is biologically reactive, while silicon is biologically inert. Natural selection informs us that the non-essentiality of aluminium is explained by its non-participation in biochemical evolution due to a complete lack of its biologically reactive forms.

On the other hand the biologically available form of silicon (silicic acid) has been extremely abundant throughout biochemical evolution and its biological essentiality has been dictated by its extremely limited biological reactivity.

It is no coincidence that one of the very few reactions of silicic acid is that with aluminium and that this reaction protects against the toxicity of aluminium.

An essential role of silicon throughout biochemical evolution has been to keep aluminium out of life! However, the activities of humans in learning how to extract aluminium from its ores and using it in myriad ways in what is now the Aluminium Age means that Earth’s inherent protection against the toxicity of aluminium is being compromised and that biologically reactive aluminium is now an active participant in biochemical (and hence human) evolution.

Some of the early results of the arrival of biochemically reactive aluminium have been worryingly obvious, including the death of fish and trees in geographical regions impacted by acid deposition, whereas others, and perhaps those which in particular are linked with the human condition, might yet be too subtle to be directly attributable to the participation of biologically-reactive aluminium in the natural selection of the elements of biological essentiality.

Link: I can’t provide a link for this report and I’m certain that this is not the complete report. The text above consists of excerpts found in other reports that reference this one using a variety of internet search terms. The complete document requires purchase:

“This unpredictability
makes biologically
available aluminium
a concern for all forms
of life on Earth.”

The immunobiology of aluminium adjuvants: how do they really work?

Author information

Exley C1, Siesjö P, Eriksson H.

The Birchall Centre
Lennard-Jones Laboratories
Keele University, Staffordshire, ST5 5BG, UK
c.exley@chem.keele.ac.uk

Abstract

Aluminium adjuvants potentiate the immune response, thereby ensuring the potency and efficacy of typically sparingly available antigen. Their concomitant critical importance in mass vaccination programmes may have prompted recent intense interest in understanding how they work and their safety. Progress in these areas is stymied, however, by a lack of accessible knowledge pertaining to the bioinorganic chemistry of aluminium adjuvants, and, consequently, the inappropriate application and interpretation of experimental models of their mode of action. The objective herein is, therefore, to identify the many ways that aluminium chemistry contributes to the wide and versatile armoury of its adjuvants, such that future research might be guided towards a fuller understanding of their role in human vaccinations.

<http://www.ncbi.nlm.nih.gov/pubmed/20153253>

“Progress in these areas [aluminum research] is stymied, however, by a lack of accessible knowledge pertaining to the bioinorganic chemistry of aluminium adjuvants, and, consequently, the inappropriate application and interpretation of experimental models of their mode of action.”

“Preterm neonates receiving parenteral nutrition are at risk of aluminum overload because of the presence of aluminum as a contaminant in parenteral formulations. Despite US Food and Drug Administration regulation, commercial products continue to present Al contamination. Moreover, premature neonates were receiving, on average, 3 times the amount considered by the Food and Drug Administration as a safe limit.”

Journal Of Pediatric Gastroenterology And Nutrition • August 2010

Aluminum loading in preterm neonates revisited

Author information

Bohrer DI, Oliveira SM, Garcia SC,
Nascimento PC, Carvalho LM.

Department of Chemistry
Universidade Federal de Santa Maria
Santa Maria, RS, Brazil
ndenise@quimica.ufsm.br

Abstract

Preterm neonates receiving parenteral nutrition are at risk of aluminum (Al) overload because of the presence of Al as a contaminant in parenteral formulations. Despite US Food and Drug Administration regulation, commercial products continue to present Al contamination. To reassess Al exposure in the premature neonatal population, the present study evaluated the Al balance (intake vs urinary excretion) in a group of preterm neonates during the period in which they stayed in the intensive care unit (NICU) under total parenteral nutrition. For the 10 patients selected, daily infusion solutions (nutrition and medication) were collected and the level of Al contamination was measured. From the urine collected daily, an aliquot was taken for Al determination. Blood was also collected for Al determination on the first and last day in the NICU. The measurements were carried out by atomic absorption spectrometry. The difference between Al administered and excreted revealed that 56.2% +/- 22.7% of the Al intake was not eliminated. The mean serum Al levels from the first to the last day decreased from 41.2 +/- 23.3 to 23.5 +/- 11.2 microg/L. The resulting mean Al daily intake of the 10 patients was 15.2 +/- 8.0 microg x kg(-1) x day(-1). Because Al intake was higher than that excreted and Al in serum decreased to practically half during the period in the NICU (+/-7.3 days), some amount of Al deposition occurred. Moreover, premature neonates were receiving, on average, 3 times the amount of 5 microg x kg(-1) x day(-1), considered by the Food and Drug Administration as a safe limit.

“... the vulnerability of infants to early exposure to aluminium serves to highlight an urgent need to reduce the aluminium content of infant formulas ...”

BMC Pediatrics • August 2010

There is (still) too much aluminium in infant formulas

Author information

Burrell SA1, Exley C.
The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, UK

Abstract

BACKGROUND

Infant formulas are sophisticated milk-based feeds for infants which are used as a substitute for breast milk. Historically they are known to be contaminated by aluminium and in the past this has raised health concerns for exposed infants. We have measured the aluminium content of a number of widely used infant formulas to determine if their contamination by aluminium and consequent issues of child health persists.

METHODS

Samples of ready-made milks and powders used to make milks were prepared by microwave digestion of acid/peroxide mixtures and their aluminium content determined by THGA.

RESULTS

The concentration of aluminium in ready-made milks varied from ca 176 to 700 $\mu\text{g/L}$. The latter concentration was for a milk for preterm infants. The aluminium content of powders used to make milks varied from ca 2.4 to 4.3 $\mu\text{g/g}$. The latter content was for a soya-based formula and equated to a ready-to-drink milk concentration of 629 $\mu\text{g/L}$. Using the manufacturer's own guidelines of formula consumption the average daily ingestion of aluminium from infant formulas for a child of 6 months varied from ca 200 to 600 μg of aluminium. Generally ingestion was higher from powdered as compared to ready-made formulas.

CONCLUSIONS

The aluminium content of a range of well known brands of infant formulas remains high and particularly so for a product designed for preterm infants and a soya-based product designed for infants with cow's milk intolerances and allergies. Recent research demonstrating the vulnerability of infants to early exposure to aluminium serves to highlight an urgent need to reduce the aluminium content of infant formulas to as low a level as is practically possible.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2939626/>

The neurotoxicity of environmental aluminum is still an issue

Author information

Bondy SC.

Program in Environmental Toxicology
Division Occupational and Environmental Health
Department of Medicine, University of California
Irvine, CA 92697-1825, USA
scbondy@uci.edu

Abstract

Evidence for the neurotoxicity of extended exposure to low levels of aluminum salts is described using an animal model treated with aluminum at low levels reflecting those found in some water supplies. Emphasis is given to the potential role of aluminum in acceleration and promotion of some indices characteristic of brain aging. These hallmarks include the appearance of excess levels of inflammation in specific brain areas. Aluminum salts can increase levels of glial activation, inflammatory cytokines and amyloid precursor protein within the brain. Both normal brain aging and to a greater extent, Alzheimer's disease are associated with elevated basal levels of markers for inflammation. These are not attributable to obvious exogenous stimuli and may reflect the lifespan history of the organism's immune responses. It is possible that aluminum salts can act as a subtle promoter of such apparently unprovoked responses.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20553758>

“Emphasis is given to the potential role of aluminum in acceleration and promotion of some indices characteristic of brain aging. These hallmarks include the appearance of excess levels of inflammation in specific brain areas.”

Infants' exposure to aluminum from vaccines and breast milk during the first 6 months

Author information

Dórea JG1, Marques RC.

Department of Nutrition
Universidade de Brasília
Brasília, DF, Brazil
dorea@rudah.com.br

Abstract

The success of vaccination programs in reducing and eliminating infectious diseases has contributed to an ever-increasing number of vaccines given at earlier ages (newborns and infants). Exposure to low levels of environmental toxic substances (including metals) at an early age raises plausible concerns over increasingly lower neuro-cognitive rates. Current immunization schedules with vaccines containing aluminum (as adjuvant) are given to infants, but thimerosal (as preservative) is found mostly in vaccines used in non-industrialized countries. Exclusively, breastfed infants (in Brazil) receiving a full recommended schedule of immunizations showed an exceedingly high exposure of Al (225 to 1750 μg per dose) when compared with estimated levels absorbed from breast milk (2.0 μg). This study does not dispute the safety of vaccines but reinforces the need to study long-term effects of early exposure to neuro-toxic substances on the developing brain. Pragmatic vaccine safety needs to embrace conventional toxicology, addressing especial characteristics of unborn fetuses, neonates and infants exposed to low levels of aluminum, and ethyl-mercury traditionally considered innocuous to the central nervous system.

<http://www.ncbi.nlm.nih.gov/pubmed/20010978>

“Exclusively, breastfed infants (in Brazil) receiving a full recommended schedule of immunizations showed an exceedingly high exposure of Aluminum (225 to 1750 μg per dose) when compared with estimated levels absorbed from breast milk (2.0 μg).”

Effects of ethylene glycol ethers on cell viability in the human neuroblastoma SH-SY5Y cell line

Author information

Regulska M1, Pomierny B, Basta-Kaim A,
Starek A, Filip M, Lason W, Budziszewska B.

Department of Experimental Neuroendocrinology
Institute of Pharmacology Polish Academy of Sciences
Smolna 12, PL 31-343 Kraków, Poland

Abstract

Ethylene glycol ethers (EGEs) are a class of chemicals used extensively in the manufacture of a wide range of domestic and industrial products, which may result in human exposure and toxicity. Hematologic and reproductive toxicity of EGEs are well known whereas their action on neuronal cell viability has not been studied so far. In the present study, we investigated the effects of some EGEs on cell viability and on the hydrogen peroxide-induced damage in the human neuroblastoma (SH-SY5Y) cells. It has been found that 2-phenoxyethanol in a concentration-dependent manner (5-25 mM, 24 h) increased the basal and H₂O₂-induced lactate dehydrogenase (LDH) release and 3-[4,5-dimethylthiazol-2-yl]2,5-diphenyl tetrazolium bromide (MTT) reduction. 2-Butoxyethanol given alone did not affect LDH release and MTT reduction but concentration-dependently enhanced the cytotoxic effect of H₂O₂. 2-Isopropoxyethanol significantly and concentration-dependently (1-25 mM) increased the basal LDH release and attenuated MTT reduction, but did not potentiate the cytotoxic effect of H₂O₂. Contrary to this, 2-methoxyethanol did not show a cytotoxic effect while 2-ethoxyethanol at high concentrations intensified the hydrogen peroxide action. This study demonstrated that among the EGEs studied, 2-phenoxyethanol showed the most consistent cytotoxic effect on neurons in in vitro conditions and enhanced the hydrogen peroxide action. 2-Isopropoxyethanol had also a potent cytotoxic effect, but it did not enhance the hydrogen peroxide action, whereas 2-butoxyethanol only potentiated cytotoxic effect of H₂O₂. It is concluded that the results of the present study should be confirmed in in vivo conditions and that some EGEs, especially 2-phenoxyethanol, 2-butoxyethanol and 2-isopropoxyethanol, may be responsible for initiation or exacerbation of neuronal cell damage.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21273685>

“2-phenoxyethanol

showed the most consistent cytotoxic effect

on neurons in in vitro conditions and enhanced

the hydrogen peroxide action.”

Gene expression in primary cultured astrocytes affected by aluminum: alteration of chaperons involved in protein folding

Author information

Aremu DA1, Ezomo OF, Meshitsuka S.

Division of Integrative Bioscience
Institute for Regenerative Medicine and Biofunction
Graduate School of Medical Science
Tottori University, Yonago, Tottori, 683-8503, Japan

Abstract

OBJECTIVES

Aluminum is notorious as a neurotoxic metal. The aim of our study was to determine whether endoplasmic reticulum (ER) stress is involved in aluminum-induced apoptosis in astrocytes.

METHODS

Mitochondrial RNA (mRNA) was analyzed by reverse transcription (RT)-PCR following pulse exposure of aluminum glycinate to primary cultured astrocytes. Tunicamycin was used as a positive control.

RESULTS

Gene expression analysis revealed that Ire1 α was up-regulated in astrocytes exposed to aluminum while Ire1 was up-regulated by tunicamycin. Exposure to aluminum glycinate, in contrast to tunicamycin, seemed to down-regulate mRNA expression of many genes, including the ER resident molecular chaperone BiP/Grp78 and Ca(2+)-binding chaperones (calnexin and calreticulin), as well as stanniocalcin 2 and OASIS. The down-regulation or non-activation of the molecular chaperons, whose expressions are known to be protective by increasing protein folding, may spell doom for the adaptive response. Exposure to aluminum did not have any significant effects on the expression of Bax and Bcl2 in astrocytes.

CONCLUSIONS

The results of this study demonstrate that aluminum may induce apoptosis in astrocytes via ER stress by impairing the protein-folding machinery.

<http://www.ncbi.nlm.nih.gov/pubmed/21432213>

“The results of this study demonstrate that aluminum may induce apoptosis in astrocytes via ER stress by impairing the protein-folding machinery.”

“aluminum (Al), plays a relevant role in affecting A β aggregation and neurotoxicity.”

PLoS One • January 2011

Microarray Analysis on Human Neuroblastoma Cells Exposed to Aluminum, β 1–42-Amyloid or the β 1–42-Amyloid Aluminum Complex

Valentina Gatta, Denise Drago, Karina Fincati, Maria Teresa Valenti,
Luca Dalle Carbonare, Stefano L. Sensi, Paolo Zatta

Abstract

Background

A typical pathological feature of Alzheimer’s disease (AD) is the appearance in the brain of senile plaques made up of β -amyloid (A β) and neurofibrillary tangles. AD is also associated with an abnormal accumulation of some metal ions, and we have recently shown that one of these, aluminum (Al), plays a relevant role in affecting A β aggregation and neurotoxicity.

Methodology

In this study, employing a microarray analysis of 35,129 genes, we investigated the effects induced by the exposure to the A β 1–42-Al (A β -Al) complex on the gene expression profile of the neuronal-like cell line, SH-SY5Y.

Principal Findings

The microarray assay indicated that, compared to A β or Al alone, exposure to A β -Al complex produced selective changes in gene expression. Some of the genes selectively over or underexpressed are directly related to AD. A further evaluation performed with Ingenuity Pathway analysis revealed that these genes are nodes of networks and pathways that are involved in the modulation of Ca²⁺ homeostasis as well as in the regulation of glutamatergic transmission and synaptic plasticity.

Conclusions and Significance

A β -Al appears to be largely involved in the molecular machinery that regulates neuronal as well as synaptic dysfunction and loss. A β -Al seems critical in modulating key AD-related pathways such as glutamatergic transmission, Ca²⁺ homeostasis, oxidative stress, inflammation, and neuronal apoptosis.

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0015965#authcontrib>

Aluminium in the human brain

Christopher Exley , Emily R. House

Abstract

An inevitable consequence of humans living in the Aluminium Age is the presence of aluminium in the brain. This non-essential, neurotoxic metal gains entry to the brain throughout all stages of human development, from the foetus through to old age. Human exposure to myriad forms of this ubiquitous and omnipresent metal makes its presence in the brain inevitable, while the structure and physiology of the brain makes it particularly susceptible to the accumulation of aluminium with age. In spite of aluminium's complete lack of biological essentiality, it actually participates avidly in brain biochemistry and substitutes for essential metals in critical biochemical processes. The degree to which such substitutions are disruptive and are manifested as biological effects will depend upon the biological availability of aluminium in any particular physical or chemical compartment, and will under all circumstances be exerting an energy load on the brain. In short, the brain must expend energy in its 'unconscious' response to an exposure to biologically available aluminium. There are many examples where 'biological effect' has resulted in aluminium-induced neurotoxicity and most potently in conditions that have resulted in an aluminium-associated encephalopathy. However, since aluminium is non-essential and not required by the brain, its biological availability will only rarely achieve such levels of acuity, and it is more pertinent to consider and investigate the brain's response to much lower though sustained levels of biologically reactive aluminium. This is the level of exposure that defines the putative role of aluminium in chronic neurodegenerative disease and, though thoroughly investigated in numerous animal models, the chronic toxicity of aluminium has yet to be addressed experimentally in humans. A feasible test of the 'aluminium hypothesis', whereby aluminium in the human brain is implicated in chronic neurodegenerative disease, would be to reduce the brain's aluminium load to the lowest possible level by non-invasive means. The simplest way that this aim can be fulfilled in a significant and relevant population is by facilitating the urinary excretion of aluminium through the regular drinking of a silicic acid-rich mineral water over an extended time period. This will lower the body and brain burden of aluminium, and by doing so will test whether brain aluminium contributes significantly to chronic neurodegenerative diseases such as Alzheimer's and Parkinson's.

<http://link.springer.com/article/10.1007%2Fs00706-010-0417-y>

Vaccine • August 2011
Letter to the Editor

Aluminium-based adjuvants should not be used as placebos in clinical trials

by Christopher Exley
The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, UK

August 2011

Report available for purchase \$39.95

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21871940>

[Vaccine manufacturers use aluminum-based adjuvants with controls
in clinical trials meaning adverse affects of aluminum will go unnoticed]

“Aluminium ... has no known biological role.

It accumulates in the body when protective gastrointestinal mechanisms are bypassed ...”

[for example, when it’s injected]

Proceedings Of The Nutrition Society • August 2011

Aluminium exposure from parenteral nutrition in preterm infants and later health outcomes during childhood and adolescence

Author information

Fewtrell MS1, Edmonds CJ, Isaacs E, Bishop NJ, Lucas A.

Childhood Nutrition Research Centre, UCL Institute of Child Health
30 Guilford Street, London WC1N 1EH, UK
m.fewtrell@ich.ucl.ac.uk

Abstract

Aluminium is the most common metallic element, but has no known biological role. It accumulates in the body when protective gastrointestinal mechanisms are bypassed, renal function is impaired, or exposure is high - all of which apply frequently to preterm infants. Recognised clinical manifestations of aluminium toxicity include dementia, anaemia and bone disease. Parenteral nutrition (PN) solutions are liable to contamination with aluminium, particularly from acidic solutions in glass vials, notably calcium gluconate. When fed parenterally, infants retain >75% of the aluminium, with high serum, urine and tissue levels. Later health effects of neonatal intravenous aluminium exposure were investigated in a randomised trial comparing standard PN solutions with solutions specially sourced for low aluminium content. Preterm infants exposed for >10 d to standard solutions had impaired neurologic development at 18 months. At 13-15 years, subjects randomised to standard PN had lower lumbar spine bone mass; and, in non-randomised analyses, those with neonatal aluminium intake above the median had lower hip bone mass. Given the sizeable number of infants undergoing intensive care and still exposed to aluminium via PN, these findings have contemporary relevance. Until recently, little progress had been made on reducing aluminium exposure, and meeting Food and Drug Administration recommendations (<5 µg/kg per d) has been impossible in patients <50 kg using available products. Recent advice from the UK Medicines and Healthcare regulatory Authority that calcium gluconate in small volume glass containers should not be used for repeated treatment in children <18 years, including preparation of PN, is an important step towards addressing this problem.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21781356>

Do aluminum vaccine adjuvants contribute to the rising prevalence of autism?

Author information

Tomljenovic L1, Shaw CA.

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia
828 W. 10th Ave, Vancouver, BC
Canada V5Z 1L8
lucijat77@gmail.com

Abstract

Autism spectrum disorders (ASD) are serious multisystem developmental disorders and an urgent global public health concern. Dysfunctional immunity and impaired brain function are core deficits in ASD. Aluminum (Al), the most commonly used vaccine adjuvant, is a demonstrated neurotoxin and a strong immune stimulator. Hence, adjuvant Al has the potential to induce neuroimmune disorders. When assessing adjuvant toxicity in children, two key points ought to be considered: (i) children should not be viewed as “small adults” as their unique physiology makes them much more vulnerable to toxic insults; and (ii) if exposure to Al from only few vaccines can lead to cognitive impairment and autoimmunity in adults, is it unreasonable to question whether the current pediatric schedules, often containing 18 Al adjuvanted vaccines, are safe for children? By applying Hill’s criteria for establishing causality between exposure and outcome we investigated whether exposure to Al from vaccines could be contributing to the rise in ASD prevalence in the Western world. Our results show that: (i) children from countries with the highest ASD prevalence appear to have the highest exposure to Al from vaccines; (ii) the increase in exposure to Al adjuvants significantly correlates with the increase in ASD prevalence in the United States observed over the last two decades (Pearson $r=0.92$, $p<0.0001$); and (iii) a significant correlation exists between the amounts of Al administered to preschool children and the current prevalence of ASD in seven Western countries, particularly at 3-4 months of age (Pearson $r=0.89-0.94$, $p=0.0018-0.0248$). The application of the Hill’s criteria to these data indicates that the correlation between Al in vaccines and ASD may be causal. Because children represent a fraction of the population most at risk for complications following exposure to Al, a more rigorous evaluation of Al adjuvant safety seems warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/22099159>

“Our results show that:

- (i) children from countries with the highest Autistic Spectrum Disorder prevalence appear to have the highest exposure to Aluminum from vaccines;
- (ii) the increase in exposure to Al adjuvants significantly correlates with the increase in Autistic Spectrum Disorder prevalence in the United States observed over the last two decades and
- (iii) a significant correlation exists between the amounts of Aluminum administered to preschool children and the current prevalence of Autistic Spectrum Disorder in seven Western countries, particularly at 3-4 months of age.”

Aluminium and human breast diseases

Author information

Darbre PD1, Pugazhendhi D, Mannello F.

Biomedical Sciences Section
School of Biological Sciences
University of Reading, Reading
RG6 6UB, UK
p.d.darbre@reading.ac.uk

Abstract

The human breast is exposed to aluminium from many sources including diet and personal care products, but dermal application of aluminium-based antiperspirant salts provides a local long-term source of exposure. Recent measurements have shown that aluminium is present in both tissue and fat of the human breast but at levels which vary both between breasts and between tissue samples from the same breast. We have recently found increased levels of aluminium in non-invasively collected nipple aspirate fluids taken from breast cancer patients (mean $268 \pm 28 \mu\text{g/l}$) compared with control healthy subjects (mean $131 \pm 10 \mu\text{g/l}$) providing evidence of raised aluminium levels in the breast microenvironment when cancer is present. The measurement of higher levels of aluminium in type I human breast cyst fluids (median $150 \mu\text{g/l}$) compared with human serum (median $6 \mu\text{g/l}$) or human milk (median $25 \mu\text{g/l}$) warrants further investigation into any possible role of aluminium in development of this benign breast disease. Emerging evidence for aluminium in several breast structures now requires biomarkers of aluminium action in order to ascertain whether the presence of aluminium has any biological impact. To this end, we report raised levels of proteins that modulate iron homeostasis (ferritin, transferrin) in parallel with raised aluminium in nipple aspirate fluids in vivo, and we report overexpression of mRNA for several S100 calcium binding proteins following long-term exposure of MCF-7 human breast cancer cells in vitro to aluminium chloride.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22099158>

“Recent measurements have shown that aluminium is present in both tissue and fat of the human breast but at levels which vary both between breasts and between tissue samples from the same breast. We have recently found increased levels of aluminium in noninvasively collected nipple aspirate fluids taken from breast cancer patients (mean $268 \pm 28 \mu\text{g/l}$) compared with control healthy subjects (mean $131 \pm 10 \mu\text{g/l}$) providing evidence of raised aluminium levels in the breast microenvironment when cancer is present.”

Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF)

Author information

Passeri E1, Villa C, Couette M, Itti E, Brugieres P, Cesaro P,
Gherardi RK, Bachoud-Levi AC, Authier FJ.

Paris Est-Creteil University & Henri-Mondor University Hospital (APHP)
Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye
Creteil, F-94010, France

Abstract

Macrophagic myofasciitis (MMF) is characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction. Representative features of MMF-associated cognitive dysfunction (MACD) include (i) dysexecutive syndrome; (ii) visual memory; (iii) left ear extinction at dichotic listening test. In present study we retrospectively evaluated the progression of MACD in 30 MMF patients. Most patients fulfilled criteria for non-amnesic/dysexecutive mild cognitive impairment, even if some cognitive deficits seemed unusually severe. MACD remained stable over time, although dysexecutive syndrome tended to worsen. Long-term follow-up of a subset of patients with 3 or 4 consecutive neuropsychological evaluations confirmed the stability of MACD with time, despite marked fluctuations.

<http://www.ncbi.nlm.nih.gov/pubmed/22099155>

“Macrophagic myofasciitis (MMF)
is characterized by specific muscle lesions
assessing long-term persistence of aluminum
hydroxide within macrophages at the site
of previous immunization.”

Towards the prevention of
potential aluminum toxic effects
and an effective treatment for
Alzheimer's disease

Author information

Percy ME1, Kruck TP, Pogue AI, Lukiw WJ.

Neurogenetics Laboratory
Surrey Place Centre, Toronto, ON
Canada M5S 2C2
maire.percy@utoronto.ca

Abstract

In 1991, treatment with low dose intramuscular desferrioxamine (DFO), a trivalent chelator that can remove excessive iron and/or aluminum from the body, was reported to slow the progression of Alzheimer's disease (AD) by a factor of two. Twenty years later this promising trial has not been followed up and why this treatment worked still is not clear. In this critical interdisciplinary review, we provide an overview of the complexities of AD and involvement of metal ions, and revisit the neglected DFO trial. We discuss research done by us and others that is helping to explain involvement of metal ion catalyzed production of reactive oxygen species in the pathogenesis of AD, and emerging strategies for inhibition of metal-ion toxicity. Highlighted are insights to be considered in the quests to prevent potentially toxic effects of aluminum toxicity and prevention and intervention in AD.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22099160>

“Highlighted are insights
to be considered in the quests
to prevent potentially toxic effects
of aluminum toxicity and prevention
and intervention in AD.”

**Aluminum toxicity
and astrocyte dysfunction:
a metabolic link to neurological disorders**

Author information

Lemire J., Appanna VD.

Department of Chemistry and Biochemistry
Laurentian University, Sudbury, Ontario
Canada P3E 2C6

Abstract

Aluminum (Al) has been implicated in a variety of neurological diseases. However, the molecular mechanisms that enable Al to be involved in these disorders have yet to be fully delineated. Using astrocytes as a model of the cerebral cellular system, we have uncovered the biochemical networks that are affected by Al toxicity. In this review, we reveal how the inhibitory influence of Al on ATP production and on mitochondrial functions help generate globular astrocytes that are fat producing machines. These biological events may be the contributing factors to Al-triggered brain disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22099161>

“Aluminum (Al) has been implicated in a variety of neurological diseases. However, the molecular mechanisms that enable Al to be involved in these disorders have yet to be fully delineated. These biological events may be the contributing factors to Al-triggered brain disorders.”

**Aluminum and Alzheimer's Disease:
After a Century of Controversy,
Is there a Plausible Link?**

Author Information

Tomljenovic, Lucija

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia
Vancouver, BC, Canada

Abstract

The brain is a highly compartmentalized organ exceptionally susceptible to accumulation of metabolic errors. Alzheimer's disease (AD) is the most prevalent neurodegenerative disease of the elderly and is characterized by regional specificity of neural aberrations associated with higher cognitive functions. Aluminum (Al) is the most abundant neurotoxic metal on earth, widely bioavailable to humans and repeatedly shown to accumulate in AD-susceptible neuronal foci. In spite of this, the role of Al in AD has been heavily disputed based on the following claims: 1) bioavailable Al cannot enter the brain in sufficient amounts to cause damage, 2) excess Al is efficiently excreted from the body, and 3) Al accumulation in neurons is a consequence rather than a cause of neuronal loss. Research, however, reveals that: 1) very small amounts of Al are needed to produce neurotoxicity and this criterion is satisfied through dietary Al intake, 2) Al sequesters different transport mechanisms to actively traverse brain barriers, 3) incremental acquisition of small amounts of Al over a lifetime favors its selective accumulation in brain tissues, and 4) since 1911, experimental evidence has repeatedly demonstrated that chronic Al intoxication reproduces neuropathological hallmarks of AD. Misconceptions about Al bioavailability may have misled scientists regarding the significance of Al in the pathogenesis of AD. The hypothesis that Al significantly contributes to AD is built upon very solid experimental evidence and should not be dismissed. Immediate steps should be taken to lessen human exposure to Al, which may be the single most aggravating and avoidable factor related to AD.

<http://content.iospress.com/articles/journal-of-alzheimers-disease/jad101494>

“Research, however, reveals that:

1) very small amounts of Al are needed to produce neurotoxicity and this criterion is satisfied through dietary Al intake

2) Al sequesters different transport mechanisms to actively traverse brain barriers

3) incremental acquisition of small amounts of Al over a lifetime favors its selective accumulation in brain tissues

4) since 1911, experimental evidence has repeatedly demonstrated that chronic Al intoxication reproduces neuropathological hallmarks of AD.”

Effect of aluminum hydroxide adjuvant
on the immunogenicity of the
2009 pandemic influenza A/H1N1 vaccine:
multi-level modeling of data with repeated measures

Author information

Yin da P1, Zhu BP, Wang HQ, Cao L, Wu WD, Jiang KY,
Xia W, Zhang GM, Zheng JS, Cao LS, Liang XF.

Chinese Center for Disease Control and Prevention
Beijing 100050, China

Abstract

OBJECTIVE

To evaluate the effect of the aluminum hydroxide (Al-OH) adjuvant on the 2009 pandemic influenza A/H1N1 (pH1N1) vaccine.

METHODS

In a multicenter, double-blind, randomized, placebo-controlled trial, participants received two doses of split-virion formulation containing 15 µg hemagglutinin antigen, with or without aluminum hydroxide (Al-OH). We classified the participants into six age categories (>61 years, 41-60 years, 19-40 years, 13-18 years, 8-12 years, and 3-7 years) and obtained four blood samples from each participant on days 0, 21, 35, and 42 following the first dose of immunization. We assessed vaccine immunogenicity by measuring the geometric mean titer (GMT) of hemagglutination inhibiting antibody. We used a two-level model to evaluate the fixed effect of aluminum Al-OH and other factors, accounting for repeated measures.

RESULTS

The predictions of repeated measurement on GMTs of formulations with or without Al-OH, were 80.35 and 112.72, respectively. Al-OH significantly reduced immunogenicity after controlling for time post immunization, age-group and gender.

CONCLUSION

The Al-OH adjuvant does not increase but actually reduces the immunogenicity of the split-virion pH1N1 vaccine.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22365398>

“The aluminum hydroxide adjuvant does not increase but actually reduces the immunogenicity of the split-virion pH1N1 vaccine.”

Aluminum Vaccine Adjuvants: Are they Safe?

L. Tomljenovic*,1 and C.A. Shaw²

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia
828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada

²Departments of Ophthalmology and Visual Sciences
and Experimental Medicine and the Graduate Program in Neuroscience
University of British Columbia, Vancouver, British Columbia
828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada

Abstract

Aluminum is an experimentally demonstrated neurotoxin and the most commonly used vaccine adjuvant. Despite almost 90 years of widespread use of aluminum adjuvants, medical science's understanding about their mechanisms of action is still remarkably poor. There is also a concerning scarcity of data on toxicology and pharmacokinetics of these compounds. In spite of this, the notion that aluminum in vaccines is safe appears to be widely accepted. Experimental research, however, clearly shows that aluminum adjuvants have a potential to induce serious immunological disorders in humans. In particular, aluminum in adjuvant form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences. In our opinion, the possibility that vaccine benefits may have been overrated and the risk of potential adverse effects underestimated, has not been rigorously evaluated in the medical and scientific community. We hope that the present paper will provide a framework for a much needed and long overdue assessment of this highly contentious medical issue.

http://www.meerwetenoverfreek.nl/images/stories/Tomljenovic_Shaw-CMC-published.pdf

“Experimental research, however, clearly shows that aluminum adjuvants have a potential to induce serious immunological disorders in humans. In particular, aluminum in adjuvant form carries a risk for autoimmunity, long-term brain inflammation and associated neurological complications and may thus have profound and widespread adverse health consequences. In our opinion, the possibility that vaccine benefits may have been overrated and the risk of potential adverse effects underestimated, has not been rigorously evaluated in the medical and scientific community.”

Entropy • 2012

Special Issue

Biosemitic Entropy: Disorder, Disease, and Mortality

Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure

Author Information

Stephanie Seneff 1,* , Robert M. Davidson 2 and Jingjing Liu 1

1. Computer Science and Artificial Intelligence Laboratory
Massachusetts Institute of Technology, Cambridge, MA 02139, USA

2. Internal Medicine Group Practice
PhyNet, Inc., Longview, TX 75604, USA

Abstract

Autism is a condition characterized by impaired cognitive and social skills, associated with compromised immune function. The incidence is alarmingly on the rise, and environmental factors are increasingly suspected to play a role. This paper investigates word frequency patterns in the U.S. CDC Vaccine Adverse Events Reporting System (VAERS) database. Our results provide strong evidence supporting a link between autism and the aluminum in vaccines. A literature review showing toxicity of aluminum in human physiology offers further support. Mentions of autism in VAERS increased steadily at the end of the last century, during a period when mercury was being phased out, while aluminum adjuvant burden was being increased. Using standard log-likelihood ratio techniques, we identify several signs and symptoms that are significantly more prevalent in vaccine reports after 2000, including cellulitis, seizure, depression, fatigue, pain and death, which are also significantly associated with aluminum-containing vaccines. We propose that children with the autism diagnosis are especially vulnerable to toxic metals such as aluminum and mercury due to insufficient serum sulfate and glutathione. A strong correlation between autism and the MMR (Measles, Mumps, Rubella) vaccine is also observed, which may be partially explained via an increased sensitivity to acetaminophen administered to control fever.

<http://www.mdpi.com/1099-4300/14/11/2227>

“Using standard log-likelihood ratio techniques, we identify several signs and symptoms that are significantly more prevalent in vaccine reports after 2000, including cellulitis, seizure, depression, fatigue, pain and death, which are also significantly associated with aluminum-containing vaccines. We propose that children with the autism diagnosis are especially vulnerable to toxic metals such as aluminum and mercury due to insufficient serum sulfate and glutathione. A strong correlation between autism and the MMR (Measles, Mumps, Rubella) vaccine is also observed, which may be partially explained via an increased sensitivity to acetaminophen administered to control fever.”

Neurotoxicology And Teratology • January 2012

Multiple toxic heavy metals and neonatal neurobehavior in China
require considering co-exposure to Thimerosal-ethylmercury and adjuvant-aluminum

Author information

Dórea JG.

Faculty of Health Sciences
Universidade de Brasília
70919-970 Brasília, DF, Brazil
dorea@rudah.com.br

<https://www.infona.pl/resource/bwmeta1.element.elsevier-5ea9d498-e159-3496-99a1-2b3c4a568a20>

Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations

Author information

Tomljenovic L1, Shaw CA.

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia
Vancouver, BC, Canada
lucijat77@gmail.com

Abstract

Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function. Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity. In some developed countries, by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of aluminum (Al) adjuvants through routine vaccinations. According to the US Food and Drug Administration, safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic. Taken together, these observations raise plausible concerns about the overall safety of current childhood vaccination programs. When assessing adjuvant toxicity in children, several key points ought to be considered: (i) infants and children should not be viewed as “small adults” with regard to toxicological risk as their unique physiology makes them much more vulnerable to toxic insults; (ii) in adult humans Al vaccine adjuvants have been linked to a variety of serious autoimmune and inflammatory conditions (i.e., “ASIA”), yet children are regularly exposed to much higher amounts of Al from vaccines than adults; (iii) it is often assumed that peripheral immune responses do not affect brain function. However, it is now clearly established that there is a bidirectional neuro-immune cross-talk that plays crucial roles in immunoregulation as well as brain function. In turn, perturbations of the neuro-immune axis have been demonstrated in many autoimmune diseases encompassed in “ASIA” and are thought to be driven by a hyperactive immune response; and (iv) the same components of the neuro-immune axis that play key roles in brain development and immune function are heavily targeted by Al adjuvants. In summary, research evidence shows that increasing concerns about current vaccination practices may indeed be warranted. Because children may be most at risk of vaccine-induced complications, a rigorous evaluation of the vaccine-related adverse health impacts in the pediatric population is urgently needed.

<http://www.ncbi.nlm.nih.gov/pubmed/22235057>

“Immune challenges during early development, including those vaccine-induced, can lead to permanent detrimental alterations of the brain and immune function.

Experimental evidence also shows that simultaneous administration of as little as two to three immune adjuvants can overcome genetic resistance to autoimmunity. In some developed countries, by the time children are 4 to 6 years old, they will have received a total of 126 antigenic compounds along with high amounts of aluminum (Al) adjuvants through routine vaccinations.

According to the US Food and Drug Administration, safety assessments for vaccines have often not included appropriate toxicity studies because vaccines have not been viewed as inherently toxic. Taken together, these observations raise plausible concerns about the overall safety of current childhood vaccination programs.”

Alum increases antigen uptake
reduces antigen degradation and
sustains antigen presentation by DCs in vitro

Author information

Ghimire TR1, Benson RA, Garside P, Brewer JM.

Strathclyde Institute of Pharmacy and Biomedical Sciences
University of Strathclyde, Glasgow, Scotland, United Kingdom

Abstract

Aluminium adjuvants (alum) have been the only widely approved adjuvants for use in human vaccines since the 1920s, however, the mechanism of action of these adjuvants remains elusive. Due to increasing demand for novel adjuvants, a clearer understanding of the mechanisms that allow these important agents to affect adaptive immune responses will make a significant contribution to the rational design of future vaccines. Using a novel approach to tracking antigen and antigen presentation, we demonstrate that alum induces higher antigen accumulation and increased antigen presentation by dendritic cells (DCs) in vitro. Antigen accumulation was 100-fold higher and antigen presentation 10-fold higher following alum treatment when compared with soluble protein alone. We also observed that alum causes an initial reduction in presentation compared with soluble antigen, but eventually increases the magnitude and duration of antigen presentation. This was associated with reduced protein degradation in DCs following alum treatment. These studies demonstrate the dynamic alterations in antigen processing and presentation induced by alum that underlie enhanced DC function in response to this adjuvant.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22732235>

“Aluminium adjuvants (alum) have been the only widely approved adjuvants for use in human vaccines since the 1920s, however, the mechanism of action of these adjuvants remains elusive.”

Metal Ions in Neurodegenerative Diseases The coordination chemistry of aluminium in neurodegenerative disease

by Christopher Exley

Abstract

The coordination chemistry of a metal ion defines its optimal association with a biomolecule such that its binding by specific ligands on that molecule confers function and biological purpose. Aluminium is a non-essential metal with no known biological role which means that its coordination neurochemistry defines aluminium's putative role in a number of neurodegenerative diseases. In examining this chemistry it is found that very little is known about the complexes formed and ligands involved in aluminium's interactions with neurochemically-relevant ligands. Aluminium's action as a pro-oxidant as well as an excitotoxin are highlighted while the evidence for its interactions with amyloid beta, tau and DNA are discussed and it is concluded that it is too early to discount these ligands as targets for the neurotoxicity of aluminium.

Highlights

- There are few quantitative data describing the coordination chemistry of aluminium in neurodegenerative disease.
- One compelling line of evidence relates to the putative aluminium superoxide semi-reduced radical ion $\text{AlO}_2^{\cdot-}$ and its powerful action as a pro-oxidant.
- Another important candidate is aluminium's complex with ATP and its potential to disrupt neuronal signalling and induce excitotoxicity.
- Though there are no quantitative data to describe aluminium's interactions with amyloid beta this does not preclude their association in the brain.
- The biological reactivity of aluminium supports myriad as yet unidentified interactions with biomolecules associated with brain function in health and disease.

<http://www.sciencedirect.com/science/article/pii/S0010854512000392>

“In examining this chemistry it is found that very little is known about the complexes formed and ligands involved in aluminium's interactions with neurochemically-relevant ligands. Aluminium's action as a pro-oxidant as well as an excitotoxin are highlighted while the evidence for its interactions with amyloid beta, tau and DNA are discussed and it is concluded that it is too early to discount these ligands as targets for the neurotoxicity of aluminium.”

Aluminium overload after 5 years in skin biopsy following post-vaccination with subcutaneous pseudolymphoma

Author information

Guillard O1, Fauconneau B, Pineau A,
Marrault A, Bellocq JP, Chenard MP.

CHU Poitiers, Department of Biochemistry
Poitiers, France
olivier.guillard@univ-poitiers.fr

Abstract

Aluminium hydroxide is used as an effective adjuvant in a wide range of vaccines for enhancing immune response to the antigen. The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. The aim of this study is to verify if the subcutaneous pseudolymphoma observed in this patient in the site of vaccine injection is linked to an aluminium overload. Many years after vaccination, a subcutaneous nodule was discovered in a 45-year-old woman with subcutaneous pseudolymphoma. In skin biopsy at the injection site for vaccines, aluminium (Al) deposits are assessed by Morin stain and quantification of Al is performed by Zeeman Electrothermal Atomic Absorption Spectrophotometry. Morin stain shows Al deposits in the macrophages, and Al assays (in $\mu\text{g/g}$, dry weight) were 768.10 ± 18 for the patient compared with the two control patients, 5.61 ± 0.59 and 9.13 ± 0.057 . Given the pathology of this patient and the high Al concentration in skin biopsy, the authors wish to draw attention when using the Al salts known to be particularly effective as adjuvants in single or repeated vaccinations. The possible release of Al may induce other pathologies ascribed to the well-known toxicity of this metal.

<http://www.ncbi.nlm.nih.gov/pubmed/22425036>

“The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines.”

Aluminum excitotoxicity and neuroautoimmunity: the role of the brain expression of CD32+ (FcγRIIa), ICAM-1+ and CD3E in aging

Author information

Jovanova-Nesic K1, Shoenfeld Y, Spector NH.

Immunology Research Center Branislav Jankovic
Department of Neuroimmunology, Institute of Virology
Vaccines and Sera-Torlak, Belgrade, Serbia

Abstract

In the central nervous system (CNS) microglia are crucial for the defense of the brain against invading microorganisms, formation of tumors, and damage following trauma. However, uncontrolled activation of these cells may have deleterious outcomes through activation of Fcγ and the complement 3 receptors and the induction of an adaptive immune reaction. Proteins contributing to this reaction are the intercellular adhesion molecule-1 (ICAM-1) and CD3 molecules, among others. Both can be expressed on the glia cells before cytokine release and may facilitate an autoimmune inflammatory reaction in the brain. Round microglial cells among the pyramidal cells of the hippocampus with increased expression of CD32+ (FcγRIIa) and near the site of injection of aluminum were detected immunohistochemically and indicate microglial activation at the site of aluminum injury. ICAM-1+ immunoreactivity significantly increased in the hippocampus and in the choroids plexus, indicating increased inflammation in the brain as well as increased CD3E+ expression in the hippocampus and non-MHC-restricted T cytotoxicity after aluminum injection. The pattern of expression of CD32+ (FcγRIIa receptor) near the site of aluminum injection indicates that microglia may play a phagocytic role at the site of aluminum-induced excitotoxicity in the brain. Significant expression of ICAM-1+ and CD3E+ immunoreactive cells with the clusters of ICAM-1+ in the choroid plexus suggests a consequently neurotoxic autoimmune reaction induced by microglial hyperactivation in the injured brain.

<http://www.ncbi.nlm.nih.gov/pubmed/23387884>

“In the central nervous system (CNS) microglia are crucial for the defense of the brain against invading microorganisms, formation of tumors, and damage following trauma. However, uncontrolled activation of these cells may have deleterious outcomes ...”

“alum has high neurotoxic potential and planning administration of continuously escalating doses of this poorly biodegradable adjuvant in the population should be carefully evaluated by regulatory agencies since the compound may be insidiously unsafe.”

BMC Medicine • April 2013

Slow CCL2-dependent translocation of biopersistent particles from muscle to brain

Author information

Khan Z1, Combadière C, Authier FJ, Itier V, Lux F, Exley C,
Mahrouf-Yorgov M, Decrouy X, Moretto P, Tillement O, Gherardi RK, Cadusseau J.

INSERM, U955, 8 rue du Général Sarrail, Créteil, 94010, France

Abstract

BACKGROUND

Long-term biodistribution of nanomaterials used in medicine is largely unknown. This is the case for alum, the most widely used vaccine adjuvant, which is a nanocrystalline compound spontaneously forming micron/sub-micron-sized agglomerates. Although generally well tolerated, alum is occasionally detected within monocyte-lineage cells long after immunization in presumably susceptible individuals with systemic/neurologic manifestations or autoimmune (inflammatory) syndrome induced by adjuvants (ASIA).

METHODS

On the grounds of preliminary investigations in 252 patients with alum-associated ASIA showing both a selective increase of circulating CCL2, the major monocyte chemoattractant, and a variation in the CCL2 gene, we designed mouse experiments to assess biodistribution of vaccine-derived aluminum and of alum-particle fluorescent surrogates injected in muscle. Aluminum was detected in tissues by Morin stain and particle induced X-ray emission (PIXE) Both 500 nm fluorescent latex beads and vaccine alum agglomerates-sized nanohybrids (Al-Rho) were used.

RESULTS

Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection. Both fluorescent materials injected into muscle translocated to draining lymph nodes

(DLNs) and thereafter were detected associated with phagocytes in blood and spleen. Particles linearly accumulated in the brain up to the six-month endpoint; they were first found in perivascular CD11b⁺ cells and then in microglia and other neural cells. DLN ablation dramatically reduced the biodistribution. Cerebral translocation was not observed after direct intravenous injection, but significantly increased in mice with chronically altered blood-brain-barrier. Loss/gain-of-function experiments consistently implicated CCL2 in systemic diffusion of Al-Rho particles captured by monocyte-lineage cells and in their subsequent neurodelivery. Stereotactic particle injection pointed out brain retention as a factor of progressive particle accumulation.

CONCLUSION

Nanomaterials can be transported by monocyte-lineage cells to DLNs, blood and spleen, and, similarly to HIV, may use CCL2-dependent mechanisms to penetrate the brain. This occurs at a very low rate in normal conditions explaining good overall tolerance of alum despite its strong neurotoxic potential. However, continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe, especially in the case of overimmunization or immature/altered blood brain barrier or high constitutive CCL-2 production.

Full Report:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3616851/>

“... a form of the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep, linked to the repetitive inoculation of aluminum-containing adjuvants through vaccination.

The syndrome shows an acute phase that affects less than 0.5% of animals in a given herd ...”

[a syndrome that affects 5,000 individuals per each 1 million]

Immunology Research • July 2013

Autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep

Author information

Luján L1, Pérez M, Salazar E, Álvarez N, Gimeno M,
Pinczowski P, Irusta S, Santamaría J, Insausti N, Cortés Y,
Figueras L, Cuartielles I, Vila M, Fantova E, Chapullé JL.

Department of Animal Pathology
Veterinary Faculty, University of Zaragoza
177 Miguel Servet Street, 50013, Saragossa, Spain
Lluis.Lujan@unizar.es

Abstract

We describe a form of the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep, linked to the repetitive inoculation of aluminum-containing adjuvants through vaccination. The syndrome shows an acute phase that affects less than 0.5% of animals in a given herd, it appears 2-6 days after an adjuvant-containing inoculation and it is characterized by an acute neurological episode with low response to external stimuli and acute meningoencephalitis, most animals apparently recovering afterward. The chronic phase is seen in a higher proportion of flocks, it can follow the acute phase, and it is triggered by external stimuli, mostly low temperatures. The chronic phase begins with an excitatory phase, followed by weakness, extreme cachexia, tetraplegia and death. Gross lesions are related to a cachectic process with muscular atrophy, and microscopic lesions are mostly linked to a neurodegenerative process in both dorsal and ventral column of the gray matter of the spinal cord. Experimental reproduction of ovine ASIA in a small group of repeatedly vaccinated animals was successful. Detection of Al(III) in tissues indicated the presence of aluminum in the nervous tissue of experimental animals. The present report is the first description of a new sheep syndrome (ovine ASIA syndrome) linked to multiple, repetitive vaccination and that can have devastating consequences as it happened after the compulsory vaccination against bluetongue in 2008. The ovine ASIA syndrome can be used as a model of other similar diseases affecting both human and animals. A major research effort is needed in order to understand its complex pathogenesis.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23579772>

Aluminum in the central nervous system (CNS):
toxicity in humans and animals,
vaccine adjuvants, and autoimmunity

Author information

Shaw CA1, Tomljenovic L.

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia (UBC)
828 W. 10th Ave., Vancouver, BC
V5Z 1L8, Canada
cashawlab@gmail.com

Abstract

We have examined the neurotoxicity of aluminum in humans and animals under various conditions, following different routes of administration, and provide an overview of the various associated disease states. The literature demonstrates clearly negative impacts of aluminum on the nervous system across the age span. In adults, aluminum exposure can lead to apparently age-related neurological deficits resembling Alzheimer's and has been linked to this disease and to the Guamanian variant, ALS-PDC. Similar outcomes have been found in animal models. In addition, injection of aluminum adjuvants in an attempt to model Gulf War syndrome and associated neurological deficits leads to an ALS phenotype in young male mice. In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders. Many of the features of aluminum-induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/23609067>

“In young children, a highly significant correlation exists between the number of pediatric aluminum-adjuvanted vaccines administered and the rate of autism spectrum disorders. Many of the features of aluminum-induced neurotoxicity may arise, in part, from autoimmune reactions, as part of the ASIA syndrome.”

Selective accumulation of aluminum in cerebral arteries in Alzheimer's disease (AD)

Author information

Bhattacharjee S1, Zhao Y, Hill JM, Culicchia F,
Kruck TP, Percy ME, Pogue AI, Walton JR, Lukiw WJ.

Neuroscience Center
Louisiana State University Health Sciences Center
New Orleans, LA 70112, USA

Abstract

Once biologically available aluminum bypasses gastrointestinal and blood-brain barriers, this environmentally-abundant neurotoxin has an exceedingly high affinity for the large pyramidal neurons of the human brain hippocampus. This same anatomical region of the brain is also targeted by the earliest evidence of Alzheimer's disease (AD) neuropathology. The mechanism for the selective targeting and transport of aluminum into the hippocampus of the human brain is not well understood. In an effort to improve our understanding of a pathological aluminum entry system into the brain, this study examined the aluminum content of 8 arteries that supply blood to the hippocampus, including the aorta and several cerebral arteries. In contrast to age-matched controls, in AD patients we found a gradient of increasing aluminum concentration from the aorta to the posterior cerebral artery that supplies blood to the hippocampus. Primary cultures of human brain endothelial cells were found to have an extremely high affinity for aluminum when compared to other types of brain cells. Together, these results suggest for the first time that endothelial cells that line the cerebral vasculature may have biochemical attributes conducive to binding and targeting aluminum to selective anatomical regions of the brain, such as the hippocampus, with potential downstream pro-inflammatory and pathogenic consequences.

<http://www.ncbi.nlm.nih.gov/pubmed/23764827>

“Once biologically available aluminum bypasses gastrointestinal and blood-brain barriers, this environmentally-abundant neurotoxin has an exceedingly high affinity for the large pyramidal neurons of the human brain hippocampus. This same anatomical region of the brain is also targeted by the earliest evidence of Alzheimer's disease (AD) neuropathology. The mechanism for the selective targeting and transport of aluminum into the hippocampus of the human brain is not well understood.”

“All 30 infant formulas were contaminated with aluminium.”

BMC Pediatrics • October 2013

The aluminium content of infant formulas remains too high

Author information

Chuchu N1, Patel B, Sebastian B, Exley C.

The Birchall Centre, Lennard-Jones Laboratories
Keele University, Staffordshire, UK
c.exley@keele.ac.uk

Abstract

BACKGROUND

Recent research published in this journal highlighted the issue of the high content of aluminium in infant formulas. The expectation was that the findings would serve as a catalyst for manufacturers to address a significant problem of these, often necessary, components of infant nutrition. It is critically important that parents and other users have confidence in the safety of infant formulas and that they have reliable information to use in choosing a product with a lower content of aluminium. Herein, we have significantly extended the scope of the previous research and the aluminium content of 30 of the most widely available and often used infant formulas has been measured.

METHODS

Both ready-to-drink milks and milk powders were subjected to microwave digestion in the presence of 15.8 M HNO₃ and 30% w/v H₂O₂ and the aluminium content of the digests was measured by TH GFAAS.

RESULTS

Both ready-to-drink milks and milk powders were contaminated with aluminium. The concentration of aluminium across all milk products ranged from ca 100 to 430 µg/L. The concentration of aluminium in two soya-based milk products was 656 and 756 µg/L. The intake of aluminium from non-soya-based infant formulas varied from ca 100 to 300 µg per day. For soya-based milks it could be as high as 700 µg per day.

CONCLUSIONS

All 30 infant formulas were contaminated with aluminium. There was no clear evidence that subsequent to the problem of aluminium being highlighted in a previous publication in this journal that contamination had been addressed and reduced. It is the opinion of the authors that regulatory and other non-voluntary methods are now required to reduce the aluminium content of infant formulas and thereby protect infants from chronic exposure to dietary aluminium.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3851493/>

“... aluminum has the potential to induce damage at a range of levels in the Central Nervous System leading to neuronal death, circuit malfunction, and ultimately system failure.”

Immunome Research • October 2013

Aluminums Role in CNS-immune System Interactions leading to Neurological Disorders

Shaw CA^{1,2,3*}, Kette SD⁴, Davidson RM⁵ and Seneff S⁶

1. Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences
828 W. 10th Ave., Vancouver, British Columbia, V5Z1L8, Canada
2. Program Experimental Medicine, University of British Columbia, Vancouver, V5Z1L8, Canada
3. Program in Neurosciences, University of British Columbia, Vancouver, V5Z1L8, Canada
4. Independent researcher, Hudson, FL 34667, USA
5. Internal Medicine Group Practice, PhyNet, Inc., 4002 Technology Center, Longview, TX 75605, USA
6. MIT Computer Science and Artificial Intelligence Laboratory, 32 Vassar Street, Cambridge, MA 02139, USA

Abstract

Multisystem interactions are well established in neurological disorders, in spite of conventional views that only the central nervous system (CNS) is impacted. We review evidence for mutual interactions between the immune and nervous systems and show how these seem to be implicated in the origin and progression of nervous system disorders. Well-established immune system triggers leading to autoimmune reactions are considered. Of these, aluminum, a known neurotoxicant, may be of particular importance. We have demonstrated elsewhere that aluminum has the potential to induce damage at a range of levels in the CNS leading to neuronal death, circuit malfunction, and ultimately system failure. Aluminum is widely used as an adjuvant in various vaccine formulations and has been implicated in a multisystem disorder termed autoimmune/inflammatory syndrome induced by adjuvants (ASIA). The implications of aluminum-induced ASIA in some disorders of the CNS are considered. We propose a unified theory capturing a progression from a local response to a systemic response initiated by disruption of water-based interfaces of exposed cells.

Human exposure to aluminium

Author information

Christopher Exley

The Birchall Centre
Lennard-Jones Laboratories
Keele University, Staffordshire, UK

c.exley@keele.ac.uk

Abstract

Human activities have circumvented the efficient geochemical cycling of aluminium within the lithosphere and therewith opened a door, which was previously only ajar, onto the biotic cycle to instigate and promote the accumulation of aluminium in biota and especially humans. Neither these relatively recent activities nor the entry of aluminium into the living cycle are showing any signs of abating and it is thus now imperative that we understand as fully as possible how humans are exposed to aluminium and the future consequences of a burgeoning exposure and body burden. The aluminium age is upon us and there is now an urgent need to understand how to live safely and effectively with aluminium.

<http://www.ncbi.nlm.nih.gov/pubmed/23982047>

“The aluminium age is upon us
and there is now an urgent need
to understand how to live safely
and effectively with aluminium.”

Aluminum and the human diet revisited

Christopher A Shaw and Thomas E Marler

Abstract

Concerns about aluminum (Al) exposure in the human diet have persisted for one century. We suggest that continued research would benefit from better reporting of environmental factors that are known to influence Al accumulation in plant organs that are consumed, focusing on subsets of the general public that exhibit the highest risk for neuropathological responses, increased evaluation of commercial processing procedures that may concentrate Al or other toxic substances, and designing studies with low dose, chronic exposure rather than further study of acute, brief exposure.

Neurological Disorders

Cognitive decline and central nervous system (CNS) pathologies that resemble those of Alzheimer are induced by Al in older rats.²⁰ Soil and water sources of Al were implicated in the ALS-parkinsonism dementia complex on Guam.²¹ Additionally, the acute effects of higher doses of Al-induced dialysis associated encephalopathy in humans are well documented.²²

The route of administration of Al plays a key role in the type of neurotoxicity exhibited. While most dietary Al is removed by the kidneys, those lacking mature or patent kidney function such as pediatric and geriatric subjects may be more likely to accumulate Al in different organs, including the CNS. Injected Al from Al adjuvants in vaccines have a very different fate and appear to be picked up from the draining lymph nodes by circulating macrophages and transported into the CNS.²³ Motor neuron loss following Al hydroxide injections in mice and sheep²⁴⁻²⁶ and macrophagic myofasciitis in humans involving cognitive dysfunction in humans.²⁷ Al adjuvants have also been linked to a series of autoimmune disorders in humans.²⁸

Developmental neurological disorders such as autism spectrum disorder (ASD) also have a potential Al link through the accumulative weight of pediatric vaccines, many of which contain Al as adjuvants.²⁹ Indeed, there is a highly significant correlation between ASD rates and cumulative Al adjuvant amount,³⁰ a correlation that satisfies eight of nine Hill criteria for causality. Similar outcomes are found in new born mice injected with Al adjuvants.³¹ A recent review also links Al to ASD.³²

“Developmental neurological disorders such as autism spectrum disorder (ASD) also have a potential Aluminum link through the accumulative weight of pediatric vaccines, many of which contain Aluminum as adjuvants.”

Administration of aluminium
to neonatal mice in vaccine-relevant amounts
is associated with adverse long term
neurological outcomes

Author information

Shaw CA1, Li Y, Tomljenovic L.

Dept. of Ophthalmology and Visual Sciences
University of British Columbia, Vancouver, British Columbia, Canada
Program in Experimental Medicine
University of British Columbia, Vancouver, British Columbia, Canada
Program in Neuroscience
University of British Columbia, Vancouver, British Columbia, Canada
cashawlab@gmail.com

Abstract

Our previous ecological studies of autism spectrum disorder (ASD) has demonstrated a correlation between increasing ASD rates and aluminium (Al) adjuvants in common use in paediatric vaccines in several Western countries. The correlation between ASD rate and Al adjuvant amounts appears to be dose-dependent and satisfies 8 of 9 Hill criteria for causality. We have now sought to provide an animal model to explore potential behavioural phenotypes and central nervous system (CNS) alterations using s.c. injections of Al hydroxide in early postnatal CD-1 mice of both sexes. Injections of a “high” and “low” Al adjuvant levels were designed to correlate to either the U.S. or Scandinavian paediatric vaccine schedules vs. control saline-injected mice. Both male and female mice in the “high Al” group showed significant weight gains following treatment up to sacrifice at 6 months of age. Male mice in the “high Al” group showed significant changes in light-dark box tests and in various measures of behaviour in an open field. Female mice showed significant changes in the light-dark box at both doses, but no significant changes in open field behaviours. These current data implicate Al injected in early postnatal life in some CNS alterations that may be relevant for a better understanding of the aetiology of ASD.

<http://www.ncbi.nlm.nih.gov/pubmed/23932735>

“Our previous ecological studies of autism spectrum disorder (ASD) has demonstrated a correlation between increasing Autism Spectrum Disorder rates and aluminium (Al) adjuvants in common use in paediatric vaccines in several Western countries.”

Aluminium based adjuvants and their effects on mitochondria and lysosomes of phagocytosing cells

Author information

Ohlsson L1, Exley C, Darabi A, Sandén E, Siesjö P, Eriksson H.

Department of Biomedical Laboratory Science
Faculty of Health and Society
Malmö University
SE-205 06 Malmö, Sweden

Abstract

Aluminium oxyhydroxide, Al(OH)₃ is one of few compounds approved as an adjuvant in human vaccines. However, the mechanism behind its immune stimulating properties is still poorly understood. In vitro co-culture of an aluminium adjuvant and the human monocytic cell line THP-1 resulted in reduced cell proliferation. Inhibition occurred at concentrations of adjuvant several times lower than would be found at the injection site using a vaccine formulation containing an aluminium adjuvant. Based on evaluation of the mitochondrial membrane potential, THP-1 cells showed no mitochondrial rupture after co-culture with the aluminium adjuvant, instead an increase in mitochondrial activity was seen. The THP-1 cells are phagocytosing cells and after co-culture with the aluminium adjuvant the phagosomal pathway was obstructed. Primary or early phagosomes mature into phagolysosomes with an internal pH of 4.5 - 5 and carry a wide variety of hydrolysing enzymes. Co-culture with the aluminium adjuvant yielded a reduced level of acidic vesicles and cathepsin L activity, a proteolytic enzyme of the phagolysosomes, was almost completely inhibited. THP-1 cells are an appropriate in vitro model in order to investigate the mechanism behind the induction of a phagocytosing antigen presenting cell into an inflammatory cell by aluminium adjuvants. Much information will be gained by investigating the phagosomal pathway and what occurs inside the phagosomes and to elucidate the ultimate fate of phagocytosed aluminium particles.

<http://www.ncbi.nlm.nih.gov/pubmed/23992993>

“Much information will be gained
by investigating the phagosomal pathway
and what occurs inside the phagosomes and
to elucidate the ultimate fate of phagocytosed
aluminium particles.”

Aluminium and breast cancer:
Sources of exposure, tissue measurements
and mechanisms of toxicological actions
on breast biology

Author information

Darbre PD1, Mannello F, Exley C.

School of Biological Sciences, University of Reading
Reading RG6 6UB, UK
p.d.darbre@reading.ac.uk

Abstract

This review examines recent evidence linking exposure to aluminium with the aetiology of breast cancer. The human population is exposed to aluminium throughout daily life including through diet, application of antiperspirants, use of antacids and vaccination. Aluminium has now been measured in a range of human breast structures at higher levels than in blood serum and experimental evidence suggests that the tissue concentrations measured have the potential to adversely influence breast epithelial cells including generation of genomic instability, induction of anchorage-independent proliferation and interference in oestrogen action. The presence of aluminium in the human breast may also alter the breast microenvironment causing disruption to iron metabolism, oxidative damage to cellular components, inflammatory responses and alterations to the motility of cells. The main research need is now to investigate whether the concentrations of aluminium measured in the human breast can lead in vivo to any of the effects observed in cells in vitro and this would be aided by the identification of biomarkers specific for aluminium action.

<http://www.ncbi.nlm.nih.gov/pubmed/23899626>

“Aluminium has now been measured in a range of human breast structures at higher levels than in blood serum and experimental evidence suggests that the tissue concentrations measured have the potential to adversely influence breast epithelial cells including generation of genomic instability, induction of anchorage-independent proliferation and interference in oestrogen action.”

Aluminum's Role in CNS-immune System Interactions leading to Neurological Disorders

Shaw CA^{1,2,3*}, Kette SD⁴, Davidson RM⁵ and Seneff S⁶

1. Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences
828 W. 10th Ave., Vancouver, British Columbia, V5Z1L8, Canada

2. Program Experimental Medicine, University of British Columbia, Vancouver, V5Z1L8, Canada

3. Program in Neurosciences, University of British Columbia, Vancouver, V5Z1L8, Canada

4. Independent researcher, Hudson, FL 34667, USA

5. Internal Medicine Group Practice, PhyNet, Inc., 4002 Technology Center, Longview, TX 75605, USA

6. MIT Computer Science and Artificial Intelligence Laboratory, 32 Vassar Street, Cambridge, MA 02139, USA

Abstract

Multisystem interactions are well established in neurological disorders, in spite of conventional views that only the central nervous system (CNS) is impacted. We review evidence for mutual interactions between the immune and nervous systems and show how these seem to be implicated in the origin and progression of nervous system disorders. Well-established immune system triggers leading to autoimmune reactions are considered. Of these, aluminum, a known neurotoxicant, may be of particular importance. We have demonstrated elsewhere that aluminum has the potential to induce damage at a range of levels in the CNS leading to neuronal death, circuit malfunction and ultimately, system failure. Aluminum is widely used as an adjuvant in various vaccine formulations and has been implicated in a multisystem disorder termed “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA). The implications of aluminum-induced ASIA in some disorders of the CNS are considered. We propose a unified theory capturing a progression from a local response to a systemic response initiated by disruption of water-based interfaces of exposed cells.

https://people.csail.mit.edu/seneff/Shaw_et_al_Immunome_Res_2013.pdf

“The implications of aluminum-induced ASIA
in some disorders of the Central Nervous System are considered.”

“Unfortunately, despite its favorable safety profile, aluminum hydroxide can only weakly or moderately potentiate antigen-specific antibody responses. Simply reducing the particle size of the traditional aluminum hydroxide adjuvant into nanometers represents a novel and effective approach to improve its adjuvanticity.”

Journal Of Controlled Release • January 2014

**Aluminum hydroxide nanoparticles
show a stronger vaccine adjuvant activity
than traditional aluminum hydroxide microparticles**

Author information

Li X, Aldayel AM, Cui Z.

The University of Texas at Austin
College of Pharmacy, Pharmaceutics Division
Austin, TX 78712, USA

Abstract

Aluminum hydroxide is used as a vaccine adjuvant in various human vaccines. Unfortunately, despite its favorable safety profile, aluminum hydroxide can only weakly or moderately potentiate antigen-specific antibody responses. When dispersed in an aqueous solution, aluminum hydroxide forms particulates of 1-20 μ m. There is increasing evidence that nanoparticles around or less than 200nm as vaccine or antigen carriers have a more potent adjuvant activity than large microparticles. In the present study, we synthesized aluminum hydroxide nanoparticles of 112nm. Using ovalbumin and Bacillus anthracis protective antigen protein as model antigens, we showed that protein antigens adsorbed on the aluminum hydroxide nanoparticles induced a stronger antigen-specific antibody response than the same protein antigens adsorbed on the traditional aluminum hydroxide microparticles of around 9.3 μ m. The potent adjuvant activity of the aluminum hydroxide nanoparticles was likely related to their ability to more effectively facilitate the uptake of the antigens adsorbed on them by antigen-presenting cells. Finally, the local inflammation induced by aluminum hydroxide nanoparticles in the injection sites was milder than that induced by microparticles. Simply reducing the particle size of the traditional aluminum hydroxide adjuvant into nanometers represents a novel and effective approach to improve its adjuvanticity.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3918952/>

Biopersistence and systemic distribution of intramuscularly injected particles: what impact on long-term tolerability of alum adjuvants?

Gherardi RK, Cadusseau J, Authier FJ.

Abstract

Aluminium oxyhydroxide (alum), a nanocrystalline compound that forms agglomerates, has been widely used as a vaccine adjuvant since 1927, but the mechanisms by which it stimulates immune responses remain poorly understood. Although generally well tolerated, alum may occasionally cause chronic health problems in presumably susceptible individuals. Some individuals may rarely develop delayed-onset diffuse myalgia, chronic exhaustion and cognitive dysfunction, associated with long-term persistence (up to 12 years) of alum-loaded macrophages at site of i.m. immunization, defining so-called macrophagic myofasciitis (MMF). Symptoms are consistent with the chronic fatigue/myalgic encephalomyelitis (CFS/ME) syndrome, and have been used as a paradigm of the “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA). Cognitive dysfunction is reminiscent of that described in workers exposed to inhaled Al particles. Individual susceptibility may influence both alum biopersistence and diffusion away from injection sites. Biopersistent particles such as fluorescent alum-coated nanohybrids, when injected into mouse muscle, are captured by monocyte-lineage cells and then carried to distant organs, draining lymph nodes and blood, probably via the thoracic duct, with delayed and accumulative translocation to the brain (microglial cells). Brain penetration occurs at extremely low levels in normal conditions, possibly explaining the good tolerance of alum despite its high neurotoxic potential. However, systemic diffusion is considerably enhanced by the potentiating effect of MCP-1, the main monocyte chemoattractant factor, the production of which is subject to marked variations linked to age and to genetic and environmental factors. Selective MCP-1 elevation is the only known circulating biomarker of MMF.

<http://www.ncbi.nlm.nih.gov/pubmed/26259285>

“Biopersistent particles such as fluorescent alum-coated nanohybrids, when injected into mouse muscle, are captured by monocyte-lineage cells and then carried to distant organs, draining lymph nodes and blood, probably via the thoracic duct, with delayed and accumulative translocation to the brain (microglial cells). Brain penetration occurs at extremely low levels in normal conditions, possibly explaining the good tolerance of alum despite its high neurotoxic potential.”

Effects of adjuvants for human use in systemic lupus erythematosus (SLE)-prone (New Zealand black/New Zealand white) F1 mice

Author information

Favoino E1, Favia EI, Digiglio L,
Racanelli V, Shoenfeld Y, Perosa F.

Department of Internal Medicine (DIMO)
Rheumatologic and Systemic Autoimmune Diseases
and Internal Medicine Section
University of Bari Medical School, Bari, Italy

Abstract

The safety of four different adjuvants was assessed in lupus-prone New Zealand black/New Zealand white (BW)F1 mice. Four groups of mice were injected intraperitoneally with incomplete Freund's adjuvant (IFA), complete Freund's adjuvant (CFA), squalene (SQU) or aluminium hydroxide (ALU). An additional group received plain phosphate-buffered saline (PBS) (UNT group). Mice were primed at week 9 and boosted every other week up to week 15. Proteinuria became detectable at weeks 17 (IFA group), 24 (CFA group), 28 (SQU and ALU groups) and 32 (UNT group). Different mean values were obtained among the groups from weeks 17 to 21 [week 17: one-way analysis of variance (anova) $P = 0.016$; weeks 18 and 19: $P = 0.048$; weeks 20 and 21: $P = 0.013$] being higher in the IFA group than the others [Tukey's honestly significant difference (HSD) post-test $P < 0.05$]. No differences in anti-DNA antibody levels were observed among groups. Anti-RNP/Sm antibody developed at week 19 in only one CFA-treated mouse. Mean mouse weight at week 18 was lower in the ALU group than the IFA (Tukey's HSD post-test $P = 0.04$), CFA ($P = 0.01$) and SQU ($P < 0.0001$) groups, while the mean weight in the SQU group was higher than in the IFA ($P = 0.009$), CFA ($P = 0.013$) and UNT ($P = 0.005$) groups. The ALU group weight decreased by almost half between weeks 29 and 31, indicating some toxic effect of ALU in the late post-immunization period. Thus, SQU was the least toxic adjuvant as it did not (i) accelerate proteinuria onset compared to IFA; (ii) induce toxicity compared to ALU or (iii) elicit anti-RNP/Sm autoantibody, as occurred in the CFA group.

<http://www.ncbi.nlm.nih.gov/pubmed/24112107>

“The aluminum group weight decreased by almost half between weeks 29 and 31, indicating some toxic effect of aluminum in the late post-immunization period.”

Aluminium adjuvants and adverse events in sub-cutaneous allergy immunotherapy

Christopher Exley

The Birchall Centre
Lennard-Jones Laboratories
Keele University, Staffordshire, UK
c.exley@keele.ac.uk

Abstract

Sub-cutaneous immunotherapy is an effective treatment for allergy. It works by helping to modify or re-balance an individual's immune response to allergens and its efficacy is greatly improved by the use of adjuvants, most commonly, aluminium hydroxide. Aluminium salts have been used in allergy therapy for many decades and are assumed to be safe with few established side-effects. This assumption belies their potency as adjuvants and their potential for biological reactivity both at injection sites and elsewhere in the body. There are very few data purporting to the safety of aluminium adjuvants in allergy immunotherapy and particularly so in relation to longer term health effects. There are, if only few, published reports of adverse events following allergy immunotherapy and aluminium adjuvants are the prime suspects in the majority of such incidents. Aluminium adjuvants are clearly capable of initiating unwanted side effects in recipients of immunotherapy and while there is as yet no evidence that such are commonplace it is complacent to consider aluminium salts as harmless constituents of allergy therapies. Future research should establish the safety of the use of aluminium adjuvants in sub-cutaneous allergy immunotherapy.

<http://www.aacijournal.com/content/10/1/4>

“Aluminium salts

have been used in allergy therapy for many decades and are assumed to be safe with few established side-effects.

This assumption belies their potency as adjuvants and their potential for biological reactivity both at injection sites and elsewhere in the body.”

Aluminium in Biological Environments: A Computational Approach

Author Information

Jon I Mujika,^a Elixabete Rezabal,^b
Jose M Mercero,^a Fernando Ruipérez,^c Dominique Costa,^d
Jesus M Ugalde,^a and Xabier Lopeza

- a. Kimika Fakultatea, Euskal Herriko Unibertsitatea (UPV/EHU)
and Donostia International Physics Center (DIPC)
P.K. 1072, 20080 Donostia, Euskadi, Spain
b. Laboratoire de Chimie Moleculaire
Department of Chemistry, Ecole Polytechnique and CNRS
91128 Palaiseau Cedex, France
c. POLYMAT, Euskal Herriko Unibertsitatea UPV/EHU
Joxe Mari Korta zentroa, Tolosa Etorbidea 72
20018 Donostia-San Sebastián, Euskadi, Spain
d. Laboratoire de Physico-Chimie des Surfaces (UMR 7045)
ENSCP Chimie-Paristech, 11 rue P. et M. Curie, 75005 Paris, France

Abstract

The increased availability of aluminium in biological environments, due to human intervention in the last century, raises concerns on the effects that this so far “excluded from biology” metal might have on living organisms. Consequently, the bioinorganic chemistry of aluminium has emerged as a very active field of research. This review will focus on our contributions to this field, based on computational studies that can yield an understanding of the aluminum biochemistry at a molecular level. Aluminium can interact and be stabilized in biological environments by complexing with both low molecular mass chelants and high molecular mass peptides. The speciation of the metal is, nonetheless, dictated by the hydrolytic species dominant in each case and which vary according to the pH condition of the medium. In blood, citrate and serum transferrin are identified as the main low molecular mass and high molecular mass molecules interacting with aluminium. The complexation of aluminium to citrate and the subsequent changes exerted on the deprotonation pathways of its tritabile groups will be discussed along with the mechanisms for the intake and release of aluminium in serum transferrin at two pH conditions, physiological neutral and endosomal acidic. Aluminium can substitute other metals, in particular magnesium, in protein buried sites and trigger conformational disorder and alteration of the protonation states of the protein’s sidechains. A detailed account of the interaction of aluminium with proteic sidechains will be given. Finally, it will be described how aluminium can exert oxidative stress by stabilizing superoxide radicals either as mononuclear aluminium or clustered in boehmite. The possibility of promotion of Fenton reaction, and production of hydroxyl radicals will also be discussed.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3995234/>

“The increased availability of aluminium in biological environments, due to human intervention in the last century, raises concerns on the effects that this so far “excluded from biology” metal might have on living organisms.”

“There is prolonged retention of a fraction of aluminium that enters the brain ...”

Neurotoxicology • March 2014

Oxidative stress and mitochondrial dysfunction in aluminium neurotoxicity and its amelioration: a review

Author information

Kumar V1, Gill KD2.

1. Department of Biochemistry, Maharshi Dayanand University, Rohtak, India

2. Department of Biochemistry, Maharshi Dayanand University, Rohtak, India

Department of Biochemistry, Postgraduate Institute of Medical Education and Research

Chandigarh, India

kdgill2002@yahoo.co.in

Abstract

Aluminium is light weight and toxic metal present ubiquitously on earth which has gained considerable attention due to its neurotoxic effects. The widespread use of products made from or containing aluminium is ensuring its presence in our body. There is prolonged retention of a fraction of aluminium that enters the brain, suggesting its potential for accumulation with repeated exposures. There is no known biological role for aluminium within the body but adverse physiological effects of this metal have been observed in mammals. The generation of oxidative stress may be attributed to its toxic consequences in animals and humans. The oxidative stress has been implicated in pathogenesis of various neurodegenerative conditions including Alzheimer's disease and Parkinson's disease. Though it remains unclear whether oxidative stress is a major cause or merely a consequence of cellular dysfunction associated with neurodegenerative diseases, an accumulating body of evidence implicates that impaired mitochondrial energy production and increased mitochondrial oxidative damage is associated with the pathogenesis of neurodegenerative disorders. Being involved in the production of reactive oxygen species, aluminium may impair mitochondrial bioenergetics and may lead to the generation of oxidative stress. In this review, we have discussed the oxidative stress and mitochondrial dysfunctions occurring in Al neurotoxicity. In addition, the ameliorative measures undertaken in aluminium induced oxidative stress and mitochondrial dysfunctions have also been highlighted.

<http://www.ncbi.nlm.nih.gov/pubmed/24560992>

If exposure to aluminium in antiperspirants presents health risks, its content should be reduced

Author information

Pineau A1, Fauconneau B2, Sappino AP3, Deloncle R4, Guillard O5.

1. Université de Nantes, Faculté de Pharmacie

Laboratoire de Toxicologie, 44035 Nantes, France

2. Université de Poitiers, Faculté de Médecine et de Pharmacie

Service de Pharmacologie clinique, CHU Poitiers, 86021 Poitiers, France

3. Clinique des Grangettes, Chemin des Grangettes 7

1224 Chêne-Bougeries, Confédération Helvétique, Switzerland

4. Université de Tours, Faculté de Pharmacie, Laboratoire de Toxicologie, 37000 Tours, France

5. Université de Poitiers, Faculté de Médecine et Pharmacie

6 rue de la Milétrie, 86034 Poitiers, France

olivier.guillard@univ-poitiers.fr

Abstract

Since aluminium (Al) pervades our environment, the scientific community has for many years raised concerns regarding its safety in humans. Al is present in numerous cosmetics such as antiperspirants, lipsticks and sunscreens. Al chlorohydrate is the active antiperspirant agent in underarm cosmetics and may constitute for Al a key exposure route to the human body and a potential source of damage. An in vitro study has demonstrated that Al from antiperspirant can be absorbed through viable human stripped skin. The potential toxicity of Al has been clearly shown and recent works convincingly argue that Al could be involved in cancerogenic processes. Nowadays, for example, Al is suspected of being involved in breast cancer. Recent work in cells in culture has lent credence to the hypothesis that this metal could accumulate in the mammary gland and selectively interfere with the biological properties of breast epithelial cells, thereby promoting a cascade of alterations reminiscent of the early phases of malignant transformation. In addition, several studies suggest that the presence of Al in human breast could influence metastatic process. As a consequence, given that the toxicity of Al has been widely recognized and that it is not a physiological component in human tissues, reducing the concentration of this metal in antiperspirants is a matter of urgency.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24418462>

“Al chlorohydrate is the active antiperspirant agent in underarm cosmetics and may constitute for Aluminum a key exposure route to the human body and a potential source of damage. An in vitro study has demonstrated that Aluminum from antiperspirant can be absorbed through viable human stripped skin. The potential toxicity of Aluminum has been clearly shown and recent works convincingly argue that Aluminum could be involved in cancerogenic processes.”

Aluminum exposure and toxicity in neonates: a practical guide to halt aluminum overload in the prenatal and perinatal periods

Author information

Fanni D1, Ambu R, Gerosa C, Nemolato S,
Iacovidou N, Van Eyken P, Fanos V, Zaffanello M, Faa G.

Department of Pathology
University Hospital San Giovanni di Dio
AOU Cagliari and University of Cagliari
Cagliari, Italy

Abstract

BACKGROUND

During the last years, human newborns have been overexposed to biologically reactive aluminum, with possible relevant consequences on their future health and on their susceptibility to a variety of diseases. Children, newborns and particularly preterm neonates are at an increased risk of aluminum toxicity because of their relative immaturity.

DATA SOURCES

Based on recent original publications and classical data of the literatures, we reviewed the aluminum content in mother's food during the intrauterine life as well as in breast milk and infant formula during lactation. We also determined the possible role of aluminum in parenteral nutrition solutions, in adjuvants of vaccines and in pharmaceutical products. A special focus is placed on the relationship between aluminum overexposure and the insur-
gence of bone diseases.

RESULTS

Practical points of management and prevention are suggested. Aluminum sources that infants may receive during the first 6 months of life are presented. In the context of prevention of possible adverse effects of aluminum overload in fetal tissues during development, simple suggestions to pregnant women are described. Finally, practical points of management and prevention are suggested.

CONCLUSIONS

Pediatricians and neonatologists must be more concerned about aluminum content in all products our newborns are exposed to, starting from monitoring aluminum concentrations in milk- and soy-based formulas in which, on the basis of recent studies, there is still too much aluminum.

“Pediatricians and neonatologists
must be more concerned about aluminum content
in all products our newborns are exposed to, starting from
monitoring aluminum concentrations in milk and soy
based formulas in which, on the basis of recent studies,
there is still too much aluminum.”

Aluminum enhances inflammation and decreases mucosal healing in experimental colitis in mice

Author information

Pineton de Chambrun G1, Body-Malapel M2, Frey-Wagner I3, Djouina M2, Deknuydt F4, Atrott K3, Esquerre N2, Altare F4, Neut C5, Arrieta MC6, Kanneganti TD7, Rogler G3, Colombel JF1, Cortot A1, Desreumaux P1, Vignal C2

1. Univ Lille Nord de France, Lille, France [2] Inserm U995, Lille, France [3] UDSL, Lille, France [4] Hepato-Gastroenterology Department, CHU Lille, Lille, France
2. Univ Lille Nord de France, Lille, France [2] Inserm U995, Lille, France [3] UDSL, Lille, France
3. Division of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland
4. INSERM, UMR892, Nantes, France [2] CNRS, UMR6299, Nantes, France [3] Université de Nantes, Nantes, France
5. Univ Lille Nord de France, Lille, France [2] Inserm U995, Lille, France [3] UDSL, Lille, France [4] Clinical Bacteriology, College of Pharmacy, Lille, France
6. Finlay Lab, Michael Smith Laboratories, University of British Columbia Vancouver, British Columbia, Canada
7. Department of Immunology, St Jude Children's Research Hospital, Memphis, Tennessee, USA

Abstract

The increasing incidence of inflammatory bowel diseases (IBDs) in developing countries has highlighted the critical role of environmental pollutants as causative factors in their pathophysiology. Despite its ubiquity and immune toxicity, the impact of aluminum in the gut is not known. This study aimed to evaluate the effects of environmentally relevant intoxication with aluminum in murine models of colitis and to explore the underlying mechanisms. Oral administration of aluminum worsened intestinal inflammation in mice with 2,4,6-trinitrobenzene sulfonic acid- and dextran sodium sulfate-induced colitis and chronic colitis in interleukin 10-negative (IL10(-/-)) mice. Aluminum increased the intensity and duration of macroscopic and histologic inflammation, colonic myeloperoxidase activity, inflammatory cytokines expression, and decreased the epithelial cell renewal compared with control animals. Under basal conditions, aluminum impaired intestinal barrier function. In vitro, aluminum induced granuloma formation and synergized with lipopolysaccharide to stimulate inflammatory cytokines expression by epithelial cells. Deleterious effects of aluminum on intestinal inflammation and mucosal repair strongly suggest that aluminum might be an environmental IBD risk factor.

<http://www.ncbi.nlm.nih.gov/pubmed/24129165>

“Deleterious effects of aluminum on intestinal inflammation and mucosal repair strongly suggest that aluminum might be an environmental Inflammatory Bowel Disease risk factor.”

What is the risk of aluminium as a neurotoxin?

by Christopher Exley

The Birchall Centre
Lennard- Jones Laboratories
Keele University, Staffordshire, UK

The body burden of aluminium:

To understand or even appreciate the risk that aluminium poses as a neurotoxin, we will need to further our understanding of the body burden of aluminium and we will need to implement measures to reduce the body burden to a lowest practical limit. I have recently reformulated the definition of aluminium's body burden placing it into the context of what I have called aluminium's exposome [13]. We have also been investigating non-invasive ways to reduce the uptake of aluminium into the body and, importantly, to facilitate the excretion of aluminium from the body. We were successful in lowering the body burden of aluminium in individuals with moderate-to-severe AD and concomitantly we were able to demonstrate clinically significant improvements in cognitive performance in some individuals [14]. These experiments offer some hope that the aluminium hypothesis of AD, and indeed other neurodegenerative diseases, might be tested by lowering the body burden of aluminium in affected individuals. Then we might be able to ascertain if AD, for example, is the human manifestation of the risk of aluminium as a known neurotoxin.

“Then we might be able to ascertain if AD, for example, is the human manifestation of the risk of aluminium as a known neurotoxin.”

“There is now sufficient evidence from both human and animal studies showing that cumulative exposure to aluminium adjuvants is not as benign as previously assumed.”

Autism • Causes & Prevalence • June 2014

Etiology of autism spectrum disorders: Genes, environment, or both?

C Shaw^{1*}, S Sheth¹, D Li¹, L Tomljenovic¹

University of British Columbia, Vancouver, British Columbia, Canada
cashawlab@gmail.com

Abstract

Thus far, most of the research on both neurodevelopmental and neurodegenerative disorders has been focused on finding the presumed underlying genetic causes, while much less emphasis has been put on potential environmental factors. While some forms of autism are clearly genetic, the fact remains that heritability factors cannot adequately explain all reported cases nor their drastic increase over the last few decades. In particular, studies on twins have now shown that common environmental factors account for 55% of their risk for developing autism while genetic susceptibility explains only 37% of cases. Because the prenatal environment and early postnatal environment are shared between twins and because overt symptoms of autism emerge around the end of the first year of life, it is likely that at least some of the environmental factors contributing to the risk of autism exert their deleterious neurodevelopmental effect during this early period of life. Indeed, evidence has now emerged showing that autism may in part result from early-life immune insults induced by environmental xenobiotics. One of the most common xenobiotic with immuno-stimulating as well as neurotoxic properties to which infants under two years of age are routinely exposed worldwide is the aluminum (Al) vaccine adjuvant. In this review we discuss the mechanisms by which Al can induce adverse neurological and immunological effects and how these may provide important clues of Al's putative role in autism. Because of the tight connection between the development of the immune and the central nervous system, the possibility that immune-overstimulation in early infancy via vaccinations may play a role in neurobehavioural disorders needs to be carefully considered.

Conclusion

There is now sufficient evidence from both human and animal studies showing that cumulative exposure to aluminium adjuvants is not as benign as previously assumed. Given that vaccines are the only medical intervention that we attempt to deliver to every living human on earth and that by far the largest target population for vaccination are healthy children, a better appreciation and understanding of vaccine adjuvant risks appears warranted.

<http://www.oapublishinglondon.com/article/1368>

Aluminium in allergen-specific subcutaneous immunotherapy— a German perspective

Author information

Kramer MF1, Heath MD2.

1. Bencard Allergie GmbH, Messerschmittstr. 4, 80992 München, Germany.
2. Allergy Therapeutics, Plc. Dominion Way, Worthing BN14 8SA, United Kingdom
matthew.heath@allergytherapeutics.com

Abstract

We are living in an “aluminium age” with increasing bioavailability of the metal for approximately 125 years, contributing significantly to the aluminium body burden of humans. Over the course of life, aluminium accumulates and is stored predominantly in the lungs, bones, liver, kidneys and brain. The toxicity of aluminium in humans is briefly summarised, highlighting links and possible causal relationships between a high aluminium body burden and a number of neurological disorders and disease states. Aluminium salts have been used as depot-adjuvants successfully in essential prophylactic vaccinations for almost 100 years, with a convincing positive benefit-risk assessment which remains unchanged. However, allergen-specific immunotherapy commonly consists of administering a long-course programme of subcutaneous injections using preparations of relevant allergens. Regulatory authorities currently set aluminium limits for vaccines per dose, rather than per treatment course. Unlike prophylactic vaccinations, numerous injections with higher proportions of aluminium-adjuvant per injection are applied in subcutaneous immunotherapy (SCIT) and will significantly contribute to a higher cumulative life dose of aluminium. While the human body may cope robustly with a daily aluminium overload from the environment, regulatory cumulative threshold values in immunotherapy need further addressing. Based on the current literature, predisposing an individual to an unusually high level of aluminium, such as through subcutaneous immunotherapy, has the potential to form focal accumulations in the body with the propensity to exert forms of toxicity. Particularly in relation to longer-term health effects, the safety of aluminium adjuvants in immunotherapy remains unchallenged by health authorities - evoking the need for more consideration, guidance, and transparency on what is known and not known about its safety in long-course therapy and what measures can be taken to prevent or minimise its risks. The possibility of providing an effective means of measuring aluminium accumulation in patients undergoing long-term SCIT treatment as well as reducing their aluminium body burden is discussed.

Full Report

<http://www.sciencedirect.com/science/article/pii/S0264410X14007397>

“... the safety of aluminium adjuvants
in immunotherapy remains unchallenged
by health authorities - evoking the need
for more consideration ...”

“... there is only a limited understanding of the response of regulatory T cells to aluminum adjuvants and the vaccines that contain them.”

Vaccine • September 2014

**A role for impaired regulatory T cell function
in adverse responses to aluminum adjuvant-containing vaccines
in genetically susceptible individuals**

Author information

Terhune TD, Deth RC.

Department of Pharmaceutical Sciences
Northeastern University, Boston, MA, USA
todderhune@comcast.net

Abstract

Regulatory T cells play a critical role in the immune response to vaccination, but there is only a limited understanding of the response of regulatory T cells to aluminum adjuvants and the vaccines that contain them. Available studies in animal models show that although induced T regulatory cells may be induced concomitantly with effector T cells following aluminum-adjuvanted vaccination, they are unable to protect against sensitization, suggesting that under the Th2 immune-stimulating effects of aluminum adjuvants, Treg cells may be functionally compromised. Allergic diseases are characterized by immune dysregulation, with increases in IL-4 and IL-6, both of which exert negative effects on Treg function. For individuals with a genetic predisposition, the beneficial influence of adjuvants on immune responsiveness may be accompanied by immune dysregulation, leading to allergic diseases. This review examines aspects of the regulatory T cell response to aluminum-adjuvanted immunization and possible genetic susceptibility factors related to that response.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25066736>

Aluminum-induced entropy in biological systems: implications for neurological disease

Author information

Shaw CA1, Seneff S2, Kette SD3,
Tomljenovic L4, Oller JW Jr5, Davidson RM6.

1. Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences
828 W. 10th Avenue, Vancouver, British Columbia, Canada V5Z 1L8; Program
Experimental Medicine, University of British Columbia, Vancouver, Canada V5Z 1L8
Program in Neurosciences, University of British Columbia, Vancouver, Canada V5Z 1L8
2. MIT Computer Science and Artificial Intelligence Laboratory
32 Vassar Street, Cambridge, MA 02139, USA
3. Hudson, FL 34667, USA
4. Neural Dynamics Research Group, Department of Ophthalmology and Visual Sciences,
828 W. 10th Avenue, Vancouver, British Columbia, Canada V5Z 1L8
5. Department of Communicative Disorders, University of Louisiana
Lafayette, LA 70504-3170, USA
6. Internal Medicine Group Practice, PhyNet Inc., 4002 Technology Center
Longview, TX 75605, USA

Abstract

Over the last 200 years, mining, smelting, and refining of aluminum (Al) in various forms have increasingly exposed living species to this naturally abundant metal. Because of its prevalence in the earth's crust, prior to its recent uses it was regarded as inert and therefore harmless. However, Al is invariably toxic to living systems and has no known beneficial role in any biological systems. Humans are increasingly exposed to Al from food, water, medicinals, vaccines, and cosmetics, as well as from industrial occupational exposure. Al disrupts biological self-ordering, energy transduction, and signaling systems, thus increasing biosemiotic entropy. Beginning with the biophysics of water, disruption progresses through the macromolecules that are crucial to living processes (DNAs, RNAs, proteoglycans, and proteins). It injures cells, circuits, and subsystems and can cause catastrophic failures ending in death. Al forms toxic complexes with other elements, such as fluorine, and interacts negatively with mercury, lead, and glyphosate. Al negatively impacts the central nervous system in all species that have been studied, including humans. Because of the global impacts of Al on water dynamics and biosemiotic systems, CNS disorders in humans are sensitive indicators of the Al toxicants to which we are being exposed.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4202242/>

“Beginning with the biophysics of water, disruption progresses through the macromolecules that are crucial to living processes (DNAs, RNAs, proteoglycans, and proteins). It injures cells, circuits, and subsystems and can cause catastrophic failures ending in death. Aluminum forms toxic complexes with other elements, such as fluorine, and interacts negatively with mercury, lead, and glyphosate.

Aluminum negatively impacts the central nervous system in all species that have been studied, including humans. Because of the global impacts of Aluminum on water dynamics and biosemiotic systems, Central Nervous System disorders in humans are sensitive indicators of the Aluminum toxicants to which we are being exposed.

... vaccine trials often treat an Aluminum adjuvant-containing injection as a harmless “ placebo “ (a comparison benchmark or control treatment) or they use another Al-containing vaccine to treat a “ control group, “ despite evidence that Aluminum in vaccine-relevant exposures is universally toxic to humans and animals. Its use in a supposed “ placebo “ or in any “ control “ treatment in vaccine trials is indefensible.”

Systematic review of potential health risks posed by pharmaceutical, occupational and consumer exposures to metallic and nanoscale aluminum, aluminum oxides, aluminum hydroxide and its soluble salts

Author information

Willhite CC1, Karyakina NA, Yokel RA, Yenugadhati N, Wisniewski TM, Arnold IM, Momoli F, Krewski D.
Risk Sciences International, Ottawa, ON , Canada

Abstract

Abstract Aluminum (Al) is a ubiquitous substance encountered both naturally (as the third most abundant element) and intentionally (used in water, foods, pharmaceuticals, and vaccines); it is also present in ambient and occupational airborne particulates. Existing data underscore the importance of Al physical and chemical forms in relation to its uptake, accumulation, and systemic bioavailability. The present review represents a systematic examination of the peer-reviewed literature on the adverse health effects of Al materials published since a previous critical evaluation compiled by Krewski et al. (2007). Challenges encountered in carrying out the present review reflected the experimental use of different physical and chemical Al forms, different routes of administration, and different target organs in relation to the magnitude, frequency, and duration of exposure. Wide variations in diet can result in Al intakes that are often higher than the World Health Organization provisional tolerable weekly intake (PTWI), which is based on studies with Al citrate. Comparing daily dietary Al exposures on the basis of “total Al” assumes that gastrointestinal bioavailability for all dietary Al forms is equivalent to that for Al citrate, an approach that requires validation. Current occupational exposure limits (OELs) for identical Al substances vary as much as 15-fold. The toxicity of different Al forms depends in large measure on their physical behavior and relative solubility in water. The toxicity of soluble Al forms depends upon the delivered dose of Al(+3) to target tissues. Trivalent Al reacts with water to produce bidentate superoxide coordination spheres $[Al(O_2)(H_2O)_4]^{+2}$ and $Al(H_2O)_6^{+3}$ that after complexation with $O_2(\bullet-)$, generate Al superoxides

$[Al(O_2(\bullet))(H_2O)_5]^{+2}$. Semireduced $AlO_2(\bullet)$ radicals deplete mitochondrial Fe and promote generation of H_2O_2 , $O_2(\bullet-)$ and $OH(\bullet)$. Thus, it is the Al(+3)-induced formation of oxygen radicals that accounts for the oxidative damage that leads to intrinsic apoptosis. In contrast, the toxicity of the insoluble Al oxides depends primarily on their behavior as particulates. Aluminum has been held responsible for human morbidity and mortality, but there is no consistent and convincing evidence to associate the Al found in food and drinking water at the doses and chemical forms presently consumed by people living in North America and Western Europe with increased risk for Alzheimer’s disease (AD). Neither is there clear evidence to show use of Al-containing underarm antiperspirants or cosmetics increases the risk of AD or breast cancer. Metallic Al, its oxides, and common Al salts have not been shown to be either genotoxic or carcinogenic. Aluminum exposures during neonatal and pediatric parenteral nutrition (PN) can impair bone mineralization and delay neurological development. Adverse effects to vaccines with Al adjuvants have occurred; however, recent controlled trials found that the immunologic response to certain vaccines with Al adjuvants was no greater, and in some cases less than, that after identical vaccination without Al adjuvants. The scientific literature on the adverse health effects of Al is extensive. Health risk assessments for Al must take into account individual co-factors (e.g., age, renal function, diet, gastric pH). Conclusions from the current review point to the need for refinement of the PTWI, reduction of Al contamination in PN solutions, justification for routine addition of Al to vaccines, and harmonization of OELs for Al substances.

“The scientific literature on the adverse health effects of Al is extensive. Conclusions from the current review point to the need for refinement of the provisional tolerable weekly intake (PTWI), reduction of Aluminum contamination in parenteral nutrition (PN) solutions, justification for routine addition of Aluminum to vaccines ...”

Why industry propaganda and political interference
cannot disguise the inevitable role played by human exposure
to aluminum in neurodegenerative diseases,
including Alzheimer's disease

Author Information

Christopher Exley

The Birchall Centre, Lennard-Jones Laboratories
Keele University, Stoke-on-Trent, UK

Abstract

In the aluminum age, it is clearly unpalatable for aluminum, the globe's most successful metal, to be implicated in human disease. It is unpalatable because for approximately 100 years human beings have reaped the rewards of the most abundant metal of the Earth's crust without seriously considering the potential consequences for human health. The aluminum industry is a pillar of the developed and developing world and irrespective of the tyranny of human exposure to aluminum it cannot be challenged without significant consequences for businesses, economies, and governments. However, no matter how deep the dependency or unthinkable the withdrawal, science continues to document, if not too slowly, a burgeoning body burden of aluminum in human beings. Herein, I will make the case that it is inevitable both today and in the future that an individual's exposure to aluminum is impacting upon their health and is already contributing to, if not causing, chronic diseases such as Alzheimer's disease. This is the logical, if uncomfortable, consequence of living in the aluminum age.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4209859/>

“Herein, I will make the case
that it is inevitable both today and in the
future that an individual's exposure to aluminum
is impacting upon their health and is already
contributing to, if not causing, chronic diseases
such as Alzheimer's disease. This is the logical,
if uncomfortable, consequence of living
in the aluminum age.”

Effects of aluminium and bacterial lipopolysaccharide on oxidative stress and immune parameters in roach, *Rutilus rutilus* L

Author information

Jolly S1, Jaffal A, Delahaut L, Palluel O, Porcher JM, Geffard A, Sanchez W, Betoulle S.

Université de Reims Champagne-Ardenne
UMR-I02 SEBIO, BP 1039, 51687
Reims Cedex 2, France
sabrina.jolly@univ-reims.fr

Abstract

Aluminium is used in diverse anthropogenic processes at the origin of pollution events in aquatic ecosystems. In the Champagne region (France), high concentrations of aluminium (Al) are detected due to vine-growing practices. In fish, little is known about the possible immune-related effects at relevant environmental concentrations. The present study analyzes the simultaneous effects of aluminium and bacterial lipopolysaccharide (LPS), alone and in combination, on toxicological biomarkers in the freshwater fish species *Rutilus rutilus*. For this purpose, roach treated or not with LPS were exposed to environmental concentrations of aluminium (100 µg/L) under laboratory-controlled conditions for 2, 7, 14 and 21 days. After each exposure time, we assessed hepatic lipoperoxidation, catalase activity, glutathione reductase activity and total glutathione content. We also analyzed cellular components related to the LPS-induced inflammatory response in possible target tissues, i.e. head kidney and spleen. Our results revealed a significant prooxidant effect in the liver cells and head kidney leukocytes of roach exposed to 100 µg of Al/L for 2 days. In liver, we observed more lipoperoxidation products and lower endogenous antioxidant activity levels such as glutathione reductase activity and total glutathione content. These prooxidant effects were associated with a higher oxidative burst in head kidney leukocytes, and they were all the more important in fish stimulated by LPS injection. These findings demonstrate that environmental concentrations of Al induce oxidative and immunotoxic effects in fish and are associated to an immunomodulatory process related to the inflammatory response.

<http://www.ncbi.nlm.nih.gov/pubmed/24996940>

“These findings demonstrate that environmental concentrations of Aluminum induce oxidative and immunotoxic effects in fish and are associated to an immunomodulatory process related to the inflammatory response.”

Unequivocal identification of intracellular aluminium adjuvant in a monocytic THP-1 cell line

Author information

Mold M1, Eriksson H2, Siesjö P3, Darabi A3, Shardlow E1, Exley C1.

1. The Birchall Centre, Lennard-Jones Laboratories, Keele University
Keele, Staffordshire, ST5 5BG, UK
2. Department of Biomedical Laboratory Science, Faculty of Health and Society
Malmö University, SE-205 06 Malmö, Sweden
3. Glioma Immunotherapy Group, Department of Clinical Sciences
BMC D14, Lund University, SE-221 84 Lund, Sweden

Abstract

Aluminium-based adjuvants (ABA) are the predominant adjuvants used in human vaccinations. While a consensus is yet to be reached on the aetiology of the biological activities of ABA several studies have identified shape, crystallinity and size as critical factors affecting their adjuvanticity. In spite of recent advances, the fate of ABA following their administration remains unclear. Few if any studies have demonstrated the unequivocal presence of intracellular ABA. Herein we demonstrate for the first time the unequivocal identification of ABA within a monocytic T helper 1 (THP-1) cell line, using lumogallion as a fluorescent molecular probe for aluminium. Use of these new methods revealed that particulate ABA was only found in the cell cytoplasm. Transmission electron microscopy revealed that ABA were contained within vesicle-like structures of approximately 0.5-1 μm in diameter.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4155332/>

“In spite of recent advances, the fate of Aluminium-based adjuvants following their administration remains unclear. Herein we demonstrate for the first time the unequivocal identification of ABA within a monocytic T helper 1 cell line, using lumogallion as a fluorescent molecular probe for aluminium. Use of these new methods revealed that particulate Aluminium-based adjuvants was only found in the cell cytoplasm.”

“This short “Opinion” paper will overview and comment on the current massive mobilization of aluminum into the earth’s biosphere.”

Frontiers In Neurology • December 2014

The mobilization of aluminum into the biosphere

Aileen I. Pogue¹ and Walter J. Lukiw^{2,3*}

1. Alchem Biotech, Toronto, ON, Canada

2. Louisiana State University Neuroscience Center and Department of Ophthalmology
Louisiana State University School of Medicine, New Orleans, LA, USA

3. Department of Neurology, Louisiana State University Health Sciences Center
New Orleans, LA, USA

Abstract

Aluminum is currently the most widely used non-ferrous metal, and its extraction and purification from geological stores exceeds that of any other metal except iron (1, 2). In 2013, global primary aluminum production was ~52 million tons (104 billion pounds) or about 15 pounds for very person on the earth (1–4). The global outlook for aluminum demand from developing countries such as Brazil, China, India, and Indonesia is rapidly increasing, due to new applications for aluminum and aluminum alloys in infrastructural support, transportation including automobiles, aviation and aerospace applications, electrical transmission, and the generation of energy, including catalytic zeolites in the petroleum and petrochemical industries (5). Interestingly, the largest “machine” built by humankind is the domestic and international networks for the transmission of electricity. Although traditionally-used copper has a higher electrical conductivity, aluminum is only slightly less so, being lighter, more ductile, and less expensive; aluminum is now widely used for both high-voltage tower construction and the electrical transmission wires themselves (2–5). It has been estimated that within the next 10 years aluminum production will exceed that of the previous 150 years (1–3). This prolific de novo generation of aluminum combined with its highly efficient recycling means this metal is becoming increasingly present in our biosphere, defined as the sum of all ecosystems and living organisms on the earth. This short “Opinion” paper will overview and comment on the current massive mobilization of aluminum into the earth’s biosphere.

<http://journal.frontiersin.org/article/10.3389/fneur.2014.00262/full>

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA): clues and pitfalls in the pediatric background

Author information

Esposito S1, Prada E, Mastrolia MV,
Tarantino G, Codecà C, Rigante D.

Pediatric Highly Intensive Care Unit
Department of Pathophysiology and Transplantation
Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Università degli Studi di Milano
Via Commenda 9, 20122, Milan, Italy
susanna.esposito@unimi.it

Abstract

The development and increasing diffusion of new vaccinations and global immunization protocols have aroused burning debates about safety of adjuvants and their immunogenicity-enhancing effect in vaccines. Shoenfeld and Agmon-Levin have grouped under the term “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA) a complex of variable signs and symptoms that may occur after a previous exposure to different adjuvants and also external environmental triggers, even eliciting specific overt immune-mediated disorders. This entity subsumes five medical conditions: post-vaccination phenomena, gulf war syndrome, macrophagic myofasciitis syndrome, siliconosis, and sick building syndrome, but the relevance and magnitude of the syndrome in the pediatric age is fundamentally limited to post-vaccination autoimmune or inflammatory disorders. The occurrence of vaccine-triggered phenomena represents a diagnostic challenge for clinicians and a research conundrum for many investigators. In this paper, we will analyze the general features of ASIA and focus on specific post-vaccination events in relation with the pediatric background. In the presence of a favorable genetic background, many autoimmune/inflammatory responses can be triggered by adjuvants and external factors, showing how the man himself might breach immune tolerance and drive many pathogenetic aspects of human diseases. Nonetheless, the elective application of ASIA diagnostic criteria to the pediatric population requires further assessment and evaluations. Additional studies are needed to help clarify connections between innate or adaptive immunity and pathological and/or protective autoantibodies mostly in the pediatric age, as children and adolescents are mainly involved in the immunization agendas related to vaccine-preventable diseases.

“In the presence of a favorable genetic background, many autoimmune/inflammatory responses can be triggered by adjuvants and external factors, showing how the man himself might breach immune tolerance and drive many pathogenetic aspects of human diseases.”

Aluminum content of human semen: implications for semen quality

Author information

Klein JP1, Mold M2, Mery L3, Cottier M4, Exley C5.

1. Université de Lyon, F-42023, Saint-Etienne, EA 4624, SFR IFRESIS, France
Université Jean Monnet and CHU de Saint-Etienne, France
2. The Birchall Centre, Lennard Jones Laboratories
Keele University, Staffordshire ST5 5BG, UK
3. Université de Lyon, F-42023, Saint-Etienne, EA 4624, SFR IFRESIS, France
Université Jean Monnet and CHU de Saint-Etienne, France
4. Université de Lyon, F-42023, Saint-Etienne, EA 4624, SFR IFRESIS, France
Université Jean Monnet and CHU de Saint-Etienne, France
5. The Birchall Centre, Lennard Jones Laboratories
Keele University, Staffordshire ST5 5BG, UK
c.exley@keele.ac.uk

Abstract

A deterioration of human semen quality has been observed over recent decades. A possible explanation could be an increased exposure to environmental pollutants, including aluminum. Our aim was to measure the aluminum concentration in the semen of 62 patients and to carry out a preliminary evaluation on its impact on specific semen parameters. For each patient, semen analyses were performed according to WHO guidelines. A graphite furnace atomic absorption spectrometry method was used to determine semen aluminum concentration. A cytological analysis using an aluminum-specific fluor, lumogallion, was also performed. The mean aluminum concentration in human semen was 339 µg/L. Patients with oligozoospermia had a statistically higher aluminum concentration than others. No significant difference was observed for other semen parameters. Cytological analysis showed the presence of aluminum in spermatozoa. This study provided unequivocal evidence of high concentrations of aluminum in human semen and suggested possible implications for spermatogenesis and sperm count.

<http://www.ncbi.nlm.nih.gov/pubmed/25461904>

“This study provided unequivocal evidence of high concentrations of aluminum in human semen and suggested possible implications for spermatogenesis and sperm count.”

**Chronic aluminum intake
causes Alzheimer's disease:
applying Sir Austin Bradford Hill's
causality criteria**

Walton JR

Faculty of Medicine
University of New South Wales
St George Hospital, Sydney, Australia

Industrialized societies produce many convenience foods with aluminum additives that enhance various food properties and use alum (aluminum sulfate or aluminum potassium sulfate) in water treatment to enable delivery of large volumes of drinking water to millions of urban consumers. The present causality analysis evaluates the extent to which the routine, life-long intake, and metabolism of aluminum compounds can account for Alzheimer's disease (AD), using Austin Bradford Hill's nine epidemiological and experimental causality criteria, including strength of the relationship, consistency, specificity, temporality, dose-dependent response, biological rationale, coherence with existing knowledge, experimental evidence, and analogy. Mechanisms that underlie the risk of low concentrations of aluminum relate to (1) aluminum's absorption rates, allowing the impression that aluminum is safe to ingest and as an additive in food and drinking water treatment, (2) aluminum's slow progressive uptake into the brain over a long prodromal phase, and (3) aluminum's similarity to iron, in terms of ionic size, allows aluminum to use iron-evolved mechanisms to enter the highly-active, iron-dependent cells responsible for memory processing. Aluminum particularly accumulates in these iron-dependent cells to toxic levels, dysregulating iron homeostasis and causing microtubule depletion, eventually producing changes that result in disconnection of neuronal afferents and efferents, loss of function and regional atrophy consistent with MRI findings in AD brains. AD is a human form of chronic aluminum neurotoxicity. The causality analysis demonstrates that chronic aluminum intake causes AD.

<http://europepmc.org/abstract/med/24577474>

“Aluminum particularly accumulates in these iron-dependent cells to toxic levels, dysregulating iron homeostasis and causing microtubule depletion, eventually producing changes that result in disconnection of neuronal afferents and efferents, loss of function and regional atrophy consistent with MRI findings in AD brains. AD is a human form of chronic aluminum neurotoxicity. The causality analysis demonstrates that chronic aluminum intake causes AD.”

Immunotherapy • 2014

Are there negative CNS impacts of aluminum adjuvants used in vaccines and immunotherapy?

Author information

Shaw CA1, Li D, Tomljenovic L.

Neural Dynamics Research Group
828 W. 10th Ave, Vancouver
BC, V5Z 1L8, Canada

Abstract

In spite of a common view that aluminum (Al) salts are inert and therefore harmless as vaccine adjuvants or in immunotherapy, the reality is quite different. In the following article we briefly review the literature on Al neurotoxicity and the use of Al salts as vaccine adjuvants and consider not only direct toxic actions on the nervous system, but also the potential impact for triggering autoimmunity. Autoimmune and inflammatory responses affecting the CNS appear to underlie some forms of neurological disease, including developmental disorders. Al has been demonstrated to impact the CNS at every level, including by changing gene expression. These outcomes should raise concerns about the increasing use of Al salts as vaccine adjuvants and for the application as more general immune stimulants.

<http://www.ncbi.nlm.nih.gov/pubmed/25428645>

“Aluminum has been demonstrated to impact the Central Nervous System at every level, including by changing gene expression. These outcomes should raise concerns about the increasing use of Aluminum salts as vaccine adjuvants and for the application as more general immune stimulants.”

“Currently, ethylmercury (EtHg) and adjuvant-Aluminum are the dominating interventional exposures encountered by fetuses, newborns, and infants due to immunization with Thimerosal-containing vaccines (TCVs). Despite their long use as active agents of medicines and fungicides, the safety levels of these substances have never been determined, either for animals or for adult humans—much less for fetuses, newborns, infants, and children.”

International Journal Of Environmental Research And Public Health • January 2015

**Exposure to mercury and aluminum in early life:
developmental vulnerability as a modifying factor
in neurologic and immunologic effects**

Author information

Dórea JG.

Department of Nutrition
Faculty of Health Sciences
Universidade de Brasilia
70919-970 DF Brasilia, Brazil
jg.dorea@gmail.com

Abstract

Currently, ethylmercury (EtHg) and adjuvant-Al are the dominating interventional exposures encountered by fetuses, newborns, and infants due to immunization with Thimerosal-containing vaccines (TCVs). Despite their long use as active agents of medicines and fungicides, the safety levels of these substances have never been determined, either for animals or for adult humans—much less for fetuses, newborns, infants, and children. I reviewed the literature for papers reporting on outcomes associated with (a) multiple exposures and metabolism of EtHg and Al during early life; (b) physiological and metabolic characteristics of newborns, neonates, and infants relevant to xenobiotic exposure and effects; (c) neurobehavioral, immunological, and inflammatory reactions to Thimerosal and Al-adjuvants resulting from TCV exposure in infancy. Immunological and neurobehavioral effects of Thimerosal-EtHg and Al-adjuvants are not extraordinary; rather, these effects are easily detected in high and low income countries, with co-exposure to methylmercury (MeHg) or other neurotoxicants. Rigorous and replicable studies (in different animal species) have shown evidence of EtHg and Al toxicities. More research attention has been given to EtHg and findings have showed a solid link with neurotoxic effects in humans; however, the potential synergic effect of both toxic agents has not been properly studied. Therefore, early life exposure to both EtHg and Al deserves due consideration.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4344667>

Biopersistence and brain translocation of aluminum adjuvants of vaccines

Author information

Gherardi RK1, Eidi H1, Crépeaux G1, Authier FJ1, Cadusseau J1.

Faculté de Médecine and Faculté des Sciences et Technologie
INSERM U955 Team 10, Université Paris Est-Créteil
Créteil, France

Abstract

Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunological adjuvant of vaccines. Concerns linked to the use of alum particles emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion detected in patients with myalgic encephalomyelitis/chronic fatigue/syndrome. MMF revealed an unexpectedly long-lasting biopersistence of alum within immune cells in presumably susceptible individuals, stressing the previous fundamental misconception of its biodisposition. We previously showed that poorly biodegradable aluminum-coated particles injected into muscle are promptly phagocytosed in muscle and the draining lymph nodes, and can disseminate within phagocytic cells throughout the body and slowly accumulate in brain. This strongly suggests that long-term adjuvant biopersistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity. The understanding of basic mechanisms of particle biopersistence and brain translocation represents a major health challenge, since it could help to define susceptibility factors to develop chronic neurotoxic damage. Biopersistence of alum may be linked to its lysosome-destabilizing effect, which is likely due to direct crystal-induced rupture of phagolysosomal membranes. Macrophages that continuously perceive foreign particles in their cytosol will likely reiterate, with variable interindividual efficiency, a dedicated form of autophagy (xenophagy) until they dispose of alien materials. Successful compartmentalization of particles within double membrane autophagosomes and subsequent fusion with repaired and re-acidified lysosomes will expose alum to lysosomal acidic pH, the sole factor that can solubilize alum particles. Brain translocation of alum particles is linked to a Trojan horse mechanism previously described for infectious particles (HIV, HCV), that obeys to CCL2, signaling the major inflammatory monocyte chemoattractant.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4318414/>

“This strongly suggests
that long-term adjuvant biopersistence
within phagocytic cells is a prerequisite for
slow brain translocation and delayed neurotoxicity.”

A histological study of toxic effects of aluminium sulfate on rat hippocampus

Author information

Çabus N1, Oguz EO, Tufan AÇ, Adıgüzel E.

Department of Histology and Embryology
Faculty of Medicine, Hacettepe University
Sihhiye Ankara, Turkey

Abstract

Aluminium has toxic effects on many organ systems of the human body. Aluminium toxicity also is a factor in many neurodegenerative diseases. We investigated changes in numbers of hippocampal neurons in rats exposed to aluminium using an optical fractionator and we investigated aluminium-induced apoptosis using the transferase mediated dUTP nick end labeling (TUNEL) assay. Twenty-four female rats were divided equally into control, sham and aluminium-exposed groups. The control group received no treatment. The two treatment groups were injected intraperitoneally with 1 ml 0.9% saline without (sham) and with 3 mg/ml aluminium sulfate every day for two weeks. Following the treatments, the brains were removed, the left hemisphere was used for hippocampal neuron counting using an optical fractionator and the right hemisphere was investigated using hippocampal TUNEL assay to determine the apoptotic index. The number of neurons in the stratum pyramidale of the hippocampus was significantly less in the aluminium group than in the control and sham groups; there was no significant difference between the control and sham groups. The apoptotic index also was significantly higher in the aluminium group than in the other two groups. We quantified the toxic effects of aluminium on the rat hippocampus and determined that apoptosis was the mechanism of aluminium-induced neuron death in the hippocampus.

<http://www.ncbi.nlm.nih.gov/pubmed/25314162>

“Aluminium has toxic effects
on many organ systems of the human body.
We quantified the toxic effects of aluminium
on the rat hippocampus and determined that
apoptosis was the mechanism of aluminium-
induced neuron death in the hippocampus.”

The binding, transport and fate of aluminium in biological cells

Author information

Exley C1, Mold MJ2.

The Birchall Centre, Lennard-Jones Laboratories
Keele University, Staffordshire ST5 5BG, UK
c.exley@keele.ac.uk

Abstract

Aluminium is the most abundant metal in the Earth's crust and yet, paradoxically, it has no known biological function. Aluminium is biochemically reactive, it is simply that it is not required for any essential process in extant biota. There is evidence neither of element-specific nor evolutionarily conserved aluminium biochemistry. This means that there are no ligands or chaperones which are specific to its transport, there are no transporters or channels to selectively facilitate its passage across membranes, there are no intracellular storage proteins to aid its cellular homeostasis and there are no pathways which evolved to enable the metabolism and excretion of aluminium. Of course, aluminium is found in every compartment of every cell of every organism, from virus through to Man. Herein we have investigated each of the 'silent' pathways and metabolic events which together constitute a form of aluminium homeostasis in biota, identifying and evaluating as far as is possible what is known and, equally importantly, what is unknown about its uptake, transport, storage and excretion.

<http://www.ncbi.nlm.nih.gov/pubmed/25498314>

“Of course, aluminium is found in every compartment of every cell of every organism, from virus through to Man. Herein we have investigated each of the ‘silent’ pathways and metabolic events which together constitute a form of aluminium homeostasis in biota, identifying and evaluating as far as is possible what is known and, equally importantly, what is unknown about its uptake, transport, storage and excretion.”

Bumblebee pupae contain high levels of aluminium

Author information

Exley C1, Rotheray E2, Goulson D2.

1. The Birchall Centre, Lennard-Jones Laboratories, Keele University
Stoke-on-Trent, Staffordshire, ST5 5BG, United Kingdom
2. Evolution, Behaviour & Ecology, School of Life Sciences
University of Sussex, Brighton, BN1 9QG, United Kingdom

Abstract

The causes of declines in bees and other pollinators remains an on-going debate. While recent attention has focussed upon pesticides, other environmental pollutants have largely been ignored. Aluminium is the most significant environmental contaminant of recent times and we speculated that it could be a factor in pollinator decline. Herein we have measured the content of aluminium in bumblebee pupae taken from naturally foraging colonies in the UK. Individual pupae were acid-digested in a microwave oven and their aluminium content determined using transversely heated graphite furnace atomic absorption spectrometry. Pupae were heavily contaminated with aluminium giving values between 13.4 and 193.4 $\mu\text{g/g}$ dry wt. and a mean (SD) value of 51.0 (33.0) $\mu\text{g/g}$ dry wt. for the 72 pupae tested. Mean aluminium content was shown to be a significant negative predictor of average pupal weight in colonies. While no other statistically significant relationships were found relating aluminium to bee or colony health, the actual content of aluminium in pupae are extremely high and demonstrate significant exposure to aluminium. Bees rely heavily on cognitive function and aluminium is a known neurotoxin with links, for example, to Alzheimer's disease in humans. The significant contamination of bumblebee pupae by aluminium raises the intriguing spectre of cognitive dysfunction playing a role in their population decline.

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4456414/>

“the actual content
of aluminium in pupae
are extremely high and
demonstrate significant
exposure to aluminium.”

Vaccines, adjuvants and autoimmunity

Author information

Guimarães LE1, Baker B1, Perricone C2, Shoenfeld Y3.

1. The Zabłudowicz Center for Autoimmune Diseases, Chaim Sheba Medical Center, Tel-Hashomer, Israel
2. Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Italy
3. Zabłudowicz Center for Autoimmune Diseases, Chaim Sheba Medical Ctr, Tel-Hashomer, Israel; Incumbent of the Laura Schwarz-kipp chair for research of autoimmune diseases, Sackler Faculty of Medicine, Tel-Aviv University, Israel
shoenfel@post.tau.ac.il

Abstract

Vaccines and autoimmunity are linked fields. Vaccine efficacy is based on whether host immune response against an antigen can elicit a memory T-cell response over time. Although the described side effects thus far have been mostly transient and acute, vaccines are able to elicit the immune system towards an autoimmune reaction. The diagnosis of a definite autoimmune disease and the occurrence of fatal outcome post-vaccination have been less frequently reported. Since vaccines are given to previously healthy hosts, who may have never developed the disease had they not been immunized, adverse events should be carefully assessed and evaluated even if they represent a limited number of occurrences. In this review of the literature, there is evidence of vaccine-induced autoimmunity and adjuvant-induced autoimmunity in both experimental models as well as human patients. Adjuvants and infectious agents may exert their immune-enhancing effects through various functional activities, encompassed by the adjuvant effect. These mechanisms are shared by different conditions triggered by adjuvants leading to the autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome). In conclusion, there are several case reports of autoimmune diseases following vaccines, however, due to the limited number of cases, the different classifications of symptoms and the long latency period of the diseases, every attempt for an epidemiological study has so far failed to deliver a connection. Despite this, efforts to unveil the connection between the triggering of the immune system by adjuvants and the development of autoimmune conditions should be undertaken. Vaccinomics is a field that may bring to light novel customized, personalized treatment approaches in the future.

<http://www.ncbi.nlm.nih.gov/pubmed/26275795>

“In this review of the literature, there is evidence of vaccine-induced autoimmunity and adjuvant-induced autoimmunity in both experimental models as well as human patients.”

Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections

Author information

Crépeaux G1, Eidi H2, David MO3, Tzavara E4,
Giros B4, Exley C5, Curmi PA3, Shaw CA6, Gherardi RK7, Cadusseau J8.

1. INSERM U955 E10, Paris Est University, Créteil, France; franceguillemette.crepeaux@gmail.com.
2. INSERM U955 E10, Paris Est University, Créteil, France; INSERM U1204, Evry University, Evry, France
3. INSERM U1204, Evry University, Evry, France
4. INSERM U1130, CNRS UMR 8246, UPMC UM CR18, Paris, France
5. Birchall Centre, Keele University, Staffordshire, UK
6. Department of Ophthalmology, University of British Columbia, Vancouver, BC, Canada
7. INSERM U955 E10, Paris Est University, Créteil, France
8. INSERM U955 E10, Paris Est University, Créteil, France; Faculté des Sciences & Technologie UPEC, Créteil, France

Abstract

Concerns regarding vaccine safety have emerged following reports of potential adverse events in both humans and animals. In the present study, alum, alum-containing vaccine and alum adjuvant tagged with fluorescent nanodiamonds were used to evaluate i) the persistence time at the injection site, ii) the translocation of alum from the injection site to lymphoid organs, and iii) the behavior of adult CD1 mice following intramuscular injection of alum (400 μ gAl/kg). Results showed for the first time a strikingly delayed systemic translocation of adjuvant particles. Alum-induced granuloma remained for a very long time in the injected muscle despite progressive shrinkage from day 45 to day 270. Concomitantly, a markedly delayed translocation of alum to the draining lymph nodes, major at day 270 endpoint, was observed. Translocation to the spleen was similarly delayed (highest number of particles at day 270). In contrast to C57BL/6J mice, no brain translocation of alum was observed by day 270 in CD1 mice. Consistently neither increase of Al cerebral content, nor behavioral changes were observed. On the basis of previous reports showing alum neurotoxic effects in CD1 mice, an additional experiment was done, and showed early brain translocation at day 45 of alum injected subcutaneously at 200 μ gAl/kg. This study confirms the striking biopersistence of alum. It points out an unexpectedly delayed diffusion of the adjuvant in lymph nodes and spleen of CD1 mice, and suggests the importance of mouse strain, route of administration, and doses, for future studies focusing on the potential toxic effects of aluminum-based adjuvants.

<http://www.ncbi.nlm.nih.gov/pubmed/26384437>

“Concerns regarding vaccine safety

have emerged following reports of potential adverse

events in both humans and animals. This study

confirms the striking biopersistence of alum. It points

out an unexpectedly delayed diffusion of the adjuvant

in lymph nodes and spleen of CD1 mice ...”

“The well-recognized manifestations of systemic aluminum toxicity include fracturing osteomalacia, dialysis encephalopathy, and microcytic hypochromic anemia. More recently, aluminum loading has been demonstrated in premature infants receiving intravenous fluid therapy.”

American Academy Of Pediatrics • December 2015
Committee on Nutrition

Aluminum Toxicity in Infants and Children

Abstract

During the last 15 years, accumulating evidence has implicated aluminum in disorders associated with chronic renal failure.¹⁻⁶ The well-recognized manifestations of systemic aluminum toxicity include fracturing osteomalacia, dialysis encephalopathy, and microcytic hypochromic anemia. More recently, aluminum loading has been demonstrated in premature infants receiving intravenous fluid therapy.⁷ Although the clinical importance of this finding is unclear, it warrants careful attention. The association between aluminum excess and neurologic dysfunction, which has been reported in patients with chronic renal failure, suggests the possibility that aluminum overload may contribute to the pathogenesis of CNS damage in the sick premature infant.^{7,8}

Aluminum Exposure

Aluminum, which is the most abundant metal in the earth's crust, is ubiquitous in its distribution.⁷ There is constant exposure to this element through ingestion of water and food and exposure to dust particles.¹⁰ Because aluminum sulfate (alum) is used as a flocculating agent in the purification of municipal water supplies, drinking water may contain high levels of aluminum (up to 1,000 µg/L). Aluminum cans, containers, and cooking utensils, as well as aluminum-containing medications, are also potential sources of oral intake of aluminum. Increase in aluminum intake as a result of transfer through the skin is probably negligible; however, exposure is common due to use of aluminum in deodorants.¹⁰ Some inhaled aluminum is retained in pulmonary tissue and in the peribronchial lymph nodes, but it is largely excluded from other tissues. Pulmonary aluminum concentration increases with age; unlike aluminum levels in other tissues, the concentration in the lung does not correlate with that in other tissues.

<http://pediatrics.aappublications.org/content/78/6/1150>

Springer Plus • 2015

The mechanisms of action of vaccines containing aluminum adjuvants: an in vitro vs in vivo paradigm

Tirth Raj Ghimire

Division of Veterinary and Primate Health
Global Primate Network, Kathmandu, Nepal
Department of Zoology, Birendra Multiple Campus
Tribhuvan University, Chitwan, Nepal

Abstract

Adjuvants such as the aluminum compounds (alum) have been dominantly used in many vaccines due to their immunopotentiality and safety records since 1920s. However, how these mineral agents influence the immune response to vaccination remains elusive. Many hypotheses exist as to the mode of action of these adjuvants, such as depot formation, antigen (Ag) targeting, and the induction of inflammation. These hypotheses are based on many in vitro and few in vivo studies. Understanding how cells interact with adjuvants in vivo will be crucial to fully understanding the mechanisms of action of these adjuvants. Interestingly, how alum influences the target cell at both the cellular and molecular level, and the consequent innate and adaptive responses, will be critical in the rational design of effective vaccines against many diseases. Thus, in this review, mechanisms of action of alum have been discussed based on available in vitro vs in vivo evidences to date.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4406982/>

“Adjuvants such as the aluminum compounds (alum) have been dominantly used in many vaccines due to their immunopotentiality and safety records since 1920s. However, how these mineral agents influence the immune response to vaccination remains elusive.”

Chapter Four

The Human Papilloma Virus Vaccine

2008 - 2015

Dr. Harper was the lead scientist for Mercks Gardasil vaccine. She explained in a presentation at the 4th International Public Conference on Vaccination in October of 2009 that the cervical cancer risk in the U.S. is already extremely low, and that vaccinations are unlikely to have any effect upon the rate of cervical cancer in the United States. In fact, 70% of all HPV infections resolve themselves without treatment in a year and the number rises to well over 90% in two years. Harper also mentioned the safety angle. All trials of the vaccines were done on children aged 15 and above, despite them currently being marketed for 9-year-olds.

So far, 15,037 girls have reported adverse side effects from Gardasil alone to the Vaccine Adverse Event Reporting System (V.A.E.R.S.), and this number only reflects parents who underwent the hurdles required for reporting adverse reactions. At the time of writing, over 100 girls are officially known to have died from this vaccine.

The reported side effects include Guillian Barré Syndrome (paralysis lasting for years, or permanently — sometimes eventually causing suffocation), lupus, seizures, blood clots, brain inflammation and more. Parents are usually not made aware of these risks. Dr. Harper, the vaccine developer, claimed that she was speaking out, so that she might finally be able to sleep at night.

“About eight in every ten women who have been sexually active will have H.P.V. at some stage of their life. Normally there are no symptoms, and in 98 per cent of cases it clears itself.”

- Dr. Diane Harper

Spanish attorney Don Manuel Saez Ochoa filed a criminal complaint against Merck-Sanofi Pasteur Laboratories and the Spanish National Health Authorities in the Spanish courts in June of 2014. The complaint alleges that Merck failed to use an inert placebo during clinical trials thereby manipulating data and thus Gardasil was marketed under false pretences. Merck-Sanofi Pasteur and Spain’s National and Regional (La Rioja) health authorities are charged with the following:

- fraudulent marketing and/or administration of an inadequately tested vaccine;
- failure to inform the public about the potential risks of using Gardasil;
- clear infringement of the right to informed consent;
- ignoring new medical conditions in those who used Gardasil despite the similarity of their symptoms and the relatively short period of time between vaccine administration and the onset of symptoms;
- ignoring established and new scientific evidence illustrating the potential harmful effects of Gardasil ingredients and manufacturing methods;
- callous disregard for those suffering new medical conditions post-Gardasil;
- failure to inform the public that HPV infections are simply one of the risk factors involved in the development of cervical cancer;
- failure to inform the public that 90% of all HPV infections clear on their own without medical intervention;
- failure to inform the public about alternative methods of controlling cervical cancer;
- and criminal liability for the injuries resulting from the administration of Gardasil.

Thousands of young women around the world are finding themselves in the same position. They have gone from being happy, active, and healthy to facing a multitude of autoimmune problems and neurological disorders. For them, the ‘possible’ adverse effects of Gardasil have become an all too harsh and brutal reality.

It is time for those responsible to be held accountable for their actions. Criminal prosecution is quite possibly the only way to accomplish that goal. Perhaps six to twelve years in prison would remind those responsible what it means to conduct yourself in an ethical manner.

Perhaps they would remember that their first duty is to maintain the public health, not destroy it. On July 30, the Judge decided to open criminal proceedings and an investigation of the facts. The first criminal case in Spain regarding Gardasil injuries and potential criminal liability now begins.

The human papillomavirus vaccine and risk of anaphylaxis

Neal A. Halsey, MD

From the Institute for Vaccine Safety
Johns Hopkins Bloomberg School of Public Health
Baltimore, Md.

Abstract

In this issue of CMAJ, Brotherton and colleagues¹ report a comprehensive investigation revealing higher than expected rates of apparent anaphylaxis following vaccination with the quadrivalent human papillomavirus (HPV) vaccine in Australian children. The cause of these reactions remains somewhat unclear and needs further investigation. Of note, rates of anaphylaxis, if confirmed, may not be as high in other populations. Further investigations may assist in clarifying differences between the Australian study and other reports.

The HPV vaccine is associated with high rates of fainting in adolescents, which can result in serious head injuries. These adverse events emphasize the need for recommendations to keep adolescents and children under close observation (preferably sitting) for at least 15 minutes after vaccination.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2527389/>

“The HPV vaccine
is associated with high rates of fainting
in adolescents, which can result
in serious head injuries.”

Development of unilateral cervical and supraclavicular lymphadenopathy after human papilloma virus vaccination

Author information

Studdiford J1, Lamb K,
Horvath K, Altshuler M, Stonehouse A.

Department of Family and Community Medicine
Jefferson University Hospital
Philadelphia Pennsylvania 19107, USA

Abstract

A 26-year-old woman developed significant unilateral anterior cervical and supraclavicular lymphadenopathy 3 days after receiving her first dose (of a total of three doses) of human papilloma virus (HPV) vaccine. She had no history of lymphadenopathy after other previous immunizations, and had received no vaccines other than HPV at that time. The left-sided lymphadenopathy developed after she was vaccinated in the left deltoid muscle. The spatial and temporal relationships between the appearance of the lymphadenopathy and receipt of the vaccine in the absence of other causal agents strongly suggest that the HPV vaccine was the causal agent. Use of the Naranjo adverse drug reaction probability scale indicated that the HPV vaccine was a probable (score of 6) cause of the patient's adverse reaction. The patient received her second dose of the HPV vaccine 2 months later without further lymphadenopathy. To prevent unnecessary lymph node biopsies and patient concern, clinicians should be aware that lymphadenopathy may occur after HPV vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18752390>

“clinicians should be aware
that lymphadenopathy may occur
after HPV vaccination.”

CNS demyelination and quadrivalent HPV vaccination

Author information

Sutton IJ, Lahoria R, Tan I,
Clouston P, Barnett M.

Department of Neurology
St Vincent's Hospital
Darlinghurst, New South Wales
Australia

Abstract

Vaccination is generally considered safe in patients with multiple sclerosis (MS). We report five patients who presented with multifocal or atypical demyelinating syndromes within 21 days of immunization with the quadrivalent human papilloma virus (HPV) vaccine, Gardasil. Although the target population for vaccination, young females, has an inherently high risk for MS, the temporal association with demyelinating events in these cases may be explained by the potent immuno-stimulatory properties of HPV virus-like particles which comprise the vaccine. A prospective case-control study of patients with MS or clinically isolated demyelinating syndromes receiving the Gardasil vaccine may provide relevant safety data in this population.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18805844>

“We report five patients who presented with multifocal or atypical demyelinating syndromes within 21 days of immunization with the quadrivalent human papilloma virus (HPV) vaccine, Gardasil ... association with demyelinating events in these cases may be explained by the potent immuno-stimulatory properties of HPV virus-like particles which comprise the vaccine.”

Cervical cancers after human papillomavirus vaccination

Author information

Beller U1, Abu-Rustum NR.

Abstract

BACKGROUND

Current randomized clinical trials have shown that the quadrivalent human papillomavirus (HPV) vaccine can reduce the morbidity of precancerous lesions associated with HPV infection of vaccine-related subtypes. However, to date, there is no definite evidence showing the vaccine reduces the incidence of invasive cervical carcinoma.

CASES

We present two cases—one young, vaccinated woman who developed cervical carcinoma that was unrelated to HPV and another who developed cervical carcinoma secondary to infection with an HPV subtype not covered by the vaccine. Both patients were treated successfully and remained well without evidence of cancer.

CONCLUSION

Long-term follow-up data are needed to evaluate the prophylactic effectiveness of the current HPV vaccine. These cases could represent non-vaccine-related HPV infections. Young women must be thoroughly counseled about the efficacy and limitations of the vaccine and about continuing lifelong screening even after vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19155953>

“However, to date,
there is no definite evidence
showing the vaccine reduces
the incidence of invasive
cervical carcinoma.”

Vaccine • August 2009

Quadrivalent Human Papillomavirus recombinant vaccine associated lipoatrophy

Author information

Ojaimi S1, Buttery JP, Korman TM.
Department of Infectious Diseases
Monash Medical Centre, Clayton, Monash University
246 Clayton Rd, Clayton, Victoria, Australia
samojaimi@yahoo.com.au

Abstract

Involitional lipoatrophy, a loss of subcutaneous fat, may be idiopathic, associated with inflammatory skin conditions, or trauma, and has also been reported following injections of medications including insulin, corticosteroids and penicillin. There have also been reports in association with Diphtheria Pertussis Tetanus (DPT) vaccine. We report on two cases of lipoatrophy associated with the new Quadrivalent Human Papillomavirus (HPV) recombinant vaccine (Gardasil).

<http://www.ncbi.nlm.nih.gov/pubmed/19555713>

“Involitional lipoatrophy, a loss of subcutaneous fat, may be idiopathic, associated with inflammatory skin conditions, or trauma, and has also been reported following injections of medications including insulin, corticosteroids and penicillin. There have also been reports in association with Diphtheria Pertussis Tetanus (DPT) vaccine. We report on two cases of lipoatrophy associated with the new Quadrivalent Human Papillomavirus (HPV) recombinant vaccine (Gardasil).”

No actual evidence that the vaccine can prevent any cancer

Dr. Diane Harper
Lead Vaccine Researcher
Merck Gardasil And Cervarix Vaccines

Abstract

Dr. Diane Harper was the lead researcher in the development of the human papilloma virus vaccines, Gardasil and Cervarix. She is the latest to come forward and question the safety and effectiveness of these vaccines. She made the surprising announcement at the 4th International Public Conference on Vaccination, which took place in Reston, Virginia on Oct. 2nd through 4th, 2009.

Her speech was supposed to promote the Gardasil and Cervarix vaccines, but she instead turned on her corporate bosses in a very public way. When questioned about the presentation, audience members remarked that they came away feeling that the vaccines should not be used. “I came away from the talk with the perception that the risk of adverse side effects is so much greater than the risk of cervical cancer, I couldn’t help but question why we need the vaccine at all.” – Joan Robinson

Dr. Harper explained in her presentation that the cervical cancer risk in the U.S. is already extremely low, and that vaccinations are unlikely to have any effect upon the rate of cervical cancer in the United States. In fact, 70% of all H.P.V. infections resolve themselves without treatment in a year, and the number rises to well over 90% in two years. Harper also mentioned the safety angle. All trials of the vaccines were done on children aged 15 and above, despite them currently being marketed for 9-year-olds.

So far, 15,037 girls have reported adverse side effects from Gardasil alone to the Vaccine Adverse Event Reporting System (V.A.E.R.S.), and this number only reflects parents who underwent the hurdles required for reporting adverse reactions. At the time of writing, 44 girls are officially known to have died from these vaccines.

The reported side effects include Guillian Barré Syndrome (paralysis lasting for years, or permanently — sometimes eventually causing suffocation), lupus, seizures, blood clots, and brain inflammation. Parents are usually not made aware of these risks. Dr. Harper, the vaccine developer, claimed that she was speaking out, so that she might finally be able to sleep at night.

“About eight in every ten women who have been sexually active will have H.P.V. at some stage of their life. Normally there are no symptoms, and in 98 per cent of cases it clears itself. But in those cases where it doesn’t, and isn’t treated, it can lead to pre-cancerous cells which may develop into cervical cancer.” - Dr. Diane Harper

One must understand how the establishment’s word games are played to truly understand the meaning of the above quote, and one needs to understand its unique version of “science”. When they report that untreated cases “can” lead to something that “may” lead to cervical cancer, it really means that the relationship is merely a hypothetical conjecture that is profitable if people actually believe it. In other words, there is no demonstrated relationship between the condition being vaccinated for and the rare cancers that the vaccine might prevent, but it is marketed to do that nonetheless. In fact, there is no actual evidence that the vaccine can prevent any cancer.

From the manufacturers own admissions, the vaccine only works on 4 strains out of 40 for a specific venereal disease that dies on its own in a relatively short period, so the chance of it actually helping an individual is about about the same as the chance of him being struck by a meteorite. Why do nine-year-old girls need vaccinations for extremely rare and symptomless venereal diseases that the immune system usually kills anyway?

The quadrivalent human papillomavirus vaccine: erythema multiforme and cutaneous side effects after administration

Author information

Pérez-Carmona L1, Aguayo-Leiva I,
González-García C, Jaén-Olasolo P.

Ramón y Cajal Hospital
Madrid, Spain
lpcarmona@hotmail.com

Abstract

The quadrivalent human papillomavirus (qHPV) vaccine, the first vaccine for use in the prevention of cervical cancer and condyloma acuminatum, was approved in June 2006. In 2008, the mass media reported suspected links between the qHPV vaccine and serious adverse events; however, several studies have found that the vaccine is safe and the main adverse events are mild local reactions. Erythema multiforme (EM) is an acute self-limited cutaneous or mucocutaneous syndrome characterized by the abrupt onset of symmetric target lesions. The clinical manifestations and histological features of EM, Stevens-Johnson syndrome and toxic epidermal necrolysis show considerable overlap, and they are classically considered to represent a spectrum of skin disorders. We present a case of EM following qHPV vaccination to review the cutaneous side effects of this vaccine and the possibility of more serious side effects with the administration of booster doses.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20861606>

“We present a case of Erythema multiforme following qHPV vaccination to review the cutaneous side effects of this vaccine and the possibility of more serious side effects with the administration of booster doses.”

Review of Gardasil

Author information

Harper DM1, Vierthaler SL, Santee JA.

Professor of Medicine, Director
Center of Excellence in Women's Health
University of Missouri-Kansas City School of Medicine
Departments of Biomedical and Health Informatics
Obstetrics and Gynecology and Community and Family Medicine

Abstract

Human papillomavirus (HPV) is necessary for the development of cervical cancer. Cervical cancer is the second most common cancer in women worldwide but 80% occurs in developing countries, not countries with Pap screening programs. Pap screening programs in industrialized countries have reduced the incidence of cervical cancer to 4-8/100,000 women. HPV vaccines may be a promising strategy for cervical cancer in women without access to screening programs. In industrialized countries, the benefit of HPV vaccines focuses on individual abnormal Pap test reduction not cancer prevention. The focus of this review is to cover the side effects of Gardasil in perspective with the limited population benefit cervical cancer reduction in countries with organized Pap screening programs. In addition, information about Gardasil benefits, risks and unknowns for individual patient decision making for vaccination is presented. Gardasil offers protection against CIN 2+ lesions caused by HPV 16/18 and against genital warts caused by HPV 6/11 for at least 5 years. Combining Gardasil with repeated cytology screenings may reduce the proportion of abnormal cytology screens and hence reduce the associated morbidity with the subsequent colposcopies and excisional procedures.

<http://www.ncbi.nlm.nih.gov/pubmed/23805398>

“Pap screening programs
in industrialized countries
have reduced the incidence of cervical cancer
to 4-8/100,000 women.

HPV vaccines
may be a promising strategy
for cervical cancer in women
without access to screening programs.”

Erythema multiforme following vaccination for human papillomavirus

Author information

Katoulis AC1, Liakou A, Bozi E, Theodorakis M,
Alevizou A, Zafeiraki A, Mistidou M, Stavrianeas NG.

National and Kapodistrian University of Athens
Medical School, 2nd Department of Dermatology and Venereology
Attikon General University Hospital, Athens, Greece
alexanderkatoulis @ yahoo.co.uk

Abstract

Erythema multiforme (EM) is an acute self-limited immune-mediated reaction manifested by target skin lesions with mucous membrane involvement. The most common causes are infections and drugs. Vaccinations have been reported as a triggering factor, and they may be a frequent cause of EM in childhood. A 19-year-old female developed several target lesions of the hands and feet 10 days after the second dose of human papillomavirus (HPV) vaccine. Clinico-histologically, a diagnosis of EM minor was made. Treatment with topical corticosteroids and oral antihistamines resulted in complete clearance of the rash. Four months later, she received the last booster dose of the vaccine. A few subtle lesions appeared and disappeared spontaneously after a few days. Gardasil is a non-infectious vaccine, developed for the prevention of cervical cancer, precancerous genital lesions and genital warts. It delivers the major capsid (L1) protein of HPV types 6, 11, 16 and 18. Mild local reactions are the main adverse events. The only serious events are very rare cases of anaphylaxis. In our patient, the temporal relationship between the development of EM and the vaccination suggests that the HPV vaccine probably was the causal agent. This is the first published case of EM following HPV vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19887766>

“In our patient,
the temporal relationship between
the development of Erythema multiforme
and the vaccination suggests that the
HPV vaccine probably was the causal agent.
This is the first published case of
Erythema multiforme following HPV vaccination.”

Vaccine • January 2011

**Guillain-Barré syndrome after Gardasil vaccination:
data from Vaccine Adverse Event Reporting System
2006-2009**

Author information

Souayah NI, Michas-Martin PA, Nasar A,
Krivitskaya N, Yacoub HA, Khan H, Qureshi AI.

Department of Neurology
University of Medicine and Dentistry of New Jersey
Newark, NJ 07103, USA
souayani@umdnj.edu

Abstract

Using data from Vaccine Adverse Event Reporting System, we identified 69 reports of Guillain-Barré Syndrome (GBS) after Gardasil vaccination that occurred in the United States between 2006 and 2009. The onset of symptoms was within 6 weeks after vaccination in 70% of the patients in whom the date of vaccination was known. The estimated weekly reporting rate of post-Gardasil GBS within the first 6 weeks (6.6 per 10,000,000) was higher than that of the general population, and higher than post-Menactra and post-influenza vaccinations. Further prospective active surveillance for accurate ascertainment and identification of high-risk groups of GBS after Gardasil vaccination is warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20869467>

“The estimated weekly reporting rate of post-Gardasil Guillain-Barré Syndrome within the first 6 weeks (6.6 per 10,000,000) was higher than that of the general population, and higher than post-Menactra and post-influenza vaccinations.”

[for every 100 million women vaccinated it is known and recognized that there will be an estimated 66 cases of collateral damage in the form of Guillain-Barré Syndrome]

Autoimmune hepatitis type 2 following anti-papillomavirus vaccination in a 11-year-old girl

Author information

Della Corte C1, Carlucci A,
Francalanci P, Alisi A, Nobili V.

Unit of Liver Research
Department of Pathology
Bambino Gesù Children's Hospital
IRCCS, P.le S. Onofrio 4, 00165 Rome, Italy
claudia.dellacorte@opbg.net

Abstract

In the last years numerous reports describing a possible association between administration of vaccines and development of autoimmune phenomena and overt autoimmune disease were published. Possible mechanisms of induction of autoimmune phenomena by vaccines and their excipients are probably similar to those implicated in induction by infectious agents. Here we report the case of an 11-year-old girl who developed autoimmune hepatitis type II after four weeks from vaccination against human papillomavirus. The possible relationships between the use of adjuvated vaccine against papillomavirus and autoimmune hepatitis are discussed. Although we do not provide evidence for a causal link, we suggest that the occurrence of the autoimmune hepatitis may be related to the stimulation of immune system by adjuvated-vaccine, that could have triggered the disease in a genetically predisposed individual. Therefore a monitoring of liver function test following administration of vaccine against papillomavirus may be useful in adolescent girl with signs of hepatopathy, as jaundice, dark urine or hepatomegaly, to early identify and to promptly treat autoimmune liver disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21596082>

“In the last years

numerous reports

describing a possible

association between

administration of

vaccines and development

of autoimmune phenomena

and overt autoimmune

disease were published.”

Systemic lupus erythematosus following HPV immunization or infection?

Author information

Soldevilla HF1, Briones SF, Navarra SV.
1University of Santo Tomas, Manila, Philippines
helmar_110576@yahoo.com

Abstract

BACKGROUND AND PURPOSE

The link between autoimmunity and infectious agents has been strongly suggested by reports of lupus or lupus-like syndromes following immunization. This report describes three patients with either newly diagnosed systemic lupus erythematosus (SLE) or SLE flare, following vaccination for human papilloma virus (HPV). CASE 1: A 17-year-old female completed two doses of HPV vaccine uneventfully. Two months later, she developed arthralgias with pruritic rashes on both lower extremities, later accompanied by livedo reticularis, bipedal edema with proteinuria, anemia, leucopenia, hypocomplementemia and high titers of anti-nuclear antibody (ANA) and anti-double-stranded DNA (anti-dsDNA). Kidney biopsy showed International Society of Nephrology/Renal Pathology Society Class III lupus nephritis. She was started on high dose steroids followed by pulse cyclophosphamide therapy protocol for lupus nephritis, and subsequently went into remission. CASE 2: A 45-year-old housewife, previously managed for 11 years as having rheumatoid arthritis, had been in clinical remission for a year when she received two doses of HPV immunization. Four months later, she developed fever accompanied by arthritis, malar rash, oral ulcers, recurrent ascites with intestinal pseudo-obstruction, and behavioral changes. Cranial MRI showed vasculitic lesions on the frontal and parietal lobes. Laboratory tests showed anemia with leucopenia, hypocomplementemia, proteinuria, ANA positive at 1:320, and antibodies against dsDNA, Ro/SSA, La/SSB and histone. She improved following pulse methylprednisolone with subsequent oral prednisone combined with hydroxychloroquine. CASE 3: A 58-year-old housewife diagnosed with SLE had been in clinical remission for 8 years when she received two doses of HPV immunization. Three months later, she was admitted to emergency because of a 1-week history of fever, malar rash, easy fatigability, cervical lymph nodes, gross hematuria and pallor. Laboratory exams showed severe anemia, thrombocytopenia, active urine sediments, and hypocomplementemia. Despite pulse steroid therapy, blood transfusions, intravenous immunoglobulin and aggressive resuscitative measures, she expired a day after hospital admission.

SUMMARY

These cases narrate instances of the onset or exacerbation of lupus following HPV immunization suggesting adjuvant-induced autoimmunity. On the other hand, there are reports of higher incidence of HPV infection in SLE, with the infection per se possibly contributing to disease activity. Thus, the benefit of HPV immunization may still outweigh the risk among these individuals.

“These cases narrate instances of the onset or exacerbation of lupus following HPV immunization suggesting adjuvant-induced autoimmunity.”

Pharmaceutical companies' role in state vaccination policymaking: the case of human papillomavirus vaccination

Author information

Mello MM1, Abiola S, Colgrove J.

Harvard School of Public Health, Boston, MA, USA
mmello@hsph.harvard.edu

Abstract

OBJECTIVES

We sought to investigate roles that Merck & Co Inc played in state human papillomavirus (HPV) immunization policymaking, to elicit key stakeholders' perceptions of the appropriateness of these activities, and to explore implications for relationships between health policymakers and industry.

METHODS

We used a series of state case studies combining data from key informant interviews with analysis of media reports and archival materials. We interviewed 73 key informants in 6 states that were actively engaged in HPV vaccine policy deliberations.

RESULTS

Merck promoted school-entry mandate legislation by serving as an information resource, lobbying legislators, drafting legislation, mobilizing female legislators and physician organizations, conducting consumer marketing campaigns, and filling gaps in access to the vaccine. Legislators relied heavily on Merck for scientific information. Most stakeholders found lobbying by vaccine manufacturers acceptable in principle, but perceived that Merck had acted too aggressively and non-transparently in this case.

CONCLUSIONS

Although policymakers acknowledge the utility of manufacturers' involvement in vaccination policymaking, industry lobbying that is overly aggressive, not fully transparent, or not divorced from financial contributions to lawmakers risks undermining the prospects for legislation to foster uptake of new vaccines.

“Most stakeholders
found lobbying by
vaccine manufacturers
acceptable in principle,
but perceived that Merck
had acted too aggressively
and nontransparently in this case.”

Who Profits From Uncritical Acceptance of Biased Estimates of Vaccine Efficacy and Safety?

Lucija Tomljenovic, PhD and Christopher A. Shaw, PhD

At the time of the writing, Lucija Tomljenovic and Christopher A. Shaw were with the Neural Dynamics Research Group University of British Columbia, Vancouver, Canada

Abstract

We read with great interest the analysis by Mello et al.¹ on how Merck & Co., Inc. (Merck) influenced state human papillomavirus (HPV) vaccination policymaking. The exclusive reliance on Merck for scientific information on behalf of the legislators is unfortunate, especially in the light of independent research which has repeatedly warned that drug companies may manipulate clinical trial designs and subsequent data analysis and reporting to make their drugs look better and safer.^{2–4} Indeed, careful scrutiny of Gardasil clinical trials shows that their design, as well as data reporting and interpretation, were largely inadequate.^{4–6}

Given this, the widespread public optimism regarding Gardasil's clinical benefits appears to rest on an extremely weak base built on a number of untested assumptions and significant misinterpretation of factual evidence. For example, the claim that Gardasil vaccination will result in approximately 70% reduction of cervical cancers^{7,8} is made despite the fact that the clinical trial data have not demonstrated to date that the vaccine has actually prevented a single case of cervical cancer (let alone cervical cancer death),⁴ nor that the current overly optimistic surrogate marker-based extrapolations are justified.⁶ A second equally fallacious claim is that life-long protection arises from three vaccine doses,^{7,8} although clinical trial follow-up data do not extend beyond five years.⁹ The third claim is that Gardasil may induce only minor side effects of negligible clinical importance,^{7,8} although such conclusions are only supported by highly flawed safety trials design.^{4,10} Additionally, we note evidence of biased and selective reporting of results from clinical trials, that is, exclusion of particular vaccine efficacy figures from peer-reviewed publications, such as those related to study subgroups in which efficacy might be lower or even negative.^{4,5}

All of the above issues suggest that the information presented by Merck to the public and the various state legislators concerning Gardasil safety and true prophylactic value were incomplete and inaccurate and thus inevitably misleading, particularly in light of data from various vaccine safety surveillance systems and case reports that continue to raise significant concerns regarding the safety of Gardasil (Table 1).⁴

Keeping in mind that “the primary interest of a pharmaceutical company is developing and selling pharmaceutical product,”¹ one must ask whether rational vaccine policy decisions should be based on conclusions derived from an uncritical acceptance of flawed vaccine safety and efficacy estimates provided by the vaccine manufacturer. Failure to adhere to principles of evidence-based medicine with respect to Gardasil promotion and vaccination policymaking inevitably raises the question of whether we have learned anything from the Vioxx debacle.

Age-Adjusted Rate Of Adverse Reactions (ADRs) Related To Gardasil Compared With All Other Vaccines In The United States Reported To The Vaccine Adverse Event Reporting System (VAERS) As Of March 25th, 2012.

Event	Gardasil	All Vaccines	Gardasil %
All	14,616	31,713	46.1
Serious	1,272	2,077	61.2
Deaths	37	58	63.8
Life-Threatening	289	444	65.1
Permanently Disabled	468	572	81.2
Prolonged Hospitalization	172	229	75.1
Emergency Room Visit	6,892	12,927	53.3

Note: Compared with all other vaccines, Gardasil alone is associated with >60% of all serious Adverse Reactions (including 63.8% of all deaths and 81.2% cases of permanent disability) in females younger than 30 years. In context, while females in this age group have a near-zero risk of dying from cervical cancer, they are faced with a risk of dying and a permanently disabling condition from a vaccine that has not prevented a single case of cervical cancer thus far. For a vaccine with uncertain benefits designed to prevent a disease that is preventable through Papanicolaou screening combined with the loop electrosurgical excision procedure, which together carry no such risks, the potential for harm to those vaccinated should be negligible. It is not.

“In context, while females in this age group have a near-zero risk of dying from cervical cancer, they are faced with a risk of dying and a permanently disabling condition from a vaccine that has not prevented a single case of cervical cancer thus far. For a vaccine with uncertain benefits designed to prevent a disease that is preventable through Papanicolaou screening combined with the loop electrosurgical excision procedure, which together carry no such risks, the potential for harm to those vaccinated should be negligible.”

Premature ovarian failure
3 years after menarche in a 16-year-old girl
following human papillomavirus vaccination

Author information

Little DT1, Ward HR.

Department of General Practice
North Bellingen Medical Services, Bellingen, Australia
dradford@wirefree.net.au

Abstract

Its occurrence raises important questions about causation, which may signal other systemic concerns. This patient presented with amenorrhoea after identifying a change from her regular cycle to irregular and scant periods following vaccinations against human papillomavirus. She declined the oral contraceptives initially prescribed for amenorrhoea. The diagnostic tasks were to determine the reason for her secondary amenorrhoea and then to investigate for possible causes of the premature ovarian failure identified. Although the cause is unknown in 90% of cases, the remaining chief identifiable causes of this condition were excluded. Premature ovarian failure was then notified as a possible adverse event following this vaccination. The young woman was counselled regarding preservation of bone density, reproductive implications and relevant follow-up. This event could hold potential implications for population health and prompts further inquiry.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4543769/>

“Premature ovarian failure in a well adolescent is a rare event. This patient presented with amenorrhoea after identifying a change from her regular cycle to irregular and scant periods following vaccinations against human papillomavirus. This event could hold potential implications for population health and prompts further inquiry.”

Letter to the Editor

No autoimmune safety signal after vaccination with quadrivalent HPV vaccine Gardasil?

L. Tomljenovic and C. A. Shaw

Dear sir,

Recently, the Journal of Internal Medicine published a study by Chao et al. [1] on autoimmune conditions following the routine use of Gardasil, which failed to identify any significant autoimmune safety concerns. This study was conducted in collaboration between two managed care organizations, Kaiser Permanente Southern California (KPSC) and Kaiser Permanente Northern California (KPNC), as a postlicensure commitment to the FDA, the European Medicines Agency (EMA) and other regulatory authorities to help evaluate the autoimmune safety of the vaccine. In particular, Chao et al. [1] noted that ‘well-designed postlicensure safety studies for newly approved vaccines facilitate proper evaluation of their autoimmune safety’ [emphasis added]. We certainly do agree with the authors that such studies are needed for determining whether or not new vaccines have adequate safety profiles. The study population for the autoimmune surveillance by the Kaiser’s research team thus included 189 629 women of diverse ethnical and socio-economic background, 99% of whom were in the recommended age range for HPV vaccination (9–26 years) [1]. Nonetheless, two potential biases might have influenced the outcome of the safety analysis conducted by the authors.

First, the study included all women who received at least one dose of Gardasil, thus making this particular population sample less sensitive for the detection of serious adverse reactions (ADRs), as such events may be expected to occur less frequently if fewer doses of the vaccine are administered. As the authors did not report how many women actually completed the recommended three-dose HPV vaccination regimen, it is impossible to know what proportion of the study population was actually at high risk from vaccine-related serious ADRs. Secondly, the Safety Review Committee (SRC) that reviewed all safety data included a general paediatrician/clinical epidemiologist, a perinatologist/teratologist, a vaccinologist, a paediatric rheumatologist and a pharmacoepidemiologist [1]. In view of the fact that the autoimmune conditions of interest to be examined by this expert Committee included (i) rheumatologic/autoimmune disorders, (ii) autoimmune endocrine conditions and (iii) autoimmune neurological/ophthalmic disorders [1]; the question must be asked about why the Kaiser’s research team failed to recruit an expert panel with similar expertise if, in fact, the study aimed to facilitate proper evaluation of autoimmune safety for Gardasil? It is thus surprising to note the absence of an immunologist/autoimmunologist, neurologist and ophthalmologist from the SRC especially because such experts were in fact present at a later stage, in the analysis of case reports selected by the SRC [1]. As demonstrated repeatedly in the scientific literature, inadequately designed research cannot be used to reliably evaluate the safety of any drug [2,3].

We have previously pointed out to existing HPV vaccine-related safety concerns as well as uncertainties about the efficacy of HPV vaccination against actual cervical cancer incidence [3, 4]. Whilst results from clinical trials show that Gardasil can reduce the incidence of a subset of abnormal CIN 2/3+ cytologies (i.e. those related to HPV-16/18) in women with no pre-existing HPV infections [5], the vaccine is unlikely to reduce the overall frequency of cervical cancers (at least not beyond what Pap screening has already accomplished) [6, 7], yet this is the primary aim for which the vaccine was developed [8]. Furthermore, current data show that antibodies against HPV-18 after Gardasil fall rapidly, with 35% of women having no measurable antibody titres by 5 years postinjec-

tion [6]. This outcome suggests that rather than preventing future cases of cervical cancer, Gardasil, at best, may only be effective in postponing them.

In addition, unlike screening and the loop electrosurgical excision procedure (LEEP), Gardasil offers no therapeutic benefits as it cannot cause regression of pre-existing HPV-16/18 infections or associated lesions. On the contrary, Gardasil may exacerbate cervical cancer disease in women with pre-existing HPV-6/11/16/18 infections [5]. It thus appears that the current widespread optimism regarding the putative long-term benefits of HPV vaccination has only been made possible by invalid and premature extrapolations from such often inadequate surrogate markers [3, 9, 10]. As recently noted by Gerhardus and Razum [9], the, ‘unwarranted confidence in the new [HPV] vaccines led to the impression that there was no need to actually evaluate their effectiveness’.

On the other hand, abundant evidence now exists that HPV vaccines can cause serious adverse events, including death and long-term disabling autoimmune conditions [3, 6]. Moreover, because currently there are no active surveillance programs for monitoring vaccine safety outcomes anywhere in the world, the true rate of serious ADRs following Gardasil remains unknown. In context, whilst 12-year-old preadolescents are at zero risk of dying from cervical cancer, they are faced with a risk of death and a permanently disabling lifelong autoimmune or neurodegenerative condition from a vaccine that thus far has not prevented a single case of cervical cancer, let alone cervical cancer death. For vaccines with uncertain benefits designed to prevent a disease that is already preventable by Pap screening and LEEP, both of which carry no such risks, the potential for harm to those vaccinated should be negligible [3, 4].

Conflict of interest statement

Authors LT and CAS conducted a histological analysis of autopsy brain samples from a Gardasil-suspected death case

<http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2796.2012.02551.x/full>

“the vaccine is unlikely to reduce the overall frequency of cervical cancers (at least not beyond what Pap screening has already accomplished), yet this is the primary aim for which the vaccine was developed. Furthermore, current data show that antibodies against HPV-18 after Gardasil fall rapidly, with 35% of women having no measurable antibody titres by 5 years postinjection. This outcome suggests that rather than preventing future cases of cervical cancer, Gardasil, at best, may only be effective in postponing them.”

Too fast or not too fast: the FDA's approval of Merck's HPV vaccine Gardasil

Author information

Tomljenovic L1, Shaw CA.
University of British Columbia

Abstract

There are not many public health issues where views are as extremely polarized as those concerning vaccines, and Merck's HPV vaccine Gardasil is a case in point. Ever since gaining the FDA's approval in 2006, Merck has been heavily criticized for their overly aggressive marketing strategies and lobbying campaigns aimed at promoting Gardasil as a mandatory vaccine. Subsequently, questions have been raised as to whether it was appropriate for vaccine manufacturers to partake in public health policies when their conflicts of interests are so obvious. Some of their advertising campaign slogans, such as "cervical cancer kills x women per year" and "your daughter could become one less life affected by cervical cancer," seemed more designed to promote fear rather than evidence-based decision making about the potential benefits of the vaccine. Although, conflicts of interests do not necessarily mean that the product itself is faulty, marketing claims should be carefully examined against factual science data. Currently Gardasil vaccination is strongly recommended by the U.S. and other health authorities while public concerns about safety and efficacy of the vaccine appear to be increasing. This discrepancy leads to some important questions that need to be resolved. The current review examines key issues of this debate in light of currently available research evidence.

<http://www.ncbi.nlm.nih.gov/pubmed/23061593>

"Some of their advertising campaign slogans, such as "cervical cancer kills x women per year" and "your daughter could become one less life affected by cervical cancer," seemed more designed to promote fear rather than evidence-based decision making about the potential benefits of the vaccine."

Death after Quadrivalent Human Papillomavirus (HPV) Vaccination: Causal or Coincidental?

Lucija Tomljenovic^{1*} and Christopher A Shaw^{1,2,3}

1. Department of Ophthalmology and Visual Sciences, University of British Columbia, Canada
2. Program in Experimental Medicine, University of British Columbia, Canada
3. Program in Neuroscience, University of British Columbia, Canada

Abstract

Background

The proper understanding of a true risk from vaccines is crucial for avoiding unnecessary adverse reactions (ADRs). However, to this date no solid tests or criteria have been established to determine whether adverse events are causally linked to vaccinations.

Objectives

This research was carried out to determine whether or not some serious autoimmune and neurological ADRs following HPV vaccination are causal or merely coincidental and to validate a biomarker-based immunohistochemical (IHC) protocol for assessing causality in case of vaccination-suspected serious adverse neurological outcomes.

Results

In both cases, the autopsy revealed no anatomical, microbiological nor toxicological findings that might have explained the death of the individuals. In contrast, our IHC analysis showed evidence of an autoimmune vasculitis potentially triggered by the cross-reactive HPV-16L1 antibodies binding to the wall of cerebral blood vessels in all examined brain samples. We also detected the presence of HPV-16L1 particles within the cerebral vasculature with some HPV-16L1 particles adhering to the blood vessel walls. HPV-18L1 antibodies did not bind to cerebral blood vessels nor any other neural tissues. IHC also showed increased T-cell signalling and marked activation of the classical antibody-dependent complement pathway in cerebral vascular tissues from both cases. This pattern of complement activation in the absence of an active brain infection indicates an abnormal triggering of the immune response in which the immune attack is directed towards self-tissue.

Conclusions

Our study suggests that HPV vaccines containing HPV-16L1 antigens pose an inherent risk for triggering potentially fatal autoimmune vasculopathies.

Practice implications

Cerebral vasculitis is a serious disease which typically results in fatal outcomes when undiagnosed and left untreated. The fact that many of the symptoms reported to vaccine safety surveillance databases following HPV vaccination are indicative of cerebral vasculitis, but are unrecognized as such (i.e., intense persistent migraines, syncope, seizures, tremors and tingling, myalgia, locomotor abnormalities, psychotic symptoms and cognitive deficits), is a serious concern in light of the present findings. It thus appears that in some cases vaccination may be the triggering factor of fatal autoimmune/neurological events. Physicians should be aware of this association.

“Our study suggests that HPV vaccines containing HPV-16L1 antigens pose an inherent risk for triggering potentially fatal autoimmune vasculopathies.”

Full Report:

<http://sanevax.org/wp-content/uploads/2012/10/Tomljenovic-Shaw-Gardasil-Causal-Coincidental-2167-7689-S12-001.pdf>

Human papillomavirus (HPV) vaccines as an option for preventing cervical malignancies: (how) effective and safe?

Author information

Tomljenovic L1, Spinosa JP, Shaw CA.

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia
828 W. 10th Ave, Vancouver, BC, V5Z 1L8, Canada
lucijat77@gmail.com

Abstract

We carried out a systematic review of HPV vaccine pre- and post-licensure trials to assess the evidence of their effectiveness and safety. We find that HPV vaccine clinical trials design, and data interpretation of both efficacy and safety outcomes, were largely inadequate. Additionally, we note evidence of selective reporting of results from clinical trials (i.e., exclusion of vaccine efficacy figures related to study subgroups in which efficacy might be lower or even negative from peer-reviewed publications). Given this, the widespread optimism regarding HPV vaccines long-term benefits appears to rest on a number of unproven assumptions (or such which are at odd with factual evidence) and significant misinterpretation of available data. For example, the claim that HPV vaccination will result in approximately 70% reduction of cervical cancers is made despite the fact that the clinical trials data have not demonstrated to date that the vaccines have actually prevented a single case of cervical cancer (let alone cervical cancer death), nor that the current overly optimistic surrogate marker-based extrapolations are justified. Likewise, the notion that HPV vaccines have an impressive safety profile is only supported by highly flawed design of safety trials and is contrary to accumulating evidence from vaccine safety surveillance databases and case reports which continue to link HPV vaccination to serious adverse outcomes (including death and permanent disabilities). We thus conclude that further reduction of cervical cancers might be best achieved by optimizing cervical screening (which carries no such risks) and targeting other factors of the disease rather than by the reliance on vaccines with questionable efficacy and safety profiles.

<http://www.ncbi.nlm.nih.gov/pubmed/23016780>

“We carried out a systematic review of HPV vaccine pre- and post-licensure trials to assess the evidence of their effectiveness and safety. We find that HPV vaccine clinical trials design, and data interpretation of both efficacy and safety outcomes, were largely inadequate. Given this, the widespread optimism regarding HPV vaccines long-term benefits appears to rest on a number of unproven assumptions (or such which are at odd with factual evidence) and significant misinterpretation of available data. Likewise, the notion that HPV vaccines have an impressive safety profile is only supported by highly flawed design of safety trials and is contrary to accumulating evidence from vaccine safety surveillance databases and case reports which continue to link HPV vaccination to serious adverse outcomes (including death and permanent disabilities).”

HPV vaccines and cancer prevention, science versus activism

Lucija Tomljenovic,¹ Judy Wilyman,² Eva Vanamee,³
Toni Bark,⁴ and Christopher A Shaw¹

1. Neural Dynamics Research Group

Vancouver General Hospital Research Pavilion
University of British Columbia, 828 W. 10th Ave
Vancouver, BC, V5Z 1L8, Canada

2. School of Social Sciences
Media and Communication

University of Wollongong, Wollongong 2522, Australia

3. Department of Structural and Chemical Biology
Mount Sinai School of Medicine, 1425 Madison Ave
Rm 1623, New York, NY, 10029, USA

4. School of Public Health-Healthcare Emergency Management
Boston University, Boston, MA, 02118, USA

Abstract

The rationale behind current worldwide human papilloma virus (HPV) vaccination programs starts from two basic premises, 1) that HPV vaccines will prevent cervical cancers and save lives and, 2) have no risk of serious side effects. Therefore, efforts should be made to get as many pre-adolescent girls vaccinated in order to decrease the burden of cervical cancer. Careful analysis of HPV vaccine pre- and post-licensure data shows however that both of these premises are at odds with factual evidence and are largely derived from significant misinterpretation of available data.

Letter

The recent Editorial by Silvia de Sanjosé* [1] is problematic from a variety of perspectives. Mainly, it attempts to portray a complex issue as a simple dichotomy between supposedly unjustified “anti-HPV vaccine activism” and alleged absolute science which has presumably provided indisputable evidence on HPV vaccine safety and efficacy.

In spite of much unwarranted and premature optimism, the fact is however that HPV vaccines have not thus far prevented a single case of cervical cancer (let alone cervical cancer death). Instead, what the clinical trials have shown is that HPV vaccines can prevent some of the pre-cancerous CIN 2/3 lesions associated with HPV-16 and HPV-18 infection, a large fraction of which would spontaneously resolve regardless of the vaccination status [2-4]. For example, in adolescent women aged 13 to 24 years, 38% of CIN 2 resolve after one year, 63% after two and 68% after three years [5]. Moreover, the validity of CIN 2 being a cancer precursor is questionable due to high misclassification rates and poor intra- and inter-observer reproducibility in diagnosis, as well as high regression rates [6-9]. According to Castle et al. [7] CIN 2 is the least reproducible of all histopathologic diagnoses and may in part reflect sampling error. While CIN 3 is a more reliable marker for cancer progression than CIN 2, the use of this marker is not without caveats [2,10].

Indeed, the optimistic assumption that HPV vaccination (even if proven effective against cervical cancer as claimed), will result in 70% reduction of cervical cancers appears to be largely based on premature, exaggerated

and invalid surrogate marker-based extrapolations [2,11]. Crucially, these assumptions failed to take into account several important real-world factors such as:

- (1) reliability of surrogate-markers (i.e., whether they can accurately measure what they are purport to measure);
- (2) efficacy against oncogenic HPV strains not covered by the vaccine;
- (3) possibility of increased frequency of infections with these types;
- (4) efficacy in women acquiring multiple HPV types;
- (5) effects in women with pre-existing HPV infections

It is also noteworthy that Merck’s HPV vaccine Gardasil received priority Fast Track approval by the U.S. Food and Drug Administration (FDA) after a 6-month review process, despite the fact that it failed (and still continues to fail) to meet a single one of the four criteria required by the FDA for Fast Track approval. Gardasil is demonstrably neither safer nor more effective than Pap screening combined with the loop electrosurgical excision procedure (LEEP) in preventing cervical cancers, nor can it improve the diagnosis of serious cervical cancer outcomes [12]. In this regard, Gerhardus and Razum have recently noted that the “...unwarranted confidence in the new HPV vaccines led to the impression that there was no need to actually evaluate their effectiveness” [11].

Similarly, the notion that HPV vaccines have an impressive safety profile can only be supported by highly flawed design of safety trials [2,13] and is contrary to accumulating evidence from vaccine safety surveillance databases and case reports which continue to link HPV vaccination to serious adverse outcomes (including death and permanent disabilities) [2,4,14]. For example, compared to all other vaccines in the U.S. vaccination schedule, Gardasil alone is associated with 61% of all serious adverse reactions (including 63.8% of all deaths and 81.2% cases of permanent disability) in females younger than 30 years of age [12].

Although a report to a vaccine safety surveillance system does not by itself prove that the vaccine caused an adverse reaction, the unusually high frequency of adverse reactions related to HPV vaccines reported worldwide, as well as their consistent pattern (i.e. nervous system-related disorders rank the highest in frequency), points to a potentially causal relationship [2]. Furthermore, matching the data from vaccine surveillance databases is an increasing number of case reports documenting similar serious adverse reactions associated with HPV vaccine administration, with nervous system and autoimmune disorders being the most frequently reported in the medical literature [15-24].

In summary, the optimistic claims that HPV vaccines will prevent cervical cancers and save lives, and that they are extremely safe, rest on assumptions which are misinterpreted and presented to the public as factual evidence. We thus conclude that further reduction of cervical cancers might be best achieved by optimizing cervical screening (which carries no serious health risks) and targeting other factors of the disease rather than by the reliance on vaccines with questionable efficacy and safety profiles [2,25].

To those who wish to promote HPV vaccination as a means for reducing cervical cancer burden, perhaps the following should be asked:

1. HPV vaccines have not been demonstrated to prevent any cervical cancers so why are they being promoted as cervical cancer vaccines?
2. If the majority of HPV infections and a great proportion of pre-cancerous lesions clear spontaneously and without medical treatment and are thus not a reliable indication of cancer later in life, then how can these end-points be used as a reliable indicator of the number of cervical cancer cases that will be prevented by HPV vaccines?
3. How can the clinical trials make an accurate estimate of the risk associated with HPV-vaccines if they are methodologically biased to produce type-2 errors (false negatives [2,4,13])? [continued next page]

4. Can a passive monitoring system such as that used by most vaccine surveillance systems world-wide allow the medical regulatory agencies to make accurate estimates on the real frequency of HPV-vaccine related adverse reactions?
5. Can an accurate estimate of the real frequency of HPV-vaccine related adverse reactions be made if appropriate follow-up and thorough investigation of suspected vaccine related ADRs is not conducted but instead, these cases are a-priori dismissed as being unrelated to the vaccine?
6. Why are women not informed of the fact that in some circumstances (i.e., prior exposure to vaccine-targeted and non-targeted HPV types), HPV vaccination may accelerate the progression of cervical abnormalities [4,26-28]?
7. How can women make a fully informed decision about whether or not to consent to vaccination if crucial information regarding HPV vaccine efficacy and safety is not being disclosed to them?
8. Should the medical health regulators and authorities rely solely on data provided by the vaccine manufacturers to make vaccine-policy decisions and recommendations [12,29]?

Competing interests

The authors declare that they have no conflict of interests

Authors' contributions

LT was involved in choosing the topic and drafting the initial manuscript. CAS, JW, EV and TB were involved in critically revising the manuscript and additional content. The authors have read and approved the manuscript. This work was supported by the Dwoskin and Katlyn Fox Family Foundations.

Full Report with References

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3565961/>

“As for all vaccines, and in particular for newly marketed ones, the surveillance of adverse events represents an essential step in the evaluation of a vaccination programme.”

[because all vaccines are part of a long-term human population-wide medical experiment]

“ Gardasil is demonstrably neither safer nor more effective than Pap screening combined with the loop electrosurgical excision procedure (LEEP) in preventing cervical cancers, nor can it improve the diagnosis of serious cervical cancer outcomes.”

Human papillomavirus (HPV) vaccine policy and evidence-based medicine: are they at odds?

Author information

Tomljenovic L1, Shaw CA.

Neural Dynamics Research Group
Department of Ophthalmology and Visual Sciences
University of British Columbia, 828 W. 10th Ave
Vancouver, BC, V5Z 1L8, Canada
lucijat77@gmail.com

Abstract

All drugs are associated with some risks of adverse reactions. Because vaccines represent a special category of drugs, generally given to healthy individuals, uncertain benefits mean that only a small level of risk for adverse reactions is acceptable. Furthermore, medical ethics demand that vaccination should be carried out with the participant's full and informed consent. This necessitates an objective disclosure of the known or foreseeable vaccination benefits and risks. The way in which HPV vaccines are often promoted to women indicates that such disclosure is not always given from the basis of the best available knowledge. For example, while the world's leading medical authorities state that HPV vaccines are an important cervical cancer prevention tool, clinical trials show no evidence that HPV vaccination can protect against cervical cancer. Similarly, contrary to claims that cervical cancer is the second most common cancer in women worldwide, existing data show that this only applies to developing countries. In the Western world cervical cancer is a rare disease with mortality rates that are several times lower than the rate of reported serious adverse reactions (including deaths) from HPV vaccination. Future vaccination policies should adhere more rigorously to evidence-based medicine and ethical guidelines for informed consent.

<http://www.ncbi.nlm.nih.gov/pubmed/22188159>

“... while the world's leading medical authorities state that HPV vaccines are an important cervical cancer prevention tool, clinical trials show no evidence that HPV vaccination can protect against cervical cancer. Similarly, contrary to claims that cervical cancer is the second most common cancer in women worldwide, existing data show that this only applies to developing countries. In the Western world cervical cancer is a rare disease with mortality rates that are several times lower than the rate of reported serious adverse reactions (including deaths) from HPV vaccination.”

Human papillomavirus vaccine and systemic lupus erythematosus

Author information

Gatto M1, Agmon-Levin N, Soriano A, Manna R,
Maoz-Segal R, Kivity S, Doria A, Shoenfeld Y.
Department of Medicine
University of Padova, Padova, Italy

Abstract

To investigate the association between human papillomavirus (HPV) vaccination and autoimmune manifestations compatible with systemic lupus erythematosus (SLE) or SLE-like disease, the medical history of six women who presented with SLE or SLE-like disease following HPV immunization was collected. Data regarding type of vaccine, number of immunization, family and personal, clinical and serological features, as well as response to treatments were analyzed. In the reported cases, several common features were observed, such as personal or familial susceptibility to autoimmunity or adverse response to a prior dose of the vaccine, both of which may be associated with a higher risk of post-vaccination autoimmunity. Favorable response to immunosuppressant was observed in all patients. In the current study, a temporal association between immunization with HPV vaccine and the appearance of a spectrum of SLE-like conditions is reported. Additionally, among the patients described, several common features were observed that may enable better identification of subjects at risk. Further studies are required to assess the safety of immunization with the HPV vaccine in patients with autoimmune-rheumatic diseases or in subject at risk of autoimmunity as well as the potential beneficial effect of preventive immunosuppressants.

<http://www.ncbi.nlm.nih.gov/pubmed/23624585>

“In the current study,
a temporal association between
immunization with HPV vaccine
and the appearance of a spectrum of
SLE-like conditions is reported.
Additionally, among the patients described,
several common features were observed
that may enable better identification
of subjects at risk.”

Association of acute cerebellar ataxia and human papilloma virus vaccination: a case report

Author information

Yonee C1, Toyoshima M, Maegaki Y, Kodama Y,
Hayami H, Takahashi Y, Kusunoki S, Uchibori A, Chiba A, Kawano Y.

Department of Pediatrics
Graduate School of Medical and Dental Sciences
Kagoshima University, Kagoshima City
Kagoshima, Japan

Abstract

INTRODUCTION

We report the case of a patient who developed symptoms of acute cerebellar ataxia (ACA) after administration of the human papilloma virus (HPV)-16/18 vaccine.

PATIENT AND METHOD

This patient developed symptoms of ACA, including nausea, vertigo, severe limb and truncal ataxia, and bilateral spontaneous continuous horizontal nystagmus with irregular rhythm, 12 days after administration of the HPV-16/18 AS04-adjuvanted cervical cancer vaccine. After this, the patient received methylprednisolone pulse and intravenous immunoglobulin (IVIG) therapies as well as immunoadsorption plasmapheresis.

RESULTS

Severe ACA symptoms did not improve after methylprednisolone pulse and IVIG therapies, but the patient recovered completely after immunoadsorption plasmapheresis.

CONCLUSION

This temporal association strongly suggests that ACA was induced by the vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23378179>

“This temporal association
strongly suggests that
acute cerebellar ataxia
was induced by the vaccination.”

Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants

Author information

Colafrancesco S1, Perricone C, Tomljenovic L, Shoenfeld Y.
Zabludowicz Center for Autoimmune Diseases Sheba Medical Center, Tel-Hashomer, Israel

Rheumatology Unit, Department of Internal Medicine and Medical Specialities
Sapienza University of Rome, Rome, Italy

Abstract

PROBLEM

Post-vaccination autoimmune phenomena are a major facet of the autoimmune/inflammatory syndrome induced by adjuvants (ASIA) and different vaccines, including HPV, have been identified as possible causes.

METHOD OF STUDY

The medical history of three young women who presented with secondary amenorrhea following HPV vaccination was collected. Data regarding type of vaccine, number of vaccination, personal, clinical and serological features, as well as response to treatments were analyzed.

RESULTS

All three patients developed secondary amenorrhea following HPV vaccinations, which did not resolve upon treatment with hormone replacement therapies. In all three cases sexual development was normal and genetic screen revealed no pertinent abnormalities (i.e., Turner's syndrome, Fragile X test were all negative). Serological evaluations showed low levels of estradiol and increased FSH and LH and in two cases, specific auto-antibodies were detected (antiovarian and anti thyroid), suggesting that the HPV vaccine triggered an autoimmune response. Pelvic ultrasound did not reveal any abnormalities in any of the three cases. All three patients experienced a range of common non-specific post-vaccine symptoms including nausea, headache, sleep disturbances, arthralgia and a range of cognitive and psychiatric disturbances. According to these clinical features, a diagnosis of primary ovarian failure (POF) was determined which also fulfilled the required criteria for the ASIA syndrome.

CONCLUSION

We documented here the evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports of post HPV vaccine-linked autoimmunity and the uncertainty of long-term clinical benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry.

“We documented here the evidence of the potential of the HPV vaccine to trigger a life-disabling autoimmune condition. The increasing number of similar reports of post HPV vaccine-linked autoimmunity and the uncertainty of long-term clinical benefits of HPV vaccination are a matter of public health that warrants further rigorous inquiry.”

Human papilloma virus vaccine associated uveitis

Author information

Holt HD, Hinkle DM, Falk NS, Fraunfelder FT, Fraunfelder FW1.

Lions Eye Institute, Albany Medical College, Slingerlands, New York, USA
hnc11983@gmail.com

Abstract

PURPOSE

To report a possible association between human papilloma virus (HPV) vaccination and uveitis.

METHODS

Spontaneous reports from the National Registry of Drug-Induced Ocular Side effects, World Health Organization and Food and Drug Administration were collected on uveitis associated with human papilloma virus vaccination. A MEDLINE search was performed using keywords “uveitis,” “iritis,” “iridocyclitis,” “human papilloma virus,” “Cervarix”, and “Gardasil.”

MAIN OUTCOME MEASURES

Data garnered from spontaneous reports included the age, gender, adverse drug reaction (ADR), date of administration, concomitant administration of other vaccinations, time until onset of ADR, other systemic reactions, and dechallenge and rechallenge data.

RESULTS

A total of 24 case reports of uveitis associated with human papilloma virus vaccination were identified, all cases were female, and the median age was 17. Median time from HPV vaccination to reported ADR was 30 days (range 0-476 days).

DISCUSSION

According to World Health Organization criteria, the relationship between human papilloma virus vaccination and uveitis is “possible.” Causality assessments are based on the time relationship of drug administration, uveitis development and rechallenge data.

CONCLUSIONS

Clinicians should be aware of a possible bilateral uveitis and papillitis following HPV vaccination.

“A total of 24 case reports of uveitis associated with human papilloma virus vaccination were identified, all cases were female, and the median age was 17. According to World Health Organization criteria, the relationship between human papilloma virus vaccination and uveitis is “possible.”

Postural tachycardia syndrome following human papillomavirus vaccination

Author information

Blitshteyn S.

Department of Neurology
State University of New York at Buffalo
School of Medicine and Biomedical Sciences
Buffalo, NY, USA

Abstract

BACKGROUND AND PURPOSE

Postural tachycardia syndrome (POTS) is a heterogeneous disorder of the autonomic nervous system that may have an autoimmune etiology.

METHODS

Six patients who developed new onset POTS 6 days to 2 months following human papillomavirus vaccination are reported.

RESULTS

Three patients also had neurocardiogenic syncope, and three patients were diagnosed with possible small fiber neuropathy. Symptoms in all patients improved over 3 years with pharmacotherapy and non-pharmacological measures but residual symptoms persisted. Molecular mimicry with formation of cross-reacting autoantibodies to the potential targets of the autonomic ganglia, neurons, cardiac proteins or vascular receptors is considered as a possible pathogenesis of new onset POTS after immunization.

CONCLUSION

Correct diagnosis of POTS and awareness that POTS may occur after vaccination in young women is essential for prompt and effective management of this condition.

<http://www.ncbi.nlm.nih.gov/pubmed/24102827>

“Six patients who developed
new onset Postural tachycardia syndrome
6 days to 2 months following human
papillomavirus vaccination are reported.”

Adolescent Premature Ovarian Insufficiency Following Human Papillomavirus Vaccination: A Case Series Seen in General Practice

Author information

Little DT1, Ward HR2.

1. Bellingen District Hospital, Bellingen, New South Wales, Australia
2. University of New South Wales, Coffs Harbour, New South Wales, Australia

Abstract

Three young women who developed premature ovarian insufficiency following quadrivalent human papillomavirus (HPV) vaccination presented to a general practitioner in rural New South Wales, Australia. The unrelated girls were aged 16, 16, and 18 years at diagnosis. Each had received HPV vaccinations prior to the onset of ovarian decline. Vaccinations had been administered in different regions of the state of New South Wales and the 3 girls lived in different towns in that state. Each had been prescribed the oral contraceptive pill to treat menstrual cycle abnormalities prior to investigation and diagnosis. Vaccine research does not present an ovary histology report of tested rats but does present a testicular histology report. Enduring ovarian capacity and duration of function following vaccination is unresearched in preclinical studies, clinical and postlicensure studies. Postmarketing surveillance does not accurately represent diagnoses in adverse event notifications and can neither represent unnotified cases nor compare incident statistics with vaccine course administration rates. The potential significance of a case series of adolescents with idiopathic premature ovarian insufficiency following HPV vaccination presenting to a general practice warrants further research. Preservation of reproductive health is a primary concern in the recipient target group. Since this group includes all prepubertal and pubertal young women, demonstration of ongoing, uncompromised safety for the ovary is urgently required. This matter needs to be resolved for the purposes of population health and public vaccine confidence.

<http://www.ncbi.nlm.nih.gov/pubmed/26425627>

“Three young women who developed premature ovarian insufficiency following quadrivalent human papillomavirus (HPV) vaccination presented to a general practitioner in rural New South Wales, Australia. The potential significance of a case series of adolescents with idiopathic premature ovarian insufficiency following HPV vaccination presenting to a general practice warrants further research. This matter needs to be resolved for the purposes of population health and public vaccine confidence.”

Comparison of adaptive and innate immune responses induced by licensed vaccines for Human Papillomavirus

Author information

Herrin DM1, Coates EE, Costner PJ, Kemp TJ, Nason MC, Saharia KK, Pan Y, Sarwar UN, Holman L, Yamshchikov G, Koup RA, Pang YY, Seder RA, Schiller JT, Graham BS, Pinto LA, Ledgerwood JE.

1. Vaccine Research Center
National Institute of Allergy and Infectious Disease
National Institutes of Health; Bethesda, MD USA

Abstract

Two HPV virus-like particle (VLP) vaccines, HPV-16/18 (GlaxoSmithKline, Cervarix®) and HPV-6/11/16/18 (Merck, Gardasil®), are currently licensed in the United States. Given the similar antigenic content but different adjuvant formulations in the 2 vaccines, they provide an efficient method for evaluating adjuvants and comparing the kinetics of the innate and adaptive immune responses. We randomized women to receive either Cervarix® or Gardasil®, followed 6 month vaccination delivery schedules per manufacturer's recommendations, and analyzed the humoral immune response, T cell response, and circulating plasma cytokine levels in response to vaccination. Cervarix® recipients had higher anti-HPV-16 antibody and neutralization titers at month 7, and elevated anti-HPV-18 antibody and neutralization titers at months 7 and 12. Antibody avidity was similar for the 2 vaccines. HPV-31 was the only phylogenetically related non-vaccine HPV type, for which there is evidence of cross-protection, to be cross-neutralized and only in response to Cervarix®. Comparing CD4+ T cell cytokine responses at month 12, there was a trend of increased levels of IL-2 and TNF- α in the Cervarix® groups versus the Gardasil® groups that was consistent across all 4 tested HPV types (16/18/33/45). Elevated levels of circulating plasma cytokine/chemokines were observed post first vaccination in Gardasil® recipients and proinflammatory cytokines were elevated following 1st and 3rd Cervarix® vaccinations. Cervarix® and Gardasil® are both highly immunogenic vaccines. Higher antibody levels and CD4 T cell responses were achieved with Cervarix® after 3 doses, although similar affinity maturation was measured for the 2 vaccines. The clinical implications of the differences in immune responses are unknown.

[proving vaccines are continuous, long-term human experiments]

HPV vaccine is neither safe nor effective

The following letter to the editor of the Baltimore Sun, with references, was written by Emily Tarsell, LCPC, and Dr. William Reichel on August 9, 2015

Dear Editor:

Your recent article in The Baltimore Sun, Medicine Briefs for August 2, 2015, states that “not enough pediatricians are strongly recommending HPV vaccine.” It appears there are excellent medical and scientific reasons why many doctors do not.

Since hpv vaccines were introduced seven years ago, it has been assumed that this vaccine will prevent cervical cancer. Yet it has never been demonstrated to prevent any cancer, cervical or otherwise (1, 2, 3).

It has also been assumed for 7 years that this vaccine is safe. Yet there have been thousands of adverse event reports. The CDC itself admits there are 3x as many adverse events for the hpv vaccine Gardasil as there are for all other vaccines combined.(4) Compared to all other vaccines in the US schedule, Gardasil alone is associated with 61% of all serious adverse events including 63.8% of all deaths and 81.2% of all permanent disabilities in females under 30 years of age. (5)

In fact, Japan, India and France have removed hpv vaccines from their recommended list due to safety and efficacy concerns.(6, 7, 8, 11) Unethical practices and serious post hpv vaccination injuries and deaths prompted the Supreme Court of India to initiate an ongoing investigation of the Bill and Melinda Gates Foundation. (7) The Health Welfare and Labor Ministry of Japan conducted a national investigation regarding post hpv vaccine injuries in their country. The outcome was the removal of funding and removal of recommendations regarding hpv vaccines. (8, 9, 10, 11) They concluded that the harm experienced is overwhelmingly greater than the benefit expected.

Prompted by medical reports of post hpv vaccination arrhythmia and motor neuron disabilities in children in Denmark, the European Medicines Agency is conducting an investigation of hpv injection adverse events. (12) Law suits for hpv injuries and deaths have also been led in Spain, France and Columbia.

Some studies have linked serious hpv vaccine adverse events to the aluminum adjuvant which is a known neurotoxin. (13, 14, 15, 16) Yet the latest version of hpv vaccine, Gardasil 9, contains double the amount of aluminum adjuvant than its predecessor.

We already have proven, safe and effective ways to prevent cervical cancer with pap screening which carries no serious health risk. So the doctors who do not recommend hpv vaccination are the ones who have done their research. The public should be grateful to those who have taken their oath seriously.

Sincerely,

William Reichel, MD Emily Tarsell, LCPC

References

1. Tomljenovic L, Shaw CA, Spinosa JP: Human Papillomavirus (HPV) Vaccines as an option for preventing cervical malignancies: (How) effective and safe? *Curr Pharm Des* 2012, :CPD-EPUB-20120924-13.Epub ahead of print.
2. Tomljenovic L, Shaw CA: Who profits from uncritical acceptance of biased estimates of vaccine efficacy and safety? *Am J Public Health* 2012, 102(9):e13–e14.
3. Tomljenovic L, Shaw CA: Human papillomavirus (HPV) vaccine policy and evidence-based medicine: are they at odds? *Ann Med* 2011, doi:10.3109/07853890.2011.645353
4. Slade BA, Leidel L, Vellozzi C, et al. Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine. *JAMA*. 2009; 302 (7): 750- 757.
5. Tomljenovic L, Wilyman J, Vanamee E, Bark T, Shaw CA. HPV vaccines and cancer prevention, science versus activism. *Infectious Agents and Cancer* 2013,8:6. <http://www.infectagentscancer.com/content/8/1/6>.
6. Vactruth. French Medical Doctors Say, “Delist & Suspend HPV Vaccines. December 28, 2011 <http://www.medocean.re/2011/09/le-gardasil-a-l%E2%80%99as-semblee-nationale/>. Accessed January 2012.
7. Sarojini N B, Sandhya Srinivasan, Madhavi Y, Srinivasan S, Anjali Shenoifie HPV Vaccine: Science, Ethics and Regulation. *Economic & Political Weekly EPW* november 27, 2010 vol xlv no 48.
8. Erickson N. Japan and the hpv vaccine controversy. www.sanevax.org. Accessed 4/29/2014.
9. Kyodo. Cervarix vaccine issues trigger health notice. *Japan Times*. June 15,2013. <http://www.japantimes.co.jp/news/2013/06/15/national/cervix-vaccine-issues-trigger-health-notice/#.VMfXIWjF8fX>. Accessed 4/29/2014.
10. Ministry of Health, Labor and Welfare. Shimbun A. Analysis: Experts at loss over pain from cervical cancer vaccination. *Asia and Japan Watch*. June 18, 2013. http://ajw.asahi.com/article/behind_news/social_a_airs/AJ201306180057. Accessed 1/27/15
11. Archive of proceedings and events regarding an investigation into hpv vaccines safety and efficacy by the Japanese Ministry of Health, Labor and Welfare. *Medwatcher Japan*. <http://www.yakugai.gr.jp/en/activity/index.php?year=2014>. Accessed 1/26/15.
12. Chustecka Z. Safety Profile of HPV Vaccines Under Review in Europe. *Medscape*. July 13, 2015. http://www.medscape.com/viewarticle/847841src=wnl_edit_news&uac=148182AN&impID=759675&faf=1 Accessed July 20, 2015.
13. Lee, SH. Detection of human papillomavirus (HPV) L1 gene DNA possibly bound to particulate aluminum adjuvant in the HPV-vaccine Gardasil. *Journal of Inorganic Biochemistry*. 117 (2012) 85-92. www.elsevier.com/locate/jinorgbio.
14. Shoenfeld Y, Agmon-Levin N. ‘ASIA’ – Autoimmune/inflammatory syndrome induced by adjuvants. *Journal of Autoimmunity* (2010), 2010; XXX: 1-5.
15. Tomljenovic L, Shaw CA. Mechanisms of Aluminum adjuvant toxicity and autoimmunity in pediatric populations. *Lupus* 2012; 21:223-230.
16. Shaw CA, Petrik MS. Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. *J Inorg Biochem* 2009; 103: 1555-1562.

“Since hpv vaccines were introduced seven years ago, it has been assumed that this vaccine will prevent cervical cancer.

Yet it has never been demonstrated to prevent any cancer, cervical or otherwise. It has also been assumed for 7 years that

this vaccine is safe. Yet there have been thousands of adverse event reports. The CDC itself admits there are 3x as many

adverse events for the hpv vaccine Gardasil as there are for all other vaccines combined.”

Suspected side effects to the quadrivalent human papilloma vaccine

Author information

Brinth L1, Theibel AC, Pors K, Mehlsen J.

Koordinerende Forskningsenhed/Synkopecenteret
Vej 3, Indgang 4, Frederiksberg Hospital, Nordre Fasanvej 57
2000 Frederiksberg, Denmark
louise.schouborg.brinth@regionh.dk

Abstract

Introduction

The quadrivalent vaccine that protects against human papilloma virus types 6, 11, 16 and 18 (Q-HPV vaccine, Gardasil) was included into the Danish childhood vaccination programme in 2009. During the past years, a collection of symptoms primarily consistent with sympathetic nervous system dysfunction have been described as suspected side effects to the Q-HPV vaccine.

Methods

We present a description of suspected side effects to the Q-HPV vaccine in 53 patients referred to our Syncope Unit for tilt table test and evaluation of autonomic nervous system function.

Results

All patients had symptoms consistent with pronounced autonomic dysfunction including different degrees of orthostatic intolerance, severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort and widespread pain of a neuropathic character.

Conclusion

We found consistency in the reported symptoms as well as between our findings and those described by others. Our findings neither confirm nor dismiss a causal link to the Q-HPV vaccine, but they suggest that further research is urgently warranted to clarify the pathophysiology behind the symptoms experienced in these patients and to evaluate the possibility and the nature of any causal link and hopefully establish targeted treatment options.

<http://www.ncbi.nlm.nih.gov/pubmed/25872549>

“During the past years, a collection of symptoms primarily consistent with sympathetic nervous system dysfunction have been described as suspected side effects to the Q-HPV vaccine. All patients had symptoms consistent with pronounced autonomic dysfunction including different degrees of orthostatic intolerance, severe non-migraine-like headache, excessive fatigue, cognitive dysfunction, gastrointestinal discomfort and widespread pain of a neuropathic character.”

Neurologic Complications in HPV Vaccination

Author information

Ikeda S.

Department of Medicine (Neurology and Rheumatology)
Shinshu University School of Medicine
Japan

Abstract

A relatively high incidence of chronic limb pain, frequently complicated by violent, tremulous involuntary movements, has been noted in Japanese girls following human papillomavirus vaccination. The average incubation period after the first dose of the vaccine was 5.47 ± 5.00 months. Frequent manifestations included headaches, general fatigue, coldness of the feet, limb pain, and weakness. The skin temperature of the girls with limb symptoms was slightly lower in the fingers and moderately lower in the toes. Digital plethysmograms revealed a reduced peak of the waves, especially in the toes. Limb symptoms of the affected girls were compatible with the diagnostic criteria for complex regional pain syndrome. The Schellong test identified a significant number of patients with orthostatic hypotension and a few with postural orthostatic tachycardia syndrome. Electron-microscopic examinations of the intradermal nerves showed an abnormal pathology in the unmyelinated fibers in two of the three girls examined. The symptoms observed in this study can be explained by abnormal peripheral sympathetic responses. The most common previous diagnosis in the patients was psychosomatic disease. Recently, delayed manifestation of cognitive dysfunction in the post-vaccinated girls has attracted attention. The symptoms include memory loss and difficulty in reading textbooks and/or calculation.

<http://www.ncbi.nlm.nih.gov/pubmed/26160812>

“A relatively high incidence
of chronic limb pain,
frequently complicated by violent,
tremulous involuntary movements,
has been noted in Japanese girls following
human papillomavirus vaccination.”

The safety of human papilloma virus-blockers and the risk of triggering autoimmune diseases

Author information

Baker B1, Eça Guimarães L, Tomljenovic L,
Agmon-Levin N, Shoenfeld Y.

The Zabłudowicz Center for Autoimmune Diseases
Chaim Sheba Medical Center, Tel-Hashomer 52621, Israel
+972 3 5302652; +972 3 5352855
shoenfel@post.tau.ac.il

Abstract

INTRODUCTION

With the safety of human papilloma virus vaccine (HPVv) being questioned, this article aims to assess the risks and benefits of the commercially available HPVv. Within the last decade, two vaccines (Gardasil and Cervarix) have been put on the market to prevent infection with the most oncogenic HPV subtypes. Both vaccines contain aluminum adjuvants that are meant to cause a hyper stimulated immune response to prevent HPV infection.

AREAS COVERED

The purpose of this paper is to consider the safety of these two vaccines based on the data from the U.S. Vaccine Adverse Event Reporting System (VAERS) and case reports.

EXPERT OPINION

The current HPVv are both effective and generally safe. However, it should be noted that autoimmune side effects have been reported in several studies. Further research should be done to understand the relationship between HPVv and autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/26216756>

“However, it should be noted that autoimmune side effects have been reported in several studies. Further research should be done to understand the relationship between HPVv and autoimmunity.”

Compensation programs after withdrawal of the recommendation for HPV vaccine in Japan

Author information

Yuji K1, Nakada H2.

1. Project Division of International Advanced Medical Research
The Institute of Medical Science, The University of Tokyo
4-6-1 Shirokanedai, Minatoku, Tokyo, Japan, 1088639
2. Research and Development Initiative Center
National Cerebral and Cardiovascular Center Research Institute
Suita City, Osaka, Japan
nakad@ncvc.go.jp

Abstract

HPV vaccinations were recommended with the backing of a Japanese government subsidy program in 2010, and were included in the National Immunization Program in April 2013. However, the Ministry of Health, Labour, and Welfare withdrew the recommendation for the HPV vaccination in June 2013. We investigated HPV vaccine injury compensation programs for both the national and local governments. Approximately 3.38 million girls were vaccinated, and 2,584 complained of health problems. The majority of these received the vaccine shot as a non-routine vaccination. In total, 98 people developed health problems and applied for assistance from 2011 to 2014, but no cases have been processed since October 2014. Several local governments are providing their own compensation program for cases of vaccine adverse reactions, but the number is extremely low (16 of 1,741 municipalities and 1 of 47 prefectures). The local governments that are providing compensation are largely those where HPV vaccine victim support groups are prominent. The confusion regarding the national program for HPV vaccine injury was caused by the discrepancy between the compensation programs for those vaccinated under the immunization law and for those who received voluntary vaccinations. The establishment of a new compensation program might be key to finding a lasting resolution.

<http://www.ncbi.nlm.nih.gov/pubmed/26513303>

HPV Vaccination Crisis In Japan link:

http://www.researchgate.net/publication/279181953_HPV_vaccination_crisis_in_Japan

“the Ministry of Health, Labour, and Welfare
withdrew the recommendation for the HPV vaccination
in June 2013.”

HPV vaccination syndrome A questionnaire-based study

Author information

Martínez-Lavín M1, Martínez-Martínez LA2, Reyes-Loyola P2.

1. Departamento de Reumatología
Instituto Nacional de Cardiología Ignacio Chávez
Juan Badiano 1, 14080, Mexico City, Mexico
drmartinezlavin@gmail.com.
2. Departamento de Reumatología
Instituto Nacional de Cardiología Ignacio Chávez
Juan Badiano 1, 14080, Mexico City, Mexico

Abstract

Isolated cases and small series have described the development of complex regional pain syndrome, postural orthostatic tachycardia, and fibromyalgia after human papillomavirus (HPV) vaccination. These illnesses are difficult to diagnose and have overlapping clinical features. Small fiber neuropathy and dysautonomia may play a major role in the pathogenesis of these entities. We used the following validated questionnaires to appraise the chronic illness that might appear after HPV vaccination: The 2010 American College of Rheumatology Fibromyalgia Diagnostic Criteria, COMPASS 31 dysautonomia questionnaire, and S-LANSS neuropathic pain form. These questionnaires and a “present illness” survey were e-mailed to persons who had the onset of a chronic ailment soon after HPV vaccination. Forty-five filled questionnaires from individuals living in 13 different countries were collected in a month’s period. Mean (\pm SD) age at vaccination time was 14 ± 5 years. Twenty-nine percent of the cases had immediate (within 24 h) post-vaccination illness onset. The most common presenting complaints were musculoskeletal pain (66 %), fatigue (57 %), headache (57 %), dizziness/vertigo (43 %), and paresthesias/allodynia (36 %). Fifty-three percent of affected individuals fulfill the fibromyalgia criteria. COMPASS-31 score was 43 ± 21 , implying advanced autonomic dysfunction. Eighty-three percent of the patients who had ongoing pain displayed S-LANSS values >12 , suggesting a neuropathic component in their pain experience. After a mean period of 4.2 ± 2.5 years post-vaccination, 93 % of patients continue to have incapacitating symptoms and remain unable to attend school or work. In conclusion, a disabling syndrome of chronic neuropathic pain, fatigue, and autonomic dysfunction may appear after HPV vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/26354426>

“Isolated cases and small series have described the development of complex regional pain syndrome, postural orthostatic tachycardia, and fibromyalgia after human papillomavirus (HPV) vaccination. In conclusion, a disabling syndrome of chronic neuropathic pain, fatigue, and autonomic dysfunction may appear after HPV vaccination.”

Chapter Five

75 Years Of Vaccine Science

1939 - 2016

Both common observation and official statistics confirm that there have been dramatic increases in chronic physical and mental illnesses in American children, such as autism, asthma, and allergies since the introduction of the MMR vaccine in 1978. Government health officials have denied a relationship with vaccines, but U.S. Congressional hearings on vaccine safety (1999 to Dec. 2004) revealed a total absence of vaccine safety tests that would meet current scientific standards, so that it can be assumed that many vaccine reactions are taking place unrecognized. Prior to the introduction of vaccines, the Th1 cellular immune system of the gastrointestinal and respiratory systems served as the primary defense systems with the Th2 humoral immune system in the bone marrow, serving a secondary role. There is a school of thought that the “minor childhood diseases” of earlier times,

including measles, mumps, chicken pox, and rubella, which involved the epithelial tissues of skin, respiratory, and/or gastrointestinal tracts, served a necessary purpose in challenging, strengthening, and establishing the dominance of the Th1 cellular immune system during early childhood. Current vaccines against these diseases, in contrast, being directed at stimulating antibody production in the bone marrow, are bypassing the cellular immune system and thereby tending to reverse the roles of the cellular and humoral systems, with the former suffering from a lack of challenge. In addition, the cellular immune system is being further compromised by the powerfully immunosuppressive effects of the MMR vaccine. The time is overdue to totally rethink and redirect our current childhood vaccine program.

~ Dr. Harold Buttram

JAMA • Vol 112, No. 19 • May 13, 1939

Diphtheria immunity in Chicago

by Herman N. Bundesen, MD., Sc.D.,
William I. Fishbein, MD., John L. White, MD

Abstract

Although diphtheria mortality and morbidity have been gradually decreasing in most parts of the United States for the past twenty-five years, they have not been reduced to the level which it was hoped would be attained. Antitoxin, control of carriers and the Schick test were important. The discovery of toxoid added new impetus to the efforts to control this disease. It was believed that the inoculation of a large proportion of the child population would result in almost complete eradication of diphtheria. The results obtained with the use of toxoid did not, however, approximate expectations. The present study explains to some extent this failure.

<http://jama.jamanetwork.com/article.aspx?articleid=288193&resultClick=3>

“It was believed that the inoculation of a large proportion of the child population would result in almost complete eradication of diphtheria. The results obtained with the use of toxoid did not, however, approximate expectations. The present study explains to some extent this failure.”

JAMA • Vol 114, No. 19 • May 11, 1940

Allergy induced by immunization with Tetanus Toxoid

by Robert A. Cooke, MD., Stanley Hampton, MD.,
William B. Sherman, MD., Arthur Stull, Ph.D.

Abstract

A toxoid for the active immunization of human beings against tetanus infection has been developed within the past few years and its efficiency as a producer of tetanus antitoxin has been well established. It has followed directly in the wake of the development of diphtheria toxoid, and today a refined alum precipitated formaldehyde detoxified tetanus toxoid standardized under rules of the National Institute of Health is commercially available. It is not within the scope of this paper to discuss the aspects of its development or its antitoxin producing capacity, all of which may be found in such recent papers, with references, as those of Bergey and Etris,¹ Jones and Moss,² Hall,³ Gold⁴ and Cowles.⁵

<http://jama.jamanetwork.com/article.aspx?articleid=1160278&resultClick=3>

“It has followed directly in the wake of the development of diphtheria toxoid, and today a refined alum precipitated formaldehyde detoxified tetanus toxoid standardized under rules of the National Institute of Health is commercially available.”

Encephalopathies Following Prophylactic Pertussis Vaccine

Randolph K. Byers, Frederic C. Moll

Abstract

Inspection of the records of the Children's Hospital for the past ten years has disclosed 15 instances in which children developed acute cerebral symptoms within a period of hours after the administration of pertussis vaccine. The children varied between 5 and 18 months in age and, in so far as it is possible to judge children of this age range, were developing normally according to histories supplied by their parents. None had had convulsions previously. Many different lots of vaccine, made by eight different manufacturers over a period of eight years, were implicated. The inoculations were given throughout the usual geographic range of children coming to this hospital. All but one, at the time of follow-up or death, showed evidence of impairment of the nervous system, which might still have been in the healing stage in three or four.

During the same period about half as many children were seen in the hospital suffering from the encephalopathy secondary to smallpox vaccination, and about twice as many from the encephalopathy complicating pertussis itself.

A variety of etiologic considerations were suggested by consideration of the reported cases and references to the literature. That constitutional factors may have been involved was suggested by both the preponderance of males as opposed to females, and by the high incidence of abnormalities of the nervous system in the family histories. The clinical course and cytologic abnormalities of spinal fluids found in acute cases indicated an encephalopathy. The literature suggested that this process might have resulted from either the activity of a specific toxin or from an antigen-antibody response. Against the former of these hypotheses was the unstable nature of the heretofore recognized toxins which could hardly survive in properly aged vaccines. The rapid onset of symptoms, occasionally within minutes of the first injection, seemed strong evidence against the second. The present study has left these etiologic considerations unanswered, but it has called attention to a risk of the prophylactic use of pertussis vaccine not hitherto recognized.

In view of the impressive evidence of the effectiveness of prophylactic pertussis vaccine now accumulating, it seems likely that babies are safer vaccinated than not. Further studies should be made to prove this point definitely, for the encephalopathy following pertussis vaccine seems more devastating than the vast majority of the nervous lesions following the use of smallpox vaccine.

“In view of the impressive evidence of the effectiveness of prophylactic pertussis vaccine now accumulating, it seems likely that babies are safer vaccinated than not. Further studies should be made to prove this point definitely, for the encephalopathy following pertussis vaccine seems more devastating than the vast majority of the nervous lesions following the use of smallpox vaccine.”

Precautions In Pediatric Immunization Procedures

by Louis W. Sauer, M.D., Ph.D.

Abstract

During the past decade, the simultaneous immunization against diphtheria, tetanus, and pertussis has become quite well established on laboratory and clinical evidence. To retard the elimination of antigen (DTP) from the body and to enhance antitoxin and antibody development, various forms of aluminum have been used as adjuvant. Most private patients are now adequately protected by the customary primary series of three or four monthly doses, and subsequent recall (stimulating or booster) doses. Needless deaths due to pertussis are still occurring, however, in infants and children from families with low incomes and orphanages in congested cities and in rural areas. To reach these children, mass immunization clinics should function at well baby clinics, primary schools, and mobile units. The diverse difficulties encountered in the execution of these immunization procedures are problems due to earlier immunization, febrile reactions, alum cyst, postinoculation encephalopathy, paralytic poliomyelitis of the injected limb, and unfavorable results.

<http://jama.jamanetwork.com/article.aspx?articleid=287046&resultClick=3>

“The diverse difficulties encountered in the execution of these immunization procedures are problems due to earlier immunization, febrile reactions, alum cyst, postinoculation encephalopathy, paralytic poliomyelitis of the injected limb, and unfavorable results.”

Science • January 1969

Secretory activity and oncogenicity of a cell line (MDCK) derived from canine kidney and

A cell line (MDCK) of dog kidney origin grows on a glass surface as a mosaic of epithelium with many multicellular hemispherical vesicles. The cells lining the blisters actively secrete into the cyst cavities. Suspensions of these cells injected intravenously in the chick embryo produce brain metastases resembling adenocarcinoma.

[Editors Note: The MDCK (NBL-2) (ATCC® CCL-34™) cell line has been used since 1958 to produce influenza and other vaccines]

<http://www.sciencemag.org/content/163/3866/472.long>

Information on the MDCK cell line

<http://www.atcc.org/products/all/CCL-34.aspx>

“A cell line (MDCK) of dog kidney origin grows on a glass surface as a mosaic of epithelium with many multicellular hemispherical vesicles. The cells lining the blisters actively secrete into the cyst cavities. Suspensions of these cells injected intravenously in the chick embryo produce brain metastases resembling adenocarcinoma.”

[In a departure from the use of traditional egg-based vaccines the FDA approved Flucelvax for Novartis on November 20th, 2012. Flucelvax was the first mammalian cell-based influenza vaccine in the US. The Madin-Darby canine kidney cell line is cultured to produce the vaccine. The primary advantage of MDCK over traditional egg-based manufacturing is rapid growth.]

“The observations of this study as well as those of similar studies suggest that vaccine failures contributed to the genesis of the epidemic.”

Canadian Medical Association Journal • November 1975

Analysis of a measles epidemic: possible role of vaccine failures

W. E. Rawls, M. L. Rawls, and M. A. Chernesky

Abstract

A measles epidemic occurred in the Greensville (Ont.) Unit schools during January and February 1975. There were 47 cases of measles in 403 students: 26 (55%) of the children had a history of being vaccinated and 18 (38%) had not been vaccinated. Among children known to have been vaccinated at less than 1 year of age 7 of 13 contracted measles, while among the 48 children who had not been vaccinated 18 contracted measles. The attack rate among vaccinees increased with increasing time since vaccination. The observations of this study as well as those of similar studies suggest that vaccine failures contributed to the genesis of the epidemic. It is recommended that all children initially vaccinated at less than 1 year of age should be revaccinated with live attenuated measles virus vaccine.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1956577/>

Journal Of Experimental Medicine • September 1977

Autoimmunity to type II collagen an experimental model of arthritis

Trentham DE, Townes AS, Kang AH.

Abstract

We have found that intradermal injection of native type II collagen extracted from human, chick or rat cartilage induces an inflammatory arthritis in approximately 40% of rats of several strains whether complete Freund's adjuvant or incomplete Freund's adjuvant is used. Type I or III collagen extracted from skin, cartilage proteoglycans and alpha1(II) chains were incapable of eliciting arthritis, as was type II collagen injected without adjuvant. The disease is a chronic proliferative synovitis, resembling adjuvant arthritis in rats and rheumatoid arthritis in humans. Native type II collagen modified by limited pepsin digestion still produces arthritis, suggesting that type-specific determinants residing in the helical region of the molecule are responsible for the induction of disease. Since homologous type II collagen emulsified in oil without bacterial preparations regularly causes the disease, this new animal model of arthritis represents a unique example of experimentally-inducible autoimmunity to a tissue component.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2180804/pdf/je1463857.pdf>

“this new animal model of arthritis represents a unique example of experimentally-inducible autoimmunity to a tissue component.”

HBe-Antigen in the course and prognosis of hepatitis B infection: a prospective study

Schulman AN, Fagen ND, Brezina M,
Silver H, Nitzze A, Morton D, Gitnick GL.

Abstract

The prognostic significance of the HBe-antigen (HBeAg) in the course and outcome of type B hepatitis was studied prospectively in 71 susceptible oncology patients. The patients had been exposed to tumor cell vaccines inadvertently contaminated with hepatitis B surface antigen (HBsAg)-containing plasma. Forty-five patients (63%) were infected. These 45 showed three types of acute seroreponse: HBsAg and HBeAg, 28 patients (62%); HBsAg alone, 8 patients (18%); and a primary antibody to HBsAg (anti-HBs) response, 9 patients (20%). There was no significant difference in acute course and outcome between the two HBs-antigenemic groups. All primary anti-HBs responders had asymptomatic infections. Seventeen patients receiving chemotherapy during the period of hepatitis B exposure were significantly more prone to symptomatic infection with acute HBs-antigenemia, and 2 of these patients developed chronic active hepatitis. The HBeAg is common early in acute hepatitis B among solid tumor patients and at this stage in disease has no prognostic significance independent of HBsAg.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=7350048>

“The patients had been exposed to tumor cell vaccines inadvertently contaminated with hepatitis B surface antigen-containing plasma. Forty-five patients (63%) were infected.”

Vaccine adjuvants

Edelman R.

Abstract

Nonreplicating, purified subunit or synthetic viral vaccines of the future are likely to be weak immunogens that will require immunopotentiality if they are to be effective. These marginal vaccines could be improved by combination with potent and safe immunologic adjuvants. The use of adjuvants should also reduce the amount of purified antigen required for successful immunization, thus making vaccine production more economical and more feasible. It may be possible to combine the recently developed relatively nontoxic synthetic immunoregulators of low molecular weight with antigens in order to modulate preselected compartments of the immune system. To date, the question of adjuvant safety has not been resolved and represents the major obstacle to the orderly development of adjuvanted vaccines. The fear of inducing cancer and other immediate or long-term perturbations of the immune system must be patiently and rationally overcome by basic and applied experimentation and by the development of appropriate guidelines for studies in humans.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=6997966>

“Nonreplicating, purified subunit or synthetic viral vaccines of the future are likely to be weak immunogens that will require immunopotentiality if they are to be effective.”

“These data suggest that Tween 80 has an effect on the Central Nervous System which could lead to misinterpretation of results in toxicology studies that use this compound as a dosage vehicle.”

Life Sciences • June 1982

**Effect of Tween 80
on exploratory behavior and locomotor activity in rats**

Brubaker CM, Taylor DH, Bull RJ.

Abstract

Exploratory behavior and locomotor activity is enhanced in male rat pups (aged 10 to 20 days) whose dams received a chronic dose (1.25 ml/l) of Tween 80 via their drinking water. This enhancement manifests itself during the diurnal period of the day. These data suggest that Tween 80 has an effect on the CNS which could lead to misinterpretation of results in toxicology studies that use this compound as a dosage vehicle.

<http://www.ncbi.nlm.nih.gov/pubmed/7202094>

Effect of pertussis toxin
on the hormonal regulation of cyclic AMP levels
in hamster fat cells

by Martínez-Olmedo MA, García-Sáinz JA.

Abstract

Pertussis toxin was purified approx. 1800-fold from pertussis vaccine. Administration of as little as 1 microgram of toxin/100 g body weight to hamsters markedly decreased the sensitivity of their adipocytes to agents that inhibit adenylate cyclase through receptor-mediated, GTP-dependent mechanisms such as alpha 2-adrenergic amines, prostaglandins, phenylisopropyladenosine and nicotinic acid. On the contrary, the inhibitory effect of 2',5'-dideoxyadenosine on cyclic AMP accumulation was not affected by the toxin. Activation of adenylate cyclase by isoproterenol, ACTH or forskolin was not diminished by the toxin but the maximum cyclic AMP accumulation was consistently increased. Furthermore, the dose-response curves for ACTH and forskolin were clearly shifted to the left in adipocytes from toxin-treated hamsters as compared to control adipocytes. It is concluded that pertussis toxin blocks the transfer of inhibitory information from the receptors to adenylate cyclase.

<http://www.ncbi.nlm.nih.gov/pubmed/6313062>

“It is concluded that pertussis toxin
blocks the transfer of inhibitory information
from the receptors to adenylate cyclase.”

New England Journal Of Medicine • January 1984

Abnormal T-lymphocyte subpopulations in healthy subjects after tetanus booster immunization

Eibl MM, Mannhalter JW, Zlabinger G.

“By way of explanation, a vaccine safety test is one in which before-and-after vaccine tests are performed, specifically designed to test for possible adverse effects on the neurological, immunological, hematologic, genetic, and other systems of the body, in sufficient numbers of test subjects and controls to be statistically significant. As an example, in a little noted study from Germany by Eibl et al. [11], a significant, though temporary, drop of T-Helper lymphocytes was found in 11 healthy adults following routine tetanus booster vaccinations. Special concern rests in the fact that, in four of the subjects, T-helper lymphocytes fell to levels seen in active AIDS patients.”

Report available for purchase:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=6228737>

“As an example, in a little noted study from Germany by Eibl et al. [11], a significant, though temporary, drop of T-Helper lymphocytes was found in 11 healthy adults following routine tetanus booster vaccinations. Special concern rests in the fact that, in four of the subjects, T-helper lymphocytes fell to levels seen in active AIDS patients.”

“This outbreak demonstrates that transmission of measles can occur within a school population with a documented immunization level of 100%. This level was validated during the outbreak investigation.”

CDC • June 22, 1984

MMWR Weekly

From December 9, 1983, to January 13, 1984, 21 cases of measles occurred in Sangamon County, Illinois.* Nine of the cases were confirmed serologically. The outbreak involved 16 high school students, all of whom had histories of measles vaccination after 15 months of age documented in their school health records. Of the five remaining cases, four occurred in unvaccinated preschool children, two of whom were under 15 months of age, and one case occurred in a previously vaccinated college student (Figure 5).

The affected high school had 276 students and was in the same building as a junior high school with 135 students. A review of health records in the high school showed that all 411 students had documentation of measles vaccination on or after the first birthday, in accordance with Illinois law.

Measles vaccination histories were obtained from the school health records of all 276 senior high school students. Risk of infection was not significantly associated with type of vaccine, medical provider, age at most recent vaccination, or revaccination. All the students with measles had received their most recent vaccinations after 15 months of age. However, the measles attack rate increased with increasing years since most recent vaccination ($p = 0.024$) (Table 3). The attack rate was four times greater for students vaccinated 10 or more years before the outbreak than for students vaccinated more recently ($p 0.05$). When these data are corrected for the number of vaccinations, the trend was still observed and achieved a borderline level of statistical significance ($p = 0.07$). Age at first or last vaccination was not a confounding variable.

The index patient, Student A, was a 17-year-old male in the 11th grade; he was present in school with a productive cough for 3 consecutive days before his onset of rash. The source of his infection was not identified. Nine students with first-generation cases developed onset of rash 10-14 days after exposure to Student A (Figure 5). The attack rate was 6% (16/276) for senior high school students and 0% (0/135) for junior high school students. The highest attack rate was 12% (9/74) for the 11th grade students ($p 0.02$).

Repeated and close exposure to Student A was associated with a greater risk of illness (Table 4). The eight patients with first-generation cases who attended the high school were used to analyze the degree of exposure to Student A. The measles attack rate was 3% for students who did have classroom exposure to Student A versus 2% for those who did not. Moreover, the attack rate was 21% for students whom Student A identified as “close friends” from the school enrollment roster, compared with 2% for students not so identified ($p 0.001$).

Editorial Note

This outbreak demonstrates that transmission of measles can occur within a school population with a documented immunization level of 100%. This level was validated during the outbreak investigation. Previous investigations of measles outbreaks among highly immunized populations have revealed risk factors such as improper storage or handling of vaccine, vaccine administered to children under 1 year of age, use of globulin with vaccine, and use of killed virus vaccine (1-5). However, these risk factors did not adequately explain the occurrence of this outbreak.

If waning immunity is not a problem, this outbreak suggests that measles transmission can occur within the 2%-10% of expected vaccine failures (5,7). However, transmission was not sustained beyond 36 days in this outbreak, and community spread was principally among unvaccinated preschool children. The infrequent occurrence of measles among highly vaccinated persons suggests that this outbreak may have resulted from chance clustering of otherwise randomly distributed vaccine failures in the community. That measles transmission can occur among vaccine failures makes it even more important to ensure persons are adequately vaccinated. Had there been a substantial number of unvaccinated or inadequately vaccinated students in the high school and the community, transmission in Sangamon County probably would have been sustained.

Bordetella pertussis whole cell vaccines efficacy and toxicity

Trollfors B.

Abstract

The literature concerning efficacy and side effects of pertussis vaccines is reviewed. With few exceptions, most vaccines induce a protective immunity lasting for 2 to 5 years. The large-scale use of pertussis vaccines has markedly contributed to the decrease in pertussis morbidity in small children but in some countries the incidence has increased in older children. Not even countries with immunisation rates of 90-95% have managed to eradicate pertussis or prevent disease in infants below the age of immunisation. The pertussis-associated mortality is currently very low in the industrialised countries and no differences can be discerned when countries with high, low and zero immunisation rates are compared. Local and benign systemic reactions are commonly seen after immunisation. The vaccines also sometimes cause convulsions, a shock-like state and, rarely, serious neurological reactions.

<http://www.ncbi.nlm.nih.gov/pubmed/6380211>

“The pertussis-associated mortality is currently very low in the industrialised countries and no differences can be discerned when countries with high, low and zero immunisation rates are compared. Local and benign systemic reactions are commonly seen after immunisation. The vaccines also sometimes cause convulsions, a shock-like state and, rarely, serious neurological reactions.”

Formaldehyde and hepatotoxicity: a review

Beall JR, Ulsamer AG.

Abstract

Exposure to formaldehyde appears to be associated with hepatotoxicity in many species, including humans, following injection, ingestion, or inhalation. Macroscopic, microscopic, and biochemical manifestations in the liver include alterations in weight, centrilobular vacuolization, focal cellular necrosis, and increased alkaline phosphatase concentrations. Time-related changes in the pattern of the effects are suggested as one goes from acute exposure by inhalation at greater concentrations to repeated exposure at lesser concentrations. Although the hepatic changes are generally not extensive and can be reversible following acute exposure, the potential exists for them to progressively become more serious with repeated exposures. There are several possible mechanisms for the toxicity. Depending on the route of exposure could include direct effects on hepatocytes and/or indirect effects through the circulatory and immune systems. The catabolism of formaldehyde includes conversion to CO₂ by reactions involving glutathione. Many hepatotoxic chemicals require glutathione for detoxification. Formaldehyde may then have the potential to cause additive toxicity with such chemicals in some circumstances.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=6389892>

“Exposure to formaldehyde appears to be associated with hepatotoxicity in many species, including humans, following injection, ingestion, or inhalation.”

“The results of the present study indicate that polysorbate 80 can neither be used as a solvent for isolated tissue experiments nor when considered for intravenous administration.”

Arzneimittelforschung • 1985

Polysorbate 80: a pharmacological study

Varma RK, Kaushal R, Junnarkar AY, Thomas GP,
Naidu MU, Singh PP, Tripathi RM, Shridhar DR.

Abstract

Polyoxyethylene (20) sorbitan monooleate (polysorbate 80, Tween 80), a surfactant, has been widely used as a solvent for pharmacological experiments. In the present study, polysorbate 80 was found to have toxicity of a low order in both the mice and rats when given by i.p. and p.o. routes. It produced mild to moderate depression of the central nervous system with a marked reduction in locomotor activity and rectal temperature, exhibited ataxia and paralytic activity and potentiated the pentobarbital sleeping time. On intravenous administration in dogs, it had a dose-dependent hypotensive effect. Polysorbate 80 did not have a direct stimulant or relaxant effect on either guinea pig ileum or rat uterus, however, it antagonised the contractions induced by acetylcholine, histamine, barium, 5-hydroxytryptamine and carbachol in a dose-dependent manner. A direct relaxant effect was observed on rabbit jejunum. A dose-dependent myocardial depressant effect was observed on guinea pig and rabbit paired atrial preparations. On the electrically-driven guinea pig left atrial preparation, polysorbate 80 exhibited a dose-dependent negative inotropic action. Polysorbate 80 did not induce diuresis in rats upto a dose of 2.5 ml/kg. The results of the present study indicate that polysorbate 80 can neither be used as a solvent for isolated tissue experiments nor when considered for intravenous administration. However, polysorbate 80 can be employed safely as a vehicle for neuropsychopharmacological experiments in doses not exceeding 1 ml/kg.

<http://www.ncbi.nlm.nih.gov/pubmed/4026903>

Polysorbate 80 and E-Ferol toxicity

Alade SL, Brown RE, Paquet A Jr.

Abstract

The relatively recent introduction and use of an intravenous form of a vitamin E preparation (E-Ferol) has been associated with the development of an unusual syndrome and fatalities among low birth weight (less than 1,500 g), premature infants in neonatal intensive care units. We have observed an inhibitory effect by this vitamin E preparation on the in vitro response of human lymphocytes to phytohemagglutinin (PHA). E-Ferol suppressed the expected response to low doses of PHA. However, this suppression was not due to the alpha-tocopherol acetate (vitamin E) component, because alpha-tocopherol acetate by itself was not inhibitory; in fact, it often enhanced the PHA response. Because a mixture of polysorbate 80 and polysorbate 20 is used as a carrier in E-Ferol, these components were also tested and were found to be responsible for the suppression, especially the polysorbate 80. Concurrent with this suppression of PHA-induced mitogenesis was a decrease in the percentage of T11 lymphocytes.

<http://www.ncbi.nlm.nih.gov/pubmed/3960626>

“The relatively recent introduction and use of an intravenous form of a vitamin E preparation has been associated with the development of an unusual syndrome and fatalities among low birth weight (less than 1,500 g), premature infants in neonatal intensive care units ... polysorbate 80 and polysorbate 20 ... were found to be responsible for the suppression, especially the polysorbate 80.”

Laboratory Animal Science • March 1989

An evaluation of distress following intraperitoneal immunization with Freund's adjuvant in mice

Author information

Toth LA1, Dunlap AW, Olson GA, Hessler JR.

Department of Comparative Medicine
University of Tennessee
Memphis 38163

Abstract

Intraperitoneal immunization with Freund's adjuvant is frequently used to stimulate antibody production in mice. To evaluate the clinical and pathological effects of this technique, mice were immunized intraperitoneally with complete Freund's adjuvant and albumin, and the injection repeated 3-4 weeks later using incomplete Freund's adjuvant. This regimen induced a mean antibody titer against albumin of 1:280 within 7 days after booster immunization and increased the abdominal width, abdominal circumference and spleen weights of immunized animals. Food intake and body weight decreased after immunization, but returned to control levels within 1-2 weeks. Open-field activity was not affected. Neutrophilia, eosinophilia and monocytosis were present 7 days after immunization and persisted for the duration of the study. Gross and histopathological lesions included multiple granulomatous abdominal adhesions and lymphoid hyperplasia. Thus, intraperitoneal immunization with Freund's adjuvant and albumin produced some adverse effects in the animal (weight loss, neutrophilia and granulomatous peritonitis). However, the animals did not appear to be severely or chronically impaired, since food intake, body weight and locomotor activity were within normal limits for most of the post-immunization period.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=2709800>

“intraperitoneal immunization
with Freund's adjuvant and albumin
produced some adverse effects in the
animal (weight loss, neutrophilia and
granulomatous peritonitis).”

The role of secondary vaccine failures in measles outbreaks

Author information

Mathias RG1, Meekison WG, Arcand TA, Schechter MT.

Department of Health Care and Epidemiology
University of British Columbia, Vancouver

Abstract

An outbreak of measles in 1985-86 in a community where measles vaccine trials had been carried out from 1974-76 allowed the assessment of the role of secondary vaccine failures in previously immunized children. A total of 188 children from the vaccine trial were followed. Of these, 175 seroconverted initially while 13 (6 per cent) required re-immunization (primary failure). A total of 13 cases of measles, eight of which were laboratory and/or physician-confirmed, were reported in this cohort. Of these, nine cases occurred in the 175 subjects who had hemagglutination inhibition test (HI) and neutralizing antibody responses following the initial immunization. These nine cases represent secondary vaccine failures. An additional four cases occurred in the 13 subjects with primary vaccine failure. We conclude that secondary vaccine failures occur and that while primary failures account for most cases, secondary vaccine failures contribute to the occurrence of measles cases in an epidemic. A booster dose of measles vaccine may be necessary to reduce susceptibility to a sufficiently low level to allow the goal of measles elimination to be achieved.

<http://www.ncbi.nlm.nih.gov/pubmed/2929807>

“These nine cases represent

secondary vaccine failures.

An additional four cases occurred

in the 13 subjects with primary

vaccine failure. We conclude that

secondary vaccine failures occur

and that while primary failures account

for most cases, secondary vaccine failures

contribute to the occurrence of measles

cases in an epidemic.”

Scope • 1990

Short-term Toxicity Tests for Non-genotoxic Effects Toxicity Tests with Mammalian Cell Cultures

B. Ekwall, V. Silano, A. Paganuzzi-Stammati, F. Zucco

Introduction

Cell culture can be used to screen for toxicity both by estimation of the basal functions of the cell (i.e. those processes common to all types of cells) or by tests on specialized cell functions (Ekwall, 1983b). General toxicity tests, aimed mainly at detection of the biological activity of test substances, can be carried out on many cell types (e.g. fibroblasts, HeLa and hepatoma cells). A number of parameters including vital staining, cytosolic enzyme release, cell growth and cloning efficiency are used as end-points to measure toxicity. Organ-specific toxic effects are tested using specialized cells by measuring alterations in membrane and metabolism integrity and/or in specific cell functions (e.g. glycogen metabolism in primary hepatocyte cultures, beating rate in mixed myocardial cells or myocytes, and phagocytosis in macrophages).

http://dge.stanford.edu/SCOPE/SCOPE_41/SCOPE_41_2.02_Chapter_7_75-98.pdf

[shows that as far back as 1990

we could test for non-genotoxic cellular toxicity]

Workshop on neurologic complications of pertussis and pertussis vaccination

Author information

Menkes JH1, Kinsbourne M.
University of California, Los Angeles

Abstract

A multidisciplinary workshop held from September 29 to October 1, 1989, at Airlie House, Warrenton, Virginia, considered the neurologic complications of whooping cough and pertussis vaccine. Pertussis mortality in the U.S. in 2-3/1000 cases. Seizures occur in 1.9% of cases, and encephalopathy in 0.3%. Reviewing all data, it appears likely that a combination of one or more bacterial toxins, asphyxia, CO₂ retention and loss of cerebral vascular autoregulation is responsible for neurologic symptoms. The timing of the encephalopathy suggests that it results from increased lysis of bacteria, and release of endotoxin. The encephalopathy is not confined to the paroxysmal phase. In evaluating side-reactions to the vaccine, the following must be kept in mind: 1. Vaccines are not standardized between manufacturers. 2. For a given manufacturer, vaccines are not standard from one batch to the next. 3. Unless the vaccine is properly prepared and refrigerated, its potency and reactivity varies with shelf life. In fact, the whole question of vaccine detoxification has never been systematically investigated. Listed in order of increasing severity, observed adverse reactions include irritability, persistent, unusually high pitched crying, somnolence, seizures, a shock-like "hypotensive, hyporesponsive" state, and an encephalopathy. Since the neurologic picture is not specific for pertussis vaccination, its temporal relationship to the vaccination is the critical variable for determining causation. Although the majority of seizures following pertussis vaccination are associated with fever, it was the consensus of the neurologists attending the workshop, that these do not represent febrile convulsions, but are non-benign convulsions. The incidence of post-vaccine encephalopathy is difficult to ascertain.

(Abstract truncated at 250 words)

<http://www.ncbi.nlm.nih.gov/pubmed/1981251>

Full Report

<https://www.thieme-connect.com/DOI/DOI?10.1055/s-2008-1071488>

“1. Vaccines are not standardized between manufacturers.

2. For a given manufacturer, vaccines are not standard from one batch to the next.

3. Unless the vaccine is properly prepared and refrigerated, its potency and reactivity varies with shelf life. In fact, the whole question of vaccine detoxification has never been systematically investigated.”

Aseptic meningitis as a complication of mumps vaccination

Author information

Sugiura A1, Yamada A.

Department of Measles Virus
National Institute of Health
Tokyo, Japan

Abstract

In 1989 a nationwide surveillance of neurologic complications after the administration of mumps vaccine was conducted in Japan, based on the notification of cases and the testing of mumps viruses isolated from cerebrospinal fluid for their relatedness to the vaccine by nucleotide sequence analysis. Among 630,157 recipients of measles-mumps-rubella trivalent (MMR) vaccine containing the Urabe Am9 mumps vaccine, there were at least 311 meningitis cases suspected to be vaccine-related. In 96 of these 311 cases, mumps virus related to the vaccine was isolated from cerebrospinal fluid. The unusually high incidence may have been partly a result of the adverse media publicity of the problem at the time of surveillance. We analyzed clinical features of 165 and 27 laboratory-confirmed mumps vaccine-related meningitis cases that occurred among the recipients of MMR and monovalent mumps vaccines, respectively, during a 1-year period after the introduction of MMR vaccine. The incidence of vaccine-related meningitis was similar among the recipients of MMR and monovalent Urabe Am9 mumps vaccines. Meningitis was generally mild and there were no sequelae from the illness. The complication was more frequent among male than among female children.

<http://www.ncbi.nlm.nih.gov/pubmed/2041668>

“Among 630,157 recipients of measles-mumps-rubella trivalent (MMR) vaccine containing the Urabe Am9 mumps vaccine, there were at least 311 meningitis cases suspected to be vaccine-related. In 96 of these 311 cases, mumps virus related to the vaccine was isolated from cerebrospinal fluid.”

Lancet • September 1991

Chronic fatigue syndrome: clinical condition associated with immune activation

Author information

Landay AL1, Jessop C, Lennette ET, Levy JA.

Department of Immunology/Microbiology
Rush-Presbyterian-St. Luke's Medical Center
Chicago, Illinois

Abstract

There is much conflicting immunological and viral data about the causes of chronic fatigue syndrome (CFS); some findings support the notion that CFS may be due to one or more immune disorders that have resulted from exposure to an infectious agent. In the present study, flow cytometry and several different monoclonal antibodies recognising T, B, and natural killer (NK) cell populations as well as activation and cell adhesion antigens were used to study 147 individuals with CFS. Compared with healthy controls, a reduced CD8 suppressor cell population and increased activation markers (CD38, HLA-DR) on CD8 cells were found. The differences were significant ($p = 0.01$) in patient with major symptoms of the disease. These immunological indices were not observed in 80 healthy individuals, in 22 contacts of CFS patients, or in 43 patients with other diseases. No correlation of these findings in CFS patients with any known human viruses could be detected by serology. The findings suggest that immune activation is associated with many cases of CFS.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1679864>

“No correlation of these findings
in chronic fatigue syndrome (CFS) patients with
any known human viruses could be detected by serology.
The findings suggest that immune activation
is associated with many cases of CFS.”

Vaccine • October 1991

Adverse reactions after injection of
adsorbed diphtheria-pertussis-tetanus (DPT) vaccine
are not due only to pertussis organisms
or pertussis components in the vaccine

Author information

Gupta RK1, Relyveld EH.

National Institutes of Health
Bethesda, MD 20892

Abstract

Reactions to adsorbed diphtheria-pertussis-tetanus (DPT) vaccine have mostly been attributed to the pertussis organisms or pertussis components in the vaccine. Nevertheless reactions may also be due to other factors such as sensitization induced by aluminium adjuvants and impurities present in crude toxoids that cannot be removed by purification of toxoids after formalinization. Aluminium compounds such as aluminium phosphate and aluminium hydroxide are the most commonly used adjuvants with vaccines for human use. Due to the increasing concern about the toxicity of aluminium, other adjuvants like calcium phosphate may be evaluated as an alternative to aluminium adjuvants. To minimize reactions after immunization with DPT vaccine due to impurities in the toxoids, the use of toxoided purified toxins is suggested.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1759487>

“... reactions may also be due to other factors
such as sensitization induced by aluminium adjuvants
and impurities present in crude toxoids that cannot be
removed by purification of toxoids after formalinization.”

Journal Of Autoimmunity • December 1991

Adjuvant oils induce arthritis in the DA rat. I. Characterization of the disease and evidence for an immunological involvement

Author information

Kleinau S1, Erlandsson H, Holmdahl R, Klareskog L.

Department of Medical and Physiological Chemistry
Uppsala University, Sweden

Abstract

An intradermal injection of Freund's incomplete adjuvant oil (FIA) without further additives was shown to induce erosive polyarthritis in dark Agouti (DA) rats, but not in Lewis rats. Histological examination revealed joint inflammation, first with polymorphonuclear cells and synovial hyperplasia, and subsequently, with multinucleated giant cells. Both constituents of FIA, mineral oil and Arlacel A, as well as Pristane oil were arthritogenic, whereas vegetable oil were not. Re-administration of adjuvant oil after recovery failed to induce arthritis, thus making possible a role of specific immunity in this new form of arthritis in rats.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1812893>

“Freund's incomplete adjuvant oil (FIA)

was shown to induce erosive polyarthritis in ... rats ...”

Washington DC National Academies Press (US) 1991
The National Academies Collection
Reports funded by National Institutes of Health

Howson CP, Howe CJ, Fineberg HV, editors

**Adverse Effects of Pertussis and Rubella Vaccines:
A Report of the Committee to Review the Adverse Consequences
of Pertussis and Rubella Vaccines**

Excerpt

Parents have come to depend on vaccines to protect their children from a variety of diseases. Some evidence suggests, however, that vaccination against pertussis (whooping cough) and rubella (German measles) is, in a small number of cases, associated with increased risk of serious illness. This book examines the controversy over the evidence and offers a comprehensively documented assessment of the risk of illness following immunization with vaccines against pertussis and rubella. Based on extensive review of the evidence from epidemiologic studies, case histories, studies in animals, and other sources of information, the book examines: The relation of pertussis vaccines to a number of serious adverse events, including encephalopathy and other central nervous system disorders, sudden infant death syndrome, autism, Guillain-Barre syndrome, learning disabilities, and Reye syndrome. The relation of rubella vaccines to arthritis, various neuropathies, and thrombocytopenic purpura. The volume, which includes a description of the committee's methods for evaluating evidence and directions for future research, will be important reading for public health officials, pediatricians, researchers, and concerned parents.

Full Report

<http://www.ncbi.nlm.nih.gov/pubmed/25121241>

“that the evidence is consistent with a causal relation between DPT vaccine and acute encephalopathy, shock and “unusual shock-like state,” and between RA 27/3 rubella vaccine and chronic arthritis; and that the evidence indicates a causal relation between DPT vaccine and anaphylaxis, between the pertussis component of DPT vaccine and protracted, inconsolable crying, and between RA 27/3 rubella vaccine and acute arthritis.”

[RA 27/3 rubella is still in use today]

Adverse events following pertussis and rubella vaccines Summary of a report of the Institute of Medicine

Author information

Howson CP1, Fineberg HV.

Institute of Medicine
National Academy of Sciences
Washington, DC 20418

Abstract

In August 1991, the Institute of Medicine released a report entitled Adverse Effects of Pertussis and Rubella Vaccines, which examined 18 adverse events in relation to diphtheria-tetanus-pertussis (DTP) vaccine and four adverse events in relation to the currently used rubella vaccine strain, RA 27/3. The committee spent 20 months reviewing a wide range of information sources, including case series and individual case reports, both published and unpublished, epidemiologic studies, studies in animals, and other laboratory studies. The committee found that the evidence indicates a causal relation between DTP vaccine and anaphylaxis and between the pertussis component of DTP vaccine and extended periods of inconsolable crying or screaming. The committee also reported that the evidence indicates a causal relation between the rubella vaccine and acute arthritis in adult women. The committee found the available evidence weaker but still consistent with a causal relation between DTP vaccine and two conditions--acute encephalopathy and hypotonic, hyporesponsive episodes--and between rubella vaccine and chronic arthritis in adult women. Estimated incidence rates of these adverse events following vaccination are provided, where possible. The committee found that the evidence does not indicate a causal relation between the DTP vaccine and infantile spasms, hypsarrhythmia, Reye's syndrome, and sudden infant death syndrome. The committee found insufficient evidence to indicate either the presence or absence of a causal relation between DTP vaccine and chronic neurologic damage, aseptic meningitis, erythema multiforme or other rash, Guillain-Barré syndrome, hemolytic anemia, juvenile diabetes, learning disabilities and attention-deficit disorder, peripheral mononeuropathy, or thrombocytopenia, and between rubella vaccine and radiculoneuritis and other neuropathies or thrombocytopenic purpura. The committee's evaluative methods are briefly described and a summary of research needs is provided.

<http://www.ncbi.nlm.nih.gov/pubmed/1727962>

“The committee found that the evidence indicates a causal relation between DTP vaccine and anaphylaxis and between the pertussis component of DTP vaccine and extended periods of inconsolable crying or screaming.

The committee also reported that the evidence indicates a causal relation between the rubella vaccine and acute arthritis in adult women.

The committee found the available evidence weaker but still consistent with a causal relation between DTP vaccine and two conditions—acute encephalopathy and hypotonic, hyporesponsive episodes—and between rubella vaccine and chronic arthritis in adult women.”

NTP Toxicology and Carcinogenesis Studies of Polysorbate 80 (CAS No. 9005-65-6) in F344/N Rats and B6C3F1 Mice (Feed Studies)

Abstract

Polysorbate 80 is a nonionic surfactant used widely as an additive in foods, pharmaceutical preparations, and cosmetics as an emulsifier, dispersant, or stabilizer. Toxicity and carcinogenicity studies were conducted by administering polysorbate 80 (which met all compendial specifications) in feed to groups of F344/N rats and B6C3F1 mice of each sex for 14 days, 13 weeks, and 2 years. Genetic toxicology studies were conducted in *Salmonella typhimurium*. 14-Day Studies: Groups of five rats and five mice of each sex received diets containing 0, 3,000, 6,000, 12,500, 25,000, or 50,000 ppm polysorbate 80. All animals survived to the end of the studies. The mean body weight change of male rats that received 50,000 ppm was significantly lower than that of the controls. The mean body weight changes in all other groups of dosed rats and in all groups of dosed mice were similar to those of the respective controls. No clinical findings or changes in absolute or relative organ weights in rats or mice were related to polysorbate 80 administration. 13-Week Studies: Groups of 10 rats and 10 mice of each sex received diets containing 0, 3,100, 6,200, 12,500, 25,000, or 50,000 ppm polysorbate 80. All animals survived to the end of the studies. The final mean body weights of dosed rats and mice were similar to those of the controls. No clinical findings, changes in absolute or relative organ weights, or gross or microscopic lesions in rats or mice were related to polysorbate 80 administration. 2-Year Studies: Doses for the 2-year studies were selected based on the lack of observed compound-related effects at the dose levels used in the 13-week studies. Groups of 60 rats and 60 mice of each sex received diets containing 0, 25,000, or 50,000 ppm polysorbate 80 for up to 103 weeks. 15-Month Interim Evaluations: Interim evaluations were performed on 7 to 10 rats and mice from each dose group at 15 months. There were no significant changes in absolute or relative organ weights. Incidences of hyperplasia and inflammation of the forestomach were increased in female mice that received 50,000 ppm. No other chemical-related lesions occurred in rats or male mice evaluated at 15 months. Body Weights, Clinical Findings, and Survival in the 2-Year Studies: The mean body weights in male and female rats and male mice administered polysorbate 80 were similar to those of the controls throughout the studies. The final mean body weight of female mice receiving 50,000 ppm was 11% lower than that of the controls. No clinical findings were associated with administration of polysorbate 80. The survival of dosed male rats was lower than that of the controls (0 ppm, 29/50; 25,000 ppm, 18/50; 50,000 ppm, 18/50); the survival of dosed female rats and male and female mice was similar to that of the respective controls (female rats: 23/50, 25/50, 25/50; male mice: 33/49, 34/50, 32/50; female mice: 30/50, 28/50, 26/50). Neoplasms and Nonneoplastic Lesions in the 2-Year Studies: The incidence of adrenal medulla pheochromocytoma was marginally increased in high-dose male rats (21/50, 19/50, 29/50). The incidence of hyperplasia of the adrenal medulla was increased in low-dose male rats but not in high-dose male rats (11/50, 22/50, 12/50). No chemical-related increases in the incidences of neoplasms occurred in male or female mice. The incidences of squamous hyperplasia and inflammation of the forestomach were significantly increased in high-dose male and female mice; forestomach ulcers were significantly increased in high-dose females. Genetic Toxicology: Polysorbate 80 was not mutagenic in *Salmonella typhimurium* strains TA100, TA1535, TA1537, and TA98 with or without exogenous metabolic activation (S9). Conclusions: Under the conditions of these 2-year feed studies, there was equivocal evidence of carcinogenic activity for polysorbate 80 in male F344/N rats based on an increased incidence of pheochromocytomas of the adrenal medulla. There was no evidence of carcinogenic activity for polysorbate 80 in female F344/N rats or in male or female B6C3F1 mice given 25,000 or 50, or 50,000 ppm. Administration of polysorbate 80 was associated with inflammation and squamous hyperplasia of the forestomach in male and female mice, and with ulcers of the forestomach in female mice.

“Administration of polysorbate 80 was associated with inflammation and squamous hyperplasia of the forestomach in male and female mice, and with ulcers of the forestomach in female mice.”

Vitamin A levels
and severity of measles
New York City

Author information

Frieden TR1, Sowell AL, Henning KJ, Huff DL, Gunn RA.

Division of Field Epidemiology
Centers for Disease Control

Abstract

Recent studies show that vitamin A levels decrease during measles and that vitamin A therapy can improve measles outcome in children in the developing world. Vitamin A levels of children with measles have not been studied in developed countries. We therefore measured vitamin A levels in 89 children with measles younger than 2 years and in a reference group in New York City, NY. Vitamin A levels in children with measles ranged from 0.42 to 3.0 $\mu\text{mol/L}$; 20 (22%) were low. Children with low levels were more likely to have fever at a temperature of 40 degrees C or higher (68% vs 44%), to have fever for 7 days or more (54% vs 23%), and to be hospitalized (55% vs 30%). Children with low vitamin A levels had lower measles-specific antibody levels. No child in the reference group had a low vitamin A level. Our data show that many children younger than 2 years in New York City have low vitamin A levels when ill with measles, and that such children seem to have lower measles-specific antibody levels and increased morbidity. Clinicians may wish to consider vitamin A therapy for children younger than 2 years with severe measles. Additional studies of vitamin A in measles and other infectious diseases, and in vaccine efficacy trials, should be done.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=1285727>

“Recent studies show that vitamin A levels decrease during measles and that vitamin A therapy can improve measles outcome in children in the developing world. Vitamin A levels of children with measles have not been studied in developed countries.”

[vitamin A and vaccination will be studied in Africa 20 years from now and those reports are included herein]

Chronic arthritis after rubella vaccination

Author information

Howson CP1, Katz M,
Johnston RB Jr, Fineberg HV.

Division of International Health
Institute of Medicine
Washington, D.C. 20418

Abstract

In August 1991 the Institute of Medicine released a report entitled "Adverse Effects of Pertussis and Rubella Vaccines" that examined, among other relations, the relation between immunization with the RA 27/3 rubella vaccine strain and chronic arthritis. The committee spent 20 months reviewing a wide range of information sources including case series and individual case reports published in peer-reviewed journals and reported by vaccine manufacturers; unpublished case reports from physicians, parents, and other concerned persons; epidemiological studies; and laboratory studies. There were no animal studies available. The committee found that the evidence is consistent with a causal relation between the RA 27/3 rubella vaccine strain and chronic arthritis in adult women, although the evidence is limited in scope. Proving that rubella vaccination can cause chronic arthritis will require a better understanding of pathogenetic mechanisms and additional well-designed studies. We briefly describe the committee's evaluative methods and present the evidence underlying its conclusion.

<http://www.ncbi.nlm.nih.gov/pubmed/1520764>

"The committee found
that the evidence is consistent
with a causal relation between the RA 27/3 rubella
vaccine strain and chronic arthritis in adult women ..."

“Tween 80 accelerated maturation, prolonged the oestrus cycle, and induced persistent vaginal oestrus.”

Food And Chemical Toxicology • March 1993

Delayed effects of neonatal exposure to Tween 80 on female reproductive organs in rats

Author information

Gajdová M1, Jakubovsky J, Války J.

Institute of Preventive and Clinical Medicine
Limbová, Bratislava

Abstract

Neonatal female rats were injected ip (0.1 ml/rat) with Tween 80 in 1, 5 or 10% aqueous solution on days 4-7 after birth. Treatment with Tween 80 accelerated maturation, prolonged the oestrus cycle, and induced persistent vaginal oestrus. The relative weight of the uterus and ovaries was decreased relative to the untreated controls. Squamous cell metaplasia of the epithelial lining of the uterus and cytological changes in the uterus were indicative of chronic oestrogenic stimulation. Ovaries were without corpora lutea, and had degenerative follicles.

<http://www.ncbi.nlm.nih.gov/pubmed/8473002>

Ocular contamination with BCG vaccine

A j Pollard
Department of Paediatrics

R H George
Department of Microbiology
Children's Hospital
Ladywood Middleway
Ladywood, Birmingham B16 8ET

Abstract

The complications of BCG vaccination in both the immunocompetent, with local and lymph node ulceration, and in the immunocompromised, with disseminated infection, are familiar to most paediatricians. Moreover, the risks to the doctor from needlestick injury are well known. There are probably few other risks for the vaccinator but we describe a case of ocular contamination with BCG vaccine. During attempted intradermal injection of BCG vaccine into a struggling neonate's upper arm, the syringe slipped out of the infant's skin discharging its contents into the attending doctor's eye. The doctor had received BCG vaccine in childhood. Despite lavage of the eye with water, a painful follicular conjunctivitis developed 24 hours later. There was a rapid response to topical steroids, and the inflammatory response settled completely over the subsequent week. Although it was assumed that this was a delayed-type hypersensitivity response, anti-BCG cover was given with a one month course of oral isoniazid.

Full Report:

<https://app.box.com/s/ev8bhi6vb3rofhrkavum3v3hpt2xlil9>

“During attempted
intradermal injection of BCG vaccine
into a struggling neonate's upper arm,
the syringe slipped out of the infant's skin
discharging its contents into the attending doctor's eye.”

DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis

Institute of Medicine US Committee to Study New Research on Vaccines

Editors

Kathleen R. Stratton, Cynthia J. Howe, and Richard B. Johnston, Jr.
Washington, DC

EXECUTIVE SUMMARY

An Institute of Medicine (IOM) committee recently concluded that the evidence is consistent with a causal relation between vaccination with DPT and acute encephalopathy (IOM, 1991), and the excess risk was estimated to range from 0 to 10.5 per million DPT immunizations. However, the same IOM committee also concluded that the evidence was insufficient to indicate a causal relation between DPT and permanent neurologic damage (IOM, 1991). In fact, the relation between DPT and chronic nervous system dysfunction had not been studied in a rigorous scientific manner until recently. Because the evidence has been so limited, the appearance of a single new report, a 10-year follow-up to the National Childhood Encephalopathy Study (NCES; Miller et al., 1993), prompted the U.S. Public Health Service to ask IOM to convene the Committee to Study New Research on Vaccines with the charge of studying the new data and, if warranted, reevaluating the causal relation between DPT and chronic nervous system dysfunction.

The NCES reported that the occurrence of hospitalization for serious neurologic disorders among 2- to 35-month-old children is very strongly related to the occurrence of death or nervous system dysfunction (neurologic, behavioral, educational, motor, sensory, or self-care impairment) up to age 10 years (Madge et al., 1993; Miller et al., 1993). Children who experienced the rare but serious acute neurologic disorder within 7 days after receiving DPT were no more or less likely to experience documented chronic nervous system dysfunction or to have died within 10 years of the acute disorder than children who had not received DPT within 7 days prior to the onset of the disorder. There were no special characteristics associated with the acute or chronic nervous system illnesses linked to DPT exposure.

The NCES did not investigate the possibility of a direct relation between DPT and chronic nervous system dysfunction, that is, in the absence of a

serious acute neurologic illness that occurs within 7 days after receiving DPT. The NCES provides data only on the limited case of a possible relation between DPT and chronic nervous system dysfunction in those children in whom a serious acute neurologic illness followed DPT vaccination within 7 days.

The committee posits three plausible scenarios whereby the acute neurologic illnesses that follow DPT might be related to chronic nervous system dysfunction.

1. DPT administration might cause serious acute neurologic illness and subsequent chronic dysfunction in children who otherwise might not have experienced either an acute neurologic illness or chronic dysfunction in the absence of DPT.
2. DPT might trigger (and thereby be an immediate or proximate cause) an acute neurologic illness and subsequent chronic dysfunction in children with underlying brain or metabolic abnormalities. Such children might experience acute neurologic illness and subsequent chronic dysfunction in association with some trigger other than DPT.
3. DPT might cause an acute neurologic illness in children with underlying brain or metabolic abnormalities that would themselves eventually have led to chronic dysfunction even in the absence of an acute neurologic illness.

The committee believes its conclusions take into account the fact that the data do not support any one of these scenarios over the others. Because the NCES did not (and probably could not) rule out the possibility that only children with underlying brain or metabolic abnormalities react to stimuli

such as DPT with acute neurologic illness, and no other studies establish or rule out such a possibility, the committee concludes that the evidence is insufficient to indicate whether or not DPT increases the overall risk in children of chronic nervous system dysfunction.

The National Childhood Encephalopathy Study data are consistent with the possibility that some children without underlying brain or metabolic abnormalities might experience serious acute neurologic illness within 7 days after receiving DPT and that acute neurologic illness will have chronic nervous system sequelae. The NCES data also are consistent with the possibility that some children with underlying brain or metabolic abnormalities (which foster a “triggering” by DPT of an acute neurologic illness) might go on to develop chronic nervous system dysfunction due to a DPT-triggered acute illness. Therefore, the committee concludes that the balance of evidence is consistent with a causal relation between DPT and the forms of chronic nervous system dysfunction described in the NCES in those children who experience a serious acute neurologic illness within 7 days after receiving DPT vaccine. This serious acute neurologic response to DPT is a rare event. The excess risk has been estimated to range from 0 to 10.5 per million immunizations (IOM, 1991). The evidence does not “establish” or “prove” a causal relation. The evidence remains insufficient to indicate the presence or absence of a causal relation between DPT and chronic nervous system dysfunction under any other circumstances. That is, because the NCES is the only systematic study of long-term dysfunctions after DPT, the committee can only comment on the causal relation between DPT and those long-term dysfunctions under the conditions studied by the NCES. In particular, it should be noted that the long-term dysfunctions associated with DPT followed a serious acute neurologic illness that occurred in children within 7 days after receiving DPT.

Immunosuppression after measles vaccination

Author information

Smedman L1, Joki A, da Silva AP,
Troye-Blomberg M, Aronsson B, Perlmann P.

Department of Immunology
Stockholm University, Sweden

Abstract

The influence of conventional live attenuated measles vaccine on cellular immune responsiveness was investigated in Sweden and Guinea-Bissau. Sixteen children in a residential area in Bissau and 16 living in southern Stockholm were examined before and 8-10 days after vaccination. Lymphoproliferation was measured to concanavalin A (con-A), PPD and tetanus toxoid (TT) using a whole-blood ³H-thymidine incorporation assay. Stimulation indices were significantly lower after vaccination than before, in the case of con-A ($p = 0.03$) and TT ($p = 0.01$) in the Guinean children and in the case of PPD ($p = 0.009$) and TT ($p = 0.03$) in the Swedish children. Stimulation of lymphocytes from measles-immune children with measles antigens resulted in weak lymphoproliferative responses. These observations may be relevant to the increased mortality found in children immunized with high-titre measles vaccines, as compared to controls, in recent studies. The study confirms the applicability and usefulness under field conditions of the whole blood version of the thymidine incorporation assay.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8193495>

“These observations may be relevant to the increased mortality found in children immunized with high-titre measles vaccines, as compared to controls, in recent studies.”

Journal Of Clinical Pharmacology • February 1994

Adverse drug reactions in neonates

Author information

Knight M.

Department of Pediatrics, College of Medicine
University of Florida Health Science Center, Gainesville 32610

Abstract

Adverse drug reactions (ADR) are uncommon causes of admission of neonates to the neonatal intensive care unit. The neonate, however, is potentially at significant risk for adverse drug reactions because of underdeveloped mechanisms and systems for handling drugs (the Gray Baby Syndrome with chloramphenicol as a classic example), the fact that infants in neonatal intensive care units are often critically ill with multiple organ system dysfunction, that they may be on multiple drugs, and that they may present with an adverse drug reaction as a result of exposure while still a fetus. There is also a history of misadventures in the neonatal intensive care unit and newborn nurseries due to exposure to antibacterial agents that produced systemic effects from percutaneous absorption. In this review, an overview of the mechanisms of adverse drug reactions will be presented, followed by a general review of the experience of adverse drug reactions in neonates and some specific examples of current adverse drug reactions and a suggested approach for the prevention and evaluation of adverse drug reactions in neonates.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8163712>

“The neonate, however,
is potentially at significant risk
for adverse drug reactions because
of underdeveloped mechanisms and
systems for handling drugs ...”

“Eighty-seven previously vaccinated school-aged children with measles that met the Advisory Committee on Epidemiology’s clinical case definition for measles.”

Canadian Medical Association Journal • April 1994

**Measles outbreak in 31 schools:
risk factors for vaccine failure
and evaluation of a selective revaccination strategy**

Author information

Yuan L.

Department of Preventive Medicine and Biostatistics
University of Toronto, Ontario, CA

Abstract

OBJECTIVE

To examine the risk factors for measles vaccine failure and to evaluate the effectiveness of a selective revaccination strategy during a measles outbreak.

DESIGN

Matched case-control study.

SETTING

Thirty-one schools in Mississauga, Ont.

SUBJECTS

Eighty-seven previously vaccinated school-aged children with measles that met the Advisory Committee on Epidemiology’s clinical case definition for measles. Two previously vaccinated control subjects were randomly selected for each case subject from the same homeroom class.

INTERVENTIONS

All susceptible contacts were vaccinated, and contacts who had been vaccinated before Jan. 1, 1980, were revaccinated. When two or more cases occurred in a school all children vaccinated before 1980 were revaccinated.

MAIN OUTCOME MEASURES

Risk of measles associated with age at vaccination, time since vaccination, vaccination before 1980 and revaccination.

RESULTS

Subjects vaccinated before 12 months of age were at greater risk of measles than those vaccinated later (adjusted odds ratio [OR] 7.7, 95% confidence interval [CI] 1.6 to 38.3; $p = 0.01$). Those vaccinated between 12 and 14 months of age were at no greater risk than those vaccinated at 15 months or over. Subjects vaccinated before 1980 were at greater risk than those vaccinated after 1980 (adjusted OR 14.5, 95% CI 1.5 to 135.6). Time since vaccination was not a risk factor. Revaccination was effective in reducing the risk of measles in both subjects vaccinated before 1980 and those vaccinated after 1980 (adjusted OR reduced to 0.6 [95% CI 0.1 to 5.3] and 0.3 [95% CI 0.13 to 2.6] respectively). However, only 18 cases were estimated to have been prevented by this strategy.

CONCLUSIONS

Adherence to routine measles vaccination for all eligible children is important in ensuring appropriate coverage with a single dose. The selective revaccination strategy’s high labour intensiveness and low measles prevention rate during the outbreak bring into question the effectiveness of such a strategy.

<http://www.ncbi.nlm.nih.gov/pubmed/8137189>

Adverse reactions after diphtheria-tetanus booster in 10-year-old schoolchildren in relation to the type of vaccine given for the primary vaccination

Author information

Blennow M1, Granström M, Strandell A.

1Department of Pediatrics
Sachs' Children's Hospital
Stockholm, Sweden

Abstract

This prospective open study investigated adverse reactions in 527 schoolchildren to a diphtheria-tetanus (DT) booster given within a national vaccination programme at 10 years of age. Evaluation was based on those whose immunization records showed that they had received either three doses of an adsorbed DT vaccine (n = 388) or a non-adsorbed DT-pertussis vaccine (DTP) (n = 69) for primary series vaccination. No differences in systemic reactions to the booster between the two groups were observed. Local reactions were significantly ($p < 0.001$) more common 1 day after vaccination in children who had received DT for primary series vaccination: redness, 73% compared with 23%; swelling, 56% versus 15%; and itching, 47% versus 21%. One and 2 weeks after the booster, itching was still more pronounced in the group who had received DT for primary series vaccination ($p < 0.001$ and 0.014, respectively). The study indicates that there was a real basis for the increase in spontaneous notifications of local side-effects to the school DT booster in Sweden. The most likely cause for the increase seems to be the aluminium adjuvant in the vaccine given for primary vaccination, a late and unexpected consequence of a change in the infant immunization programme.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8023551>

“This prospective open study investigated adverse reactions in 527 schoolchildren to a diphtheria-tetanus (DT) booster ... The most likely cause for the increase seems to be the aluminium adjuvant in the vaccine given for primary vaccination, a late and unexpected consequence of a change in the infant immunization programme.”

**Adverse events associated with childhood vaccines
other than pertussis and rubella.
Summary of a report from the Institute of Medicine**

Author information

Stratton KR1, Howe CJ, Johnston RB Jr.

Institute of Medicine, National Academy of Sciences
Washington, DC

Abstract

In September 1993, the Institute of Medicine released a report entitled *Adverse Events Associated With Childhood Vaccines: Evidence Bearing on Causality*. The report examined putative serious adverse consequences associated with administration of diphtheria and tetanus toxoids; measles, mumps, and measles-mumps-rubella vaccines; oral polio vaccine and inactivated polio vaccine; hepatitis B vaccines; and *Haemophilus influenzae* type b (Hib) vaccines. The committee spent 18 months reviewing all available scientific and medical data, from individual case reports (published and unpublished) to controlled clinical trials. The committee found that the evidence favored the rejection of a causal relation between diphtheria and tetanus toxoids and encephalopathy, infantile spasms, and sudden infant death syndrome, and between conjugate Hib vaccines and susceptibility to Hib disease. The committee found that the evidence favored acceptance of a causal relation between diphtheria and tetanus toxoids and Guillain-Barré syndrome and brachial neuritis, between measles vaccine and anaphylaxis, between oral polio vaccine and Guillain-Barré syndrome, and between unconjugated Hib vaccine and susceptibility to Hib disease. The committee found that the evidence established causality between diphtheria and tetanus toxoids and anaphylaxis, between measles vaccine and death from measles vaccine-strain viral infection, between measles-mumps-rubella vaccine and thrombocytopenia and anaphylaxis, between oral polio vaccine and poliomyelitis and death from polio vaccine-strain viral infection, and between hepatitis B vaccine and anaphylaxis. For five vaccine-related adverse events, there was no evidence identified. For the remaining 33 vaccine-related adverse events, the evidence was inadequate to accept or reject a causal relation.

<http://www.ncbi.nlm.nih.gov/pubmed/8182813>

“The committee found that the evidence favored acceptance of a causal relation between diphtheria and tetanus toxoids and Guillain-Barré syndrome and brachial neuritis, between measles vaccine and anaphylaxis, between oral polio vaccine and Guillain-Barré syndrome, and between unconjugated Hib vaccine and susceptibility to Hib disease.

The committee found that the evidence established causality between diphtheria and tetanus toxoids and anaphylaxis, between measles vaccine and death from measles vaccine-strain viral infection, between measles-mumps-rubella vaccine and thrombocytopenia and anaphylaxis, between oral polio vaccine and poliomyelitis and death from polio vaccine-strain viral infection, and between hepatitis B vaccine and anaphylaxis.”

“In 1993 we found 17 cases of Adverse Events Following Immunization (AEFI)
out of 1440 children between 0 and 2 years of age ...”

Przegląd Epidemiologiczny • 1994

Adverse events following immunization: AEFI in 17 children between 0 and 2 years of age

Author information

Taraszkiewicz F1, Bogus-Parafieniuk W, Oldak E, Sulik A.
Klinika Chorób Zakaznych Dzieci Akademii Medycznej w Białymstoku

Abstract

Adverse Events Following Immunization (AEFI) are disadvantageous side effects of preventive vaccination. In 1993 we found 17 cases of AEFI out of 1440 children between 0 and 2 years of age who had received BCG, diphtheria-tetanus-pertussis, measles or poliomyelitis vaccine. They were classified as reactions in 14 children (0.9%) or complications in 3 children (0.2%). Twelve adverse reactions followed DTP vaccination (0.8%), two followed BCG vaccination (0.14%), another two measles vaccination (0.14%) and one followed poliomyelitis vaccination (0.07%). Both generalized and local symptoms were present and they regressed with no further complications. Two children who had received BCG were noted to have a deeply placed abscess at the injection site remaining scar as well as axillary, submandibular and cervical lymph nodes enlargement within 6 months. In a 3 months old child, after the first injection of DTP vaccine, convulsions and consciousness disorder occurred. Transfontanel ultrasonography revealed intraventricular haemorrhage. After one year of intensive neurological care child's health state was improved. In spite of using still more and more safe vaccines none of them is the ideal one—the one with no adverse events following vaccination. Vaccination technics, distribution and storage of vaccines are to be improved which may result in decrease number of AEFI.

<http://www.ncbi.nlm.nih.gov/pubmed/7597191>

Update:
Vaccine Side Effects, Adverse Reactions, Contraindications,
and Precautions Recommendations of the
Advisory Committee on Immunization Practices (ACIP)

Summary

This report provides updated information concerning the potential adverse events associated with vaccination for hepatitis B, poliomyelitis, measles, mumps, diphtheria, tetanus, and pertussis. This information incorporates findings from a series of recent literature reviews, conducted by an expert committee at the Institute of Medicine (IOM), of all evidence regarding the possible adverse consequences of vaccines administered to children. This report contains modifications to the previously published recommendations of the Advisory Committee on Immunization Practices (ACIP) and is based on an ACIP review of the IOM findings and new research on vaccine safety. In addition, this report incorporates information contained in the "Recommendations of the Advisory Committee on Immunization Practices: Use of Vaccines and Immune Globulins in Persons with Altered Immunocompetence" (MMWR 1993;42 {No. RR-4}) and the "General Recommendations on Immunization: Recommendations of the Advisory Committee on Immunization Practices (ACIP)" (MMWR 1994;43 {No. RR-1}). Major changes to the previous recommendations are highlighted within the text, and specific information concerning the following vaccines and the possible adverse events associated with their administration are included: hepatitis B vaccine and anaphylaxis; measles vaccine and a) thrombocytopenia and b) possible risk for death resulting from anaphylaxis or disseminated disease in immunocompromised persons; diphtheria and tetanus toxoids and pertussis vaccine (DTP) and chronic encephalopathy; and tetanus-toxoid-containing vaccines and a) Guillain-Barre syndrome, b) brachial neuritis, and c) possible risk for death resulting from anaphylaxis. These modifications will be incorporated into more comprehensive ACIP recommendations for each vaccine when such statements are revised. Also included in this report are interim recommendations concerning the use of measles and mumps vaccines in:

- a. persons who are infected with human immunodeficiency virus and
- b. persons who are allergic to eggs; ACIP is still evaluating these recommendations.

Measles outbreaks in the United States, 1987 through 1990

Author information

Hutchins S1, Markowitz L, Atkinson W, Swint E, Hadler S.

National Immunization Program
Centers for Disease Control and Prevention
Atlanta, GA, USA

Abstract

BACKGROUND

During 1989 and 1990 reported measles cases in the United States increased 6- to 9-fold over the annual mean of 3000 between 1985 and 1988. To evaluate recent epidemiology we summarized measles outbreaks.

METHODS

Confirmed measles cases reported to the National Notifiable Disease Surveillance System during 1987 through 1990 were analyzed. An outbreak was defined as ≥ 5 epidemiologically linked cases.

RESULTS

There were 815 outbreaks, accounting for 94% of the 52,846 cases reported. Similar to 1985 and 1986, 3 patterns of measles transmission during outbreaks were identified: (1) predominantly among unvaccinated pre-school age children < 5 years of age (38% of outbreaks); (2) predominantly among vaccinated school age children 5 to 17 years of age (40%); and (3) predominantly among unvaccinated and vaccinated post-school age persons ≥ 18 years of age (22%). Most outbreaks were small (median, 12 cases), but very large outbreaks occurred (maximum size, 10,670). Although school age outbreaks (58%) predominated during 1987 and 1988, preschool age (40%) and post-school age (23%) outbreaks were more important during 1989 and 1990.

CONCLUSIONS

Recent epidemiology suggests that to achieve elimination of measles, ACIP recommendations must be fully implemented, including (1) routine administration of the first dose of measles vaccine from 12 to 15 months of age and (2) use of a routine two-dose schedule to prevent school age and post-school age outbreaks.

<http://www.ncbi.nlm.nih.gov/pubmed/8684873>

“There were 815 outbreaks,
accounting for 94% of the 52,846 cases reported.

3 patterns of measles transmission during
outbreaks were identified:

(1) predominantly among unvaccinated
pre-school age children (38% of outbreaks)

(2) predominantly among vaccinated
school age children 5 to 17 years of age (40%)

(3) predominantly among unvaccinated
and vaccinated post-school age persons (22%) ...”

DNA—
protein crosslinks, a biomarker of exposure to formaldehyde—
in vitro and in vivo studies

Author information

Shaham JI, Bomstein Y,
Meltzer A, Kaufman Z, Palma E, Ribak J.

Occupational Cancer Unit
Occupational Health and Rehabilitation Institute
Raanana, Israel

Abstract

Formaldehyde (FA) is a widely produced industrial chemical. Sufficient evidence exists to consider FA as an animal carcinogen. In humans the evidence is not conclusive. DNA-protein crosslinks (DPC) may be one of the early lesions in the carcinogenesis process in cells following exposures to carcinogens. It has been shown in in vitro tests that FA can form DPC. We examined the amount of DPC formation in human white blood cells exposed to FA in vitro and in white blood cells taken from 12 workers exposed to FA and eight controls. We found a significant difference ($P = 0.03$) in the amount of DPC among exposed (mean \pm SD 28 \pm 5%, minimum 21%, maximum 38%) than among the unexposed controls (mean \pm SD 22 \pm 6%, minimum 16%, maximum 32%). Of the 12 exposed workers, four (33%) showed crosslink values above the upper range of controls. We also found a linear relationship between years of exposure and the amount of DPC. We conclude that our data indicate a possible mechanism of FA carcinogenicity in humans and that DPC can be used as a method for biological monitoring of exposure to FA.

Full Report

<http://carcin.oxfordjournals.org/content/17/1/121.long>

“We conclude that our data indicate a possible
mechanism of Formaldehyde carcinogenicity in humans ...”

Adverse events associated with MMR vaccines in Japan

Author information

Kimura M1, Kuno-Sakai H, Yamazaki S,
Yamada A, Hishiyama M, Kamiya H, Ueda K,
Murase T, Hirayama M, Oya A, Nozaki S, Murata R.

School of Medicine
Tokai University, Isehara, Japan

Abstract

The largest nationwide active surveillance of four Measles-Mumps-Rubella (MMR) vaccines was conducted in Japan. A total of 1255 pediatricians actively participated in the study, which comprised 8.6% of all members of the Japanese Pediatric Society. The total number of registered recipients of MMR vaccines was 38 203. They were arbitrarily given one of the MMR vaccines produced by three makers (Takeda, Osaka city, Kitasato Minato-ku, Tokyo and Biken Suita city, Japan) or the standard MMR vaccine made of designated strains (Kitasato's measles-AIK-C, Biken's mumps-Urabe Am9 and Takeda's rubella-To336) produced by Takeda, Kitasato and Biken and were observed for 35 days. The rates of virologically confirmed aseptic meningitis per 10,000 recipients were 16.6, 11.6, 3.2 and 0 for the standard MMR, Takeda MMR, Kitasato MMR and Biken MMR vaccines, respectively. The incidence of convulsions between 15 and 35 days was the highest with the standard MMR vaccine and the incidence of fever associated with vomiting occurring between 15 and 35 days (symptoms relevant to aseptic meningitis) were also the highest with the standard MMR vaccine. The incidence of parotid swelling was the lowest with Takeda MMR vaccine. This surveillance revealed that incidences of aseptic meningitis after administration of the standard MMR vaccine and of Biken MMR vaccine were different. This posed questions about the manufacturing consistency of the Urabe Am9 mumps virus vaccines. On the other hand, the National Institute of Health found that the biological characteristics of the Urabe Am9 mumps virus contained in the standard MMR vaccine and in the Biken MMR vaccine were different. The Biken Company reported that the mumps vaccine in the standard MMR vaccine was a mixture of two Urabe Am9 mumps vaccine bulks; one identical to that contained in the Biken MMR vaccine and the other produced by a different manufacturing process.

<http://www.ncbi.nlm.nih.gov/pubmed/8741307>

“The incidence of convulsions between 15 and 35 days was the highest with the standard MMR vaccine and the incidence of fever associated with vomiting occurring between 15 and 35 days (symptoms relevant to aseptic meningitis) were also the highest with the standard MMR vaccine. The incidence of parotid swelling was the lowest with Takeda MMR vaccine. This surveillance revealed that incidences of aseptic meningitis after administration of the standard MMR vaccine and of Biken MMR vaccine were different. This posed questions about the manufacturing consistency of the Urabe Am9 mumps virus vaccines.”

Measles and atopy in Guinea-Bissau

Author information

Shaheen SO1, Aaby P, Hall AJ, Barker DJ, Heyes CB, Shiell AW, Goudiaby A.

1Medical Research Council Environmental Epidemiology Unit
University of Southampton, Southampton General Hospital, UK

Abstract

BACKGROUND

Epidemiological studies have led to speculation that infections in early childhood may prevent allergic sensitisation but evidence to support this hypothesis is lacking. We investigated whether measles infection protects against the development of atopy in children of Guinea-Bissau, West Africa.

METHODS

We conducted a historical cohort study in Bandim, a semi-rural district of Bissau, the capital of Guinea-Bissau. 395 young adults, first surveyed in 1978-80 aged 0-6 years, were followed up in 1994. Our analyses were restricted to 262 individuals still living in Bandim for whom a measles history, documented in childhood, was judged to be reliable. We defined atopy as skin-prick test positivity ($>$ or $=$ 3 mm weal) to one or more of seven allergens.

FINDINGS

17 (12.8 percent) of 133 participants who had had measles infection were atopic compared with 33 (25.6 percent) of 129 of those who had been vaccinated and not had measles (odds ratio, adjusted for potential confounding variables 0.36 [95 percent CI 0.17-0.78], $p=0.01$). Participants who had been breastfed for more than a year were less likely to have a positive skin test to housedust mite. After adjustment for breast-feeding and other variables, measles infection was associated with a large reduction in the risk of skin-prick test positivity to housedust mite (odds ratio for *Dermatophagoides pteronyssinus* 0.20 [0.05-0.81], $p=0.02$; *D farinae* 0.20 [0.06-0.71], $p=0.01$).

INTERPRETATION

Measles infection may prevent the development of atopy in African children.

<http://www.ncbi.nlm.nih.gov/pubmed/8667923>

“Measles infection may prevent

the development of atopy [allergies] in African children.”

[as Dr. Buttram stated, challenge viruses like measles and chicken pox strengthen the child’s immune system]

“Triton X-100 efficiently induces the apoptotic cell death ...”

Yonsei Medical Journal • February 1997

Triton X-100 induces apoptosis in human hepatoma cell lines

Author information

Ahn JM1, Kim SJ, Kim H, Park C, Kim WH, Park JH.

Department of Microbiology
Yonsei University College of Medicine
Seoul, Korea

Abstract

The detergent Triton X-100 was used to establish a model for apoptosis in hepatoma cell lines. The electrophoresis of DNA extracted from 0.01% Triton X-100 treated hepatoma cell lines showed DNA ladder formation, a hallmark of apoptosis. The DNA fragmentation appeared within less than 60 min of the Triton X-100 treatment. Chromatin condensation and apoptotic bodies were observed by hematoxylin and eosin (H & E) stain, and fragmented nucleosome was detected by terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling (TUNEL) test. Apoptosis was semi-quantitated by measuring the lactate dehydrogenase (LDH) level for cytotoxicity. It was found that apoptosis had been induced in more than 90% of the cells treated with Triton X-100 for 150 min. These data show that Triton X-100 efficiently induces the apoptotic cell death in hepatoma cell lines.

<http://www.ncbi.nlm.nih.gov/pubmed/9100483>

Is infant immunization a risk factor for childhood asthma or allergy?

Author information

Kemp T1, Pearce N, Fitzharris P, Crane J, Fergusson D, St George I, Wickens K, Beasley R.

1Department of Medicine
Wellington School of Medicine
New Zealand

Abstract

The Christchurch Health and Development Study comprises 1,265 children born in 1977. The 23 children who received no diphtheria/pertussis/tetanus (DPT) and polio immunizations had no recorded asthma episodes or consultations for asthma or other allergic illness before age 10 years; in the immunized children, 23.1% had asthma episodes, 22.5% asthma consultations, and 30.0% consultations for other allergic illness. Similar differences were observed at ages 5 and 16 years. These findings do not appear to be due to differential use of health services (although this possibility cannot be excluded) or confounding by ethnicity, socioeconomic status, parental atopy, or parental smoking.

<http://www.ncbi.nlm.nih.gov/pubmed/9345669>

“The 23 children who received no diphtheria/pertussis/tetanus (DPT) and polio immunizations had no recorded asthma episodes or consultations for asthma or other allergic illness before age 10 years; in the immunized children, 23.1% had asthma episodes, 22.5% asthma consultations, and 30.0% consultations for other allergic illness. Similar differences were observed at ages 5 and 16 years.”

Measles and atopy in Guinea-Bissau

Author information

Shaheen SO1, Aaby P, Hall AJ,
Barker DJ, Heyes CB, Shiell AW, Goudiaby A.

Medical Research Council Environmental Epidemiology Unit
University of Southampton, Southampton General Hospital, UK

Abstract

BACKGROUND

Epidemiological studies have led to speculation that infections in early childhood may prevent allergic sensitisation but evidence to support this hypothesis is lacking. We investigated whether measles infection protects against the development of atopy in children of Guinea-Bissau, West Africa.

METHODS

We conducted a historical cohort study in Bandim, a semi-rural district of Bissau, the capital of Guinea-Bissau. 395 young adults, first surveyed in 1978-80 aged 0-6 years, were followed up in 1994. Our analyses were restricted to 262 individuals still living in Bandim for whom a measles history, documented in childhood, was judged to be reliable. We defined atopy as skin-prick test positivity (≥ 3 mm weal) to one or more of seven allergens.

FINDINGS

17 (12.8 percent) of 133 participants who had had measles infection were atopic compared with 33 (25.6 percent) of 129 of those who had been vaccinated and not had measles (odds ratio, adjusted for potential confounding variables 0.36 [95 percent CI 0.17-0.78], $p=0.01$). Participants who had been breastfed for more than a year were less likely to have a positive skin test to housedust mite. After adjustment for breastfeeding and other variables, measles infection was associated with a large reduction in the risk of skin-prick test positivity to housedust mite (odds ratio for *Dermatophagoides pteronyssinus* 0.20 [0.05-0.81], $p=0.02$; *D farinae* 0.20 [0.06-0.71], $p=0.01$).

INTERPRETATION

Measles infection may prevent the development of atopy in African children.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=8667923>

“Measles infection may prevent the development of atopy [allergies] in African children.”

Lancet • June 1997

**Gulf War syndrome:
is it due to a systemic shift
in cytokine balance towards a Th2 profile**

Author information

Rook GA1, Zumla A.

Department of Bacteriology
University College London Medical School, UK

Abstract

The symptoms of Gulf War syndrome are compatible with the hypothesis that the immune system of affected individuals is biased towards a Th2-cytokine pattern. Factors that could lead to a Th2 shift among Gulf War veterans include exposure to multiple Th2-inducing vaccinations under stressful circumstances and the way in which such vaccinations were administered, which would be expected to maximise Th2 immunogenicity. These factors may have led to a long-term systemic shift towards a Th2-cytokine balance and to mood changes related to the immunoendocrine state. Other vaccines that lead to similar long-term, non-specific shifts in cytokine balance are well-established. If our hypothesis is proven, treatment may be possible with regimens that induce a systemic Th1 bias.

<http://www.ncbi.nlm.nih.gov/pubmed/9269228>

“The symptoms of Gulf War syndrome are compatible with the hypothesis that the immune system of affected individuals is biased towards a Th2-cytokine pattern. Factors that could lead to a Th2 shift among Gulf War veterans include exposure to multiple Th2-inducing vaccinations under stressful circumstances and the way in which such vaccinations were administered, which would be expected to maximise Th2 immunogenicity.”

“Although the use of adjuvants in veterinary vaccines enhances the immunogenicity of vaccines, they have been responsible for a number of side effects.”

Seminars In Veterinary Medicine And Surgery (Small Animal) • August 1997

Vaccine adjuvants

Author information

Macy DW.

Department of Clinical Sciences
Colorado State University
College of Veterinary Medicine and Biomedical Sciences
Fort Collins 80523, USA

Abstract

Vaccine adjuvants provide enhanced immune responses to a variety of antigens. Unlike human vaccines that are limited to aluminum-based adjuvants, veterinary vaccines may contain a large number of substances either alone or in combination that act as vaccine adjuvants. Although the use of adjuvants in veterinary vaccines enhances the immunogenicity of vaccines, they have been responsible for a number of side effects. This article explores the rationale of currently used vaccine adjuvants and some of the adverse events associated with their use in veterinary medicine.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9283246>

Incidence of apnoea and bradycardia in preterm infants following DTPw and Hib immunization: a prospective study

Author information

Botham SJ1, Isaacs D, Henderson-Smart DJ.

Abstract

OBJECTIVE

To evaluate the incidence and severity of apnoea and bradycardia in hospitalized preterm infants following immunization at 2 months of age, and identify risk factors.

METHODOLOGY

A prospective study of 98 preterm infants, of gestational age 24-31 weeks, immunized at approximately 2 months post natal age with diphtheria-tetanus-whole cell pertussis vaccine (DTPw) in the neonatal intensive care unit (NICU) at King George V Hospital Sydney. Half the infants also received Haemophilus influenzae type b conjugate vaccine (Hib) simultaneously. All infants were monitored for apnoea and bradycardia in the 24 h periods pre- and post immunization.

RESULTS

Only one infant had apnoea and/or bradycardia pre-immunization compared with 17 post immunization. For 12 infants these events were brief, self-limiting and not associated with desaturations (oxygen saturation < 90%). However, for five infants (30%) these events were associated with oxygen desaturation and two of these infants required supplemental oxygen. The group that had apnoea and/or bradycardia and the group that did not were not significantly different in terms of gestational age, birth weight and other variables. Infants who received Hib together with DTPw were less likely to have apnoea and/or bradycardia than those given DTPw alone.

CONCLUSION

When considering immunization for preterm infants, the benefits of early immunization must be balanced against the risk of apnoea and bradycardia. We recommend that the cardio-respiratory function of hospitalized infants born at less than 31 weeks gestation be monitored for 48 h post immunization.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9401886>

“Only one infant had apnoea and/or bradycardia pre-immunization compared with 17 post immunization. For 12 infants these events were brief, self-limiting and not associated with desaturations (oxygen saturation < 90%). However, for five infants (30%) these events were associated with oxygen desaturation and two of these infants required supplemental oxygen.”

Is infant immunization a risk factor for childhood asthma or allergy?

Author information

Kemp T1, Pearce N, Fitzharris P, Crane J, Fergusson D, St George I, Wickens K, Beasley R.

Department of Medicine
Wellington School of Medicine
New Zealand

Abstract

The Christchurch Health and Development Study comprises 1,265 children born in 1977. The 23 children who received no diphtheria/pertussis/tetanus (DPT) and polio immunizations had no recorded asthma episodes or consultations for asthma or other allergic illness before age 10 years; in the immunized children, 23.1% had asthma episodes, 22.5% asthma consultations, and 30.0% consultations for other allergic illness. Similar differences were observed at ages 5 and 16 years. These findings do not appear to be due to differential use of health services (although this possibility cannot be excluded) or con-founding by ethnicity, socioeconomic status, parental atopy, or parental smoking.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9345669>

“The 23 children who received no diphtheria/pertussis/tetanus (DPT) and polio immunizations had no recorded asthma episodes or consultations for asthma or other allergic illness before age 10 years; in the immunized children, 23.1% had asthma episodes, 22.5% asthma consultations, and 30.0% consultations for other allergic illness.”

Variability in Immune Response to Pathogens: Using Measles Vaccine to Probe Immunogenetic Determinants of Response

Gregory A. Poland

Mayo Vaccine Research Group
Clinical Pharmacology Unit
Mayo Clinic and Foundation
Rochester, MN

Abstract

“The measles had not prevailed on the Faroes since 1781; they broke out early in April, 1846. Of the 7,782 inhabitants, about 6,000 were taken with measles) 225 persons in all died. Of the many old people still living on the Faroes who had had the measles in 1781, not one was attacked the second time.”

Quote from P. L. Panum in the report titled
“Observations Made during the Epidemic of Measles
on the Faroe Islands in the Year 1846”

The Faroe Islands measles outbreak described above is of interest to geneticists in several regards: Why did some people survive and some die? Why was the case fatality rate so high? Why was the protective effect of prior exposure so high? Understanding the genetic influences on the phenotypes of protective and nonprotective antibody responses provides a unique window to understand the variability in host response to pathogens.

Vaccine Response as a Marker of Disease Susceptibility

Postimmunization antibody response can be used as a marker of disease susceptibility. For example, the level of antibody response after hepatitis B immunization predicts susceptibility to disease on exposure (Ellis 1993). In studies of measles, postimmunization measles antibody in the “low positive” range did not protect against clinical measles when subjects were exposed to the wild measles virus, whereas high levels were protective (Chen et al. 1990). Furthermore, nonresponders to a single dose of measles vaccine who demonstrated an antibody response only after a second immunization were still six times more likely than were responders to a single dose of measles vaccine to develop measles on exposure to wild virus (Mathias et al. 1989). Others examined “poor responders,” who were reimmunized and developed poor or low-level antibody responses only to lose detectable antibody and develop measles on exposure 2–5 years later. They concluded that there is a strong correlation between low antibody levels after a single dose of vaccine and high susceptibility to infection with exposure (Deseda-Tous et al. 1978).

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1376909/pdf/9463343.pdf>

Vaccine

Non-Responders

And

Low Responders

“... nonresponders to a single dose of measles vaccine who demonstrated an antibody response only after a second immunization were still six times more likely than were responders to a single dose of measles vaccine to develop measles on exposure to wild virus (Mathias et al. 1989). Others examined “poor responders,” who were reimmunized and developed poor or low-level antibody responses only to lose detectable antibody and develop measles on exposure 2–5 years later. They concluded that there is a strong correlation between low antibody levels after a single dose of vaccine and high susceptibility to infection with exposure.”
(Deseda-Tous et al. 1978)

Acute Encephalopathy
Followed by Permanent Brain Injury or Death
Associated With Further Attenuated Measles Vaccines:
A Review of Claims Submitted to the
National Vaccine Injury Compensation Program

by Robert E. Weibel, Vito Caserta, David E. Benor, Geoffrey Evans

Abstract

Objective

To determine if there is evidence for a causal relationship between acute encephalopathy followed by permanent brain injury or death associated with the administration of further attenuated measles vaccines (Attenuvax or Lirugen, Hoechst Marion Roussel, Kansas City, MO), mumps vaccine (Mumpsvax, Merck and Co, Inc, West Point, PA), or rubella vaccines (Meruvax or Meruvax II, Merck and Co, Inc, West Point, PA), combined measles and rubella vaccine (M-R-Vax or M-R-Vax II, Merck and Co, Inc, West Point, PA), or combined measles, mumps, and rubella vaccine (M-M-R or M-M-R II, Merck and Co, Inc, West Point, PA), the lead author reviewed claims submitted to the National Vaccine Injury Compensation Program.

Methods

The medical records of children who met the inclusion criteria of receiving the first dose of these vaccines between 1970 and 1993 and who developed such an encephalopathy with no determined cause within 15 days were identified and analyzed.

Results

A total of 48 children, ages 10 to 49 months, met the inclusion criteria after receiving measles vaccine, alone or in combination. Eight children died, and the remainder had mental regression and retardation, chronic seizures, motor and sensory deficits, and movement disorders. The onset of neurologic signs or symptoms occurred with a nonrandom, statistically significant distribution of cases on days 8 and 9. No cases were identified after the administration of monovalent mumps or rubella vaccine.

Conclusions

This clustering suggests that a causal relationship between measles vaccine and encephalopathy may exist as a rare complication of measles immunization.

<http://www.ncbi.nlm.nih.gov/pubmed/9481001>

“A total of 48 children, ages 10 to 49 months, met the inclusion criteria after receiving measles vaccine, alone or in combination. Eight children died, and the remainder had mental regression and retardation, chronic seizures, motor and sensory deficits, and movement disorders. This clustering suggests that a causal relationship between measles vaccine and encephalopathy may exist as a rare complication of measles immunization.”

Detection of cytogenetic effects
in peripheral lymphocytes
of students exposed to formaldehyde
with cytokinesis-blocked micronucleus assay

Author information

He JL1, Jin LF, Jin HY.

School of Public Health
Zhejiang Medical University
Hangzhou, China

Abstract

Cytokinesis-blocked micronucleus assay was applied as a biological dosimeter to detect abnormalities in human peripheral lymphocytes of thirteen students exposed to formaldehyde (FA) during a 12-week (10 h per week) anatomy class. Breathing-zone air samples collected during dissection procedures showed a mean concentration of 2.37 ppm (3.17 mg/m³). Ten students from the same school but without FA exposure served as controls. Chromosome aberrations (CA) and sister chromatid exchanges (SCE) were detected in both groups. The micronuclei (MN) rate (6.38 +/- 2.50 /1000) and CA rate (5.92 +/- 2.40%) in the FA-exposed group showed a significant increase ($P < 0.01$) when compared with those of the controls (3.15 +/- 1.46 /1000 and 3.40 +/- 1.57% respectively). A correlation between MN and CA in individuals was observed. SCE in the exposed group were also increased ($P < 0.05$), but not so greatly as MN or CA. The results indicated that FA might damage the chromosomes of human lymphocytes.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9559107>

“The results indicated that FA might damage the chromosomes of human lymphocytes.”

“The reader will notice an emerging clear picture that the majority (if not all) of these advances have been achieved from studies funded by independent or charity organizations rather than by the responsible authorities who are supposed and are duty bound to take on this task.”

Adverse Drug Reactions And Toxicological Reviews • March 1998

**Gulf War syndrome—
a model for the complexity of biological and environmental
interaction with human health**

Author information

Jamal GA.

University Department of Neurology
Southern General Hospital NHS Trust, Glasgow

Abstract

Since the end of the Gulf War, tens of thousands of American, Canadian and British soldiers who participated in that war have claimed to be suffering from a variety of incapacitating symptoms which are generally termed as Gulf War Syndrome (GWS). The symptoms are multiple but mainly consist of excessive tiredness, muscle and joint pain, loss of balance, sensory symptoms, neurobehavioural manifestations, diarrhoea, bladder dysfunction, sweating disturbances, and respiratory, gastrointestinal, musculoskeletal and skin manifestations. These veterans have been exposed to a variety of damaging or potentially damaging risk factors including environmental adversities, pesticides such as organophosphate chemicals, skin insect repellents, medical agents such as pyridostigmine bromide (NAPS), possible low-levels of chemical warfare agents, multiple vaccinations in combinations, depleted uranium, and other factors. A large number of basic research findings, clinical epidemiological studies, and case control studies are reviewed to try and link them together to produce a coherent picture and to demonstrate the complexity of the interaction of biological systems, environmental and genetic factors, combinations of drugs and toxins with human health. The findings of these studies so far have demonstrated that many of the previous assumptions made about the ‘safety’ of certain drugs and toxic substances or vaccines must be radically reviewed. Many of the findings have far reaching implications not only in terms of explanation of what might have gone wrong during the Gulf War, but also have wider implications for many occupational groups who are exposed daily to some of these risk factors. More open-mindedness and much less prejudice are required concerning the basic biology of interactions of the above factors and their effects on cell functions and wider intelligent research is urgently required with high priority. This review highlights the importance of intelligent research for answers for a new phenomenon, and demonstrates the necessity for a combination of this approach with high quality epidemiological research. The reader will notice an emerging clear picture that the majority (if not all) of these advances have been achieved from studies funded by independent or charity organizations rather than by the responsible authorities who are supposed and are duty bound to take on this task.

<http://www.ncbi.nlm.nih.gov/pubmed/9638279>

Identification of rat susceptibility loci for adjuvant-oil-induced arthritis

Author information

Lorentzen JC1, Glaser A, Jacobsson L, Galli J,
Fakhrai-rad H, Klareskog L, Luthman H.

Department of Medicine, Rheumatology Unit
CMM L8:04, Karolinska Hospital, S-171 76 Stockholm, Sweden
johnny.lorentzen@cmm.ki.se

Abstract

One intradermal injection of incomplete Freund's adjuvant-oil induces a T cell-mediated inflammatory joint disease in DA rats. Susceptibility genes for oil-induced arthritis (OIA) are located both within and outside the major histocompatibility complex (MHC, Oia1). We have searched for disease-linked non-MHC loci in an F2 intercross between DA rats and MHC-identical but arthritis-resistant LEW.1AV1 rats. A genome-wide scan with microsatellite markers revealed two major chromosome regions that control disease incidence and severity: Oia2 on chromosome 4 ($P = 4 \times 10^{-13}$) and Oia3 on chromosome 10 ($P = 1 \times 10^{-6}$). All animals homozygous for DA alleles at both loci developed severe arthritis, whereas all those homozygous for LEW.1AV1 alleles were resistant. These results have general implications for situations where nonspecific activation of the immune system (e.g., incomplete Freund's adjuvant-oil) causes inflammation and disease, either alone or in conjunction with specific antigens. They may also provide clues to the etiology of inflammatory diseases in humans, including rheumatoid arthritis.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC27729/>

“These results have general implications for situations where nonspecific activation of the immune system (e.g., incomplete Freund's adjuvant-oil) causes inflammation and disease, either alone or in conjunction with specific antigens. They may also provide clues to the etiology of inflammatory diseases in humans, including rheumatoid arthritis.”

**Neurologic complications
associated with oral poliovirus vaccine
and genomic variability of the vaccine strains
after multiplication in humans**

Author information

Friedrich F.

Departamento de Virologia
Instituto Oswaldo Cruz/FIOCRUZ
Rio de Janeiro, RJ, Brazil

Abstract

The oral poliovirus vaccine (OPV) has been effectively used in the reduction and control of poliomyelitis cases on the planet. Despite several advantages of using the attenuated OPV strains, the rare occurrence of vaccine-associated paralytic poliomyelitis (VAPP) cases in vaccine recipients and their susceptible contacts is a disadvantage. Molecular biology studies of polioviruses isolated from stool and central nervous system (CNS) of patients with VAPP have confirmed the vaccine origin of the isolates and demonstrated genomic modifications known or suspected to increase the neurovirulence. Similar genomic modifications have also been identified in OPV-derived strains isolated from healthy vaccinees and healthy contacts, suggesting that host factors are also involved in the establishment of poliomyelitis. Other neurologic complications such as meningitis, encephalitis, convulsions, transverse myelitis and Guillain-Barré syndrome have also been rarely associated with the use of this vaccine. The characterization of polioviruses isolated from such cases has demonstrated their OPV origin.

<http://www.ncbi.nlm.nih.gov/pubmed/9842449>

“Molecular biology studies of polioviruses isolated from stool and central nervous system (CNS) of patients with VAPP have confirmed the vaccine origin of the isolates and demonstrated genomic modifications known or suspected to increase the neurovirulence. Similar genomic modifications have also been identified in OPV-derived strains isolated from healthy vaccinees and healthy contacts, suggesting that host factors are also involved in the establishment of poliomyelitis. Other neurologic complications such as meningitis, encephalitis, convulsions, transverse myelitis and Guillain-Barré syndrome have also been rarely associated with the use of this vaccine.”

Macrophagic myofasciitis: an emerging entity

Groupe d'Etudes et Recherche sur les Maladies Musculaires Acquisées et Dysimmunitaires (GERMMAD)
de l'Association Française contre les Myopathies (AFM)

Author information

Gherardi RK1, Coquet M, Chérin P, Authier FJ,
Laforêt P, Bélec L, Figarella-Branger D, Mussini JM, Pellissier JF, Fardeau M.

Université Paris XII-Val de Marne
Département de Pathologie, Hôpital Henri Mondor
Créteil, France
gherardi@univ-paris12.fr

Abstract

BACKGROUND

An unusual inflammatory myopathy characterised by an infiltration of non-epithelioid histiocytic cells has been recorded with increasing frequency in the past 5 years in France. We reassessed some of these cases.

METHODS

We did a retrospective analysis of 18 such cases seen in five myopathology centres between May, 1993, and December, 1997. The myopathological changes were reassessed at a clinopathology seminar.

FINDINGS

Detailed clinical information was available for 14 patients. The main presumptive diagnoses were polymyositis and polymyalgia rheumatica. Symptoms included myalgias in 12 patients, arthralgias in nine, muscle weakness in six, pronounced asthenia in five, and fever in four. Abnormal laboratory findings were occasionally observed, and included raised creatine kinase concentrations, increased erythrocyte sedimentation rate, and myopathic electromyography. Muscle biopsy showed infiltration of the subcutaneous tissue, epimysium, perimysium, and perifascicular endomysium by sheets of large macrophages, with a finely granular PAS-positive content. Also present were occasional CD8 T cells, and inconspicuous muscle-fibre damage. Epithelioid and giant cells, necrosis, and mitotic figures were not seen. The images were easily distinguishable from sarcoid myopathy and fasciitis-panniculitis syndromes. Whipple's disease, Mycobacterium avium intracellulare infection, and malakoplakia could not be confirmed. Ten patients were treated with various combinations of steroids and antibiotics; symptoms improved in eight patients, and stabilised in two.

INTERPRETATION

A new inflammatory muscle disorder of unknown cause, characterized by a distinctive pathological pattern of macrophagic myofasciitis, is emerging in France.

“A new inflammatory muscle disorder of unknown cause, characterised by a distinctive pathological pattern of macrophagic myofasciitis, is emerging in France.”

Serological association of measles virus and human herpesvirus-6 with brain autoantibodies in autism

Author information

Singh VK1, Lin SX, Yang VC.
College of Pharmacy
University of Michigan
Ann Arbor, Michigan, 48109-1065, USA

Abstract

Considering an autoimmunity and autism connection, brain autoantibodies to myelin basic protein (anti-MBP) and neuron-axon filament protein (anti-NAFP) have been found in autistic children. In this current study, we examined associations between virus serology and autoantibody by simultaneous analysis of measles virus antibody (measles-IgG), human herpesvirus-6 antibody (HHV-6-IgG), anti-MBP, and anti-NAFP. We found that measles-IgG and HHV-6-IgG titers were moderately higher in autistic children but they did not significantly differ from normal controls. Moreover, we found that a vast majority of virus serology-positive autistic sera was also positive for brain autoantibody: (i) 90% of measles-IgG-positive autistic sera was also positive for anti-MBP; (ii) 73% of measles-IgG-positive autistic sera was also positive for anti-NAFP; (iii) 84% of HHV-6-IgG-positive autistic sera was also positive for anti-MBP; and (iv) 72% of HHV-6-IgG-positive autistic sera was also positive for anti-NAFP. This study is the first to report an association between virus serology and brain autoantibody in autism; it supports the hypothesis that a virus-induced autoimmune response may play a causal role in autism.

<http://www.ncbi.nlm.nih.gov/pubmed/9756729>

“This study is the first to report an association between virus serology and brain autoantibody in autism; it supports the hypothesis that a virus-induced autoimmune response may play a causal role in autism.”

Report of a US public health service workshop on hypotonic-hypo-responsive episode (HHE) after pertussis immunization

Author information

Braun MM1, Terracciano G, Salive ME, Blumberg DA, Vermeer-de Bondt PE, Heijbel H, Evans G, Patriarca PA, Ellenberg SS.

Center for Biologics Evaluation and Research, Food and Drug Administration
Rockville, MD 20852, USA

Abstract

Hypotonic-hypo-responsive episode (HHE) is a term used to describe a somewhat heterogeneous group of clinical disorders that have been reported primarily in association with whole-cell pertussis vaccination. A 1991 review by the Institute of Medicine determined that the evidence available was indeed consistent with a causal relation between whole-cell pertussis-diphtheria-tetanus immunization and HHE, but that the evidence was insufficient to indicate a causal relationship between HHE and the subsequent development of permanent neurologic damage. More recent data from clinical trials conducted in Europe suggest that HHE also occurs after vaccination with acellular pertussis vaccines. The US Food and Drug Administration, in collaboration with the US Public Health Service, sponsored a workshop on HHE in Rockville, Maryland, on June 19, 1997. The primary goals of the workshop were to develop a case definition of HHE and to evaluate the general design and feasibility of possible studies of HHE using the federal Vaccine Adverse Event Reporting System (VAERS), a national passive surveillance system. The goals of such studies would be to understand better the acute HHE event and to evaluate the possibility of long-term sequelae. Case Definition. There has been no generally accepted definition of HHE, and a standard definition would be useful for vaccine safety work and would potentially facilitate interstudy comparisons of the growing number of licensed vaccines containing acellular pertussis components. The workshop defined HHE as an event of sudden onset occurring within 48 hours of immunization, with duration of the episode ranging from 1 minute to 48 hours, in children younger than 10 years of age. All of the following must be present: 1) limpness or hypotonia, 2) reduced responsiveness or hypo-responsiveness, and 3) pallor or cyanosis or failure to observe or to recall skin coloration. HHE is not considered to have occurred if there is a known cause for

these signs (eg, postictal), if urticaria is present during the event, if normal skin coloration is observed throughout the episode, or if the child is simply sleeping. This inclusive (sensitive) case definition will allow investigators, through the technique of stratification according to certain characteristics (eg, time from vaccination to onset of HHE), to attempt to hone the definition and make it more specific. Refinement of the definition of HHE has been hindered by the lack of information on its pathophysiology and by the lack of pathognomonic signs, symptoms, and diagnostic tests. Another hindrance is that by the time the child presents for medical evaluation, the signs of HHE often have normalized. Moreover, different mechanisms may be involved in different individuals whose events meet this workshop's HHE definition. Probably the most important question about HHE is whether it has any permanent sequelae. The workshop assessed the possible contribution VAERS-based studies could make to answering this question and found substantial methodologic problems; however, ongoing studies in Sweden and The Netherlands have the potential to provide useful information on this question. The most useful contribution of VAERS data would be in a descriptive study of HHE, with a possible case-control study of factors that may affect the risk of HHE after vaccination, rather than a study of possible permanent sequelae. The workshop participants felt that a detailed descriptive study of approximately 100 HHE events reported during a 1- to 2-year period could provide a more in-depth description of HHE cases in greater numbers than has been published previously, but the study would not address the issue of long-term sequelae of HHE. Better descriptive data may lead to new hypotheses concerning risk factors, etiology, and pathophysiology of HHE that might be evaluated further by studying subsequent cases and controls from VAERS or from other sources.

Toxicity of formaldehyde to human oral fibroblasts and epithelial cells: influences of culture conditions and role of thiol status

Author information

Nilsson JA1, Zheng X, Sundqvist K, Liu Y,
Atzori L, Elfving A, Arvidson K, Grafström RC.

Division of Experimental Carcinogenesis
Institute of Environmental Medicine
Karolinska Institutet, Stockholm, Sweden

Abstract

The toxicity of formaldehyde, a monomer released from certain polymeric dental materials, was studied in cultured human oral fibroblasts and epithelial cells. The influences of growth conditions were evaluated for both cell types, as well as the role of the internal and external thiol states. A one-hour exposure to formaldehyde decreased the colony-forming efficiency (CFE) of both cell types in a concentration-dependent manner, although the toxicity varied up to 100-fold with the conditions. Clearly, the presence of serum and the thiol cysteine counteracted the toxicity in fibroblasts. Similarly, pituitary extract and cysteine, or a mixture of amino acids and ethanolamines, counteracted the formaldehyde toxicity in serum-free cultures of epithelial cells. In contrast, a growth-promoting surface matrix of fibronectin and collagen did not influence the formaldehyde toxicity, as shown by both the CFE assay and a dye reduction assay. Further, a short-term change to the various growth media per se with or without the supplements serum or cysteine did not significantly alter the CFE. Analysis of the thiol state demonstrated significant differences between epithelial cells and fibroblasts, i.e., comparatively lower cellular levels of the free low-molecular-weight thiols glutathione and cysteine in fibroblasts. This result correlated to significantly higher formaldehyde toxicity in the fibroblasts than in the epithelial cells. Taken together, the results indicated the cytoprotective function of both intracellular and extracellular thiols toward formaldehyde, as well as the usefulness of thiol-free and chemically defined conditions for toxicity assessments in oral epithelial cells and fibroblasts. We conclude that the combined use of a controlled external milieu and the presumed target cell type may be advantageous in evaluations of oral toxicity mechanisms or the toxic potency of dental materials, particularly those which, like formaldehyde, may react with thiols or amines.

“A one-hour exposure to formaldehyde decreased the colony-forming efficiency of both cell types in a concentration-dependent manner, although the toxicity varied up to 100-fold with the conditions.”

Identification of arthritogenic adjuvants of self and foreign origin

Author information

Lorentzen JC.

Department of Medicine, Karolinska Hospital
Karolinska Institute, Stockholm, Sweden

Abstract

The lack of defined triggers for human inflammatory joint diseases warrants efforts to identify candidate molecules. For this task, it may be an important lead that nonspecific activation of the immune system can precipitate arthritis in rats. Consequently, arthritis-prone rat strains were used to search for disease-triggering factors among molecules which initially induce innate defence reactions rather than specific immune responses. A variety of immunological adjuvants were investigated by intradermal injection into DA and LEW.1AV1 rats and monitoring of clinical signs for 30 days. Several arthritogenic cell-wall structures from yeast and bacteria were identified, such as beta-glucan, lipopolysaccharide and trehalosedimycolate. The test procedures also revealed arthritogens of chemical origin, such as dioctadecyldiammoniumbromide (DDA = C₃₈H₈₀NBr) and heptadecane (C₁₇H₃₆). Furthermore, it allowed the precise definition of arthritogenic determinants of lipids, since C₁₆H₃₄ induced arthritis, whereas the closely related linear hydrocarbons C₁₆H₃₂, C₁₆H₃₃Br and C₁₅H₃₂ did not. The observed pathogenicity of organic lipids raised the question of whether endogenous lipids can also precipitate arthritis. Indeed, this was true for the cholesterol precursor squalene (C₃₀H₅₀). In conclusion, this article describes the rational use of arthritis-prone rat strains to identify arthritogenic factors of both foreign and self origin. Although structurally unrelated, the pathogenic molecules defined here share the feature of being nonspecific triggers of the immune system. This consolidates a general principle for the induction of adjuvant arthritis which may provide clues to the aetiology of human arthritides, including rheumatoid arthritis.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10023856>

“The observed pathogenicity
of organic lipids raised the question of whether
endogenous lipids can also precipitate arthritis.
Indeed, this was true for the
cholesterol precursor squalene ...”

Archives Of Toxicology • February 1999

Effects of 2-phenoxyethanol on N-methyl-D-aspartate (NMDA) receptor-mediated ion currents

Author information

Musshoff U1, Madeja M, Binding N, Witting U, Speckmann EJ.

Institut für Physiologie
Universität Münster, Germany
mushoff@uni-muenster.de

Abstract

The actions were examined of 17 frequently used glycol ether compounds on the glutamate receptor-mediated ion currents. The receptors were expressed in *Xenopus* oocytes by injection of rat brain mRNA. Most of the 17 glycol ethers exerted no effects on the glutamate sub-receptors activated by kainate and N-methyl-D-aspartate (NMDA), whereas 2-phenoxyethanol (ethylene glycol monophenyl ether) caused a considerable reduction of NMDA-induced membrane currents in a reversible and concentration-dependent manner. The threshold concentration of the ethylene glycol monophenyl ether effect was < 10 $\mu\text{mol/l}$. The concentration for a 50% inhibition (IC_{50}) was approximately 360 $\mu\text{mol/l}$. The results indicate a neurotoxic potential for 2-phenoxyethanol.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10207615>

“The results indicate
a neurotoxic potential for 2-phenoxyethanol.”
[2-phenoxyethanol is a vaccine ingredient]

Epidemiology • May 1999

Hepatitis B vaccine and liver problems in U.S. children less than 6 years old 1993 and 1994

Author information

Fisher MA1, Eklund SA.

Department of Epidemiology
University of Michigan
Ann Arbor 48109, USA

Abstract

Data to assess the benefits and risks of hepatitis B vaccine for the general population of U.S. children are sparse. This study addressed the problem of external validity found in previous studies of high risk populations by evaluating the benefit of hepatitis B vaccination for the general population of American children. We calculated the risk of liver problems among hepatitis B vaccinated and non-hepatitis B vaccinated children using logistic regression. Hepatitis B vaccinated children had an unadjusted odds ratio of 2.94 and age-adjusted odds ratio of 2.35 for liver problems compared with non-hepatitis B vaccinated children in the 1993 National Health Interview Survey. Hepatitis B vaccinated children had an unadjusted odds ratio of 2.57 and age-adjusted odds ratio of 1.53 for liver problems compared with non-hepatitis B vaccinated children in the 1994 National Health Interview Survey dataset.

<http://www.ncbi.nlm.nih.gov/pubmed/10230847>

“Hepatitis B vaccinated children had an unadjusted odds ratio of 2.94 and age-adjusted odds ratio of 2.35 for liver problems compared with non-hepatitis B vaccinated children in the 1993 National Health Interview Survey.”

Vaccine • July 1999

**An overview
of the vaccine adverse event reporting system
(VAERS)
as a surveillance system
VAERS Working Group**

Author information

Singleton JA1, Lloyd JC, Mootrey GT, Salive ME, Chen RT.

Vaccine Safety and Development Activity
National Immunization Program
Centers for Disease Control and Prevention
Atlanta, GA 30333, USA

Abstract

We evaluated the Vaccine Adverse Event Reporting System (VAERS), the spontaneous reporting system for vaccine-associated adverse events in the United States, as a public health surveillance system, using evaluation guidelines from the Centers for Disease Control and Prevention. We found that VAERS is simple for reporters to use, flexible by design and its data are available in a timely fashion. The predictive value positive for one severe event is known to be high, but for most events is unknown. The acceptability, sensitivity and representativeness of VAERS are unknown. The study of vaccine safety is complicated by underreporting, erroneous reporting, frequent multiple exposures and multiple outcomes.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10438063>

“The acceptability, sensitivity and representativeness of VAERS are unknown. The study of vaccine safety is complicated by underreporting, erroneous reporting, frequent multiple exposures and multiple outcomes.”

“... A non specific permeabilization of the Blood Brain Barrier ...”

Pharmaceutical Research • December 1999

**Indirect evidence
that drug brain targeting using polysorbate 80-coated
polybutylcyanoacrylate nanoparticles is related to toxicity**

Author information

Olivier JC1, Fenart L, Chauvet R, Pariat C, Cecchelli R, Couet W.

Laboratoire de Pharmacie Galénique et Biopharmacie UPRES EA 1223 34, Poitiers, France
jc.olivier@campus.univ-poitiers.fr

Abstract

PURPOSE

To investigate the mechanism underlying the entry of the analgesic peptide dalargin into brain using biodegradable polybutylcyanoacrylate (PBCA) nanoparticles (NP) overcoated with polysorbate 80.

METHODS

The investigations were carried out with PBCA NP and with non biodegradable polystyrene (PS) NP (200 nm diameter). Dalargin adsorption was assessed by HPLC. Its entry into the CNS in mice was evaluated using the tail-flick procedure. Locomotor activity measurements were performed to compare NP toxicities. BBB permeabilization by PBCA NP was studied in vitro using a coculture of bovine brain capillary endothelial cells and rat astrocytes.

RESULTS

Dalargin loading was 11.7 microg/mg on PBCA NP and 16.5 microg/ mg on PS NP. Adding polysorbate 80 to NP led to a complete desorption. Nevertheless, dalargin associated with PBCA NP and polysorbate 80 induced a potent and prolonged analgesia, which could not be obtained using PS NP in place of PBCA NP. Locomotor activity dramatically decreased in mice dosed with PBCA NP, but not with PS NP. PBCA NP also caused occasional mortality. In vitro, PBCA NP (10 microg/ml) induced a permeabilization of the BBB model.

CONCLUSIONS

A non specific permeabilization of the BBB, probably related to the toxicity of the carrier, may account for the CNS penetration of dalargin associated with PBCA NP and polysorbate 80.

<http://www.ncbi.nlm.nih.gov/pubmed/10644071>

Gait disturbance
interpreted as cerebellar ataxia
after MMR vaccination at 15 months of age:
a follow-up study

Author information

Plesner AM1, Hansen FJ, Taudorf K,
Nielsen LH, Larsen CB, Pedersen E.

Department of Epidemiology
Statens Serum Institute
Copenhagen, Denmark

Abstract

Measles, mumps and rubella (MMR) vaccination was included in the Danish childhood vaccination programme in 1987. During the following 10-y period, 550 notification records of adverse events after MMR vaccination at 15 mo of age have been registered, and a total of 41 notifications have included "gait disturbance". This corresponds to a frequency of 8 per 100,000 doses of MMR vaccine used for 15-mo-old children. The symptoms and signs are characteristic of cerebellar ataxia. In 28 notifications, the descriptions by the doctors included only "gait disturbance", while in 13 an additional interpretation was included. Thirty-two parents (78%) filled in a questionnaire and 26 (63%) agreed to participate in a clinical follow-up study. The gait disturbance symptoms mainly occurred 7-14 d after the vaccination, and the duration was median 1-2 wk (range 1 d to more than 4 mo). One-third of the children had symptoms lasting more than 2 wk. Significantly more children with long duration of symptoms had some kind of complaint or clinical signs at the follow-up in 1997. Gait disturbance registered after MMR vaccination seems to be more frequent than hitherto reported. Most cases are mild and short-lasting and a longer duration of symptoms seems to be predictive of late sequelae. A clinical diagnosis of cerebellar ataxia after MMR and the exact frequency of this adverse event remains to be tested in prospective studies.

<http://www.ncbi.nlm.nih.gov/pubmed/10677059>

"Gait disturbance registered after MMR vaccination seems to be more frequent than hitherto reported. Most cases are mild and short-lasting and a longer duration of symptoms seems to be predictive of late sequelae."

**Immune-mediated pathology
following hepatitis B vaccination.
Two cases of polyarteritis nodosa and
one case of pityriasis rosea-like drug eruption**

Author information

De Keyser F1, Naeyaert JM, Hindryckx P, Elewaut D,
Verplancke P, Peene I, Praet M, Veys E.

Department of Rheumatology
University Hospital Gent, Belgium
Filip.Dekeyser@rug.ac.be

Abstract

The association of hepatitis B virus infection and vasculitis or other immune-mediated manifestations is well documented. Reports on such manifestations in relation to hepatitis B vaccination are scarce, however. We report 2 patients who developed polyarteritis nodosa following vaccination against hepatitis B. In one patient this resulted in an ischemic and necrotic digital ulcer, necessitating surgical amputation. The other patient presented with typical cutaneous polyarteritis nodosa which responded well to corticosteroid treatment. A third patient developed a severe pityriasis rosea-like eruption. He was treated with topical steroids with healing of the lesions, leaving only post-inflammatory hyperpigmentation. The literature on these associations is reviewed.

<http://www.ncbi.nlm.nih.gov/pubmed/10728450>

“We report 2 patients who developed polyarteritis nodosa following vaccination against hepatitis B. In one patient this resulted in an ischemic and necrotic digital ulcer, necessitating surgical amputation. The other patient presented with typical cutaneous polyarteritis nodosa which responded well to corticosteroid treatment. A third patient developed a severe pityriasis rosea-like eruption. He was treated with topical steroids with healing of the lesions, leaving only post-inflammatory hyperpigmentation.”

Vaccination and autoimmunity- 'vaccinosis': a dangerous liaison?

Author information

Shoenfeld Y1, Aron-Maor A.

Department of Internal Medicine B,
Sheba Medical Center, Tel Hashomer, Israel
shoefel@post.tau.ac.il

Abstract

The question of a connection between vaccination and autoimmune illness (or phenomena) is surrounded by controversy. A heated debate is going on regarding the causality between vaccines, such as measles and anti-hepatitis B virus (HBV), and multiple sclerosis (MS). Brain antibodies as well as clinical symptoms have been found in patients vaccinated against those diseases. Other autoimmune illnesses have been associated with vaccinations. Tetanus toxoid, influenza vaccines, polio vaccine, and others, have been related to phenomena ranging from autoantibodies production to full-blown illness (such as rheumatoid arthritis (RA)). Conflicting data exists regarding also the connection between autism and vaccination with measles vaccine. So far only one controlled study of an experimental animal model has been published, in which the possible causal relation between vaccines and autoimmune findings has been examined: in healthy puppies immunized with a variety of commonly given vaccines, a variety of autoantibodies have been documented but no frank autoimmune illness was recorded. The findings could also represent a polyclonal activation (adjuvant reaction). The mechanism (or mechanisms) of autoimmune reactions following immunization has not yet been elucidated. One of the possibilities is molecular mimicry; when a structural similarity exists between some viral antigen (or other component of the vaccine) and a self-antigen. This similarity may be the trigger to the autoimmune reaction. Other possible mechanisms are discussed. Even though the data regarding the relation between vaccination and autoimmune disease is conflicting, it seems that some autoimmune phenomena are clearly related to immunization (e.g. Guillain-Barre syndrome). The issue of the risk of vaccination remains a philosophical one, since to date the advantages of this policy have not been refuted, while the risk for autoimmune disease has not been irrevocably proved. We discuss the pros and cons of this issue (although the temporal relationship (i.e. always 2-3 months following immunization) is impressive).

<http://www.ncbi.nlm.nih.gov/pubmed/10648110>

“Even though the data regarding the relation between vaccination and autoimmune disease is conflicting, it seems that some autoimmune phenomena are clearly related to immunization (e.g. Guillain-Barre syndrome).”

Effects of diphtheria-tetanus-pertussis or tetanus vaccination on allergies and allergy-related respiratory symptoms among children and adolescents in the United States

Author information

Hurwitz EL1, Morgenstern H.

Abstract

BACKGROUND

Findings from animal and human studies confirm that diphtheria and tetanus toxoids and pertussis (DTP) and tetanus vaccinations induce allergic responses; associations between childhood vaccinations and subsequent allergies have been reported recently.

OBJECTIVE

The association of DTP or tetanus vaccination with allergies and allergy-related respiratory symptoms among children and adolescents in the United States was assessed.

METHODS

Data were used from the Third National Health and Nutrition Examination Survey on infants aged 2 months through adolescents aged 16 years. DTP or tetanus vaccination, lifetime allergy history, and allergy symptoms in the past 12 months were based on parental or guardian recall. Logistic regression modeling was performed to estimate the effects of DTP or tetanus vaccination on each allergy.

RESULTS

The odds of having a history of asthma was twice as great among vaccinated subjects than among unvaccinated subjects (adjusted odds ratio, 2.00; 95% confidence interval, 0.59 to 6.74). The odds of having had any allergy-related respiratory symptom in the past 12 months was 63% greater among vaccinated subjects than unvaccinated subjects (adjusted odds ratio, 1.63; 95% confidence interval, 1.05 to 2.54). The associations between vaccination and subsequent allergies and symptoms were greatest among children aged 5 through 10 years.

CONCLUSIONS

DTP or tetanus vaccination appears to increase the risk of allergies and related respiratory symptoms in children and adolescents. Although it is unlikely that these results are entirely because of any sources of bias, the small number of unvaccinated subjects and the study design limit our ability to make firm causal inferences about the true magnitude of effect.

“DTP or tetanus vaccination
appears to increase the risk of allergies
and related respiratory symptoms
in children and adolescents.”

Outbreak of aseptic meningitis
associated with mass vaccination
with a urabe-containing measles-mumps-rubella vaccine:
implications for immunization programs

Author information

Dourado II, Cunha S, Teixeira MG,
Farrington CP, Melo A, Lucena R, Barreto ML.

Instituto de Saúde Coletiva
Universidade Federal da Bahia
Salvador, Brazil

Abstract

A mass immunization campaign with a Urabe-containing measles-mumps-rubella vaccine was carried out in 1997 in the city of Salvador, northeastern Brazil, with a target population of children aged 1-11 years. There was an outbreak of aseptic meningitis following the mass campaign. Cases of aseptic meningitis were ascertained through data collected from the records of children admitted to the local referral hospital for infectious diseases between March and October of 1997, using previously defined eligibility criteria. Vaccination histories were obtained through home visits or telephone calls. Eighty-seven cases fulfilled the study criteria. Of those, 58 cases were diagnosed after the vaccination campaign. An elevated risk of aseptic meningitis was observed 3 weeks after Brazil's national vaccination day compared with the risk in the prevaccination period (relative risk = 14.3; 95% confidence interval: 7.9, 25.7). This result was confirmed by a case series analysis (relative risk = 30.4; 95% confidence interval: 11.5, 80.8). The estimated risk of aseptic meningitis was 1 in 14,000 doses. This study confirms a link between measles-mumps-rubella vaccination and aseptic meningitis. The authors discuss the implications of this for the organization and planning of mass immunization campaigns.

<http://www.ncbi.nlm.nih.gov/pubmed/10707922>

Full Report: <http://aje.oxfordjournals.org/content/151/5/524.long>

“An elevated risk of aseptic meningitis was observed 3 weeks after Brazil's national vaccination day compared with the risk in the prevaccination period (relative risk = 14.3; 95% confidence interval: 7.9, 25.7). This result was confirmed by a case series analysis (relative risk = 30.4; 95% confidence interval: 11.5, 80.8). The estimated risk of aseptic meningitis was 1 in 14,000 doses. This study confirms a link between measles-mumps-rubella vaccination and aseptic meningitis.”

Gender differences in the reactogenicity of measles-mumps-rubella vaccine

Author information

Shohat T1, Green MS, Nakar O, Ballin A,
Duvdevani P, Cohen A, Shohat M.

Israel Center for Disease Control
Gertner Institute for Policy Research
Tel-Hashomer, Israel
shohat@trendline.co.il

Abstract

BACKGROUND

In trials comparing different formulations of measles vaccine, excess non-specific mortality occurred in female children who received high titer vaccine. These findings suggest a gender-specific effect of measles vaccine.

OBJECTIVES

To determine whether gender differences exist in the rates of adverse reactions and morbidity in the month following immunization with measles-containing vaccine, and to evaluate whether there is a gender-specific association between the humoral immune response to measles vaccination and post-vaccination morbidity.

METHODS

Parents completed questionnaires on the health status of 755 infants aged 15-20 months, during the month preceding and the month following the measles-mumps-rubella vaccination. Blood samples were tested for measles antibody titers in a subsample of 237 infants.

RESULTS

After controlling background morbidity in the infants, the relative risk of fever and rash following vaccination was 2.35 in females and 1.36 in males. The geometric mean antibody titers against measles were similar in both sexes and there was no significant association between antibody titer and post-vaccination morbidity in either sex.

CONCLUSIONS

Our findings demonstrate higher rates of adverse effects in females following vaccination with MMR vaccine, irrespective of the humoral response. This study emphasizes the need to consider possible gender differences when evaluating new vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=10774264>

Full Report: <http://www.ima.org.il/FilesUpload/IMAJ/0/61/30887.pdf>

“Our findings demonstrate higher rates of adverse effects in females following vaccination with MMR vaccine, irrespective of the humoral response. This study emphasizes the need to consider possible gender differences when evaluating new vaccines.”

Detection and sequencing of measles virus from peripheral mononuclear cells from patients with inflammatory bowel disease and autism

Author information

Kawashima H1, Mori T, Kashiwagi Y,
Takekuma K, Hoshika A, Wakefield A.

Department of Paediatrics
Tokyo Medical University, Japan

Abstract

It has been reported that measles virus may be present in the intestine of patients with Crohn's disease. Additionally, a new syndrome has been reported in children with autism who exhibited developmental regression and gastrointestinal symptoms (autistic enterocolitis), in some cases soon after MMR vaccine. It is not known whether the virus, if confirmed to be present in these patients, derives from either wild strains or vaccine strains. In order to characterize the strains that may be present, we have carried out the detection of measles genomic RNA in peripheral mononuclear cells (PBMC) in eight patients with Crohn's disease, three patients with ulcerative colitis, and nine children with autistic enterocolitis. As controls, we examined healthy children and patients with SSPE, SLE, HIV-1 (a total of eight cases). RNA was purified from PBMC by Ficoll-paque, followed by reverse transcription using AMV; cDNAs were subjected to nested PCR for detection of specific regions of the hemagglutinin (H) and fusion (F) gene regions. Positive samples were sequenced directly, in nucleotides 8393-8676 (H region) or 5325-5465 (from noncoding F to coding F region). One of eight patients with Crohn disease, one of three patients with ulcerative colitis, and three of nine children with autism, were positive. Controls were all negative. The sequences obtained from the patients with Crohn's disease shared the characteristics with wild-strain virus. The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with being vaccine strains. The results were concordant with the exposure history of the patients. Persistence of measles virus was confirmed in PBMC in some patients with chronic intestinal inflammation.

<http://www.ncbi.nlm.nih.gov/pubmed/10759242>

“The sequences obtained from the patients with ulcerative colitis and children with autism were consistent with being vaccine strains. The results were concordant with the exposure history of the patients. Persistence of measles virus was confirmed in PBMC in some patients with chronic intestinal inflammation.”

Role of vaccinations as risk factors for ill health in veterans of the Gulf war: cross sectional study

Author information

Hotopf M1, David A, Hull L, Ismail K, Unwin C, Wessely S.
Gulf War Research Unit
King's College and St Thomas's School of Medicine
King's College London, London SE5 8AZ
m.hotopf@iop.kcl.ac.uk

Abstract

OBJECTIVES

To explore the relation between ill health after the Gulf war and vaccines received before or during the conflict. To test the hypothesis that such ill health is limited to military personnel who received multiple vaccines during deployment and that pesticide use modifies any effect.

DESIGN

Cross sectional study of Gulf war veterans followed for six to eight years after deployment.

SETTING

UK armed forces.

PARTICIPANTS

Military personnel who served in the Gulf and who still had their vaccine records.

MAIN OUTCOME MEASURES

Multisymptom illness as classified by the Centers for Disease Control and Prevention; fatigue; psychological distress; post-traumatic stress reaction; health perception; and physical functioning.

RESULTS

The response rate for the original survey was 70.4% (n=3284). Of these, 28% (923) had vaccine records. Receipt of multiple vaccines before deployment was associated with only one of the six health outcomes (post-traumatic stress reaction). By contrast five of the six outcomes (all but post-traumatic stress reaction) were associated with multiple vaccines received during deployment. The strongest association was for the multisymptom illness (odds ratio 5.0; 95% confidence interval 2.5 to 9.8).

CONCLUSION

Among veterans of the Gulf war there is a specific relation between multiple vaccinations given during deployment and later ill health. Multiple vaccinations in themselves do not seem to be harmful but combined with the "stress" of deployment they may be associated with adverse health outcomes. These results imply that every effort should be made to maintain routine vaccines during peacetime.

“Among veterans of the Gulf war there is a specific relation between multiple vaccinations given during deployment and later ill health.”

The Endogenous Adjuvant Squalene Can Induce a Chronic T-Cell-Mediated Arthritis in Rats

Barbro C. Carlson,* Åsa M. Jansson,*
Anders Larsson,† Anders Bucht,‡* and Johnny C. Lorentzen*

From the Department of Medicine,*
Unit of Rheumatology, Karolinska Institutet, Stockholm
the Department of Medical Sciences,†
University Hospital, Uppsala
and the Department of Biomedicine,‡
Division of NBC Defense, Defense Research Establishment
Umeå, Sweden

Abstract

Squalene is a cholesterol precursor, which stimulates the immune system nonspecifically. We demonstrate that one intradermal injection of this adjuvant lipid can induce joint-specific inflammation in arthritis-prone DA rats. Histopathological and immunohistochemical analyses revealed erosion of bone and cartilage, and that development of polyarthritis coincided with infiltration of CD4⁺ T cells. Depletion of these cells with anti-CD4⁺ TcR monoclonal antibody (R73) resulted in complete recovery, whereas anti-CD8 and anti-CD4⁺ TcR injections were ineffective. The apparent dependence on CD4⁺ T cells suggested a role for genes within the major histocompatibility complex (MHC), and this was concluded from comparative studies of MHC congenic rat strains, in which DA.1H rats were less susceptible than DA rats. Furthermore, LEW.1AV1 and PVG.1AV1 rats with MHC identical to DA rats were arthritis-resistant, demonstrating that non-MHC genes also determine susceptibility. Some of these genetic influences could be linked to previously described arthritis susceptibility loci in an F2 intercross between DA and LEW.1AV1 rats (ie, Cia3, Oia2 and Cia5). Interestingly, some F2 hybrid rats developed chronic arthritis, a phenotype not apparent in the parental inbred strains. Our demonstration that an autoadjuvant can trigger chronic, immune-mediated joint-specific inflammation may give clues to the pathogenesis of rheumatoid arthritis, and it raises new questions concerning the role of endogenous molecules with adjuvant properties in chronic inflammatory diseases.

In conclusion, arthritis induced with the cholesterol precursor squalene shares notable similarities with rheumatoid arthritis, and raises interesting questions concerning the role of endogenous molecules with adjuvant properties in chronic inflammatory diseases.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1850095/>

“arthritis induced with the cholesterol precursor squalene shares notable similarities with rheumatoid arthritis, and raises interesting questions concerning the role of endogenous molecules with adjuvant properties in chronic inflammatory diseases.”

Aluminum And Health

Recommendations

Aluminum is an environmentally abundant element to which we are all exposed. The neurotoxicity of this metal has been known for more than a century. More recently, it has been implicated as an etiological factor in some pathologies (including encephalopathy, bone disease, anemia) related to dialysis treatment. In addition, it has been hypothesized to be a cofactor in the etiopathogenesis of some neurodegenerative diseases, including Alzheimer's disease (AD), although, despite many studies in several laboratories in different countries, direct evidence is still, so far controversial. Thus, examples of aluminum neurotoxicity are well recognized in experimental animals and in individuals with renal failure (consequent upon aging, intoxication or renal disease) - and there are grounds to link neurodegenerative disorders to aluminum exposure. Furthermore, an increased concentration of Al in infant formulas and in solutions for home parenteral nutrition has been associated with neurological consequences and metabolic bone disease, characterized by low-bone formation rate, respectively.

For all these reasons and on the basis of our many years of scientific experience in this field, we propose the following recommendations as guidelines to avoid risks due to aluminum accumulation and potential intoxication. These recommendations are not rigid and will be updated when relevant new scientific data is available.

General Recommendations

1. It would be valuable to define as completely as possible which patient groups are at risk for iatrogenic aluminum loading, and under which conditions aluminum represents a health hazard. The more complete knowledge we have for the clinical, iatrogenic setting, the better basis we will have to judge whether different types of aluminum exposure are hazardous to the general population or to susceptible subgroups.

2. A provisional list of patients groups at risk of iatrogenic aluminum loading should include, at least, people with impaired renal function,

infants, old people and patients on total home parenteral nutrition. Where such exposure occurs, serum aluminum concentrations should be less than 30 $\mu\text{g/l}$ and possibly lower. However, further studies are necessary.

3. Urinary aluminum is also an indicator of aluminum absorption, the excreted Al/retained Al ratio depends on the integrity of the renal function.

4. Al may enter human body by mouth, intravenous infusions and by environment. Specific controls have to be adopted in order to reduce each risk of exposure.

Oral Exposure

5. Aluminum in drinking water should be less than 50 $\mu\text{g L}^{-1}$. Silicon is relevant to aluminum toxicity and, therefore, the water silicon concentrations should be monitored in parallel.

6. The aluminum content should be declared in all food preparations and pharmacological products.

7. Citrate-containing compounds appear to increase the bioavailability of ingested aluminum. Therefore, particular care should be taken to avoid these compounds in combination with Al-containing drugs. With citric acid, the enhanced gastrointestinal absorption may be compensated for by a parallel increase in urinary Al excretion, where there is good renal function. However, it is strongly suspected from recent simulation studies that other dietary acids (e.g., succinic and tartaric acids) also increase Al-bioavailability but do not cause any compensatory increase in urinary excretion. Ascorbate and lactate also significantly enhance gastrointestinal absorption of Al, as was recently demonstrated in animal studies.

8. It is recommended that acidic food, e.g., acid cabbage, tomato, etc. should not be cooked or stored in aluminum ware. In this connection, it has been demonstrated that in the juice of acidic cabbage, cooked in aluminum, the metal ion content is up to 20 mg/L.

9. Individual susceptibility to aluminum has been reported by the scientific literature. Thus, special efforts should be taken to prevent contamination of food and beverages etc. with aluminum either directly or during preparation, with special regard to infants, old people or individuals with suboptimal renal functionality.

10. Magnesium depletion is considered a high risk for aluminum accumulation especially during pregnancy and in the neonate with possible consequent problems for normal development and growth. Magnesium depletion is also common with aging.

11. Iron depletion is considered a high risk for aluminium accumulation, as iron and Al share common carriers.

Parenteral Exposure

12. Aluminum in all intravenous (i.v.) fluids should be controlled monitored and labeled. There is a general consensus that the aluminum content of i.v. fluids used in children and adults with renal failure or undergoing dialysis, should be as low as possible and in any case no higher than 10 $\mu\text{g/L}$.

13. The use of parenteral nutrition fluids that are high in aluminum should be eliminated or significantly reduced.

This document will be published in relevant scientific journals, and will be sent to all Health Ministers of the European Community as well as to other Public Health Authorities. (FDA, WHO etc.). For further information, please contact Prof. P. Zatta: zatta@civ.bio.unipd.it

Routine vaccinations and child survival: follow up study in Guinea-Bissau, West Africa

Ines Kristensen, physician,^a Peter Aaby, anthropologist,^a and
Henrik Jensen, statistician^b

^aBandim Health Project, Apartado 861, Bissau
Guinea-Bissau, ^bDanish Epidemiology Science Centre
Statens Serum Institut, Copenhagen, Denmark

Contributors: IK supervised the last year of data
collection and wrote the first draft of the paper.
HJ supervised data control and carried out the statistical anal-
yses. PA initiated the study, supervised data collection, carried
out the first analyses, and wrote the final version of the paper.
HJ and PA will act as guarantors.

Abstract

Objective

To examine the association between routine childhood
vaccinations and survival among infants in Guinea-Bissau.

Design

Follow up study.

Participants

15 351 women and their children born during 1990 and 1996.

Setting

Rural Guinea-Bissau.

Main Outcome Measures

Infant mortality over six months (between age 0-6
months and 7-13 months for BCG, diphtheria, tetanus,
and pertussis, and polio vaccines and between 7-13
months and 14-20 months for measles vaccine).

Results

Mortality was lower in the group vaccinated with any vac-
cine compared with those not vaccinated, the mortality
ratio being 0.74 (95% confidence interval 0.53 to 1.03).
After cluster, age, and other vaccines were adjusted for,
BCG was associated with significantly lower mortality
(0.55 (0.36 to 0.85)). However, recipients of one dose of
diphtheria, tetanus, and pertussis or polio vaccines had
higher mortality than children who had received none of
these vaccines (1.84 (1.10 to 3.10) for diphtheria, teta-
nus, and pertussis). Recipients of measles vaccine had a
mortality ratio of 0.48 (0.27 to 0.87). When deaths from
measles were excluded from the analysis the mortality
ratio was 0.51 (0.28 to 0.95). Estimates were unchanged
by controls for background factors.

Conclusions

These trends are unlikely to be explained exclusively by
selection biases since different vaccines were associated
with opposite tendencies. Measles and BCG vaccines
may have beneficial effects in addition to protection
against measles and tuberculosis. Diphtheria, tetanus,
and pertussis and polio vaccines were associated with
higher infant mortality.

Full Report:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC27544/>

“Diphtheria, tetanus, and pertussis
and polio vaccines were associated
with higher infant mortality.”

“... in rats, the pertussis component of DTPoP
acts on the cardiovascular system and disturbs its circadian rhythm.”

Laboratory Animals • 2000

Disturbance of cardiovascular circadian rhythms by pertussis vaccine in freely-moving rats

W. Vleeming, A. van de Kuil, J. D. te Biesebeek,
J. W. van der Laan, D. J. de Wildt & J. G. C. van Amsterdam

National Institute of Public Health and the Environment
Laboratory of Health Effects Research
PO Box 1, NL 3720 BA Bilthoven, The Netherlands

Summary

Vaccination of young children with diphtheria, tetanus, poliomyelitis and pertussis (DTPoP) vaccine is effective in preventing outbreaks of whooping cough but adverse events sometimes occur. This pilot study shows that in freely-moving rats, multiple treatment with DTPoP (at day 0 and day 5, 6 ml/kg i.v.) increased heart rate (HR) for 5 days after the first treatment and decreased diastolic blood pressure (DBP) for at least 26 days after the first treatment and inhibited the circadian rhythm of HR and DBP for at least 10 days. DTPo vaccine, containing no pertussis vaccine, was free of such effects. Thus, in rats, the pertussis component of DTPoP acts on the cardiovascular system and disturbs its circadian rhythm. The contribution of these findings to clinical adverse effects is as yet unknown and needs further research.

<http://lan.sagepub.com/content/34/4/399.long>

Feline vaccine-associated fibrosarcoma: an ultrastructural study of 20 tumors 1996-1999

Author information

Madewell BR1, Griffey SM, McEntee MC, Leppert VJ, Munn RJ.

Department of Surgical and Radiological Sciences, School of Veterinary Medicine
University of California, Davis 95616 USA
brmadewell@ucdavis.edu

Abstract

Twenty feline vaccine-associated sarcomas were examined by transmission electron microscopy. Tumors contained pleomorphic spindle cells, histiocytoid cells, and giant cells. Most tumors contained myofibroblasts, which had morphologic features similar to those of fibroblasts. These cells were further distinguished by subplasmalemmal dense plaques and thin cytoplasmic actin myofilaments organized as elongated bundles concentrated at irregular intervals forming characteristic dense bodies. Intracellular crystalline particulate material was found in 5 of the 20 tumors. Energy dispersive X-ray spectroscopy was used to identify the crystalline material within one tumor as aluminum-based. One tumor from a feline leukemia virus-infected cat contained budding and immature retroviral particles.

In one of the first reports of feline vaccine-associated sarcomas, dense crystalline material was recognized by electron microscopy within macrophages surrounding tumor cells.⁹ Subsequent electron-probe microanalytical studies demonstrated aluminum in the cytoplasm of the macrophages within these sarcomas, suggesting the role of aluminum-containing adjuvant as irritant in the pathogenesis of vaccine-associated sarcomas.⁹ The role of vaccine adjuvant in the etiopathogenesis of these tumors remains unclear. The most prevalent adjuvants used in licensed veterinary vaccines are aluminum salts and oil emulsions; all of these formulations are considered to act as depots for injected vaccines.¹ Aluminum hydroxide adjuvants are used in many human and veterinary vaccines, presumably because of their safety and low cost. Aluminum has been detected at the site of subcutaneous injections for up to 1 year in animals.³ That the tissues collected in this study represented tumors that developed months to years after vaccination when the precise site of vaccination was unknown and that most tumors were several centimeters in diameter or greater at the time of excision suggest that a large amount of aluminum, indeed, was contained within these adjuvanted vaccines to allow its detection in randomly selected ultrathin (60–90 nm thick) tissue sections examined in the electron microscope.

The results of this study support previous morphologic observations of feline vaccine-associated sarcomas. The role of the myofibroblast in vaccine-associated sarcomas is unclear but perhaps reflects a continuum of the inflammatory response that characterizes, in part, these unique neoplasms. The role of adjuvant, similarly, in these tumors is unknown.

Full Report: <http://vet.sagepub.com/content/38/2/196.long>

“The results of this study support previous morphologic observations of feline vaccine-associated sarcomas. The role of the myofibroblast in vaccine-associated sarcomas is unclear but perhaps reflects a continuum of the inflammatory response that characterizes, in part, these unique neoplasms. The role of adjuvant, similarly, in these tumors is unknown.”

Central nervous system disease in patients with macrophagic myofasciitis

Author information

Authier FJ1, Cherin P, Creange A, Bonnotte B,
Ferrer X, Abdelmoumni A, Ranoux D, Pelletier J,
Figarella-Branger D, Granel B, Maisonobe T, Coquet M,
Degos JD, Gherardi RK.

Groupe d'Etudes et de Recherches sur le Muscle et le Nerf
(GERMEN, EA Université Paris XII-Val de Marne)
Faculté de Médecine de Créteil, Département de Pathologie
Hôpital Henri Mondor, AP-HP, Créteil, France
authier@univ-paris12.fr

Abstract

Macrophagic myofasciitis (MMF), a condition newly recognized in France, is manifested by diffuse myalgias and characterized by highly specific myopathological alterations which have recently been shown to represent an unusually persistent local reaction to intramuscular injections of aluminium-containing vaccines. Among 92 MMF patients recognized so far, eight of them, which included the seven patients reported here, had a symptomatic demyelinating CNS disorder. CNS manifestations included hemisensory or sensorimotor symptoms (four out of seven), bilateral pyramidal signs (six out of seven), cerebellar signs (four out of seven), visual loss (two out of seven), cognitive and behavioural disorders (one out of seven) and bladder dysfunction (one out of seven). Brain T(2)-weighted MRI showed single (two out of seven) or multiple (four out of seven) supratentorial white matter hyperintense signals and corpus callosum atrophy (one out of seven). Evoked potentials were abnormal in four out of six patients and CSF in four out of seven. According to Poser's criteria for multiple sclerosis, the diagnosis was clinically definite (five out of seven) or clinically probable multiple sclerosis (two out of seven). Six out of seven patients had diffuse myalgias. Deltoid muscle biopsy showed stereotypical accumulations of PAS (periodic acid-Schiff)-positive macrophages, sparse CD8+ T cells and minimal myofibre damage. Aluminium-containing vaccines had been administered 3-78 months (median = 33 months) before muscle biopsy (hepatitis B virus: four out of seven, tetanus toxoid: one out of seven, both hepatitis B virus and tetanus toxoid: two out of seven). The association between MMF and multiple sclerosis-like disorders may give new insights into the controversial issues surrounding vaccinations and demyelinating CNS disorders. Deltoid muscle biopsy searching for myopathological alterations of MMF should be performed in multiple sclerosis patients with diffuse myalgias.

Full Report

<http://brain.oxfordjournals.org/content/124/5/974>

“Macrophagic myofasciitis (MMF),
a condition newly recognized in France,
is manifested by diffuse myalgias and characterized by
highly specific myopathological alterations which have recently
been shown to represent an unusually persistent local reaction
to intramuscular injections of aluminium-containing vaccines.
Among 92 MMF patients recognized so far, eight of them, which
included the seven patients reported here, had a symptomatic
demyelinating Central Nervous System disorder.”

Antiphospholipid syndrome, antiphospholipid antibodies, and atherosclerosis

Author information

Sherer Y1, Shoenfeld Y.

Department of Medicine 'B'
Sheba Medical Center
Tel-Hashomer 52621, Israel

Abstract

The antiphospholipid syndrome is characterized by arterial and venous thrombosis, as well as pregnancy morbidity, in the presence of elevated levels of antiphospholipid antibodies. These autoantibodies have procoagulant activity, as they affect platelets, humoral coagulation factors, and endothelial cells. In addition, they are proatherogenic, as demonstrated by animal models and by the increased prevalence of cardiovascular diseases in patients with systemic lupus erythematosus and antiphospholipid syndrome. Moreover, antiphospholipid antibodies, including anticardiolipin, anti-b2-glycoprotein-I, and anti-oxidized low-density lipoprotein, are associated with atherosclerosis and its consequences in the general population as well. This autoimmune aspect of atherosclerosis in the presence or absence of an autoimmune disease suggests benefit from development of immunomodulating therapies.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11389799>

“The antiphospholipid syndrome is characterized by arterial and venous thrombosis, as well as pregnancy morbidity, in the presence of elevated levels of antiphospholipid antibodies.”

“Vaccine-related cardiorespiratory events are relatively common in preterm babies.”

Acta Paediatrica • August 2001

Adverse events following vaccination in premature infants

S Sen¹, Y Cloete², K Hassan¹ and P Buss¹,

Department of Paediatrics and Neonatology, Royal Gwent Hospital, Newport, UK
Nevill Hall Hospital, Abergavenny, UK
Royal Gwent Hospital, Cardiff Road, Newport NP9 2UB, UK

Abstract

The aims of this study were to study the frequency, severity and types of adverse reactions following DPT/Hib (diphtheria and tetanus toxoids and pertussisHaemophilus influenzae type B conjugate) immunization in very preterm infants and to identify possible risk factors. Case notes of 45 preterm babies vaccinated in the neonatal intensive care unit between January 1993 and December 1998 were studied retrospectively. Birthweight, gestational age, duration of ventilation, oxygen dependency, timing of vaccination, weight, corrected gestation at vaccination and apparent adverse effects were noted. Apparent adverse events were noted in 17 of 45 (37.8%) babies: 9 (20%) had major events, i.e. apnoea, bradycardia or desaturations, and 8 (17.8%) had minor events, i.e. increased oxygen requirements, temperature instability, poor handling and feed intolerance. Babies with major events were significantly younger ($p < 0.05$), had a lower postmenstrual age ($p < 0.05$) and weighed less ($p < 0.05$) at the time of vaccination compared with babies without major events. No differences in the mean birthweight, gestational age, duration of ventilation or oxygen dependency were found between the two groups. Age at vaccination of 70 days or less was significantly associated with increased risk ($p < 0.01$). Of 27 babies vaccinated at 70 days or less, 9 (33.3%) developed major events compared with none when vaccinated over 70d.

Conclusion

Vaccine-related cardiorespiratory events are relatively common in preterm babies. Problems were much more common if vaccine is administered at or before 70 d. These babies should therefore be monitored postvaccination. Further prospective studies are needed to clarify whether delaying vaccination offers protection against these adverse events.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1651-2227.2001.tb02457.x/abstract>

Comparative analysis of host responses
related to immunosuppression between measles patients
and vaccine recipients with live
attenuated measles vaccines

Author information

Okada H1, Sato TA, Katayama A, Higuchi K, Shichijo K,
Tsuchiya T, Takayama N, Takeuchi Y, Abe T, Okabe N, Tashiro M.

Department of Viral Diseases and Vaccine Control
National Institute of Infectious Diseases
Musashi-Murayama, Tokyo, Japan

Abstract

Measles virus infection induces a profound immunosuppression. We analyzed in a time-dependent manner peripheral bloods of one to two-year-old children immunized with live attenuated measles vaccines, compared with age-matched measles patients, for immunosuppression. In contrast to transient severe lymphopenia with measles patients, primarily due to extensive apoptosis of a broad spectrum of uninfected lymphocytes, neither apoptosis nor lymphopenia occurred with measles vaccine recipients. Increase in number and activation of NK cells, which might compensate for the lymphopenia in measles patients, were not found with the vaccinees. While cell surface expression of apoptosis-related molecules such as TNF-related apoptosis-inducing ligand (TRAIL), TRAIL-receptors, CD95(Fas) and Fas-ligand, and plasma interferon-gamma were increased for measles patients, they remained unchanged after vaccination. Plasma interleukin (IL)-18, which is responsible for inducing apoptosis in several infectious diseases, was increased predominantly with measles patients, whereas the increase remained marginal with the vaccinees. IL-10 was elevated transiently in both measles patients and vaccinees. Decrease in plasma IL-12, which is often correlated with T cell suppression, was not found for both cases. Serum IgM and IgG antibodies to measles virus were induced at lower titers in the vaccinees than measles patients. These results indicate that in contrast to wild-type measles virus, live measles vaccines hardly provoked host cytokine responses that lead to apoptotic cytolysis of uninfected lymphocytes, lymphopenia and immunosuppression, and thereby induced weaker immune responses to the virus.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11448026>

“These results indicate that in contrast to wild-type measles virus, live measles vaccines hardly provoked host cytokine responses that lead to apoptotic cytolysis of uninfected lymphocytes, lymphopenia and immunosuppression, and thereby induced weaker immune responses to the virus.”

Adverse events following vaccination in premature infants

Author information

Sen S1, Cloete Y, Hassan K, Buss P.

Department of Paediatrics and Neonatology
Royal Gwent Hospital, Newport, UK

Abstract

The aims of this study were to study the frequency, severity and types of adverse reactions following DPT/Hib (diphtheria and tetanus toxoids and pertussis/Haemophilus influenzae type B conjugate) immunization in very preterm infants and to identify possible risk factors. Case notes of 45 preterm babies vaccinated in the neonatal intensive care unit between January 1993 and December 1998 were studied retrospectively. Birthweight, gestational age, duration of ventilation, oxygen dependency, timing of vaccination, weight, corrected gestation at vaccination and apparent adverse effects were noted. Apparent adverse events were noted in 17 of 45 (37.8%) babies: 9 (20%) had major events, i.e. apnoea, bradycardia or desaturations, and 8 (17.8%) had minor events, i.e. increased oxygen requirements, temperature instability, poor handling and feed intolerance. Babies with major events were significantly younger ($p < 0.05$), had a lower postmenstrual age ($p < 0.05$) and weighed less ($p < 0.05$) at the time of vaccination compared with babies without major events. No differences in the mean birthweight, gestational age, duration of ventilation or oxygen dependency were found between the two groups. Age at vaccination of 70 days or less was significantly associated with increased risk ($p < 0.01$). Of 27 babies vaccinated at 70 days or less, 9 (33.3%) developed major events compared with none when vaccinated over 70 days.

CONCLUSION:

Vaccine-related cardiorespiratory events are relatively common in preterm babies. Problems were much more common if vaccine is administered at or before 70 d. These babies should therefore be monitored postvaccination. Further prospective studies are needed to clarify whether delaying vaccination offers protection against these adverse events.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11529542>

“Vaccine-related cardiorespiratory events are relatively common in preterm babies. Problems were much more common if vaccine is administered at or before 70 days.”

**Infection of
human B lymphocytes
with MMR vaccine
induces IgE class switching**

Author information

Imani F1, Kehoe KE.

Division of Clinical Immunology, Department of Medicine
The Johns Hopkins University School of Medicine
Asthma and Allergy Center, 5501 Hopkins Bayview Circle
Baltimore, Maryland 21224, USA
fimani@mail.jhmi.edu

Abstract

Circulating immunoglobulin E (IgE) is one of the characteristics of human allergic diseases including allergic asthma. We recently showed that infection of human B cells with rhinovirus or measles virus could lead to the initial steps of IgE class switching. Since many viral vaccines are live viruses, we speculated that live virus vaccines may also induce IgE class switching in human B cells. To examine this possibility, we selected the commonly used live attenuated measles mumps rubella (MMR) vaccine. Here, we show that infection of a human IgM(+) B cell line with MMR resulted in the expression of germline epsilon transcript. In addition, infection of freshly prepared human PBLs with this vaccine resulted in the expression of mature IgE mRNA transcript. Our data suggest that a potential side effect of vaccination with live attenuated viruses may be an increase in the expression of IgE.

<http://www.ncbi.nlm.nih.gov/pubmed/11513549>

“Circulating immunoglobulin E (IgE) is one of the characteristics of human allergic diseases including allergic asthma. We recently showed that infection of human B cells with rhinovirus or measles virus could lead to the initial steps of IgE class switching. Our data suggest that a potential side effect of vaccination with live attenuated viruses may be an increase in the expression of IgE.”

[Based on these findings, the authors concluded that viral vaccines might be playing a role in the increasing incidence of asthma and other allergic diseases]

“From October 1998 to December 1999, 112 cases of intussusception were reported.”

Vaccine • September 2001

Data mining in the US Vaccine Adverse Event Reporting System (VAERS): early detection of intussusception and other events after rotavirus vaccination

Author Information

Manette T. Niu.a, Diane E. Erwin.c, M.Miles Braun.b

a. Vaccine Safety Branch, Division of Epidemiology,
Office of Biostatistics and Epidemiology, Center for Biologic Evaluation and Research,
US Food and Drug Administration, 1401 Rockville Pike, HFM-210, Rockville, MD

b. Division of Epidemiology, Office of Biostatistics and Epidemiology
Center for Biologic Evaluation and Research, US Food and Drug Administration, Rockville, MD

c. Information Management Services, Inc., Rockville, MD, USA

Abstract

The Vaccine Adverse Event Reporting System (VAERS) is the US passive surveillance system monitoring vaccine safety. A major limitation of VAERS is the lack of denominator data (number of doses of administered vaccine), an element necessary for calculating reporting rates. Empirical Bayesian data mining, a data analysis method, utilizes the number of events reported for each vaccine and statistically screens the database for higher than expected vaccine-event combinations signaling a potential vaccine-associated event. This is the first study of data mining in VAERS designed to test the utility of this method to detect retrospectively a known side effect of vaccination—intussusception following rotavirus (RV) vaccine. From October 1998 to December 1999, 112 cases of intussusception were reported. The data mining method was able to detect a signal for RV-intussusception in February 1999 when only four cases were reported. These results demonstrate the utility of data mining to detect significant vaccine-associated events at early date. Data mining appears to be an efficient and effective computer-based program that may enhance early detection of adverse events in passive surveillance systems.

<http://www.sciencedirect.com/science/article/pii/S0264410X01002377>

Adaptation of *Bordetella pertussis* to vaccination: a cause for its reemergence?

Author information

Mooi FR1, van Loo IH, King AJ.

National Institute for Public Health and the Environment
Bilthoven, the Netherlands
fr.mooi@rivm.nl

Abstract

In the Netherlands, as in many other western countries, pertussis vaccines have been used extensively for more than 40 years. Therefore, it is conceivable that vaccine-induced immunity has affected the evolution of *Bordetella pertussis*. Consistent with this notion, pertussis has reemerged in the Netherlands, despite high vaccination coverage. Further, a notable change in the population structure of *B. pertussis* was observed in the Netherlands subsequent to the introduction of vaccination in the 1950s. Finally, we observed antigenic divergence between clinical isolates and vaccine strains, in particular with respect to the surface-associated proteins pertactin and pertussis toxin. Adaptation may have allowed *B. pertussis* to remain endemic despite widespread vaccination and may have contributed to the reemergence of pertussis in the Netherlands.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2631860/>

“Adaptation
may have allowed *B. pertussis*
to remain endemic despite
widespread vaccination and
may have contributed to the
reemergence of pertussis in
the Netherlands.”

Immunization with the adjuvant MF59 induces macrophage trafficking and apoptosis

Author information

Dupuis M1, Denis-Mize K, LaBarbara A,
Peters W, Charo IF, McDonald DM, Ott G.

Cardiovascular Research Institute and Department of Anatomy
University of California, San Francisco, USA

Abstract

The mechanisms associated with the immunostimulatory activity of vaccine adjuvants are still poorly understood. We have undertaken a study to determine whether antigen-presenting cell trafficking is modified by administration of the submicron emulsion adjuvant MF59. We investigated the fate of inflammatory macrophages after intramuscular injection of the antigen herpes simplex virus gD2 with fluorescence-labeled MF59. A homogeneous population of macrophages infiltrated the muscle, internalized adjuvant and expressed markers characteristic of mature macrophages over a 48-h period. Macrophage influx to the injection site was reduced by 70% in mice deficient for the chemokine receptor 2 (CCR2). Two distinct cell populations were shown to contain fluorescence-labeled MF59 in the draining lymph node at 48 h post injection. The first population had a round morphology, exhibited bright fluorescence, was located in the subcapsular sinus, and was apoptotic. The second population had a dendritic morphology, was weakly fluorescent, and was located in the T cell area where adjuvant-containing apoptotic bodies identified by TUNEL labeling were present. We propose that lymph node-resident dendritic cells can acquire antigen and MF59 after intramuscular immunization by uptake of the apoptotic macrophages.

<http://www.ncbi.nlm.nih.gov/pubmed/11592066>

“We propose that lymph node-resident dendritic cells can acquire antigen and MF59 [squalene] after intramuscular immunization by uptake of the apoptotic macrophages.”

“There are significantly elevated risks
of febrile seizures after receipt of DTP vaccine or MMR vaccine ...”

CDC New England Journal Of Medicine • 2001

The Risk of Seizures after Receipt of Whole-Cell Pertussis or Measles, Mumps, and Rubella Vaccine

William E. Barlow, Ph.D., Robert L. Davis, M.D., M.P.H., John W. Glasser, Ph.D., M.P.H.,
Phillip H. Rhodes, Ph.D., Robert S. Thompson, M.D., John P. Mullooly, Ph.D., Steven B. Black, M.D.,
Henry R. Shinefield, M.D., Joel I. Ward, M.D., S. Michael Marcy, M.D., Frank DeStefano, M.D.,
Virginia Immanuel, M.P.H., John A. Pearson, M.D., Constance M. Vadheim, Ph.D., Viviana Rebolledo, B.S.,
Dimitri Christakis, M.D., M.P.H., Patti J. Benson, M.P.H., Ned Lewis, M.P.H., and Robert T. Chen, M.D.
for the Centers for Disease Control and Prevention Vaccine Safety Datalink Working Group

BACKGROUND

The administration of the diphtheria and tetanus toxoids and whole-cell pertussis (DTP) vaccine and measles, mumps, and rubella (MMR) vaccine has been associated with seizures. We studied the relation between these vaccinations and the risk of a first seizure, subsequent seizures, and neurodevelopmental disability in children.

METHODS

This cohort study was conducted at four large health maintenance organizations and included reviews of the medical records of children with seizures. We calculated the relative risks of febrile and nonfebrile seizures among 679,942 children after 340,386 vaccinations with DTP vaccine, 137,457 vaccinations with MMR vaccine, or no recent vaccination. Children who had febrile seizures after vaccination were followed to identify the risk of subsequent seizures and other neurologic disabilities.

RESULTS

Receipt of DTP vaccine was associated with an increased risk of febrile seizures only on the day of vaccination (adjusted relative risk, 5.70; 95 percent confidence interval, 1.98 to 16.42). Receipt of MMR vaccine was associated with an increased risk of febrile seizures 8 to 14 days after vaccination (relative risk, 2.83; 95 percent confidence interval, 1.44 to 5.55). Neither vaccination was associated with an increased risk of nonfebrile seizures. The number of febrile seizures attributable to the administration of DTP and MMR vaccines was estimated to be 6 to 9 and 25 to 34 per 100,000 children, respectively. As compared with other children with febrile seizures that were not associated with vaccination, the children who had febrile seizures after vaccination were not found to be at higher risk for subsequent seizures or neurodevelopmental disabilities.

CONCLUSIONS

There are significantly elevated risks of febrile seizures after receipt of DTP vaccine or MMR vaccine, but these risks do not appear to be associated with any long-term, adverse consequences.

Formaldehyde cytotoxicity in three human cell types assessed in three different assays

Author information

Lovschall H1, Eiskjaer M, Arenholt-Bindslev D.

Tissue Culture Laboratory
Department of Dental Pathology
Royal Dental College, Faculty of Health Sciences
University of Aarhus, DK-8000 Aarhus C, Denmark
loev@odont.au.dk

Abstract

International standards for preclinical screening of the cytotoxicity of dental materials so far recommend the use of established cell lines. The aim of this study was to assess the relative susceptibility of human dental pulp fibroblasts (HPF), human buccal epithelial cells (HBE) and HeLa cervix cancer cells exposed to identical cytotoxic challenges. Formaldehyde, which may be released from dental materials such as dental composites, glassionomer cements, and endodontic sealers, was used as test chemical. Cytotoxicity data including dose-response relations and TC(50) values were assessed in three different assays: BrdU incorporation, neutral red uptake and MTT assays. HBE and HPF demonstrated statistically significant lower TC(50) values in both the neutral red and the BrdU assay in comparison to HeLa cells. In the MTT assay no statistically significant differences were observed between the cell types. In the two target-tissue cell types (HPF and HBE) the Neutral Red assay revealed lower TC(50) values in comparison to the BrdU assay. In HeLa cells no statistically significant differences were observed between the assays. In conclusion, the present study confirms that cytotoxicity data obtained by cell culture studies are influenced by both cell culture model and choice of assay. Under identical experimental conditions, human target tissue cells appeared to be more sensitive to formaldehyde toxicity than human HeLa cancer cells.

“Under identical experimental conditions,
human target tissue cells appeared to be more
sensitive to formaldehyde toxicity than
human HeLa cancer cells.”

“antivaccination activists use: highly emotive content,
conspiratorial claims and privately published material and newspapers articles ...”

[the reason for the publication of this eBook]

Archives Of Disease In Childhood • March 2002

Antivaccination activists on the world wide web

Author Information

P Davies¹, S Chapman¹, J Leask²

1. Department of Public Health and Community Medicine, University of Sydney A27, NSW 2006, Australia

2. National Centre for Immunisation Research and Surveillance

Simonc@health.usyd.edu.au

Abstract

Aims

To determine the likelihood of finding an antivaccination site on the world wide web and to characterise their explicit claims and rhetorical appeals.

Methods

Using “vaccination” and “immunisation”, examining the first 10 sites displayed on seven leading search engines. Detailed examination of content of 100 antivaccination sites found on Google.

Results

43% of websites were antivaccination (all of the first 10 on Google). Main rhetorical appeals involve themes of the scientific veracity of antivaccination argument; rapport with parents seeking to protect their children from harm; and alleged collusion between doctors, the pharmaceutical industry, and government to deny vaccine harm.

Conclusions

There is a high probability that parents will encounter elaborate antivaccination material on the world wide web. Factual refutational strategies alone are unlikely to counter the highly rhetorical appeals that shape these sites. Campaigns by those opposed to immunisation have been followed by falling immunisation rates and outbreaks of vaccine preventable disease.¹ The internet has provided antivaccinationists with unprecedented opportunities for exposure. In the USA, 55% of adults with internet access use it to seek health related information.² For all its benefits, the internet has great potential to disseminate health information that is incorrect and potentially dangerous.³ To date, all studies on health information on the internet have assessed content against

a priori standards of evidence, and have not considered the rhetorical subtexts and wider social discourses in which this information is embedded.^{4,5} We examined the content of 100 antivaccination websites, considering not only the explicit claims made about vaccination, but also the ways these claims are framed to maximise their appeal and influence.

Response to the problem

To defuse conspiratorial claims the public should be made aware of efforts to address the issue of vaccine safety through more active surveillance of adverse events and studies investigating hypothesised links between vaccination and serious chronic diseases.^{9,10} Since antivaccination websites share many of the characteristics we have described, the themes identified in this article might act as a tool for parents to discern whether the source is trustworthy. The checklist might include:

- Highly emotive content
- Conspiratorial claims
- Privately published material, newspapers articles, etc., given as sources of information
- Claims to have privileged information unknown to medical authorities

Where refuting antivaccination arguments on the basis of fact alone is insufficient, it may be possible to use similarly emotive tactics to promote immunisation. Emphasis could be given to images and stories of children harmed by vaccine preventable illnesses (see, for example, <http://www.immunize.org/stories/unprot.htm>).

“Several recent epidemiological studies have shown that vaccinations against biological warfare using pertussis as an adjuvant were associated with the Gulf war syndrome.”

Medical Hypotheses • April 2002

**Gulf war syndrome:
could it be triggered by biological warfare-vaccines
using pertussis as an adjuvant?**

Author information

Tournier JN1, Jouan A, Mathieu J, Drouet E.

Département de biologie des agents transmissibles
CRSSA, La Tronche, France
j.tournier@eudoramail.com

Abstract

Several recent epidemiological studies have shown that vaccinations against biological warfare using pertussis as an adjuvant were associated with the Gulf war syndrome. If such epidemiological findings are confirmed, we propose that the use of pertussis as an adjuvant could trigger neurodegeneration through induction of interleukin-1beta secretion in the brain. In turn, neuronal lesions may be sustained by stress or neurotoxic chemical combinations. Particular susceptibility for IL-1beta secretion and potential distant neuronal damage could provide an explanation for the diversity of the symptoms observed on veterans.

<http://www.ncbi.nlm.nih.gov/pubmed/12027522>

The effect of vaccination on the epidemiology of varicella zoster virus

Author information

Edmunds WJ1, Brisson M.

Immunisation Division
Colindale, London
NW9 5EQ, UK
jedmunds@phls.org.uk

Abstract

Varicella zoster virus (VZV) causes chickenpox (varicella) on primary exposure and can reactivate later in life to cause shingles (zoster). As primary infection is more serious in adults than children, and exposure to the virus might boost the immune response to both chickenpox and shingles, there are two main concerns regarding infant VZV vaccination: that it could lead to an increase in adult disease; and/or that it could lead to a temporary increase in the incidence of shingles. This paper reviews the evidence for such outcomes. The consensus view of mathematical modelling studies is that the overall varicella associated burden is likely to decrease in the long term, regardless of the level of vaccine coverage. On the other hand, recent evidence suggests that an increase in zoster incidence appears likely, and the more effective vaccination is at preventing varicella, the larger the increase in zoster incidence. Targeted vaccination of susceptible adolescents and/or the contacts of high-risk individuals can be effective at preventing disease in these individuals with minimal risk to the community. However, targeted strategies would not prevent most disease (including most severe disease), and will not lead to a long-term reduction in the incidence of zoster. Understanding the mechanisms for maintaining immunity against varicella and zoster is critical for predicting the long-term effects of vaccination. Meanwhile sensitive surveillance of both chickenpox and shingles is essential in countries that have implemented, or are about to implement, varicella vaccination.

<http://www.ncbi.nlm.nih.gov/pubmed/12099726>

“... recent evidence suggests that an increase in zoster [shingles] incidence appears likely, and the more effective vaccination is at preventing varicella, the larger the increase in zoster incidence.”

[varicella is chicken pox]

Neurological adverse events associated with vaccination

Author information

Piyasirisilp S1, Hemachudha T.

Division of Neurology, Department of Medicine
Chiang Mai University, Chiang Mai 50200, Thailand
spiyasir@mail.med.cmu.ac.th

Abstract

Public tolerance to adverse reactions is minimal. Several reporting systems have been established to monitor adverse events following immunization. The present review summarizes data on neurologic complications following vaccination, and provides evidence that indicates whether they were directly associated with the vaccines. These complications include autism (measles vaccine), multiple sclerosis (hepatitis B vaccine), meningoencephalitis (Japanese encephalitis vaccine), Guillain-Barré syndrome and giant cell arteritis (influenza vaccine), and reactions after exposure to animal rabies vaccine. Seizures and hypotonic/hyporesponsive episodes following pertussis vaccination and potential risks associated with varicella vaccination, as well as vaccine-associated paralytic poliomyelitis following oral poliovirus vaccination, are also described. In addition, claims that complications are caused by adjuvants, preservatives and contaminants [i.e. macrophagic myofasciitis (aluminium), neurotoxicity (thimerosal), and new variant Creutzfeldt-Jakob disease (bovine-derived materials)] are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12045734>

“These complications include autism (measles vaccine), multiple sclerosis (hepatitis B vaccine), meningoencephalitis (Japanese encephalitis vaccine), Guillain-Barré syndrome and giant cell arteritis (influenza vaccine), and reactions after exposure to animal rabies vaccine. Seizures and hypotonic/hyporesponsive episodes following pertussis vaccination and potential risks associated with varicella vaccination, as well as vaccine-associated paralytic poliomyelitis following oral poliovirus vaccination, are also described.”

“The present review summarizes data on neurologic complications following vaccination ...”

Current Opinion in Neurology • June 2002

Neurological adverse events associated with vaccination

Piyasirisilp, Sucheepa; Hemachudha, Thiravatb

Abstract

Public tolerance to adverse reactions is minimal. Several reporting systems have been established to monitor adverse events following immunization. The present review summarizes data on neurologic complications following vaccination, and provides evidence that indicates whether they were directly associated with the vaccines. These complications include autism (measles vaccine), multiple sclerosis (hepatitis B vaccine), meningoencephalitis (Japanese encephalitis vaccine), Guillain-Barré syndrome and giant cell arteritis (influenza vaccine), and reactions after exposure to animal rabies vaccine. Seizures and hypotonic/hyporesponsive episodes following pertussis vaccination and potential risks associated with varicella vaccination, as well as vaccine-associated paralytic poliomyelitis following oral poliovirus vaccination, are also described. In addition, claims that complications are caused by adjuvants, preservatives and contaminants [i.e. macrophagic myofasciitis (aluminium), neurotoxicity (thimerosal), and new variant Creutzfeldt-Jakob disease (bovine-derived materials)] are discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/12045734>

Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism

Author information

Singh VK1, Lin SX, Newell E, Nelson C.

Department of Biology and Biotechnology Center
Utah State University, Logan, Utah 84322, USA
singhvk@cc.usu.edu

Abstract

Autoimmunity to the central nervous system (CNS), especially to myelin basic protein (MBP), may play a causal role in autism, a neurodevelopmental disorder. Because many autistic children harbor elevated levels of measles antibodies, we conducted a serological study of measles-mumps-rubella (MMR) and MBP autoantibodies. Using serum samples of 125 autistic children and 92 control children, antibodies were assayed by ELISA or immunoblotting methods. ELISA analysis showed a significant increase in the level of MMR antibodies in autistic children. Immunoblotting analysis revealed the presence of an unusual MMR antibody in 75 of 125 (60%) autistic sera but not in control sera. This antibody specifically detected a protein of 73-75 kD of MMR. This protein band, as analyzed with monoclonal antibodies, was immunopositive for measles hemagglutinin (HA) protein but not for measles nucleoprotein and rubella or mumps viral proteins. Thus the MMR antibody in autistic sera detected measles HA protein, which is unique to the measles subunit of the vaccine. Furthermore, over 90% of MMR antibody-positive autistic sera were also positive for MBP autoantibodies, suggesting a strong association between MMR and CNS autoimmunity in autism. Stemming from this evidence, we suggest that an inappropriate antibody response to MMR, specifically the measles component thereof, might be related to pathogenesis of autism.

<http://www.ncbi.nlm.nih.gov/pubmed/12145534>

“... over 90% of MMR antibody-positive autistic sera were also positive for MBP autoantibodies, suggesting a strong association between MMR and CNS autoimmunity in autism. Stemming from this evidence, we suggest that an inappropriate antibody response to MMR, specifically the measles component thereof, might be related to pathogenesis of autism.”

“The results indicated that whole-cell DTP vaccine contained high levels of endotoxin and was statistically significantly more reactogenic than acellular DTaP vaccine.”

Pediatric Rehabilitation • July 2002

**Serious neurological conditions following pertussis immunization:
an analysis of endotoxin levels, the vaccine adverse events reporting
system (VAERS) database and literature review**

Author information

Geier DA1, Geier MR.
MedCon, Inc., Silver Spring, MD, USA

Abstract

The purpose of this study was to determine the potential risks for the development and outcome of serious neurological illnesses following whole-cell DTP vaccination and also to determine if the switch to using acellular DTaP vaccine in the US has had any effect on the incidence rate of serious neurological illnesses following vaccination. This study used the Limulus amoebocyte lysate (LAL) endotoxin assay to determine the levels of endotoxin in various commercially available whole-cell and acellular DTaP vaccines, analysed the Vaccine Adverse Events Reporting System (VAERS) database to determine the clinical effects of the use of whole-cell DTP and acellular DTaP vaccines in the US and reviewed recently published pertinent studies that analysed the incidence rates of serious neurological illness following whole-cell DTP and acellular DTaP vaccines. The results indicated that whole-cell DTP vaccine contained high levels of endotoxin and was statistically significantly more reactogenic than acellular DTaP vaccine. The presence of bias in the VAERS database was not borne-out. The recommendation by the American Academy of Paediatrics to use acellular DTaP vaccine for the entire childhood vaccination schedule beginning in 1996 and the absence of the availability of whole-cell DTP in the US beginning in 2001 seems well justified based upon the results of this study.

<http://www.ncbi.nlm.nih.gov/pubmed/12587565>

Antibodies to squalene in recipients of anthrax vaccine

Author information

Asa PB1, Wilson RB, Garry RF.

Department of Microbiology
Tulane University Medical School
New Orleans, Louisiana 70112, USA

Abstract

We previously reported that antibodies to squalene, an experimental vaccine adjuvant, are present in persons with symptoms consistent with Gulf War Syndrome (GWS) (P. B. Asa et al., *Exp. Mol. Pathol* 68, 196-197, 2000). The United States Department of Defense initiated the Anthrax Vaccine Immunization Program (AVIP) in 1997 to immunize 2.4 million military personnel. Because adverse reactions in vaccinated personnel were similar to symptoms of GWS, we tested AVIP participants for anti-squalene antibodies (ASA). In a pilot study, 6 of 6 vaccine recipients with GWS-like symptoms were positive for ASA. In a larger blinded study, only 32% (8/25) of AVIP personnel compared to 15.7% (3/19) of controls were positive ($P > 0.05$). Further analysis revealed that ASA were associated with specific lots of vaccine. The incidence of ASA in personnel in the blinded study receiving these lots was 47% (8/17) compared to an incidence of 0% (0/8; $P < 0.025$) of the AVIP participants receiving other lots of vaccine. Analysis of additional personnel revealed that in all but one case (19/20; 95%), ASA were restricted to personnel immunized with lots of vaccine known to contain squalene. Except for one symptomatic individual, positive clinical findings in 17 ASA-negative personnel were restricted to 4 individuals receiving vaccine from lots containing squalene. ASA were not present prior to vaccination in preimmunization sera available from 4 AVIP personnel. Three of these individuals became ASA positive after vaccination. These results suggest that the production of ASA in GWS patients is linked to the presence of squalene in certain lots of anthrax vaccine.

<http://www.ncbi.nlm.nih.gov/pubmed/12127050>

“Three of these individuals became anti-squalene antibody positive after vaccination. These results suggest that the production of anti-squalene antibody in Gulf War Syndrome patients is linked to the presence of squalene in certain lots of anthrax vaccine.”

Vaccines and Autism

by Bernard Rimland, PhD, Woody McGinnis, MD

Autism Research Institute, San Diego, CA

Abstract

Autism research is characterized by diverse findings. There is no consensus about the biological determinants of autism. This paper examines the autistic immune profile and the possible role of vaccines in autism.

Vaccinations may be one of the triggers for autism. Substantial data demonstrate immune abnormality in many autistic children consistent with impaired resistance to infection, activation of inflammatory response, and autoimmunity. Impaired resistance may predispose to vaccine injury in autism.

A mercurial preservative in childhood vaccines, thimerosal, may cause direct neurotoxic, immunodepressive, and autoimmune injury and contribute to early-onset and regressed autism. Live viruses in measles, mumps, and rubella (MMR) may result in chronic infection of the gut and trigger regressed autism. Thimerosal injection may potentiate MMR injury.

Consideration of vaccine etiology must include recognition of compromised gut and nutrition in most autistic children. An integrated view of the underlying biological problems in autistic children serves our understanding of the possible role of vaccines. Development of screening methods for deferral of vaccines in at-risk children is a worthy goal.

<http://labmed.oxfordjournals.org/content/labmed/33/9/708.full.pdf>

“Vaccinations may be one of the triggers for autism. Substantial data demonstrate immune abnormality in many autistic children consistent with impaired resistance to infection, activation of inflammatory response, and autoimmunity. Impaired resistance may predispose to vaccine injury in autism.

A mercurial preservative in childhood vaccines, thimerosal, may cause direct neurotoxic, immunodepressive, and autoimmune injury and contribute to early-onset and regressed autism. Live viruses in measles, mumps, and rubella (MMR) may result in chronic infection of the gut and trigger regressed autism. Thimerosal injection may potentiate MMR injury.”

Peroxide formation in polysorbate 80 and protein stability

Author information

Ha E1, Wang W, Wang YJ.

Analytics & Formulation Department
Process Sciences, Bayer Biotechnology
800 Dwight Way, Berkeley, California 94701, USA

Abstract

Nonionic surfactants are widely used in the development of protein pharmaceuticals. However, the low level of residual peroxides in surfactants can potentially affect the stability of oxidation-sensitive proteins. In this report, we examined the peroxide formation in polysorbate 80 under a variety of storage conditions and tested the potential of peroxides in polysorbate 80 to oxidize a model protein, IL-2 mutein. For the first time, we demonstrated that peroxides can be easily generated in neat polysorbate 80 in the presence of air during incubation at elevated temperatures. Polysorbate 80 in aqueous solution exhibited a faster rate of peroxide formation and a greater amount of peroxides during incubation, which is further promoted/catalyzed by light. Peroxide formation can be greatly inhibited by preventing any contact with air/oxygen during storage. IL-2 mutein can be easily oxidized both in liquid and solid states. A lower level of peroxides in polysorbate 80 did not change the rate of IL-2 mutein oxidation in liquid state but significantly accelerated its oxidation in solid state under air. A higher level of peroxides in polysorbate 80 caused a significant increase in IL-2 mutein oxidation both in liquid and solid states, and glutathione can significantly inhibit the peroxide-induced oxidation of IL-2 mutein in a lyophilized formulation. In addition, a higher level of peroxides in polysorbate 80 caused immediate IL-2 mutein oxidation during annealing in lyophilization, suggesting that implementation of an annealing step needs to be carefully evaluated in the development of a lyophilization process for oxidation-sensitive proteins in the presence of polysorbate.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12226852>

“For the first time,
we demonstrated that
peroxides can be easily generated
in neat polysorbate 80 ...”

Routine vaccinations and child survival in a war situation with high mortality: effect of gender

Author information

Aaby P1, Jensen H, Garly ML, Balé C, Martins C, Lisse I.

Bandim Health Project, Apartado 861 Bissau
Guinea-Bissau and Danish Epidemiology Science Centre
Artillerivej 5, 2300 Copenhagen S, Denmark
psb@sol.gtelecom.gw

Abstract

Non-specific effects of vaccination may be different for boys and girls. Due to the sequential administration of vaccines, it is difficult to separate the effect of different vaccines. We tested sex-specific effects of diphtheria, tetanus, pertussis (DTP) and polio vaccines and measles vaccines during the recent war (1998) in Guinea-Bissau when there was no functioning immunisation programme in the country. The study included 1491 children aged 1-17 months in four urban districts in Bissau. Vaccination status had been assessed in the study area in the 3 months before the war. The effect of DTP and polio vaccines was assessed for children who had not received measles vaccine. The effect of measles vaccine was evaluated for children aged 6-17 months. Compared with measles-unvaccinated children, measles-vaccinated children had lower mortality (mortality ratio (MR)=0.44 (95% CI 0.20-1.00)), the difference being marked for girls (0.25 (0.09-0.71)) but not for boys (0.84 (0.26-2.75)) (test of homogeneity, $P=0.095$). If measles cases were censored in the analysis, the mortality ratio for vaccinated and unvaccinated children was 0.38 (0.16-0.89). DTP and polio-vaccinated children did not have lower mortality than unvaccinated children. The female-male mortality ratio for DTP and polio-vaccinated children was 3.08 (1.11-8.56) and 0.63 (0.28-1.40) for measles-vaccinated children, a significant inversion of the ratios (test of homogeneity, $P=0.013$). The divergent female-male mortality ratios are unlikely to be explained by a selection bias going in different directions for different vaccines. The reduction associated with measles vaccination was unrelated to prevention against measles infection. Non-specific effects of vaccination should be assessed separately for boys and girls. Taking these effects into consideration may have implications for child mortality patterns in developing countries.

<http://www.ncbi.nlm.nih.gov/pubmed/12443658>

“The divergent female-male mortality ratios are unlikely to be explained by a selection bias going in different directions for different vaccines. Non-specific effects of vaccination should be assessed separately for boys and girls.”

Diabetes • December 2002

The rise of childhood type 1 diabetes in the 20th century

Author information

Gale EA

Department of Diabetes and Metabolism
Division of Medicine, University of Bristol
Medical School Unit, Southmead Hospital
Bristol BS10 5NB, U.K.

Abstract

The incidence of childhood type 1 diabetes increased worldwide in the closing decades of the 20th century, but the origins of this increase are poorly documented. A search through the early literature revealed a number of useful but neglected sources, particularly in Scandinavia. While these do not meet the exacting standards of more recent surveys, tentative conclusions can be drawn concerning long-term changes in the demography of the disease. Childhood type 1 diabetes was rare but well recognized before the introduction of insulin. Low incidence and prevalence rates were recorded in several countries over the period 1920-1950, and one carefully performed study showed no change in childhood incidence over the period 1925-1955. An almost simultaneous upturn was documented in several countries around the mid-century. The overall pattern since then is one of linear increase, with evidence of a plateau in some high-incidence populations and of a catch-up phenomenon in some low-incidence areas. Steep rises in the age-group under 5 years have been recorded recently. The disease process underlying type 1 diabetes has changed over time and continues to evolve. Understanding why and how this produced the pandemic of childhood diabetes would be an important step toward reversing it.

<http://www.ncbi.nlm.nih.gov/pubmed/12453886>

“Understanding why and how
this produced the pandemic of childhood diabetes
would be an important step toward reversing it.”

“... probably because the pertussis component of most currently available acellular DPT vaccines contains toxoided pertussis toxin that has a significant rate of reversion to active toxin.”

Toxicology Mechanisms And Methods • 2002

An analysis of the occurrence of convulsions and death after childhood vaccination

Author information

Geier DA1, Geier MR.
MedCon, Inc., Silver Spring, Maryland USA

Abstract

The association between the whole-cell diphtheria, tetanus, and pertussis (DTP) vaccine and the occurrence of convulsions and death has long been debated by the medical and scientific communities. A certified copy of the Vaccine Adverse Events Reporting System database was obtained from the Centers for Disease Control, and the data were analyzed using the Microsoft Access program. The results of this analysis reveal a statistically ($p < .01$) higher rate of occurrence of convulsions and death after whole-cell DTP vaccination than after acellular DTP and DT vaccination, showing, as do the previous findings of many other scientists, that acellular DTP vaccine is much less reactogenic than is whole-cell DTP vaccine. This study helps to validate the decision by American vaccine manufactures and the Food and Drug Administration to use only acellular DTP for the American childhood vaccination schedule. However, acellular DTP vaccine is still more reactogenic than is DT vaccine, probably because the pertussis component of most currently available acellular DPT vaccines contains toxoided pertussis toxin that has a significant rate of reversion to active toxin. This suggests the need to use the newer acellular pertussis vaccines, which are of higher purity and in which the reversion of the pertussis toxin is prevented.

<http://www.ncbi.nlm.nih.gov/pubmed/20597817>

“DTP and MMR vaccine are associated with a transiently increased risk of febrile seizures ...”

Paediatric Drugs • 2003

Placing the risk of seizures with pediatric vaccines in a clinical context

Author information

Davis RL1, Barlow W.

Departments of Pediatrics and Epidemiology
University of Washington, Seattle, Washington 98101, USA
rdavis@u.washington.edu

Abstract

In this review we discuss the relationship between commonly administered childhood vaccines such as diphtheria-tetanus-whole cell pertussis (DTP) and measles-mumps-rubella (MMR), and the risk of nonfebrile and febrile seizure. We summarize data from the Vaccine Safety Datalink Study and other studies that suggest that DTP and MMR vaccine are associated with a transiently increased risk of febrile seizures, and cause between 5-9 and 25-34 additional extra febrile seizures per 100 000 immunized children, respectively. DTP and MMR do not appear to increase the risk of nonfebrile seizures. We discuss some methodologic challenges in studies of vaccines and seizures. Because there is no adequate comparison group that would allow for the study of seizures long after vaccination, studies of seizures are limited to acute events shortly following vaccination. Additionally, while seizures following vaccination are worrisome to parents and physicians alike, observational studies of the neurodevelopmental outcomes of these children are particularly problematic. We discuss how such studies are confounded by the natural history of predisposition to febrile seizures and by the increased diagnostic scrutiny that children with febrile seizures might undergo. Nevertheless, current data suggest that children with febrile seizures do not experience long-term negative effects. Finally, we discuss the creation of new clinics designed specifically to assist physicians in managing the vaccination of children with a personal or family history of seizures. Data from these clinics suggest that vaccination is safe for children with a personal or family history of seizures, but statistical power has been limited. We conclude by discussing the introduction of new vaccines, and note that, even with widespread use, it will take many years before we can be knowledgeable about the risk of rare events with these newly licensed products.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14580221>

by Mark R. Geier, MD, PhD; David A Geier

Pediatric MMR Vaccination Safety

Abstract

Measles, mumps and rubella are viral infections that have the potential to result in globally destructive disorders. Measles, mumps and rubella (MMR) vaccine has helped to dramatically reduce the number of cases of measles, mumps and rubella infection, as well as to reduce the amount of pain and suffering associated with each of these natural infections. The purpose of this study was to analyze the incidence of serious neurologic disorders in a comparative examination between MMR vaccine and a vaccine control group. The Vaccine Adverse Events Reporting System (VAERS) database was analyzed for the incidence rate of permanent brain damage, cerebellar ataxia, autism and mental retardation reported following MMR vaccine and diphtheria, tetanus and whole-cell pertussis (DTwcp) containing-vaccines from 1994 through 2000 in the US.

Statistically significant increases in the incidence of serious neurologic disorders following pediatric MMR vaccine in comparison to DTwcP vaccine were found. The potentially globally destructive effects of natural measles, mumps and rubella infections means that continued vaccination is necessary, but improvements in MMR vaccines are needed to improve its safety.

These results show that primary pediatric MMR vaccination in children is associated with a marked increase in serious neurologic disorders in comparison to DTwcP vaccination. The increase is statistically significant for cerebellar ataxia, autism, mental retardation and permanent brain damage following primary pediatric MMR vaccination in comparison to DTwcP vaccination. These results are remarkable considering that DTwcP vaccination has been found by the scientific and medical communities to be responsible for permanent neurologic sequelae in children.

Another study found 18 cases of neurological complications following live measles vaccine administered between 1971 to 1978 in Hamburg, Germany. A causal connection was assumed by the author in 14 of the cases, resulting in an incidence of 1 per 2,500 vaccinees. The author observed an incidence of 1 per 17,650 vaccinees of abortive encephalopathy following live measles vaccination.

In conclusion, this study showed a highly statistically significant increase in serious neurologic conditions following primary pediatric MMR vaccination in comparison to a DTwcP vaccine control group. This finding confirms and extends a number of previous studies showing that patients are at increased risk for developing serious neurologic disorders for about 5-10 days following pediatric MMR vaccination. The pathogenesis of these reactions appears to follow a similar course as in the natural viral infections. In order to alleviate the potential for serious neurologic disorders following primary pediatric MMR vaccination, we recommend that killed MMR vaccine be made available. If live MMR vaccine is to be used, parents should have the option to have each viral component of MMR vaccine administered separately.

“These results show that primary pediatric MMR vaccination in children is associated with a marked increase in serious neurologic disorders in comparison to DTwcP vaccination. The increase is statistically significant for cerebellar ataxia, autism, mental retardation and permanent brain damage following primary pediatric MMR vaccination in comparison to DTwcP vaccination. These results are remarkable considering that DTwcP vaccination has been found by the scientific and medical communities to be responsible for permanent neurologic sequellae in children.”

Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome

Author information

Gherardi RK.

Groupe Nerf-Muscle, Département de Pathologie
Hôpital Henri Mondor, Créteil
romain.gherardi@hmn.ap-hop-paris.fr

Abstract

Macrophagic myofasciitis is a condition first reported in 1998, which cause remained obscure until 2001. Over 200 definite cases have been identified in France, and isolated cases have been recorded in other countries. The condition manifests by diffuse myalgias and chronic fatigue, forming a syndrome that meets both Center for Disease Control and Oxford criteria for the so-called chronic fatigue syndrome in about half of patients. One third of patients develop an autoimmune disease, such as multiple sclerosis. Even in the absence of overt autoimmune disease they commonly show subtle signs of chronic immune stimulation, and most of them are of the HLADRB1*01 group, a phenotype at risk to develop polymyalgia rheumatica and rheumatoid arthritis. Macrophagic myofasciitis is characterized by a stereotyped and immunologically active lesion at deltoid muscle biopsy. Electron microscopy, microanalytical studies, experimental procedures, and an epidemiological study recently demonstrated that the lesion is due to persistence for years at site of injection of an aluminum adjuvant used in vaccines against hepatitis B virus, hepatitis A virus, and tetanus toxoid. Aluminum hydroxide is known to potently stimulate the immune system and to shift immune responses towards a Th-2 profile. It is plausible that persistent systemic immune activation that fails to switch off represents the pathophysiological basis of chronic fatigue syndrome associated with macrophagic myofasciitis, similarly to what happens in patients with post-infectious chronic fatigue and possibly idiopathic chronic fatigue syndrome. Therefore, the WHO recommended an epidemiological survey, currently conducted by the French agency AFSSAPS, aimed at substantiating the possible link between the focal macrophagic myofasciitis lesion (or previous immunization with aluminium-containing vaccines) and systemic symptoms. Interestingly, special emphasis has been put on Th-2 biased immune responses as a possible explanation of chronic fatigue and associated manifestations known as the Gulf war syndrome. Results concerning macrophagic myofasciitis may well open new avenues for etiologic investigation of this syndrome. Indeed, both type and structure of symptoms are strikingly similar in Gulf war veterans and patients with macrophagic myofasciitis. Multiple vaccinations performed over a short period of time in the Persian gulf area have been recognized as the main risk factor for Gulf War syndrome. Moreover, the war vaccine against anthrax, which is administered in a 6-shot regimen and seems to be crucially involved, is adjuvanted by aluminium hydroxide and, possibly, squalene, another Th-2 adjuvant. If safety concerns about long-term effects of aluminium hydroxide are confirmed it will become mandatory to propose novel and alternative vaccine adjuvants to rescue vaccine-based strategies and the enormous benefit for public health they provide worldwide.

<http://www.ncbi.nlm.nih.gov/pubmed/12660567>

“Macrophagic myofasciitis is a condition first reported in 1998, which cause remained obscure until 2001. Over 200 definite cases have been identified in France, and isolated cases have been recorded in other countries [many thousands of cases have since been identified]. Electron microscopy, microanalytical studies, experimental procedures, and an epidemiological study recently demonstrated that the lesion is due to persistence for years at site of injection of an aluminum adjuvant used in vaccines against hepatitis B virus, hepatitis A virus, and tetanus toxoid ... If safety concerns about long-term effects of aluminium hydroxide are confirmed it will become mandatory to propose novel and alternative vaccine adjuvants to *rescue* vaccine-based strategies ...”

Chronic fatigue syndrome in patients with macrophagic myofasciitis

François-Jérôme Authier MD, PhD, Stéphane Sauvat MD,
Julien Champey MD, Irène Drogou MD, Michèle Coquet MD and Romain K. Gherardi MD

Abstract

Macrophagic myofasciitis (MMF), a condition first reported in France in 1998, is defined by the presence of a stereotyped and immunologically active lesion at deltoid muscle biopsy (1, 2). It was recently demonstrated that this lesion is an indicator of long-term persistence of the immunologic adjuvant aluminum hydroxide within the cytoplasm of macrophages at the site of previous intramuscular (IM) injection (2). MMF is typically detected in patients with diffuse arthromyalgias that have appeared subsequent to aluminum hydroxide administration in the absence of a clearly defined anatomic substratum (2). Patients also report unexplained chronic fatigue (1). These manifestations are reminiscent of the so-called chronic fatigue syndrome (CFS), a poorly understood condition manifesting as disabling fatigue, musculoskeletal pain, sleep disturbance, impaired concentration, and headaches (3). The present study was conducted to determine the proportion of MMF patients fulfilling international criteria for CFS.

Thirty unselected consecutive patients with biopsy-proven MMF identified in Créteil and Bordeaux were retrospectively included, regardless of symptoms that led to indication of muscle biopsy. As previously described (2), MMF was assessed by 1) well-circumscribed sheets of densely packed, large, nonepithelioid macrophages with a finely granular, periodic acid–Schiff–positive content, in the connective structures of deltoid muscle; 2) lymphocytic infiltrates intermingled with macrophages and forming microvascular cuffs; and 3) absence of significant muscle fiber injury (see Figure 1). In each patient, we determined, through both chart review and either direct patient questioning or telephone interview, 1) the presence of chronic fatigue of >6 months' duration, 2) the alleged severity of fatigue, and 3) the presence of CFS according to Centers for Disease Control and Prevention (CDC) criteria (1994) (4) or Oxford criteria (1991) (5). In addition, in 20 patients, we retrospectively evaluated history of immunization as well as prevalence of fever and neurologic features suggestive of central nervous system demyelinating disease; laboratory findings, including erythrocyte sedimentation rate, creatine kinase levels, and ⁶⁷Ga scintigraphy; and responsiveness to steroids.

Figure 1. Deltoid muscle biopsy samples from patients with macrophagic myofasciitis (MMF). A, Tightly packed, large, basophilic macrophages intermingled with lymphocytes in perifascicular endomysium (frozen section, hematoxylin and eosin stained; original magnification ×400). B, MMF lesion in perimuscular adipose tissue showing immunolocalization of the macrophage marker CD68 (paraffin section, immunoperoxidase procedure; original magnification ×400). C, Adjacent section of the same biopsy sample showing immunolocalization of the T cell marker CD3 (paraffin section, immunoperoxidase procedure; original magnification ×400).

The male:female ratio was 1:2. The mean age of patients was 52 years (range 12–78 years). Chronic fatigue was found in 28 of 30 patients (93%) and was considered disabling in 26 of 30 patients (87%). Sixteen patients (53%) fulfilled CFS criteria from either the CDC (14 of 30 patients, 47%) or Oxford (12 of 30 patients, 40%), 11 of 30 patients (37%) fulfilled both CDC and Oxford criteria. Other symptoms, laboratory findings, and steroid responsiveness are detailed in Table 1. ⁶⁷Ga scintigraphy was performed in 5 patients and showed increased levels of ⁶⁷Ga uptake in muscle and para-articular areas, mainly in lower limbs. A history of vaccination was available for 19 of 20 patients. All 19 patients had received IM administration of aluminum-containing vaccine prior to the onset of CFS symptoms, and the delay from the last vaccination to the first manifestations ranged from 1 month to 72 months (median 12 months).

We have previously determined that myalgias are a major symptom in patients with MMF. The prevalence of myalgias was much higher in such patients than in other patients who had undergone deltoid muscle biopsies at the same time in the same centers (85% versus 45%; $P < 0.0001$ by Fisher's exact test) (2). We show now that chronic disabling fatigue is a symptom as frequent as diffuse myalgias in patients with MMF (87%), a finding also noted in the French Institut de Veille Sanitaire exploratory investigation report (6). More than half of the patients also reported other manifestations of CFS. Therefore, MMF should be alternatively considered as a cause of CFS or as an additional exclusion criterion, along with rheumatoid arthritis, lupus, and other diseases, for the diagnosis of idiopathic CFS (4). Consequently, we suggest that patients with CFS should be carefully checked for a history of IM administration of aluminum hydroxide, and, if there is consistent chronology, a muscle biopsy to search for MMF at the site of injection should be considered, even many years after onset of symptoms.

Pathophysiology of CFS is still fiercely debated by psychologists, neuroendocrinologists, and immunologists. Chronic immune stimulation that fails to switch off has been previously reported as a possible cause of CFS (7–9), and such a situation may very well result from persistence of the immunologic adjuvant aluminum hydroxide within antigen-presenting cells (2, 10). Therefore, MMF may well represent a paradigm for CFS of immunologic origin. We believe that clarification of MMF pathophysiology would significantly contribute to the understanding of the whole spectrum of chronic fatigue and its syndromes.

Full Report: <http://onlinelibrary.wiley.com/doi/10.1002/art.10740/full>

PDF: <http://onlinelibrary.wiley.com/doi/10.1002/art.10740/epdf>

A review of hepatitis B vaccination

Author information

Geier MR1, Geier DA, Zahalsky AC.

The Genetic Centers of America
14 Redgate Ct, Silver Spring, MD 20905, USA
mgeier@erols.com

Abstract

Hepatitis B is one of the most important infectious causes of acute and chronic liver disease both in the US and world-wide. In order to combat the life-threatening effects of hepatitis B infection, recombinant hepatitis B vaccines have been developed. The medical and scientific communities have generally accepted that recombinant hepatitis B vaccine - a highly purified, genetically engineered, single antigen vaccine - is a safe vaccine. Information is presented showing that hepatitis B vaccine contains yeast, aluminium, thimerosal and hepatitis B surface antigen epitopes, which may result in hepatitis B vaccine being associated with autoimmune diseases among susceptible adult vaccine recipients. There is little doubt that the benefits of this vaccine overall far outweigh its risks. Physicians and patients should evaluate the risks and benefits of hepatitis B vaccination and, together, make an informed consent decision as to whether to undergo vaccination. Individuals who experience an adverse reaction to hepatitis B vaccination should report it to the Vaccine Adverse Event Reporting System database and be advised that they may be eligible for compensation from the no-fault National Vaccine Injury Compensation Program, administered by the US Court of Claims. The authors strongly urge that additional research be conducted into the molecular basis of adverse events following hepatitis B vaccine administration, so that further recommendations may be made on how to improve their safety profiles.

<http://www.ncbi.nlm.nih.gov/pubmed/12904111>

“Information is presented showing that hepatitis B vaccine contains yeast, aluminium, thimerosal and hepatitis B surface antigen epitopes, which may result in hepatitis B vaccine being associated with autoimmune diseases among susceptible adult vaccine recipients.”

Elevated levels of measles antibodies in children with autism

Author information

Singh VK1, Jensen RL.
Department of Biology and Biotechnology Center
Utah State University, Logan, Utah, USA

Abstract

Virus-induced autoimmunity may play a causal role in autism. To examine the etiologic link of viruses in this brain disorder, we conducted a serologic study of measles virus, mumps virus, and rubella virus. Viral antibodies were measured by enzyme-linked immunosorbent assay in the serum of autistic children, normal children, and siblings of autistic children. The level of measles antibody, but not mumps or rubella antibodies, was significantly higher in autistic children as compared with normal children ($P = 0.003$) or siblings of autistic children ($P \leq 0.0001$). Furthermore, immunoblotting of measles vaccine virus revealed that the antibody was directed against a protein of approximately 74 kd molecular weight. The antibody to this antigen was found in 83% of autistic children but not in normal children or siblings of autistic children. Thus autistic children have a hyperimmune response to measles virus, which in the absence of a wild type of measles infection might be a sign of an abnormal immune reaction to the vaccine strain or virus reactivation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12849883>

“Thus autistic children have a hyperimmune response to measles virus, which in the absence of a wild type of measles infection might be a sign of an abnormal immune reaction to the vaccine strain or virus reactivation.”

Influenza vaccination and Guillain Barre syndrome

Author information

Geier MR1, Geier DA, Zahalsky AC.
The Genetic Centers of America
14 Redgate Court, Silver Spring, MD 20905, USA
mgeier@erols.com

Abstract

Acute and severe Guillain Barre Syndrome (GBS) cases reported following influenza vaccine to the Vaccine Adverse Events Reporting System (VAERS) database from 1991 through 1999 were examined. Endotoxin concentrations were measured using the Limulus amoebocyte lysate assay in influenza vaccines. There were a total of 382 cases of GBS reported to the VAERS database following influenza vaccination (male/female ratio, 1.2). The median onset of GBS following influenza vaccine was 12 days (interquartile range, 7 days to 21 days). There was an increased risk of acute GBS (relative risk, 4.3; 95% confidence interval, 3.0 to 6.4) and severe GBS (relative risk, 8.5; 95% confidence interval, 3.7 to 18.9) in comparison to an adult tetanus-diphtheria (Td) vaccine control group. There were maximums in the incidence of GBS following influenza vaccine that occurred approximately every third year (1993, 1996, and 1998) and statistically significant variation in the incidence of GBS among different influenza manufacturers. Influenza vaccines contained from a 125- to a 1250-fold increase in endotoxin concentrations in comparison to an adult Td vaccine control and endotoxin concentrations varied up to 10-fold among different lots and manufacturers of influenza vaccine. The biologic mechanism for GBS following influenza vaccine may involve the synergistic effects of endotoxin and vaccine-induced autoimmunity. There were minimal potential reporting biases in the data reported to the VAERS database in this study. Patients should make an informed consent decision on whether to take this optional vaccine based upon its safety and efficacy and physicians should vigilantly report GBS following influenza vaccination to the VAERS in the United States so that continued evaluation of the safety of influenza vaccine may be undertaken.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12763480>

“from 1991 through 1999 ...

There were a total of 382 cases of

Guillain-Barre Syndrome reported to

the VAERS database following influenza vaccination ...”

Cytokine profile after rubella vaccine inoculation: evidence of the immunosuppressive effect of vaccination

Author information

Pukhalsky AL1, Shmarina GV, Bliacher MS,
Fedorova IM, Toptygina AP, Fisenko JJ, Alioshkin VA

Research Centre for Medical Genetics
1 Moskvorechie Street
Moscow 11547 Russia

Abstract

BACKGROUND AND AIM:

Immunization with live virus vaccines may cause an immunosuppression with lymphopaenia, impaired cytokine production and defective lymphocyte response to mitogenes. These abnormalities were described in subjects vaccinated against measles. This study was performed to analyse the host immune response related to immunosuppression in subjects vaccinated with live attenuated rubella vaccine.

METHODS:

Eighteen schoolgirls, aged 11-13 years, were vaccinated with live attenuated rubella vaccine Rudivax. Before immunization, and 7 and 30 days after, peripheral blood was collected. Cellular fractions were subjected to flow cytometric analysis, and the lymphocyte response to phytohaemagglutinin was investigated. Plasma samples were analysed for cytokines (interleukin (IL)-4, IL-10, tumour necrosis factor-alpha, and interferon-gamma) by enzyme-linked immunosorbent assay techniques.

RESULTS:

On day 7 after vaccination, the number of each lymphocyte subset was decreased; however, only for CD3 and CD4 lymphocytes has a significant reduction been shown. On the contrary, tumour necrosis factor-alpha and IL-10 levels markedly increased and amounted to its maximum on day 30. Simultaneously, a significant reduction in plasma interferon-gamma and a profound decrease of the lymphocyte response to phytohaemagglutinin were shown. The changes were accompanied with marked elevation of plasma IL-4.

CONCLUSIONS:

Our data indicate that the vaccination with live attenuated rubella vaccine results in moderate but sustained immune disturbance. The signs of immunosuppression, including defective lymphocyte response to mitogene and impaired cytokine production, may persist for at least 1 month after vaccination.

“Immunization with live virus vaccines may cause an immunosuppression with lymphopaenia, impaired cytokine production and defective lymphocyte response to mitogenes. These abnormalities were described in subjects vaccinated against measles. Our data indicate that the vaccination with live attenuated rubella vaccine results in moderate but sustained immune disturbance.”

“The potential to induce autoimmunity may complicate the use of
oil adjuvants in human and veterinary vaccines.”

Journal Of Autoimmunity • August 2003

Induction of lupus autoantibodies by adjuvants

Author information

Satoh M1, Kuroda Y, Yoshida H, Behney KM, Mizutani A,
Akaogi J, Nacionales DC, Lorenson TD, Rosenbauer RJ, Reeves WH.

Division of Rheumatology and Clinical Immunology
Department of Medicine, University of Florida
P.O. Box 100221, 1600 SW Archer Road
Gainesville, FL 32610-0221, USA
satohm@medicine.ufl.edu

Abstract

Exposure to the hydrocarbon oil pristane induces lupus specific autoantibodies in non-autoimmune mice. We investigated whether the capacity to induce lupus-like autoimmunity is a unique property of pristane or is shared by other adjuvant oils. Seven groups of 3-month-old female BALB/cJ mice received a single intraperitoneal injection of pristane, squalene (used in the adjuvant MF59), incomplete Freund's adjuvant (IFA), three different medicinal mineral oils, or saline, respectively. Serum autoantibodies and peritoneal cytokine production were measured. In addition to pristane, the mineral oil Bayol F (IFA) and the endogenous hydrocarbon squalene both induced anti-nRNP/Sm and -Su autoantibodies (20% and 25% of mice, respectively). All of these hydrocarbons had prolonged effects on cytokine production by peritoneal APCs. However, high levels of IL-6, IL-12, and TNFalpha production 2-3 months after intraperitoneal injection appeared to be associated with the ability to induce lupus autoantibodies. The ability to induce lupus autoantibodies is shared by several hydrocarbons and is not unique to pristane. It correlates with stimulation of the production of IL-12 and other cytokines, suggesting a relationship with a hydrocarbon's adjuvanticity. The potential to induce autoimmunity may complicate the use of oil adjuvants in human and veterinary vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=12892730>

Excess incidence of ALS in young Gulf War veterans

Author information

Haley RW.

Epidemiology Division
Department of Internal Medicine
University of Texas Southwestern Medical Center
Dallas, TX 75390-8874, USA
Robert.Haley@UTSouthwestern.edu

Abstract

BACKGROUND

Reported cases of ALS in young veterans of the 1991 Gulf War have suggested excess incidence.

OBJECTIVE

To compare observed and expected incidence of ALS in Gulf War veterans diagnosed before age 45 years (young veterans).

METHODS

Cases of ALS diagnosed from 1991 through 1998 were collected from military registries and a publicity campaign in late 1998. Diagnoses were established from neurologists' medical records using El Escorial criteria. Expected incidence was estimated from the age distribution of the Gulf War veteran population, weighted by age-specific death rates of the US population. Secular changes in nationwide ALS rates were assessed using calculations of the age-specific US population death rates from vital statistics data of 1979 to 1998.

RESULTS

During 8 postwar years, 20 ALS cases were confirmed in approximately 690,000 Gulf War veterans, and 17 were diagnosed before age 45 years. All developed bulbar and spinal involvement, and 11 have died. In young veterans, the expected incidence increased from 0.93 cases/year in 1991 to 1.57 cases/year in 1998, but the observed incidence increased from 1 to 5 cases/year. The observed incidence was 0.94 (95% CI, 0.26 to 2.41) times that expected in the baseline period from 1991 to 1994 (4 vs 4.25 cases; $p = 0.6$); it increased to 2.27 (95% CI, 1.27 to 3.88) times that expected during the 4-year period from 1995 to 1998 (13 vs 5.72 cases; $p = 0.006$); and it peaked at 3.19 (95% CI, 1.03 to 7.43) times that expected in 1998 (5 vs 1.57 cases; $p = 0.02$). The magnitude of the excess of ALS cases over the expected incidence increased during the 8-year period (Poisson trend test, $p = 0.05$), and the increase was not explained by a change in the interval from onset to diagnosis or by a change in the US population death rate of ALS in those aged <45 years.

CONCLUSIONS

The observed incidence of ALS in young Gulf War veterans exceeded the expected, suggesting a war-related environmental trigger.

“The observed incidence of Amyotrophic Lateral Sclerosis in young Gulf War veterans exceeded the expected ...”

Analysis of neurological disease in four dimensions: insight from ALS-PDC epidemiology and animal models

Author information

Shaw CA1, Wilson JM.

Program in Neuroscience
University of British Columbia
Vancouver, BC, Canada
cshaw@interchange.ubc.ca

Abstract

The causal factor(s) responsible for sporadic neurological diseases are unknown and the stages of disease progression remain undefined and poorly understood. We have developed an animal model of amyotrophic lateral sclerosis-parkinsonism dementia complex which mimics all the essential features of the disease with the initial neurological insult arising from neurotoxins contained in washed cycad seeds. Animals fed washed cycad develop deficits in motor, cognitive, and sensory behaviors that correlate with the loss of neurons in specific regions of the central nervous system. The ability to recreate the disease by exposure to cycad allows us to extend the model in multiple dimensions by analyzing behavioral, cellular, and biochemical changes over time. In addition, the ability to induce toxin-based neurodegeneration allows us to probe the interactions between genetic and epigenetic factors. Our results show that the impact of both genetic causal and susceptibility factors with the cycad neurotoxins are complex. The article describes the features of the model and suggests ways that our understanding of cycad-induced neurodegeneration can be used to decipher and identify the early events in various human neurological diseases.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14599431>

“... causal factor(s) responsible
for sporadic neurological diseases
are unknown and the stages of
disease progression remain
undefined and poorly understood.”

Aluminum inclusion macrophagic myofasciitis: a recently identified condition

Author information

Gherardi RK1, Authier FJ.

Muscle and Nerve Group
Henri Mondor University Hospital
Créteil, France
lauret@univ-paris12.fr

Abstract

The authors conclude that the persistence of aluminum hydroxide at the site of intramuscular injection is a novel finding which has an exact significance that remains to be established fully. It seems mandatory to evaluate possible long-term adverse effects induced by this compound, because this issue has not been addressed (in the past, aluminum hydroxide was believed to be cleared quickly from the body). If safety concerns about the long-term effects of aluminum hydroxide are confirmed, novel and alternative vaccine adjuvants to rescue vaccine-based strategies should be proposed to ensure the enormous benefit for public health that these vaccines provide worldwide.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14753387>

“The authors conclude that the persistence of aluminum hydroxide at the site of intramuscular injection is a novel finding which has an exact significance that remains to be established fully.”

“... it has become apparent over the past 20 years, and most notably during the past 10 years,
that an array of metabolic machinery is also expressed in this organ ...”

Drug Metabolism & Disposition • December 2003

The Small Intestine As A Xenobiotic-Metabolizing Organ

Author Information

Laurence S. Kaminsky and Qing-Yu Zhang

Wadsworth Center, New York State Department of Health
Albany, New York (L.S.K., Q-Y.Z.)

Department of Environmental Health and Toxicology
School of Public Health, University at Albany
State University of New York, Albany, New York (L.S.K.)

Address correspondence to:

Dr. Laurence Kaminsky, New York State Department of Health
Wadsworth Center, P.O. Box 509, Albany, NY 12201-0509
kaminsky@wadsworth.org

Abstract

The mammalian small intestine serves principally as the site for absorption of nutrients, water, and both beneficial and potentially harmful xenobiotics. However, it has become apparent over the past 20 years, and most notably during the past 10 years, that an array of metabolic machinery is also expressed in this organ (Kaminsky and Fasco, 1992; Lin et al., 1999; Doherty and Charman, 2002; Ding and Kaminsky, 2003). Both phase I and phase II metabolic enzymes are expressed, together with associated transporters. In this minireview we discuss some of the most prominent phase I and II enzymes in the metabolic systems in the small intestine. The transporters, despite their importance for the fate of enterocyte- absorbed xenobiotics, are beyond the scope of this minireview (Suzuki and Sugiyama, 2000).

<http://dmd.aspetjournals.org/content/31/12/1520.long>

[vaccines are xenobiotics]

Addressing parents' concerns:
do vaccines contain harmful preservatives,
adjuvants, additives, or residuals?

Author information

Offit PA1, Jew RK.

Division of Infectious Diseases
Children's Hospital of Philadelphia
University of Pennsylvania School of Medicine
and Wistar Institute of Anatomy and Biology
Philadelphia, Pennsylvania 19104, USA
offit@email.chop.edu

Abstract

Vaccines often contain preservatives, adjuvants, additives, or manufacturing residuals in addition to pathogen-specific immunogens. Some parents, alerted by stories in the news media or information contained on the World Wide Web, are concerned that some of the substances contained in vaccines might harm their children. We reviewed data on thimerosal, aluminum, gelatin, human serum albumin, formaldehyde, antibiotics, egg proteins, and yeast proteins. Both gelatin and egg proteins are contained in vaccines in quantities sufficient to induce rare instances of severe, immediate-type hypersensitivity reactions. However, quantities of mercury, aluminum, formaldehyde, human serum albumin, antibiotics, and yeast proteins in vaccines have not been found to be harmful in humans or experimental animals.

<http://www.ncbi.nlm.nih.gov/pubmed/14654615>

[Dr. Offit, pro-vaccine media pundit,
discusses vaccine safety with parents]

Th1/Th2 Balance: The Hypothesis, its Limitations, and Implications for Health and Disease

Parris Kidd, PhD

Abstract

One theory of immune regulation involves homeostasis between T-helper 1 (Th1) and T-helper 2 (Th2) activity. The Th1/Th2 hypothesis arose from 1986 research suggesting mouse T-helper cells expressed differing cytokine patterns. This hypothesis was adapted to human immunity, with Th1- and Th2-helper cells directing different immune response pathways. Th1 cells drive the type-1 pathway (“cellular immunity”) to fight viruses and other intracellular pathogens, eliminate cancerous cells, and stimulate delayed-type hypersensitivity (DTH) skin reactions. Th2 cells drive the type-2 pathway (“humoral immunity”) and up-regulate antibody production to fight extracellular organisms; type 2 dominance is credited with tolerance of xenografts and of the fetus during pregnancy. Overactivation of either pattern can cause disease, and either pathway can down-regulate the other. But the hypothesis has major inconsistencies; human cytokine activities rarely fall into exclusive pro- Th1 or -Th2 patterns. The non-helper regulatory T cells, or the antigen-presenting cells (APC), likely influence immunity in a manner comparable to Th1 and Th2 cells. Many diseases previously classified as Th1 or Th2 dominant fail to meet the set criteria. Experimentally, Th1 polarization is readily transformed to Th2 dominance through depletion of intracellular glutathione, and vice versa. Mercury depletes glutathione and polarizes toward Th2 dominance. Several nutrients and hormones measurably influence Th1/Th2 balance, including plant sterols/sterolins, melatonin, probiotics, progesterone, and the minerals selenium and zinc. The long-chain omega-3 fatty acids EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) significantly benefit diverse inflammatory and autoimmune conditions without any specific Th1/Th2 effect. Th1/Th2-based immunotherapies, e.g., T-cell receptor (TCR) peptides and interleukin-4 (IL- 4) injections, have produced mixed results to date.

Conclusion

In managing immune hypofunction or other dysfunction, it is crucial to manage all forms of stress. Rooks reported diverse stressors, including sleep deprivation, calorie restriction, excessive exercise, examination stress, and cardiopulmonary bypass surgery, down-regulate Th1 and up-regulate Th2 activity.⁹⁵ These effects are mediated mainly by glucocorticoids, but also by the catecholamine hormones epinephrine and norepinephrine.⁹² As heroic efforts to tailor technological immune therapies go forward, the best immune intervention tools continue to be lifestyle modification, vitamins, minerals, orthomolecules, and selected nontoxic phytotherapies.

<http://www.altmedrev.com/publications/8/3/223.pdf>

“As heroic efforts to tailor technological immune therapies go forward, the best immune intervention tools continue to be lifestyle modification, vitamins, minerals, orthomolecules, and selected nontoxic phytotherapies.”

Brain Pathology • January 2004

The July 2003 Case of the Month (COM)
62-year-old female with progressive muscular weakness

Author information

Bornemann A1, Bohl J, Schneider HM,
Goebel HH, Schmidt PF, Gherardi RK.

Institute of Brain Research
Eberhard-Karls University
Tübingen, Germany

Abstract

The July 2003 Case of the Month (COM). A 62-year-old female patient experienced progressive muscular weakness over the last ten years, involving shoulder and pelvic girdle muscles, paraspinal and facial muscles. A biopsy was taken from the left deltoid muscle where hepatitis vaccination had taken place 4 weeks previously. The specimen revealed macrophagic myofasciitis due to the injection of aluminium-bound vaccines. The finding can be reproduced experimentally by injecting vaccines in rats. The pathomechanism is supposed to involve immune stimulation due to long term persistence of the adjuvant. Macrophagic myofasciitis has been suggested to occasionally cause myopathy but is supposed to be unrelated to the underlying myopathy in our patient.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14997943>

“The specimen revealed
macrophagic myofasciitis due to
the injection of aluminium-bound vaccines.”

“When mass vaccination programs encompass billions of lives, even relatively rare toxicity events cannot be tolerated.”

Presentation to the Vaccine Safety Committee of the Institute of Medicine
The National Academies of Science • February 9, 2004

Jeff Bradstreet MD, ICDRC 321-953-0278

Biological Evidence of Significant Vaccine Related Side-effects Resulting in Neurodevelopmental Disorders

Hypothesis

Evident for many individuals experienced with these issues, is the data supporting unprecedented levels of neurodevelopmental and immune disorders within the last two decades. The prevalence has risen to the point that many believe it has reached epidemic proportions. Our group of researchers and clinicians, have hypothesized that a subset of neurodevelopmental and medical disorders including: encephalopathy with autistic features, a unique inflammatory bowel disease, along with speech, learning and sensorimotor dysfunction, represent the manifestations of injuries related to vaccine components, especially mercury in the form of Thimerosal and measles virus from the MMR. Part of this hypothesis has been the existence of specific genetic vulnerability or environmental susceptibility cofactors. Our group represents researchers and clinicians with heterogeneous experience and expertise, that when taken together, provide the substance for a broad understanding of this phenomena.

Thesis

It must be recognized I am defining the data of a subgroup of children and in no way making estimates about autism or autism spectrum disorders in general. These terms will be discussed further in a moment. For what is often referred to as the broader autism phenotype, numerous candidate genes have been presented in the literature which I will not discuss here. To my knowledge, none of these genes would serve as susceptibility genes for measles viral persistence, mercury toxicity or autoimmunity of the type we will describe in this presentation, with the exception of the haplotype B44-SC30-DR4. Within this population, specific vulnerability factors, i.e. single nucleotide polymorphisms (SNP) within genes for enzymes regulating the methionine transsulfuration and glutathione systems, occur at statistically significant greater frequency than within the general or control populations. The biochemical defects predicted by these SNP are all present as well. These include: low methionine, thiol deficiencies, heavy metal (particularly mercury) accumulation, immunological disorders including autoimmunity and neurotransmitter malregulation, and the probability of viral persistence. Proteomic studies are presently underway and will help to further define and confirm these associations. Other environmental factors include oxidative stress, which has broad implications on chemistry, and in utero exposure to mercury (methylmercury from fish and Thimerosal in anti-Rho immunoglobulin preparations). In all endpoint issues, the findings have been reproduced by at least two independent laboratories, and as in the case of SNP identification and low thiols, by multiple laboratories using various methodologies. These data will be presented in summary form to the committee during the brief time allotted, but will be presented in toto in written form with supporting literature.

Vaccine Contribution to Public Health

The well-accepted benefits of vaccinations to prevention of many childhood and serious illnesses are without question. All the data presented herein are intended to improve vaccine safety and long-term public confidence in vaccines. When mass vaccination programs encompass billions of lives, even relatively rare toxicity events cannot be tolerated. While others may debate the frequency of specific adverse events and the appropriate detection and surveillance methodologies, medicine remains governed by the foundational tenet, *primum non nocere*. Where options exist, as is the case with Thimerosal, there is no acceptable rationale for continued use of a known, suspected or plausible neurotoxin in vaccines for developing children. Safe vaccine policy can now completely eliminate any concern of mercury for every age-group. This way, none of us need to fear even subtle potential effects of mercury.

The sixth month cut-off, which seems to be in practice (whereby children over 6 months are routinely advised to take vaccines with 25 mcg of ethylmercury, e.g. influenza vaccine) is equally untenable. As has been eloquently demonstrated by Landing et al, (full paper submitted: *Pediatric Pathology and Molecular Medicine* 21: 321-342, 2002) the organization of the six layers of the human neocortex undergoes repeated and dynamic changes during the exact time when a known neurotoxicant (ethylmercury) has been and is continuing to be administered. Strides to reduce Thimerosal in vaccines have been partially successful in the youngest children, but incompletely understood potential risks remain in older children who are still being exposed through Diphtheria Tetanus boosters, Influenza and other vaccines. Since no market-ready alternative for MMR exists in the US, this is a more challenging issue until new options emerge. I did receive notice from Secretary Tommy Thompson that a nasal measles vaccine was in development and expected within 2-3 years. No safety data is available, nor will be available for some time. Researchers at Johns Hopkins are working on a DNA MV vaccine. The concept is designed to further improve safety, but I have serious reservation regarding those within the population at risk for DNA hypomethylation, i.e. the same individuals with deficient methionine production secondary to folate deficiency, MTHFR defects or other factors. Methylation of viral DNA is a critical pathway to viral replication regulation/suppression. A discussion of this is beyond the scope of this paper. Below are two graphs from the Landing paper, presented here to allow easier understanding of the timing issue on neocortical development.

<http://www.vaccinationnews.org/DailyNews/2004/February/IOMBradstreet14.htm>

Full Report: <http://iom.nationalacademies.org/~media/4B8DAC4AD18F432283E67D91DB81F49B.ashx>

Macrophagic myofasciitis: an infantile Italian case

Author information

Di Muzio A1, Capasso M, Verrotti A, Trotta D,
Lupo S, Pappalepore N, Manzoli C, Chiarelli F, Uncini A.

Center for Neuromuscular Diseases
University 'G. d'Annunzio', Chieti, Italy

Abstract

Macrophagic myofasciitis is a recently identified inflammatory myopathy mostly described in adult French patients complaining of arthro-myalgias and fatigue. It is probably due to intramuscular injection of aluminium-containing vaccines and is characterized by a typical muscular infiltrate of large macrophages with aluminium inclusions. We report a 1-year-old Italian child presenting irritability, delayed motor development, hyperCKemia (up to 10 times the normal value), and typical features of macrophagic myofasciitis on muscle biopsy. The child recovered fully after steroid therapy. Macrophagic myofasciitis is a new treatable cause of motor retardation and hyperCKemia in children, and is probably more common than reported. Diagnosis requires a high index of suspicion and can be missed if biopsy is performed outside the vaccination site.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=14733966>

“It is probably due to intramuscular injection of aluminium-containing vaccines and is characterized by a typical muscular infiltrate of large macrophages with aluminium inclusions.”

An analysis of rotavirus vaccine reports to the vaccine adverse event reporting system: more than intussusception alone?

Author information

Haber P1, Chen RT, Zanardi LR, Mootrey GT, English R, Braun MM; VAERS Working Group.

National Immunization Program
Centers for Disease Control and Prevention
Atlanta, Georgia 30333, USA
phaber@cdc.gov

Abstract

BACKGROUND

The rhesus-human rotavirus reassortant-tetravalent vaccine (RRV-TV) was licensed on August, 31, 1998, and subsequently recommended for routine infant immunizations in the United States. After approximately 1 million doses had been administered, an increase in acute risk of intussusception in vaccinees led to the suspension of the use of RRV-TV and its withdrawal from the market. These postmarketing safety studies focused on a single adverse event (intussusception) and, to minimize the risk of a false-positive finding, accepted only cases that met a strict case definition. Safer rotavirus vaccines are needed to prevent the substantial global morbidity and mortality caused by rotavirus infections; their development and future use may benefit from a better understanding of the postmarketing safety profile of RRV-TV beyond intussusception.

OBJECTIVE

To characterize more completely the postmarketing surveillance safety profile of RRV-TV more completely by review and analysis of Vaccine Adverse Event Reporting System (VAERS) case reports to better understand 1) whether severe adverse events other than intussusception may have occurred after RRV-TV and 2) the likely scope of gastrointestinal illnesses, of which the previously identified, highly specific intussusception cases may account for just a fraction.

SETTING AND PARTICIPANTS

Infants vaccinated with RRV-TV and other vaccines in the United States and for whom a report was submitted to VAERS during September 1, 1998, to December 31, 1999.

METHODOLOGY

To detect adverse events of interest other than intussusception, we used proportional morbidity analysis to compare the adverse event profile of VAERS reports among infants who received routine vaccines including RRV-TV

(after excluding confirmed and suspected intussusception reports) with infants who received identical vaccine combinations but without RRV-TV. Next, to better capture all described diagnoses, signs, and symptoms associated with the suspected adverse events, a set of new codes was developed and assigned to each VAERS report. All 448 nonfatal RRV-TV-associated reports (including intussusception) were recoded manually from the clinical description on the VAERS report and categorized into clinical groups to better describe a spectrum of reported illnesses after the vaccine. Each report was assigned to one of the following hierarchical and mutually exclusive clinical groups: 1) diagnosed intussusception; 2) suspected intussusception; 3) illness consistent with either gastroenteritis or intussusception; 4) gastroenteritis; 5) other gastrointestinal diagnoses (ie, not consistent with intussusception or rotavirus-like gastroenteritis); and 6) nongastrointestinal diagnoses.

RESULTS

Even after excluding intussusception cases, a higher proportion of RRV-TV reports than non-RRV-TV reports included fever and various gastrointestinal symptoms, most notably bloody stool but also vomiting, diarrhea, abdominal pain, gastroenteritis, abnormal stool, and dehydration. Distribution of RRV-TV reports by clinical groups was as follows: diagnosed intussusception (109 [24%], suspected intussusception (36 [8%]), and illness consistent with gastroenteritis or intussusception (33 [7%]), gastroenteritis (101 [22%]), other gastrointestinal diagnoses (10 [2%]), and nongastrointestinal outcomes (159 [35%]). The median time interval between vaccination and illness onset decreased incrementally among the first 4 clinical groups: from 7 days for diagnosed intussusceptions to 3 days for gastroenteritis.

CONCLUSIONS

Intussusception and gastroenteritis were the most commonly reported outcomes; however, a substantial number of reports indicate signs and symptoms consistent with either illness, possibly suggestive of a spectrum of gastrointestinal illness(es) related to RRV-TV. Although VAERS data have recognized limitations such as underreporting (that may differ by vaccine) and are nearly always insufficient to prove causality between a vaccine and an adverse event, this safety profile of RRV-TV may aid better understanding of the pathophysiology of intussusception as well as development of future safer rotavirus vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/15060267>

“Intussusception and gastroenteritis were the most commonly reported outcomes; however, a substantial number of reports indicate signs and symptoms consistent with either illness, possibly suggestive of a spectrum of gastrointestinal illness(es) related to RRV-TV.”

“Induction of autoantibodies by mineral oils considered nontoxic also may have pathogenetic implications in human autoimmune diseases.”

Toxicology Science • April 2004

Distinctive patterns of autoimmune response induced by different types of mineral oil

Author information

Kuroda Y1, Akaogi J, Nacionales DC,
Wasdo SC, Szabo NJ, Reeves WH, Satoh M.

Division of Rheumatology and Clinical Immunology
Department of Medicine, University of Florida
Gainesville, Florida 32610-0221, USA

Abstract

Although mineral oils are generally considered nontoxic and have a long history of use in humans, the mineral oil Bayol F (incomplete Freund's adjuvant, IFA) and certain mineral oil components (squalene and n-hexadecane) induce lupus-related anti-nRNP/Sm or -Su autoantibodies in nonautoimmune mice. In the present study, we investigated whether medicinal mineral oils can induce other types of autoantibodies and whether structural features of hydrocarbons influence autoantibody specificity. Female 3-month-old BALB/c (16-45/group) mice each received an i.p. injection of pristane (C19), squalene (C30), IFA, three medicinal mineral oils (MO-F, MO-HT, MO-S), or PBS. Sera were tested for autoantibodies and immunoglobulin levels. Hydrocarbons were analyzed by gas chromatography/mass spectrometry. IFA contained mainly C15-C25 hydrocarbons, whereas MO-HT and MO-S contained C20-C40, and MO-F contained C15-C40. Pristane and n-hexadecane were found in IFA (0.17% and 0.10% w/v, respectively) and MOs (0.0026-0.027%). At 3 months, pristane and IFA induced mainly IgG2a, squalene IgG1, and MOs IgG3 and IgM in sera. Anti-cytoplasmic antibodies were common in mice treated with MO-F, as well as those treated with pristane, squalene, and IFA. Anti-ssDNA and -chromatin antibodies were higher in MO-F and MO-S than in untreated/PBS, squalene-, or IFA-treated mice, suggesting that there is variability in the induction of anti-nRNP/Sm versus -chromatin/DNA antibodies. The preferential induction of anti-chromatin/ssDNA antibodies without anti-nRNP/Sm/Su by MO-S and MO-F is consistent with the idea that different types of autoantibodies are regulated differently. Induction of autoantibodies by mineral oils considered nontoxic also may have pathogenetic implications in human autoimmune diseases.

Full Report

<http://toxsci.oxfordjournals.org/content/78/2/222.long>

Chronic Microglial Activation and Excitotoxicity Secondary to Excessive Immune Stimulation: Possible Factors in Gulf War Syndrome and Autism

Russell L. Blaylock, M.D.

Abstract

There is considerable and growing evidence that chronic microglial activation plays a major role in numerous neurological conditions including Alzheimer's dementia, Parkinson's disease, ALS, strokes, and inflammatory brain diseases. The release of toxic elements from activated microglia, such as cytokines and excitotoxins, is known to produce neurodegeneration. Peripheral immune stimulation has been shown to activate CNS microglia, and when excessive can lead to neurodegeneration and cognitive defects commonly associated with both the Gulf War Syndrome (GWS) and autism. This paper summarizes the mechanism linking these two disorders with excessive immune stimulation secondary to overvaccination.

The Role of Vaccines

As stated above, peripheral immune stimulation readily activates the brain's immune system. In most instances this is short-lived, and neuron damage is minimal. Chronic activation of microglia, however, can lead to substantial disruption of neuronal function and even neurodegeneration.

Two basic processes seem to be responsible for the chronic stimulation of brain immunity: repeated, closely spaced inoculation without allowing brain recovery, and inoculation with live viruses or contaminant organisms that persist in the brain. Gulf War veterans were given some 17 inoculations very close together. Children are often given as many as five to seven inoculations during one visit to the pediatrician's office, several as combined vaccines, such as measles-mumps-rubella (MMR).

Of particular concern is the use of live organisms and contaminant organisms. Garth Nicolson and co-workers have demonstrated polymerase chain reaction (PCR) evidence of mycoplasma species in the blood samples of Gulf War veterans suffering from ALS, the incidence of which was found to be increased by 200 percent in this population.⁴⁰ Nicolson et al. found that 83 percent of veterans with ALS had positive tests, whereas positives were rarely seen in controls. It is hypothesized that the vaccines were contaminated primarily with *Mycoplasma fermentans*. Numerous activated microglia are found in the spinal cord of affected veterans. The involvement of live *M. fermentans* could also explain the appearance of similar illnesses in other household members.

Excitotoxins contribute to the damage in central nervous system infections. Cerebrospinal fluid glutamate levels rise in bacterial meningitis, and levels are directly correlated with prognosis. Extracellular glutamate levels are elevated in all cases of viral encephalopathies, including that of the acquired immunodeficiency

syndrome (AIDS). Glutamate and aspartate levels in the plasma were also found to be elevated in 11 of 14 autistic children.⁴¹ There is also evidence that viruses can enhance the toxicity of glutamate.⁴²

Injection of the immune adjuvant lipopolysaccharide (LPS) closely resembles the vaccination process. In one study, it was shown for the first time that peripherally administered LPS decreased learning in mice.⁴³ The dose used did not produce observable injury to the neurons, but significantly impaired the animals' completing the Morris water maze and spontaneous alternation Y-maze, which tests spatial learning requiring a functional hippocampus. Associative learning was affected most. Memory retention was spared. LPS injection, by elevating IL-1 levels, has been shown to alter hippocampal norepinephrine and serotonin levels, as well as increasing glutamate levels.⁴⁴ Elevated serotonin levels have been described in autism.⁴⁵

Long-term persistent immune activation and low-grade brain inflammation have been described in three children who recovered from Herpes simplex encephalitis before age two.⁴⁶ The children all demonstrated abundant activated microglia at brain biopsy and continued to deteriorate after viral treatment, indicating continued microglial activation. Viral fragments, without active infection, can produce this phenomenon.

Not all persistent viral infections are associated with obvious inflammatory responses. Using a hamster neurotrophic strain of measles, it was found that a noninflammatory encephalopathy could occur with destruction of the CA1 and CA3 segments of the hippocampus.⁴⁷ This could more closely resemble the situation in autistic child and some cases of GWS, since obvious clinical and laboratory signs of inflammation would be absent. Neurodegeneration caused by this neurotrophic measles virus was blocked using the NMDA receptor antagonist, MK-801, indicating an excitotoxic mechanism. (The NMDA receptor is the postsynaptic receptor for L-glutamate that can be activated by the drug N-methyl-D-aspartate.)

The smallpox vaccine is associated with postvaccinal encephalitis at a rate of 1 in 110,000 vaccinations. This includes only obvious cases of encephalitis; more chronic, subtle cases involving ill-defined neurological symptoms remote from the vaccination would be overlooked. Most vaccine follow-up studies do not extend beyond two weeks. It is obvious from the above studies that this follow-up period is far too short. More persistent neurotropic viruses now being discovered appear to be related to chronic neurodegeneration. These include HSV-1, coronavirus, measles virus, and human herpes viruses 6 and 7 (HHV-6 and HHV-7). A postvaccinal encephalopathy has been described in children under age two years following the smallpox vaccine.⁴⁸ Most of these occur as chronic conditions.

Flow-cytometric analysis on adverse effects of polysorbate 80 in rat thymocytes

Author information

Hirama S1, Tatsuishi T, Iwase K, Nakao H, Umebayashi C,
Nishizaki Y, Kobayashi M, Ishida S, Okano Y, Oyama Y.

Department of Pharmaceutical Care and Clinical Pharmacy
Faculty of Pharmaceutical Sciences, Tokushima Bunri University
Tokushima 770-8514, Japan

Abstract

The effects of polysorbate 80, a non-ionic surfactant widely used in pharmaceutical products, on rat thymocytes were examined to reveal its toxic property at the cellular level. Polysorbate 80 at concentrations of 1-100 microg/ml did not significantly affect the cell viability. This surfactant at 30 microg/ml or more augmented the intensity of fluo-3 fluorescence, indicating the increase in intracellular Ca(2+) concentration. Such an augmentation of fluo-3 fluorescence by polysorbate 80 was not seen under the Ca(2+)-free condition, suggesting that polysorbate 80 increased membrane Ca(2+) permeability. The concentration-dependent polysorbate 80 at 10 microg/ml or more attenuated the intensity of 5-chloromethylfluorescein, indicating a decrease in cellular content of glutathione by polysorbate 80. Furthermore, the agent at 1 microg/ml or more attenuated the intensity of bis-(1,3-dibutylbarbituric acid) trimethine oxonol fluorescence, being independent from the changes in membrane potential. This phenomenon indicates that polysorbate 80 at 1 microg/ml or more may attenuate the incorporation of anionic compounds into the membranes. It can be suggested that polysorbate 80 modifies some of membranes and intracellular physiological parameters without affecting the cell viability.

<http://www.ncbi.nlm.nih.gov/pubmed/15147788>

“ It can be suggested
that polysorbate 80 modifies
some of membranes and
intracellular physiological
parameters without affecting
the cell viability.”

MMR vaccination and febrile seizures: evaluation of susceptible subgroups and long-term prognosis

Author information

Vestergaard M1, Hviid A, Madsen KM, Wohlfahrt J, Thorsen P, Schendel D, Melbye M, Olsen J.
The Danish Epidemiology Science Centre
Department of Epidemiology and Social Medicine
Aarhus University, Aarhus, Denmark
mv@soci.au.dk

Abstract

CONTEXT

The rate of febrile seizures increases following measles, mumps, and rubella (MMR) vaccination but it is unknown whether the rate varies according to personal or family history of seizures, perinatal factors, or socioeconomic status. Furthermore, little is known about the long-term outcome of febrile seizures following vaccination.

OBJECTIVES

To estimate incidence rate ratios (RRs) and risk differences of febrile seizures following MMR vaccination within subgroups of children and to evaluate the clinical outcome of febrile seizures following vaccination.

DESIGN, SETTING, AND PARTICIPANTS

A population-based cohort study of all children born in Denmark between January 1, 1991, and December 31, 1998, who were alive at 3 months; 537,171 children were followed up until December 31, 1999, by using data from the Danish Civil Registration System and 4 other national registries.

MAIN OUTCOME MEASURES

Incidence of first febrile seizure, recurrent febrile seizures, and subsequent epilepsy.

RESULTS

A total of 439,251 children (82%) received MMR vaccination and 17,986 children developed febrile seizures at least once; 973 of these febrile seizures occurred within 2 weeks of MMR vaccination. The RR of febrile seizures increased during the 2 weeks following MMR vaccination (2.75; 95% confidence interval [CI], 2.55-2.97), and thereafter was close to the observed RR for nonvaccinated children. The RR did not vary significantly in the subgroups of children that had been defined by their family history of seizures, perinatal factors, or socioeconomic status. At 15 to 17 months, the risk difference of febrile seizures within 2 weeks following MMR vaccination was 1.56 per 1000 children overall (95% CI, 1.44-1.68), 3.97 per 1000 (95% CI, 2.90-5.40) for siblings of children with a history of febrile seizures, and 19.47 per 1000 (95% CI, 16.05-23.55) for children with a personal history of febrile seizures. Children with febrile seizures following MMR vaccinations had a slightly increased rate of recurrent febrile seizures (RR, 1.19; 95% CI, 1.01-1.41) but no increased rate of epilepsy (RR, 0.70; 95% CI, 0.33-1.50) compared with children who were nonvaccinated at the time of their first febrile seizure.

CONCLUSIONS

MMR vaccination was associated with a transient increased rate of febrile seizures but the risk difference was small even in high-risk children. The long-term rate of epilepsy was not increased in children who had febrile seizures following vaccination compared with children who had febrile seizures of a different etiology.

“439,251

children

received MMR

vaccination and

17,986

children

developed

febrile

seizures

at least once ...”

An evaluation of serious neurological disorders following immunization: a comparison of whole-cell pertussis and acellular pertussis vaccines

Author information

Geier DA1, Geier MR.
MedCon, Inc., Silver Spring, MD 20905, USA

Abstract

Serious neurological disorders reported following whole-cell pertussis in comparison to acellular pertussis vaccines were evaluated. The Vaccine Adverse Events Reporting System (VAERS) was analyzed for Emergency Department (ED) visits, life-threatening reactions, hospitalizations, disabilities, deaths, seizures, infantile spasms, encephalitis/encephalopathy, autism, Sudden Infant Death Syndrome (SIDS) and speech disorders reported with an initial onset of symptoms within 3 days following whole-cell pertussis and acellular pertussis vaccines among those residing in the US from 1997 to 1999. Controls were employed to evaluate potential biases in VAERS. Evaluations as to whether whole-cell and acellular vaccines were administered to populations of similar age and sex were undertaken because these factors might influence the study's results. Statistical increases were observed for all events examined following whole-cell pertussis vaccination in comparison to acellular pertussis vaccination, excepting cerebellar ataxia. Reporting biases were minimal in VAERS, and whole-cell and acellular pertussis vaccines were administered to populations of similar age and sex. Biologic mechanisms for the increased reactogenicity of whole-cell pertussis vaccines may stem from the fact that whole-cell pertussis vaccines contain 3,000 different proteins, whereas DTaP contains two to five proteins. Whole-cell pertussis vaccine contains known neurotoxins including: endotoxin, pertussis toxin and adenylate cyclase. Our results, and conclusions by the US Institute of Medicine, suggest an association between serious neurological disorders and whole-cell pertussis immunization. In light of the presence of a safer and at least equally efficacious acellular pertussis vaccine alternative, the Japanese and US switch to using acellular pertussis vaccine seems well justified. Other countries using whole-cell pertussis-containing vaccines should consider following suite in the near future.

<http://www.ncbi.nlm.nih.gov/pubmed/15165669>

“... results, and conclusions by the US Institute of Medicine, suggest an association between serious neurological disorders and whole-cell pertussis immunization.”

Granuloma with
lymphocytic hyperplasia
following vaccination: 10 cases
Presence of aluminium in the biopsies

Author information

Lafaye S1, Authier FJ, Fraitag S, Rethers L, Bagot M, Wechsler J.

Département de Pathologie, Hôpital Henri Mondor,
51 avenue du Maréchal de Lattre de Tassigny
94010 Créteil, France

Abstract

BACKGROUND

Few cases of cutaneous lymphocytic hyperplasia secondary to vaccination have been published, although such lesions are not rare.

PATIENTS AND METHODS

We report a series of 10 cases registered between 1993 and 2003.

RESULTS

Mean age was 25. The clinical aspect was solitary or multiple subcutaneous nodules, located on the arm, developing after a delay of 1 to 18 months after vaccination. Histologic examination showed a lymphocytic infiltration of the subcutaneous fat, with diffuse and/or follicular pattern, without nuclear atypia, the morphological and immunohistochemical analysis of which revealed the benign nature. In all cases, there was fibrosis and granuloma composed of lymphocytes, plasma cells, eosinophils and macrophages with basophilic cytoplasm. Morin stain showed intralesional aluminium in the 6 investigated cases. Evolution was always benign, with no relapse following exeresis.

DISCUSSION

Cutaneous lymphocytic hyperplasia secondary to vaccination has to be suspected in a young patient with subcutaneous nodules appearing at a vaccination site. Evidence of aluminium in the lesions supports the diagnosis and the hypothesis that aluminium in the vaccine excipient might have a role in the onset of such lesions.

“Cutaneous lymphocytic hyperplasia secondary to vaccination has to be suspected in a young patient with subcutaneous nodules appearing at a vaccination site. Evidence of aluminium in the lesions supports the diagnosis ...”

Urinary tract diseases revealed after DTP vaccination
in infants and young children: cytokine irregularities and
down-regulation of cytochrome P-450 enzymes induced by the vaccine
may uncover latent diseases in genetically predisposed subjects

Author information

Prandota J.

Faculty of Medicine and Dentistry, University Medical School, Wroclaw, Poland
Jzef.854735@pharmanet.com.pl

Abstract

Prophylactic vaccinations may sometimes shorten the incubation period of some illnesses and/or convert a latent infection/inflammation into a clinically apparent disease. Cytokines play a major role in mediating the inflammatory process in various clinical entities and represent a potential source of tissue damage if their production is not sufficiently well controlled. It seems that irregularities in production of proinflammatory cytokines may be responsible for the abnormalities associated with full-blown clinical symptoms of various urinary tract diseases observed after DTP vaccination in 13 infants and young children hospitalized over the past 24 years. On admission, upper respiratory tract diseases, atopic dermatitis, and/or latent urinary tract infection/inflammation were found in these children. It is suggested that the whole-cell pertussis present in DTP vaccine, acting as an excessive stimulus in these patients, produced symptoms reminiscent of biologic responses to circulating proinflammatory monokines such as IL-1beta, TNF-alpha, and IL-6 because earlier it was reported that in vitro the whole-cell vaccine induced significantly more such cytokine production than did the acellular pertussis or diphtheria-tetanus-only vaccine. Analysis of the cellular immune disturbances previously reported in urinary tract infection/inflammation (increased serum and/or urinary IL-1alpha, IL-1 receptor antagonist, IL-6 and IL-8), steroid-sensitive nephrotic syndrome (increased IL-2, IFN-gamma, TNF-alpha, and decreased or increased IL-4, depending on the cells studied), and atopic dermatitis (decreased IFN-gamma and increased IL-4 production), may suggest that similar subclinical chronic cytokine-mediated abnormalities produced in the course of latent diseases revealed in our patients, combined with those caused by DTP vaccination stimulus, were responsible for the pathomechanism of these clinical entities. This speculation is in agreement with the reports on the long-lasting induction of cytokine release and down-regulation of hepatic cytochrome P-450 isoenzyme activities after administration of DTP vaccine to mice and may be supported by the fact that TH1 phenotype is associated with the up-regulation of intercellular adhesion molecule-1 and RANTES, whereas TH2 phenotype is associated with the up-regulation of the vascular cell adhesion molecule and P-selectin, which are key players in the migration into inflamed tissues and localization of lymphocytes and other allergic effector and inflammatory cells. Because several inflammatory cytokines down-regulate gene expression of major cytochrome P-450 and/or other enzymes with the specific effects on mRNA levels, protein expression, and enzyme activity, thus affecting the metabolism of several endogenous lipophilic substances such as steroids, lipid-soluble vitamins, prostaglandins, leukotrienes, thromboxanes, and exogenous substances, their irregularities in the body may eventually lead to the flare of latent diseases in some predisposed subjects. Also, interleukin genetic polymorphisms, especially the constellation of TNF-alpha and IL-6 genetic variants, might predispose some infants with infection to a more than usually intense inflammatory response in the kidneys after vaccination. It seems that the aforementioned pathomechanism may also be responsible for some cases of sudden infant death syndrome, which is often preceded by infection/inflammation.

“It seems that the aforementioned
pathomechanism may also be responsible
for some cases of sudden infant death syndrome,
which is often preceded by infection/inflammation.”

Recombinant hepatitis B vaccine and the risk of multiple sclerosis: a prospective study

Author information

Hernán MA1, Jick SS, Olek MJ, Jick H.

Department of Epidemiology
Harvard School of Public Health
677 Huntington Avenue, Boston, MA 02115, USA
miguel_hernan@post.harvard.edu

Abstract

BACKGROUND

A potential link between the recombinant hepatitis B vaccine and an increased risk of multiple sclerosis (MS) has been evaluated in several studies, but some of them have substantial methodologic limitations.

METHODS

The authors conducted a nested case-control study within the General Practice Research Database (GPRD) in the United Kingdom. The authors identified patients who had a first MS diagnosis recorded in the GPRD between January 1993 and December 2000. Cases were patients with a diagnosis of MS confirmed through examination of medical records, and with at least 3 years of continuous recording in the GPRD before their date of first symptoms (index date). Up to 10 controls per case were randomly selected, matched on age, sex, practice, and date of joining the practice. Information on receipt of immunizations was obtained from the computer records.

RESULTS

The analyses include 163 cases of MS and 1,604 controls. The OR of MS for vaccination within 3 years before the index date compared to no vaccination was 3.1 (95% CI 1.5, 6.3). No increased risk of MS was associated with tetanus and influenza vaccinations.

CONCLUSIONS

These findings are consistent with the hypothesis that immunization with the recombinant hepatitis B vaccine is associated with an increased risk of MS, and challenge the idea that the relation between hepatitis B vaccination and risk of MS is well understood.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15365133>

“These findings are consistent with the hypothesis that immunization with the recombinant hepatitis B vaccine is associated with an increased risk of MS, and challenge the idea that the relation between hepatitis B vaccination and risk of MS is well understood.”

“In this review, we discuss recent articles and controversies pertaining to vaccine-associated adverse events.”

Current Allergy And Asthma Reports • November 2004

Update on side effects from common vaccines

Author information

Song BJ1, Katial RK.

Division of Adult Allergy and Immunology
National Jewish Medical and Research Center
1400 Jackson Street, Denver, CO 80206, USA

Abstract

Vaccines have had a tremendous impact on public health by reducing morbidity and mortality from a variety of virulent pathogens. However, unintended side effects continue to pose a potential risk that may outweigh the vaccine's protective attributes. In this review, we discuss recent articles and controversies pertaining to vaccine-associated adverse events. Included in the discussion are influenza, hepatitis B, measles-mumps-rubella, diphtheria-tetanus-pertussis, polio, Haemophilus influenzae type b, and rotavirus vaccines. The importance and contribution of vaccine constituents (such as thimerosal) to side effects is also reviewed.

<http://www.ncbi.nlm.nih.gov/pubmed/15462710>

Guillain-Barré syndrome following influenza vaccination

Author information

Haber P1, DeStefano F, Angulo FJ, Iskander J, Shadomy SV, Weintraub E, Chen RT.

Immunization Safety Branch
Epidemiology and Surveillance Division
National Immunization Program
Centers for Disease Control and Prevention
Atlanta, Ga 30333, USA
PHaber@cdc.gov

Abstract

CONTEXT

An unexplained increase in the risk of Guillain-Barre syndrome (GBS) occurred among recipients of the swine influenza vaccine in 1976-1977. Guillain-Barre syndrome remains the most frequent neurological condition reported after influenza vaccination to the Vaccine Adverse Events Reporting System (VAERS) since its inception in 1990.

OBJECTIVE

To evaluate trends of reports to VAERS of GBS following influenza vaccination in adults.

DESIGN, SETTING, AND PARTICIPANTS

VAERS is the US national spontaneous reporting system for adverse events following vaccination. Reports of GBS in persons 18 years or older following influenza vaccination were evaluated for each influenza season from July 1, 1990, through June 30, 2003. The number of people vaccinated was estimated from the National Health Interview Survey and US census data. Beginning in 1994, active follow-up was conducted to verify GBS diagnosis and obtain other clinical details.

MAIN OUTCOME MEASURE

Reporting rates of GBS following influenza vaccination over time.

RESULTS

From July 1990 through June 2003, VAERS received 501 reports of GBS following influenza vaccination in adults. The median onset interval (13 days) was longer than that of non-GBS reports of adverse events after influenza vaccine (1 day) ($P < .001$). The annual reporting rate decreased 4-fold from a high of 0.17 per 100,000 vaccinees in 1993-1994 to 0.04 in 2002-2003 ($P < .001$). A GBS diagnosis was confirmed in 82% of reports. Preceding illness within 4 weeks of vaccination was identified in 24% of reported cases.

CONCLUSIONS

From 1990 to 2003, VAERS reporting rates of GBS after influenza vaccination decreased. The long onset interval and low prevalence of other preexisting illnesses are consistent with a possible causal association between GBS and influenza vaccine. These findings require additional research, which can lead to a fuller understanding of the causes of GBS and its possible relationship with influenza vaccine.

“An unexplained increase in the risk of Guillain-Barre syndrome (GBS) occurred among recipients of the swine influenza vaccine in 1976-1977. Guillain-Barre syndrome remains the most frequent neurological condition reported after influenza vaccination to the Vaccine Adverse Events Reporting System (VAERS) since its inception in 1990.”

“... the whole cell vaccine may lead to the acute encephalopathy, fever seizures, hypotonic-hyporeactive episodes, inconsolable crying or anaphylactic reactions.”

Przeegląd Epidemiologiczny • 2004

Prevention of pertussis and high expectations concerning vaccines

Author information

Wysocki J.

Katedra Profilaktyki Zdrowotnej
Akademia Medyczna im Karola Marcinkowskiego w Poznaniu

Abstract

The basic vaccine used in the prevention of pertussis is the combined vaccine including a whole cell pertussis component and tetanus and diphtheria toxoids. Although this type of vaccine has been used more than 50 years in USA and more than 40 years in Poland it is still effective what can be evidenced by the decreased number of pertussis cases since the vaccine has been implemented. There are however some evidences that the whole cell vaccine may lead to the acute encephalopathy, fever seizures, hypotonic-hyporeactive episodes, inconsolable crying or anaphylactic reactions. But still is a lack of convincing evidences that the vaccine may be a cause of persistent brain damage. It was also shown that the longer is the period after the last dose of the vaccine the lower effectiveness was observed. Improving the safety of the pertussis vaccine was the reason of introducing the acellular vaccines in the eightieth. All these products contain pertussis toxoid and some of them contain also filamentous hemagglutinin, pertactin and fimbrial agglutinogens. Some published studies have shown that the effectiveness of these vaccines is similar to the whole cells vaccines and that the incidence of some adverse events especially seizures, hypotonic-hyporeactive episodes and inconsolable crying is lower.

<http://www.ncbi.nlm.nih.gov/pubmed/15807156>

Vaccine adjuvants and macrophagic myofasciitis

Author information

Siegrist CA.

Département de pathologie
centre de vaccinologie, université de Genève
CMU, Suisse
claire-anne.siegrist@medecine.unige.ch

Abstract

Aluminium-based adjuvants have been used throughout the world since 1926, and their safety profile is such that they have long been the sole adjuvants registered for clinical use. Their safety has nevertheless been questioned in France over the last few years following the demonstration that aluminium could persist for prolonged periods at the injection site, within macrophages gathered around the muscular fibres and forming a microscopic histological lesion called “macrophagic myofasciitis (MMF)”. This image has been observed in patients undergoing a deltoid muscular biopsy for diagnostic purposes of various symptoms essentially including muscular pain and fatigue, in association with a large panel of various symptoms and diseases, including those of an autoimmune nature. Studies of the clinical, biological and epidemiological characteristics undertaken to identify a possible association between the MMF histological image and a systematic disease have remained negative. As of today, available evidence indicates that although vaccine aluminium may persist at the site of injection for years (“vaccine tattoo”), this does not reflect the existence of a diffuse inflammatory muscular disease and is not associated with a specific clinical disease. The existence of sampling bias inherent to the complexity of the clinical and pathological diagnoses remains the most likely hypothesis.

<http://www.ncbi.nlm.nih.gov/pubmed/15653065>

“Aluminium-based adjuvants have been used throughout the world since 1926, and their safety profile is such that they have long been the sole adjuvants registered for clinical use. Their safety has nevertheless been questioned in France over the last few years following the demonstration that aluminium could persist for prolonged periods at the injection site, within macrophages gathered around the muscular fibres and forming a microscopic histological lesion called “macrophagic myofasciitis (MMF)”.”

Combining vitamin A and vaccines: convenience or conflict?

Author information

Benn CS1.
Bandim Health Project, Statens Serum Institut, Copenhagen S, Denmark
cb@ssi.dk

Abstract

The present thesis is based on 11 papers from 1995-2010. The studies have mainly taken place at the Bandim Health Project in Guinea-Bissau, West Africa, but a reanalysis of a randomised trial from Ghana is also included. My research has explored the consequences of combining high-dose vitamin A supplementation and childhood vaccines. Vitamin A deficiency is associated with increased mortality. To protect against the consequences of vitamin A deficiency the World Health Organization recommends that high-dose vitamin A supplements be given together with routine vaccines to children between 6 months and 5 years of age in more than 100 low-income countries. The recommendation is based on logistical considerations. The consequences of combining vitamin A and vaccines were not investigated in randomised trials prior to the implementation of this policy - it was assumed that the interventions were independent. My first project aimed to study the effect on the immune response to measles of providing vitamin A together with measles vaccine. We found that the two interventions were not independent. Vitamin A enhanced the antibody response to measles vaccine given at 9 months of age significantly, especially in boys. The effects were sustained over time; the children who had received vitamin A with their measles vaccine were more protected against measles at 6-8 years of age. Though vitamin A supplementation had a beneficial effect on the immune response to measles vaccine, it intrigued me that the effect of vitamin A supplementation on overall mortality was not always beneficial. While vitamin A was beneficial when given after 6 months of age, and two studies had shown a beneficial effect when given at birth, all studies testing the effect between 1-5 months of age had found no effect. These time windows are dominated by three different childhood vaccines: BCG vaccine given at birth, diphtheria-tetanus-pertussis (DTP) vaccine given between 1-5 months of age, and measles vaccine given at 9 months of age. These vaccines have been shown to have strong effects on mortality from infectious diseases in general, so-called non-specific effects. The live BCG and measles vaccine protects against more mortality than can be ascribed to the prevention of tuberculosis and measles, respectively. The inactivated DTP vaccine worryingly has been associated with increased mortality from other infectious diseases. Both positive and negative effects are strongest for girls. I proposed the hypothesis that vitamin A amplifies not only the specific vaccine effects, as we saw for measles vaccine, but also the non-specific effects of vaccines on mortality from other infectious diseases. According to my hypothesis, vitamin A would enhance the non-specific beneficial effects on mortality of BCG and measles vaccine, but also the negative effects of DTP vaccine. Hence, the hypothesis offered an explanation for the mortality-age pattern after vitamin A supplementation. Since it was formulated, I have aimed to test this hypothesis. Since it is associated with ethical problems to randomise

children above 6 months of age to vitamin A supplementation, and to randomise children in general to recommended vaccines, we have had to be pragmatic when designing the trials. Hence, our studies have taken many different forms. We conducted an observational study during a vitamin A campaign in which missing vaccines were also provided, and a randomised trial testing the effect of two different doses of vitamin A during another campaign; we tested the effect of providing vitamin A with BCG at birth in two randomised trials, and we reanalysed data from one of the original randomised trials of vitamin A supplementation from the perspective of vaccination status. In all studies the main outcome was mortality. The results document that vitamin A supplements do more than protect against vitamin A deficiency. They support the hypothesis that vitamin A supplements interact with vaccines with important consequences for mortality. First, a smaller dose of vitamin A was more beneficial than a larger dose for girls. Second, the effect of vitamin A given with DTP vaccine was significantly different from the effect of vitamin A given with measles vaccine, and children, who received vitamin A with DTP vaccine, had higher mortality than children, who had received vitamin A alone, or who did not receive anything. Third, vitamin A given with BCG at birth interacted negatively with subsequent DTP vaccines in girls. Fourth, the effect of vitamin A to older children in Ghana depended on vaccination status, being beneficial in boys, but harmful in girls who received DTP vaccine during follow-up. The results also show that boys and girls respond differently to vitamin A and vaccines. It is a common assumption within public health in low-income countries that interventions can be combined without producing unexpected consequences. The work presented in this thesis confronts this assumption; the results show that vitamin A and vaccines should be seen not only as specific interventions with specific and independent effects, but as immuno-modulators, which can interact with important consequences for overall mortality. Combining interventions can be convenient and lead to synergistic health benefits, but we documented several examples, where it also leads to unexpectedly increased mortality. Thus, to optimise the child health intervention policy in low-income countries a shift in paradigm is needed. Health interventions should no longer be seen as merely specific and independent, and the policy should probably not be the same for boys and girls. Though more complex, it is necessary to evaluate all health interventions in terms of their effect on overall mortality - and their potential interactions with other health interventions and potential sex-differential effects should always be investigated. Only in this way can we assure that the children in the poorest countries get the best possible treatment and avoid using large amounts of money and resources on interventions which may, in worst case, kill them.

“In all studies the main outcome was mortality. The results document that vitamin A supplements do more than protect against vitamin A deficiency. They support the hypothesis that vitamin A supplements interact with vaccines with important consequences for mortality. First, a smaller dose of vitamin A was more beneficial than a larger dose for girls. Second, the effect of vitamin A given with DTP vaccine was significantly different from the effect of vitamin A given with measles vaccine, and children, who received vitamin A with DTP vaccine, had higher mortality than children, who had received vitamin A alone, or who did not receive anything. Third, vitamin A given with BCG at birth interacted negatively with subsequent DTP vaccines in girls. Fourth, the effect of vitamin A to older children in Ghana depended on vaccination status, being beneficial in boys, but harmful in girls who received DTP vaccine during follow-up. The results also show that boys and girls respond differently to vitamin A and vaccines. It is a common assumption within public health in low-income countries that interventions can be combined without producing unexpected consequences. The work presented in this thesis confronts this assumption; the results show that vitamin A and vaccines should be seen not only as specific interventions with specific and independent effects, but as immuno-modulators, which can interact with important consequences for overall mortality. Combining interventions can be convenient and lead to synergistic health benefits, but we documented several examples, where it also leads to unexpectedly increased mortality.”

Routine vaccinations
associated with divergent effects on female and male mortality
at the paediatric ward in Bissau, Guinea-Bissau

Author information

Veirum JE1, Sodemann M, Biai S,
Jakobsen M, Garly ML, Hedegaard K, Jensen H, Aaby P.

Projecto de Saúde de Bandim, Apartado 861
Bissau, Guinea-Bissau

Abstract

Several studies have suggested that routine childhood immunisations may have non-specific effects on mortality. To examine which disease categories might be affected, we investigated whether immunisation status had an impact on the case fatality for hospitalised children. Between 1990 and 1996, the Bandim Health Project maintained a register of all children from the study area hospitalised at the paediatric ward of the central hospital in Bissau, Guinea-Bissau. The study included 2079 hospitalised children aged 1.5-17 months coming from the Bandim study area. Among children whose vaccination card had been seen at admission, the case fatality ratio for measles-vaccinated children versus measles-unvaccinated children was 0.51 (0.27-0.98), the beneficial effect being significantly stronger for girls than for boys (test of interaction, $p=0.050$). The protective effect of measles vaccine remained unchanged when hospitalised measles cases were excluded from the analysis (0.49 (0.26-0.94)). The effect of measles vaccine was strongest for children with pneumonia (MR=0.28 (0.07-0.91)) and presumptive malaria (MR=0.40 (0.13-1.18)). For measles-vaccinated children, the female to male case fatality ratio was 0.54 (0.28-0.97). Among children having received diphtheria-tetanus-pertussis (DTP) and oral polio (OPV) as the last vaccines, girls had higher case fatality than boys, the mortality ratio being 1.63 (1.03-2.59). The female to male ratios were significantly inversed for DTP and OPV versus measles vaccine (test of interaction, $p=0.003$). These results remained unchanged if 1-month post-discharge deaths were included in the analysis, and in multivariate analyses controlling for determinants of mortality. In conclusion, measles vaccine was associated with reduced mortality from diseases other than measles, the beneficial effect being stronger for girls than for boys. On the other hand, DTP and OPV vaccine were associated with higher case fatality for girls than for boys. Understanding the divergent non-specific effects of common vaccines may contribute to better child survival in developing countries.

<http://www.ncbi.nlm.nih.gov/pubmed/15629363>

“Diphtheria-Tetanus-Pertussis
and Oral Polio Vaccine were associated
with higher case fatality for girls than for boys.”

Viruses as adjuvants for autoimmunity: evidence from Coxsackievirus-induced myocarditis

Author information

Fairweather D1, Frisancho-Kiss S, Rose NR.

The Department of Pathology
Johns Hopkins School of Medicine
Baltimore, MD 21205, USA

Abstract

Adjuvants historically are considered to stimulate immune responses ‘non-specifically’. Recently, a renewed understanding of the critical role of innate immunity in influencing the development of an adaptive immune response has led researchers to a better understanding of ‘the adjuvant effect’. Although innate immune cells do not respond to specific antigenic epitopes on pathogens, they do produce restricted responses to particular classes of pathogens via pattern recognition receptors such as Toll-like receptors (TLR). Coxsackievirus infection was found to upregulate TLR4 on mast cells and macrophages immediately following infection. Although both susceptible and resistant mice produce a mixture of Th1 and Th2 cytokines, susceptible mice have increased levels of key proinflammatory cytokines, increased numbers of mast cells, and go on to develop chronic autoimmune heart disease. TLR4 signaling also increases acute myocarditis and proinflammatory cytokines in the heart. Many similarities are described in the pathogenesis of Coxsackievirus and the adjuvant-induced model of myocarditis including upregulation of particular TLRs and cytokines soon after inoculation. Recent findings suggest that mast cell activation by viruses or adjuvants may be important in initiating autoimmune disease.

<http://www.ncbi.nlm.nih.gov/pubmed/15386590>

“... mast cell activation by viruses or adjuvants may be important in initiating autoimmune disease.”

Autoimmune hazards of hepatitis B vaccine

Author information

Girard M1.

1 bd de la République 78000-Versailles, France
agosgirard@aol.com

Abstract

According to Hippocratic tradition, the safety level of a preventive medicine must be very high, as it is aimed at protecting people against diseases that they may not contract. This paper points out that information on the safety of hepatitis B vaccine (HBV) is biased as compared to classical requirements of evidence-based medicine (EBM), as exemplified by a documented selectivity in the presentation or even publication of available clinical or epidemiological data. Then, a review is made of data suggesting that HBV is remarkable by the frequency, the severity and the variety of its complications, some of them probably related to a mechanism of molecular mimicry leading to demyelinating diseases, and the others reproducing the spectrum of non-hepatic manifestations of natural hepatitis B. To be explained, this unusual spectrum of toxicity requires additional investigations based upon complete release of available data.

<http://www.ncbi.nlm.nih.gov/pubmed/15722255>

“... a review is made of data suggesting that Hepatitis B Vaccine is remarkable by the frequency, the severity and the variety of its complications, some of them probably related to a mechanism of molecular mimicry leading to demyelinating diseases, and the others reproducing the spectrum of non-hepatic manifestations of natural hepatitis B.”

“Result suggests that polysorbate 80 (at clinically-relevant concentrations)
may increase the susceptibility of cells to oxidative stress.”

Toxicology • February 2005

**Polysorbate 80
increases the susceptibility to oxidative stress in rat thymocytes**

Author information

Tatsuishi T1, Oyama Y, Iwase K, Yamaguchi JY,
Kobayashi M, Nishimura Y, Kanada A, Hiramasa S.

Laboratory of Cellular Signaling
Faculty of Integrated Arts and Sciences
The University of Tokushima
Tokushima 770-8502, Japan

Abstract

Effect of simultaneous application of polysorbate 80, a nonionic surfactant widely used in pharmaceutical products, and hydrogen peroxide on rat thymocytes was examined to see if polysorbate 80 increases the susceptibility to oxidative stress because this surfactant decreases the cellular content of glutathione. Polysorbate 80 at clinically-relevant concentrations increases the cytotoxicity of hydrogen peroxide under the in vitro condition. Result suggests that polysorbate 80 may increase the susceptibility of cells to oxidative stress.

<http://www.ncbi.nlm.nih.gov/pubmed/15590117>

Vaccination-induced cutaneous pseudolymphoma

Author information

Maubec E1, Pinguier L, Viguier M, Caux F,
Amsler E, Aractingi S, Chafi H, Janin A, Cayuela JM,
Dubertret L, Authier FJ, Bachelez H.

Institut de Recherche sur la Peau
Université Paris 7, Paris, France

Abstract

BACKGROUND

Although mild early cutaneous transient reactions to vaccinations are common, late-onset chronic lesions have been scarcely reported. We report herein a series of 9 patients presenting with cutaneous and subcutaneous pseudolymphoma.

OBSERVATIONS

Nine patients presenting with late-onset, chronic skin lesions occurring at the site of antihepatitis B (8 cases) and antihepatitis A (one case) vaccination were reported. Histopathologic and immunohistochemical studies, and molecular analysis of clonality of skin biopsy specimens, were performed. Furthermore, the presence of vaccine products was investigated in skin lesions by using histochemical, microanalytic, and electronic microscopy techniques.

RESULTS

Histopathologic studies showed dermal and hypodermal lymphocytic follicular infiltrates with germinal center formation. The center of follicles was mostly composed of B cells without atypia, whereas CD4+ T cells were predominant at the periphery. Molecular analysis of clonality revealed a polyclonal pattern of B-cell and T-cell subsets. Aluminium deposits were evidenced in all cases by using histochemical staining in all cases, and by microanalysis and ultrastructural studies in one case. Associated manifestations were vitiligo (one case) and chronic fatigue with myalgia (two cases).

CONCLUSION

Cutaneous lymphoid hyperplasia is a potential adverse effect of vaccinations including aluminium hydroxide as an adjuvant. Further prospective studies are warranted to evaluate the incidence of this complication in the immunized population.

“Cutaneous lymphoid hyperplasia
is a potential adverse effect of vaccinations
including aluminium hydroxide as an adjuvant.”

Infection, vaccines and other environmental triggers of autoimmunity

Author information

Molina V1, Shoenfeld Y.

Department of Medicine B and The Center for Autoimmune Diseases
Sheba Medical Center, Tel-Hashomer, Israel

Abstract

The etiology of autoimmune diseases is still not clear but genetic, immunological, hormonal and environmental factors are considered to be important triggers. Most often autoimmunity is not followed by clinical symptoms unless an additional event such as an environmental factor favors an overt expression. Many environmental factors are known to affect the immune system and may play a role as triggers of the autoimmune mosaic. Infections: bacterial, viral and parasitic infections are known to induce and exacerbate autoimmune diseases, mainly by the mechanism of molecular mimicry. This was studied for some syndromes as for the association between SLE and EBV infection, pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection and more. Vaccines, in several reports were found to be temporally followed by a new onset of autoimmune diseases. The same mechanisms that act in infectious invasion of the host, apply equally to the host response to vaccination. It has been accepted for diphtheria and tetanus toxoid, polio and measles vaccines and GBS. Also this theory has been accepted for MMR vaccination and development of autoimmune thrombocytopenia, MS has been associated with HBV vaccination. Occupational and other chemical exposures are considered as triggers for autoimmunity. A debate still exists about the role of silicone implants in induction of scleroderma like disease. Not only foreign chemicals and agents have been associated with induction of autoimmunity, but also an intrinsic hormonal exposure, such as estrogens. This might explain the sexual dimorphism in autoimmunity. Better understanding of these environmental risk factors will likely lead to explanation of the mechanisms of onset and progression of autoimmune diseases and may lead to effective preventive involvement in specific high-risk groups. So by diagnosing a new patient with autoimmune disease a wide anamnesis work should be done.

<http://www.ncbi.nlm.nih.gov/pubmed/16126512>

“The same mechanisms that act in infectious invasion of the host, apply equally to the host response to vaccination. It has been accepted for diphtheria and tetanus toxoid, polio and measles vaccines and Guillain Barre Syndrome. Also this theory has been accepted for MMR vaccination and development of autoimmune thrombocytopenia, Multiple Sclerosis has been associated with HBV vaccination.”

Neurodegenerative memory disorders: a potential role of environmental toxins

Author information

Caban-Holt A1, Mattingly M, Cooper G, Schmitt FA.

Sanders-Brown Center on Aging
University of Kentucky Medical Center
Lexington, KY 40536, USA

Abstract

The hypothesis that neurotoxins may play a role in neurodegenerative disorders remains an elusive one, given that epidemiologic studies often provide conflicting results. Although these conflicting results may result from methodological differences within and between studies, the complexity of chemical disruption of the central nervous system cannot be ignored in attempts to evaluate this hypothesis in different neurodegenerative disorders. Spencer provides a detailed review of the complex processes involved in defining the neurotoxic potential of naturally occurring and synthetic agents. Even concepts such as exposure and dose, as often reported in studies attempting to evaluate the risk imparted by a potential compound, can be deceptive. For example, although dose reflects “that amount of chemical transferred to the exposed subject”, factors such as time and concentration in the organism, the ability to access the central nervous system, and how a compound reaches the central nervous system (routes of administration) or secondarily affects other organ systems leading to central nervous system disruption are clearly important to the concept of neurotoxic risk in neurodegenerative disorders. These factors would appear to explain the observed disagreements between studies using animal or neuronal models of neurotoxicity and population-based studies in humans. The importance of these factors and how a potential neurotoxin is investigated are clearly seen in the data on AD and aluminum. In contrast, the impact of MTPT on the central nervous system is more direct and compelling. Added complexity in the study of neurotoxins in human neurodegeneration is derived from data showing that agents may have additive, potentiating, synergistic, or antagonistic effects. Therefore, data from studies evaluating EMF risks could be readily confounded by the presence or absence of heavy metals (eg, arc welding). Other factors that may conceal neurotoxic causes for a given disorder focus on additional features such as genetic predispositions, physiologic changes that occur in aging, and even nutritional status that can support or hinder the affect of a given agent on the central nervous system. Finally, many studies that investigate exposure risk do not readily incorporate the five criteria proposed by Schaumburg for establishing causation. For example, if we apply Schaumburg’s first criterion, epidemiologic studies often determines the presence of an agent through history, yet they cannot readily confirm exposure based on environmental or clinical chemical analyses to fulfill this criterion for causation. Additional limitations in research design along with the populations and methods that are used to study neurotoxins in human neurodegenerative disorders often fail to meet other criteria such as linking the severity and onset with duration and exposure level. Therefore, although studies of agents such as MTPT provide compelling models of neurotoxins and neurodegeneration in humans, disorders such as ALS, PD, and particularly AD will require additional effort if research is to determine the contribution (presence or absence) of neurotoxins to these neurologic disorders.

“Added complexity
in the study of neurotoxins
in human neurodegeneration
is derived from data showing that
agents may have additive, potentiating,
synergistic, or antagonistic effects.”

Vaccination alone or in combination with
pyridostigmine promotes and prolongs activation of
stress-activated kinases induced by
stress in the mouse brain

Author information

Wang D1, Perides G, Liu YF.

Department of Pharmacology
Boston University School of Medicine
Massachusetts 02118, USA

Abstract

Gulf war illnesses (GWI) are currently affecting thousands of veterans. To date, the molecular mechanisms underlying the pathogenesis of these illnesses remain unknown. During Gulf war I, military personnel were exposed to multiple stressors, one or more vaccines, pyridostigmine (PY), and other chemicals. In our previous studies, we found that stress induces activation of mitogen activated protein-kinase kinase 4 (MKK4) and c-Jun-N-terminal kinase (JNK) in the mouse brain (Liu et al. 2004). Our working hypothesis is that stress, vaccination, and PY may synergistically induce activation of MKK4 and JNK in the brain, leading to over-activation of these kinases and neurological injuries. To test our hypothesis, we examined the effect of keyhole limpet hemocyanin (KLH) immunization alone or in combination with PY on activation of MKK4 and JNK induced by stress. We found that KLH immunization alone had a small effect on MKK4 or JNK activity but it significantly enhanced and prolonged activation of these kinases induced by stress, from a few hours to several days. Additionally, KLH immunization caused activation of p38MAPK. PY treatment further enhanced and prolonged activation of these kinases induced by stress in combination with KLH immunization and triggered activation of caspase-3. Our current studies suggest that stress, vaccination, and PY may synergistically act on multiple stress-activated kinases in the brain to cause neurological impairments in GWI.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15857404>

“Our current studies suggest that stress, vaccination, and pyridostigmine may synergistically act on multiple stress-activated kinases in the brain to cause neurological impairments in Gulf War Illness.”

Effect of formaldehyde on energy metabolism in postnatal rat cortex neurons in culture

Author information

Liu T1, Bai XT.

Department of Toxicology
Institute of Environment Health and Related Product Safety
China CDC, Beijing 100021, China

Abstract

OBJECTIVE:

The mechanism of the effect of formaldehyde on CNS which is much concerned to formaldehyde poisoning was studied.

METHODS:

In the present study, incubation of postnatal rat cortex neurons in culture with formaldehyde at 1, 2, 4, 8 mg/L (medium) was carried out to evaluate the effect of formaldehyde on energy metabolism.

RESULTS:

The result of cytochemistry showed a significant down-regulation of cytochrome oxidase activity after consecutive formaldehyde treatment for 4 hours compared with the control ($P < 0.01$), the significant dosage-response relationship was also observed (R value is - 0.92, $P < 0.01$).

CONCLUSION:

The result demonstrates that excessive exposure of formaldehyde can decrease cytochrome oxidase activity in cortex neurons which indicates energy metabolism will be decreased and therefore normal physiology function would be damaged.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16111027>

“The result demonstrates that excessive exposure of formaldehyde can decrease cytochrome oxidase activity in cortex neurons which indicates energy metabolism will be decreased and therefore normal physiology function would be damaged.”

**A case-control study
of serious autoimmune adverse events
following hepatitis B immunization**

Author information

Geier DA1, Geier MR.
MedCon, Inc., Silver Spring, MD 20905, USA

Abstract

Hepatitis B infection is one of the most important causes of acute and chronic liver disease. During the 1980s, genetically engineered hepatitis B vaccines (HBVs) were introduced in the United States. A large-series of serious autoimmune conditions have been reported following HBVs, despite the fact that HBVs have been reported to be “generally well-tolerated.” A case-control epidemiological study was conducted to evaluate serious autoimmune adverse events prospectively reported to the vaccine adverse events reporting system (VAERS) database following HBVs, in comparison to an age, sex, and vaccine year matched unexposed tetanus-containing vaccine (TCV) group for conditions that have been previously identified on an a priori basis from case-reports. Adults receiving HBV had significantly increased odds ratios (OR) for multiple sclerosis (OR = 5.2, $p < 0.0003$, 95% Confidence Interval (CI) = 1.9 - 20), optic neuritis (OR = 14, $p < 0.0002$, 95% CI = 2.3 - 560), vasculitis (OR = 2.6, $p < 0.04$, 95% CI = 1.03 - 8.7), arthritis (OR = 2.01, $p < 0.0003$, 95% CI = 1.3 - 3.1), alopecia (OR = 7.2, $p < 0.0001$, 95% CI = 3.2 - 20), lupus erythematosus (OR = 9.1, $p < 0.0001$, 95% CI = 2.3 - 76), rheumatoid arthritis (OR = 18, $p < 0.0001$, 95% CI = 3.1 - 740), and thrombocytopenia (OR = 2.3, $p < 0.04$, 95% CI = 1.02 - 6.2) in comparison to the TCV group. Minimal confounding or systematic error was observed. Despite the negative findings of the present study regarding the rare serious adverse effects of HBVs, it is clear that HBV does, indeed, offer significant benefits, but it is also clear that chances of exposure to hepatitis B virus in adults is largely life-style dependent. Adults should make an informed consent decision, weighing the risks and benefits of HBV, as to whether or not to be immunized.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16206512>

“Adults receiving
Hepatitis B Vaccine
had significantly increased
odds ratios (OR) for
multiple sclerosis ...
optic neuritis ...
vasculitis ...
arthritis ...
alopecia ...
lupus erythematosus ...
rheumatoid arthritis and
thrombocytopenia”

Meeting report:
summary of IARC monographs
on formaldehyde, 2-butoxyethanol,
and 1-tert-butoxy-2-propanol

Author information

Cogliano VJ1, Grosse Y, Baan RA, Straif K,
Secretan MB, El Ghissassi F; Working Group for Volume 88

International Agency for Research on Cancer
Lyon, France

Abstract

An international, interdisciplinary working group of expert scientists met in June 2004 to develop IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans (IARC Monographs) on formaldehyde, 2-butoxyethanol, and 1-tert-butoxy-2-propanol. Each IARC Monograph includes a critical review of the pertinent scientific literature and an evaluation of an agent's potential to cause cancer in humans. After a thorough discussion of the epidemiologic, experimental, and other relevant data, the working group concluded that formaldehyde is carcinogenic to humans, based on sufficient evidence in humans and in experimental animals. In the epidemiologic studies, there was sufficient evidence that formaldehyde causes nasopharyngeal cancer, "strong but not sufficient" evidence of leukemia, and limited evidence of sinonasal cancer. The working group also concluded that 2-butoxyethanol and 1-tert-butoxy-2-propanol are not classifiable as to their carcinogenicity to humans, each having limited evidence in experimental animals and inadequate evidence in humans. These three evaluations and the supporting data will be published as Volume 88 of the IARC Monographs.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16140628>

“there was sufficient evidence
that formaldehyde causes
nasopharyngeal cancer,
“strong but not sufficient” evidence
of leukemia, and limited evidence
of sinonasal cancer.”

Vaccines for measles, mumps and rubella in children

Author information

Demicheli V1, Jefferson T, Rivetti A, Price D.
Servizio Sovrazonale di Epidemiologia, ASL 20
Via Venezia 6, Alessandria, Piemonte, Italy 15100
demichelivittorio@asl20.piemonte.it

Abstract

BACKGROUND

Public debate over the safety of the trivalent measles, mumps and rubella (MMR) vaccine, and the resultant drop in vaccination rates in several countries, persists despite its almost universal use and accepted effectiveness.

OBJECTIVES

We carried out a systematic review to assess the evidence of effectiveness and unintended effects associated with MMR.

SEARCH STRATEGY

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 4, 2004), MEDLINE (1966 to December 2004), EMBASE (1974 to December 2004), Biological Abstracts (from 1985 to December 2004), and Science Citation Index (from 1980 to December 2004). Results from reviews, handsearching and from the consultation of manufacturers and authors were also used.

SELECTION CRITERIA

Eligible studies were comparative prospective or retrospective trials testing the effects of MMR compared to placebo, do-nothing or a combination of measles, mumps and rubella antigens on healthy individuals up to 15 years of age. These studies were carried out or published by 2004.

DATA COLLECTION AND ANALYSIS

We identified 139 articles possibly satisfying our inclusion criteria and included 31 in the review.

MAIN RESULTS

MMR was associated with a lower incidence of upper respiratory tract infections, a higher incidence of irritability, and similar incidence of other adverse effects compared to placebo. The vaccine was likely to be associated with benign thrombocytopenic purpura, parotitis, joint and limb complaints, febrile convulsions within two weeks of vaccination and aseptic meningitis (mumps) (Urabe strain-containing MMR). Exposure to MMR was unlikely to be associated with Crohn's disease, ulcerative colitis, autism or aseptic meningitis (mumps) (Jeryl-Lynn strain-containing MMR). We could not identify studies assessing the effectiveness of MMR that fulfilled our inclusion criteria even though the impact of mass immunisation on the elimination of the diseases has been largely demonstrated.

AUTHORS' CONCLUSIONS

The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate. The evidence of adverse events following immunisation with MMR cannot be separated from its role in preventing the target diseases.

<http://www.ncbi.nlm.nih.gov/pubmed/16235361>

“The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate. The evidence of adverse events following immunisation with MMR cannot be separated from its role in preventing the target diseases.”

Anti-phospholipid antibodies following vaccination with recombinant hepatitis B vaccine

Author information

Martinuc Porobic J1, Avcin T, Bozic B, Kuhar M, Cucnik S, Zupancic M, Prosenec K, Kveder T, Rozman B.

Department of Allergology
Rheumatology and Clinical Immunology
University Children's Hospital Ljubljana, Slovenia

Abstract

This study was undertaken to evaluate the possible role of hepatitis B recombinant vaccine inducing the synthesis of IgG and IgM anti-cardiolipin antibodies (aCL), antibodies against beta(2)GPI (anti-beta(2)GPI), lupus anti-coagulant (LA), anti-nuclear antibodies and antibodies against extractable nuclear antigens (anti-ENA). The study population consisted of 85 healthy students (63 female, 22 male; mean age 20.8 years), vaccinated with three doses of recombinant DNA hepatitis B vaccine. One month after vaccination with the first dose of hepatitis B vaccine a minority of vaccinated individuals showed changes in IgG or IgM aCL or anti-beta(2)GPI or LA activity ($P < 0.001$). Among subjects in whom changes of IgG anti-beta(2)GPI were observed, a significantly higher number of increased (8/85) than decreased (2/85) values were found ($P < 0.01$). Analyses of paired data showed that differences in aCL or anti-beta(2)GPI levels before vaccination or 1 month later did not reach statistical significance. In two people aCL transitorily reached medium positivity after the first dose of hepatitis B vaccine with a drop 5 months later. Similar evident anti-beta(2)GPI fluctuation was also observed in one person. Another participant was initially low positive for IgG anti-beta2GPI and the levels were increasing after vaccination. Two participants became positive for anti-nuclear antibodies during 6 months' follow-up. There were no sex-dependent differences in tested antibodies observed and no associations between levels of aPL and levels of anti-HBV antibodies. We conclude that HBV can induce aPL, although rarely. In genetically susceptible individuals or together with some other triggers such combination might confer the risk of developing a continuous autoimmune response in an individual.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1809502/>

“ In genetically susceptible individuals or together with some other triggers such combination might confer the risk of developing a continuous autoimmune response in an individual.”

Editors Note:

aPL or Antiphospholipid Syndrome

Antiphospholipid syndrome or antiphospholipid antibody syndrome (APS or APLS), or often also Hughes syndrome, is an autoimmune, hypercoagulable state caused by antiphospholipid antibodies. APS provokes blood clots (thrombosis) in both arteries and veins as well as pregnancy-related complications such as miscarriage, stillbirth, preterm delivery, and severe preeclampsia.

Antiphospholipid syndrome can be primary or secondary. Primary antiphospholipid syndrome occurs in the absence of any other related disease. Secondary antiphospholipid syndrome occurs with other autoimmune diseases, such as systemic lupus erythematosus (SLE). In rare cases, APS leads to rapid organ failure due to generalised thrombosis; this is termed “catastrophic antiphospholipid syndrome” (CAPS) and is associated with a high risk of death.

Antiphospholipid syndrome often requires treatment with anticoagulant medication such as heparin to reduce the risk of further episodes of thrombosis and improve the prognosis of pregnancy. Warfarin/Coumadin is not used during pregnancy because it can cross the placenta, unlike heparin, and is teratogenic.

Macrophagic myofasciitis in childhood: a controversial entity

Author information

Rivas E1, Gómez-Arnáiz M, Ricoy JR, Mateos F,
Simón R, García-Peñas JJ, Garcia-Silva MT, Martín E,
Vázquez M, Ferreiro A, Cabello A.

Department of Pathology, Neuropathology Section
Hospital Universitario 12 de Octubre, Madrid, Spain

Abstract

Macrophagic myofasciitis is an unusual inflammatory myopathy, which has been almost exclusively reported in French adults with diffuse arthromyalgias and asthenia. It is characterized by an infiltrate of densely packed macrophages, with granular periodic-acid-Schiff positive content, on muscle biopsies at the site of vaccination. The presence of aluminum inclusions in these macrophages points to an inappropriate reaction to aluminum used as an adjuvant in some vaccines. Although in adults this entity is well defined, less than 15 cases have been reported in children. This study describes seven children, younger than 3 years of age, with typical lesions of macrophagic myofasciitis on quadriceps muscle biopsy. In five cases, biopsies were performed to exclude mitochondrial pathology. All the children developed hypotonia and motor or psychomotor delay, associated with others symptoms. Abnormal neuroimaging was evident in six cases. Spectrometry studies detected elevated levels of aluminum in muscle in three of four cases tested. Despite the wide use of vaccines in childhood, macrophagic myofasciitis was rarely observed in children and its characteristic histologic pattern could not be correlated with a distinctive clinical syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16243223>

“Although in adults this entity is well defined,
less than 15 cases have been reported in children.
This study describes seven children, younger than 3
years of age, with typical lesions of macrophagic
myofasciitis on quadriceps muscle biopsy.”

Nineteen cases
of persistent pruritic nodules and contact allergy
to aluminium after injection of commonly used
aluminium-adsorbed vaccines

Author information

Bergfors E1, Björkelund C, Trollfors B.

Department of Primary Health Care
Göteborg University, Box 454
40530 Gothenburg, Sweden
elisabet.bergfors@allmed.gu.se

Abstract

Rare cases of persistent pruritic nodules, sometimes associated with aluminium (Al) allergy, have been reported after the use of several Al adsorbed vaccines. During vaccine trials in the 1990s a high incidence of pruritic nodules (645 cases/76,000 recipients), in 77% associated with Al allergy, was observed after the administration of diphtheria-tetanus / acellular pertussis (DT/aP) vaccines from a single producer. In the present report 19 children with pruritic nodules after vaccination with Al hydroxide-adsorbed DTaP/polio+Hib (Infanrix, Pentavac) are described. The children had intensely itching nodules at the injection site, often aggravated during upper respiratory tract infections, and local skin alterations. So far, the symptoms have persisted for up to 7 years. The median time between vaccination and onset of symptoms was 1 month. 16 children were epicutaneously tested for Al, all with positive reactions indicating delayed hypersensitivity to Al. The condition is not commonly known but is important to recognise, as the child and the family may suffer considerably. Future vaccinations with Al-adsorbed vaccines may cause aggravation of the symptoms and the Al allergy. Al-containing skin products, such as antiperspirants, may cause contact dermatitis. Nodules may be mistaken for tumours. Even though the incidence of itching nodules and Al allergy after administration of Infanrix, Pentavac and other Al-adsorbed vaccines is probably low, research to replace Al adjuvants seems appropriate. We conclude that intensely itching subcutaneous nodules, lasting for many years, and hypersensitivity to aluminium may occur after DTaP/polio+Hib vaccination of infants.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16044278>

“... intensely itching subcutaneous nodules,
lasting for many years, and hypersensitivity to
aluminium may occur after DTaP/polio + Hib
vaccination of infants.”

Do cytosine guanine dinucleotide (CpG) fragments induce vasoactive neuropeptide mediated fatigue-related autoimmune disorders?

Author information

Staines DR.

Gold Coast Public Health Unit
10-12 Young Street, Southport 4215
Qld., Australia
don_staines@health.qld.gov.au

Abstract

Autoimmune dysfunction of certain vasoactive neuropeptides (e.g., vasoactive intestinal peptide, pituitary adenylate cyclase activating polypeptide) may be implicated in a range of disorders associated with fatigue-like states (chronic fatigue syndrome, Gulf War syndrome) and even sudden infant death syndrome (SIDS). The important roles of these vasoactive neuropeptides make them a vulnerable target for autoimmune dysfunction. They are known to be associated with heat shock proteins for intracellular functioning with which they may form immunostimulating complexes. Cytosine guanine dinucleotide (CpG) fragments are potentially immunogenic DNA fragments which serve as friend or foe recognition systems between bacterial (hypomethylated) and mammalian (methylated) DNA and are being assessed for suitability for use in human vaccines as adjuvants. Interactions between CpG fragments, heat shock proteins and vasoactive neuropeptides may be associated with fatigue-related autoimmune conditions.

<http://www.ncbi.nlm.nih.gov/pubmed/15922114>

“Interactions between CpG fragments, heat shock proteins and vasoactive neuropeptides may be associated with fatigue-related autoimmune conditions.”

“In this study, 24.5% of asymptomatic children from 6 months to 5 years of age were sensitized to one or more contact allergens, and thimerosal was the second most prevalent allergen ...”

Dermatitis • 2005

Hypersensitivity Reactions to Vaccine Components

Noushin Heidary; David E. Cohen

Department of Dermatology and Allergic, Occupational and Environmental Dermatology
New York University School of Medicine, New York, NY

Excerpt

This article will review adverse cutaneous events consistent with hypersensitivity reactions to the following ingredients in vaccines: aluminum, thimerosal, 2-phenoxyethanol, formaldehyde, and neomycin.

Despite the low clinical relevance of thimerosal allergy, the rate of thimerosal sensitivity has increased during the last decade, probably because of the increase in vaccines administered during infancy. With the initiation of a mass vaccination campaign in Austria in 1981, the administration of thimerosal-containing vaccines for tick-borne encephalitis (TBE) increased from 6% in 1980 to 86% in 2001. The growing number of people immunized to TBE has been concomitant with an increase in thimerosal-sensitized individuals in Austria.[14,20]

Bruckner and colleagues investigated the prevalence of positive patch-test results using the TRUE Test system (Mekos Laboratories A/S, Hillerød, Denmark) on children under 5 years of age to determine whether sensitization to contact allergens was common in infancy.[21]

In this study, 24.5% of asymptomatic children from 6 months to 5 years of age were sensitized to one or more contact allergens, and thimerosal was the second most prevalent allergen (after nickel). Vaccines thus appear to sensitize children to thimerosal at a younger age than expected, given the unlikelihood of contact exposure in this age group to other thimerosal-containing products. Osawa and colleagues also demonstrated this phenomenon by associating DTP vaccination with thimerosal sensitivity in a guinea pig model.[22]

To determine whether patients with thimerosal allergy could tolerate vaccination, Audicana and colleagues evaluated tolerance to thimerosal-containing vaccines in 125 patients sensitized to mercury derivatives and/or thimerosal.[23] Patch-test results in this patient population revealed that 45% of patients had positive reactions to thimerosal (0.05% in petrolatum), 74% had positive reactions to metallic mercury (0.5% in petrolatum), and 70% had positive reactions to mercury chloride (0.1% in water). In 10 cases, of all mercury derivatives tested, thimerosal yielded the only positive patch-test result. A questionnaire revealed that the likely source of sensitization in the 57 thimerosal patch-test-positive patients was vaccination.

Full Report

<http://www.medscape.com/viewarticle/516045>

Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination: another pathology in suspected SIDS?

Author information

Ottaviani G1, Lavezzi AM, Maturri L.

Institute of Pathology, University of Milan
Via della Commenda 19, Milan 20122, Italy

Abstract

Experts from panels of the European Agency for the Evaluation of Medical Products have investigated whether there might be a link between hexavalent vaccines and some cases of deaths that occurred. Participants included pathologists with experience in the field of vaccines and sudden infant death syndrome who conducted autopsies. However, to the best of our knowledge, little, if any, attention was paid to examination of the brainstem and the cardiac conduction systems on serial sections, nor was the possibility of a triggering role of the vaccine in these deaths considered. Herein we report the case of a 3-month-old female infant dying suddenly and unexpectedly shortly after being given a hexavalent vaccination. Examination of the brainstem on serial sections revealed bilateral hypoplasia of the arcuate nucleus. The cardiac conduction system presented persistent fetal dispersion and resorptive degeneration. This case offers a unique insight into the possible role of hexavalent vaccine in triggering a lethal outcome in a vulnerable baby. Any case of sudden unexpected death occurring perinatally and in infancy, especially soon after a vaccination, should always undergo a full necropsy study according to our guidelines.

<http://www.ncbi.nlm.nih.gov/pubmed/16231176>

“This case offers a unique insight into the possible role of hexavalent vaccine in triggering a lethal outcome in a vulnerable baby. Any case of sudden unexpected death occurring perinatally and in infancy, especially soon after a vaccination, should always undergo a full necropsy study according to our guidelines.”

Low-dose intraperitoneal Freund's adjuvant:
toxicity and immunogenicity in mice
using an immunogen targeting amyloid-beta peptide

Author information

Oscherwitz J1, Hankenson FC, Yu F, Cease KB.

Division of Hematology-Oncology, Department of Internal Medicine
University of Michigan Medical School, Ann Arbor, MI 48105, USA
joscher@umich.edu

Abstract

Complete Freund's adjuvant (CFA) is effective for potentiating immune responses in mice when administered subcutaneously, and is often more potent when given intraperitoneally (i.p.). However, the the potential toxicity of i.p. administration in mice has led investigators and Institutional Animal Care and Use committees to increasingly view the use of CFA i.p. with reservation. We evaluated whether an 80% reduction in the dose of CFA administered i.p. to mice, compared to the i.p. doses used in a previous analysis, could abrogate the untoward effects associated with its use, while still maintaining adjuvanticity. Using a novel immunogen targeting the N-terminus of the 42-amino acid amyloid-beta peptide, we compared low dose CFA administered i.p., with three other commonly used adjuvants given i.p.: alum, incomplete Freund's adjuvant (IFA) and monophosphoryl lipid A + trehalose dicorynomycolate (MPL + TDM). The results of the study showed that, though the reduction in intraperitoneal dose of CFA mitigated transient weight loss and leukocytosis observed previously with higher doses of i.p. CFA, all mice administered CFA or IFA i.p. developed abdominal adhesions and granulomatous peritonitis. Mice from all adjuvant groups, however, appeared to tolerate the respective adjuvants well and excellent comparative immunogenicity was observed in mice immunized with the Freund's and MPL + TDM adjuvants. Consequently, we conclude that though a high-titered, humoral response may be generated using low dose CFA administered i.p., the accompanying toxicity remains significant, and thus alternative adjuvants and/or routes should be considered.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16307832>

“Consequently, we conclude that though a high-titered, humoral response may be generated using low dose CFA [still used in several vaccines today] administered i.p., the accompanying toxicity remains significant, and thus alternative adjuvants and/or routes should be considered.”

“Adverse cardiorespiratory events including apnea, bradycardia, and desaturations have been described following administration of the first diphtheria-tetanus-pertussis-inactivated polio-Haemophilus influenzae type B (DTP-IPV-Hib) immunization to preterm infants.”

BMC Pediatrics • June 2006

**Frequency of apnea, bradycardia, and desaturations
following first diphtheria-tetanus-pertussis-inactivated
polio-Haemophilus influenzae type B immunization
in hospitalized preterm infants**

Jackie Lee,¹ Joan L Robinson,¹ and Donald W Spady¹

Stollery Children’s Hospital and Department of Pediatrics
University of Alberta, Edmonton, Alberta, Canada
jr3@ualberta.ca

Abstract

Background

Adverse cardiorespiratory events including apnea, bradycardia, and desaturations have been described following administration of the first diphtheria-tetanus-pertussis-inactivated polio-Haemophilus influenzae type B (DTP-IPV-Hib) immunization to preterm infants. The effect of the recent substitution of acellular pertussis vaccine for whole cell pertussis vaccine on the frequency of these events requires further study.

<http://www.ncbi.nlm.nih.gov/pubmed/16784533>

“... the outbreak lasted for approximately 2 months, suggesting that varicella in vaccinated persons was contagious and that 99% varicella vaccination coverage was not sufficient to prevent the outbreak.”

Pediatrics • June 2006

One dose of varicella vaccine does not prevent school outbreaks: is it time for a second dose?

Author information

Lopez AS1, Guris D, Zimmerman L, Gladden L, Moore T, Haselow DT, Loparev VN, Schmid DS, Jumaan AO, Snow SL.
Centers for Disease Control and Prevention, Atlanta, GA 30333, USA
alopez@cdc.gov

OBJECTIVES

The implementation of a routine childhood varicella vaccination program in the United States in 1995 has resulted in a dramatic decline in varicella morbidity and mortality. Although disease incidence has decreased, outbreaks of varicella continue to be reported, increasingly in highly vaccinated populations. In 2000, a varicella vaccination requirement was introduced for kindergarten entry in Arkansas. In October 2003, large numbers of varicella cases were reported in a school with high vaccination coverage. We investigated this outbreak to examine transmission patterns of varicella in this highly vaccinated population, to estimate the effectiveness of 1 dose of varicella vaccine, to identify risk factors for vaccine failure, and to implement outbreak control measures.

METHODS

A retrospective cohort study involving students attending an elementary school was conducted. A questionnaire was distributed to parents of all of the students in the school to collect varicella disease and vaccination history; parents of varicella case patients were interviewed by telephone. A case of varicella was defined as an acute, generalized, maculopapulovesicular rash without other apparent cause in a student or staff member in the school from September 1 to November 20, 2003. Varicella among vaccinated persons was defined as varicella-like rash that developed >42 days after vaccination. In vaccinated persons, the rash may be atypical, maculopapular with few or no vesicles. Cases were laboratory confirmed by polymerase chain reaction, and genotyping was performed to identify the strain associated with the outbreak.

RESULTS

Of the 545 students who attended the school, 88% returned the questionnaire. Overall varicella vaccination coverage was 96%. Forty-nine varicella cases were identified; 43 were vaccinated. Three of 6 specimens tested were positive by polymerase chain reaction. The median age at vaccination of vaccinated students in the school was 18 months, and the median time since vaccination was 59 months. Forty-four cases occurred in the East Wing, where 275 students in grades kindergarten through 2 were located, and vaccination coverage was 99%. In this wing, varicella attack rates among unvaccinated and vaccinated students were 100% and 18%, respectively. Vaccine effectiveness against varicella of any severity was 82% and 97% for moderate/severe varicella. Vaccinated cases were significantly milder compared with unvaccinated cases. Among the case patients in the East Wing, the median age at vaccination was 18.5 and 14 months among non-case patients. Four cases in the West Wing did not result in further transmission in that wing. The Arkansas strains were the same as the common varicella-zoster virus strain circulating in the United States (European varicella-zoster virus strain).

CONCLUSIONS

Although disease was mostly mild, the outbreak lasted for approximately 2 months, suggesting that varicella in vaccinated persons was contagious and that 99% varicella vaccination coverage was not sufficient to prevent the outbreak. This investigation highlights several challenges related to the prevention and control of varicella outbreaks with the 1-dose varicella vaccination program and the need for further prevention of varicella through improved vaccine-induced immunity with a routine 2-dose vaccination program. The challenges include: 1-dose varicella vaccination not providing sufficient herd immunity levels to prevent outbreaks in school settings where exposure can be intense, the effective transmission of varicella among vaccinated children, and the difficulty in the diagnosis of mild cases in vaccinated persons and early recognition of outbreaks for implementing control measures. The efficacy of 2 doses of varicella vaccine compared with 1 dose was assessed in a trial conducted among healthy children who were followed for 10 years. The efficacy for 2 doses was significantly higher than for 1 dose of varicella vaccine. This higher efficacy translated into a 3.3-fold lower risk of developing varicella >42 days after vaccination in 2- vs 1-dose recipients. Of the children receiving 2 doses, 99% achieved a glycoprotein-based enzyme-linked immunosorbent assay level of > or =5 units (considered a correlate of protection) 6 weeks after vaccination compared with 86% of children who received 1 dose. The 6-week glycoprotein-based enzyme-linked immunosorbent assay level of > or =5 units has been shown to be a good surrogate for protection from natural disease. Ten years after the implementation of the varicella vaccination program, disease incidence has declined dramatically, and vaccination coverage has increased greatly. However, varicella outbreaks continue to occur among vaccinated persons. Although varicella disease among vaccinated persons is mild, they are contagious and able to sustain transmission. As a step toward better control of varicella outbreaks and to reduce the impact on schools and public health officials, in June 2005, the Advisory Committee on Immunization Practices recommended the use of a second dose of varicella vaccine in outbreak settings. Early recognition of outbreaks is important to effectively implement a 2-dose vaccination response and to prevent more cases. Although the current recommendation of providing a second dose of varicella vaccine during an outbreak offers a tool for controlling outbreaks, a routine 2-dose recommendation would be more effective at preventing cases. Based on published data on immunogenicity and efficacy of 2 doses of varicella vaccine, routine 2-dose vaccination will provide improved protection against disease and further reduce morbidity and mortality from varicella.

<http://www.ncbi.nlm.nih.gov/pubmed/16740809>

Environmental mercury release,
special education rates, and autism disorder:
an ecological study of Texas

Author information

Palmer RF1, Blanchard S, Stein Z, Mandell D, Miller C.

University of Texas Health Science Center
San Antonio Department of Family and Community Medicine
7703 Floyd Curl Drive, San Antonio, Texas 78229-3900, USA
palmer@uthscsa.edu

Abstract

The association between environmentally released mercury, special education and autism rates in Texas was investigated using data from the Texas Education Department and the United States Environmental Protection Agency. A Poisson regression analysis adjusted for school district population size, economic and demographic factors was used. There was a significant increase in the rates of special education students and autism rates associated with increases in environmentally released mercury. On average, for each 1,000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism. The association between environmentally released mercury and special education rates were fully mediated by increased autism rates. This ecological study suggests the need for further research regarding the association between environmentally released mercury and developmental disorders such as autism. These results have implications for policy planning and cost analysis.

<http://www.ncbi.nlm.nih.gov/pubmed/16338635>

“On average,
for each 1,000 lb of
environmentally released mercury,
there was a 43% increase in the rate
of special education services and a
61% increase in the rate of autism.”

Vaccine • Volume 24, Issues 31–32 • July 2006

Unexplained cases of sudden infant death
shortly after hexavalent vaccination

Author Information

Zinka B, Rauch E, Buettner A, Ruëff F, Penning R.

Report available for purchase:

<http://www.sciencedirect.com/science/article/pii/S0264410X05004688>

Two successive outbreaks of mumps in Nova Scotia among vaccinated adolescents and young adults

Author Information

Gaynor Watson-Creed, Andrea Saunders, Jeffrey Scott, Luis Lowe, Janice Pettipas, and Todd F. Hatchette

From Nova Scotia Health Promotion and Protection (Watson-Creed, Saunders, Scott)
the Departments of Community Health and Epidemiology (Watson-Creed, Scott), Pediatrics (Scott) and Pathology (Hatchette)
Dalhousie University, and the Department of Pathology and Laboratory Medicine (Pettipas, Hatchette)
QEII Health Science Centre, Halifax, NS; the Canadian Field Epidemiology Program (Saunders), Public Health Agency of Canada, Ottawa, Ontario
and the Respiratory and Enteric Virus Branch (Lowe), Centers for Disease Control and Prevention, Atlanta, GA

Abstract

Background

Before the widespread use of vaccine, mumps was the most common cause of viral meningitis (up to 10% of mumps infections). Vaccination programs have resulted in a drop of more than 99% in the number of reported mumps cases in the United States and Canada. Although rare in Canada, outbreaks have recently occurred throughout the world, including a large outbreak in the United Kingdom, where more than 56,000 cases were reported in 2004–2005.

Methods

Two recent outbreaks in Nova Scotia were investigated by public health officials. Cases were defined by laboratory confirmation of infection (i.e., isolation of mumps virus by culture) or clinical diagnosis in people epidemiologically linked to a laboratory-confirmed case. The people infected were interviewed to determine possible links and to identify contacts. Mumps virus was cultured from urine and throat specimens, identified via reverse-transcriptase polymerase chain reaction (RT-PCR) and subjected to phylogenetic analysis to identify the origin of the strain.

Results

The first outbreak involved 13 high-school students (median age 14 yr): 9 who had previously received 2 doses of measles–mumps–rubella vaccine (MMR) and 4 who received a single dose. The second outbreak comprised 19 cases of mumps among students and some staff at a local university (median age 23 yr), of whom 18 had received only 1 dose of MMR (the other received a second dose). The viruses identified in the outbreaks were phylogenetically similar and belonged to a genotype commonly reported in the UK. The virus from the second outbreak is identical to the strain currently circulating in the UK and United States.

Interpretation

The predominance in these outbreaks of infected people of university age not only highlights an environment with potential for increased transmission but also raises questions about the efficacy of the MMR vaccine. The people affected may represent a “lost cohort” who do not have immunity from natural mumps infection and were not offered a 2-dose schedule. Given the current level of mumps activity around the world, clinicians should remain vigilant for symptoms of mumps.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1550754>

“... studies especially on neurotoxicity, genotoxicity, or carcinogenicity, are previously published in numerous articles.”

Biometals • August 2006

Occurrence, use and potential toxic effects of metals and metal compounds

Ana-Maria Florea, Dietrich Büsselberg

Abstract

Metals and metal compounds are constituents of our natural environment. Their distribution depends on the existence of natural sources (e.g. volcanoes or erosion) and their use in human's activity. They are transformed naturally (e.g. by bacterial activity) with formation of organic species that influence their mobility and accumulation in abiotic as well as biotic systems. Up to date metal species are released into the environment questioning their influence on human health. Due to their widespread use in human activities such as industry, agriculture and even as medicine (e.g. As, Se, Pt), numerous health risks may be associated with exposure to these substances. Different reports on metal intoxication are documented and studies especially on neurotoxicity, genotoxicity, or carcinogenicity, are previously published in numerous articles. This mini-review gives an overview on the use and the actions of selected metal species of actual scientific concern, with a focus on neuronal cells.

<http://link.springer.com/article/10.1007%2Fs10534-005-4451-x>

Acute metabolic crisis induced by vaccination in seven Chinese patients

Author information

Yang Y1, Sujan S, Sun F, Zhang Y, Jiang Y, Song J, Qin J, Wu X.

Department of Pediatrics, Peking University First Hospital
Beijing, China
yanlingy@vip.sina.com

Abstract

Seven Chinese patients (5 males and 2 females) with vaccination-induced acute metabolic crisis were reported. Only one male with 21-hydroxylase deficiency had been diagnosed before vaccination. In the remaining six patients, the preexisting diagnoses were not confirmed before the vaccination. Acute metabolic crisis occurred in seven patients between 3 and 12 hours after the administration of Japanese encephalitis, diphtheria, and tetanus toxoids and acellular pertussis, hepatitis B, or measles vaccines. Patients 1 and 2 displayed acute adrenal insufficiencies at the ages of 5 years and 3 months, respectively. Patient 3 had presented with mild motor retardation previously. Patients 4 to 7 were previously healthy, but suffered from fever, seizures, coma, acidosis, and hypoglycemia after being vaccinated. Glutaric aciduria type 1 was evident in case 4. Leigh syndromes were present in Patients 5, 6, and 7. They all died from respiratory failure before 2 years of age. Symmetric foci, cystic cavitations with neuronal loss, and vascular proliferation were observed by postmortem examination. Among the seven patients, although the vaccines were not the primary cause of the acute metabolic crisis, the severe acute episodes occurred coincidentally.

<http://www.ncbi.nlm.nih.gov/pubmed/16876007>

“Seven Chinese patients with vaccination-induced acute metabolic crisis were reported.”

“The first rotavirus vaccine ... left instead the unfortunate legacy that live oral rotavirus vaccines may be associated with a serious but rare adverse event: intussusception.”

Pediatrics • August 2006

Rotavirus Vaccination and Intussusception: Can We Decrease Temporally Associated Background Cases of Intussusception by Restricting the Vaccination Schedule?

Author Information

Jennifer H. Tai, MDa, Aaron T. Curns, MPHb,
Umesh D. Parashar, MBBS, MPHa, Joseph S. Bresee, MDa, Roger I. Glass, MD, PhDa

- a. Viral Gastroenteritis Section
- b. Office of the Director, Division of Viral and Rickettsial Diseases
Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

OBJECTIVE

The first rotavirus vaccine that was licensed in the United States, RotaShield, could have prevented the enormous burden of rotavirus diarrhea in American children but left instead the unfortunate legacy that live oral rotavirus vaccines may be associated with a serious but rare adverse event: intussusception. Although large trials indicate that the next generation of rotavirus vaccines is not associated with this complication, many children likely will develop intussusception by chance alone in the 2-week window after immunization, raising concerns about whether these cases might be “caused” by the vaccine. Our objective for this study was to model and compare the number of temporally associated intussusception events that are expected by chance alone under 2 rotavirus vaccination strategies.

CONCLUSIONS

Although an age-restricted vaccination schedule substantially reduced the number of intussusception events that were observed in the 2-week postvaccination window when compared with a schedule with fewer restrictions, this decrease was attributable to a lower rate of vaccine coverage rather than a safer schedule of vaccination. The risk for intussusception did not differ significantly between vaccination strategies. Public health policy and education messages for physicians and parents should be developed to anticipate intussusception events that will occur by chance alone but are temporally related to rotavirus vaccination.

<http://pediatrics.aappublications.org/content/118/2/e258>

Elevated urinary excretion of aluminium and iron in multiple sclerosis

Author information

Exley C1, Mamutse G, Korchazhkina O,
Pye E, Strekopytov S, Polwart A, Hawkins C.

Birchall Centre for Inorganic Chemistry and Materials Science
Lennard-Jones Laboratories, Keele University, Staffordshire, UK
c.exley@chem.keele.ac.uk

Abstract

Multiple sclerosis (MS) is a chronic, immune-mediated, demyelinating disease of the central nervous system of as yet unknown aetiology. A consensus of opinion has suggested that the disorder is the result of an interplay between environmental factors and susceptibility genes. We have used a battery of analytical techniques to determine if the urinary excretion of i) markers of oxidative damage; ii) iron and iii) the environmental toxin aluminium and its antagonist, silicon, are altered in relapsing-remitting (RRMS) and secondary progressive MS (SPMS). Urinary concentrations of oxidative biomarkers, MDA and TBARS, were not found to be useful indicators of inflammatory disease in MS. However, urinary concentrations of another potential marker for inflammation and oxidative stress, iron, were significantly increased in SPMS ($P < 0.01$) and insignificantly increased in RRMS ($P > 0.05$). Urinary concentrations of aluminium were also significantly increased in RRMS ($P < 0.001$) and SPMS ($P < 0.05$) such that the levels of aluminium excretion in the former were similar to those observed in individuals undergoing metal chelation therapy. The excretion of silicon was lower in MS and significantly so in SPMS ($P < 0.05$). Increased excretion of iron in urine supported a role for iron dysmetabolism in MS. Levels of urinary aluminium excretion similar to those seen in aluminium intoxication suggested that aluminium may be a hitherto unrecognized environmental factor associated with the aetiology of MS. If aluminium is involved in MS then an increased dietary intake of its natural antagonist, silicon, might be a therapeutic option.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17086897>

“Levels of urinary aluminium excretion similar to those seen in aluminium intoxication suggested that aluminium may be a hitherto unrecognized environmental factor associated with the aetiology of Multiple Sclerosis.”

Fibromyalgia, infection and vaccination: two more parts in the etiological puzzle

Author information

Ablin JN1, Shoenfeld Y, Buskila D.

Department of Rheumatology
Tel-Aviv Sourasky Medical Center and Sackler Faculty of Medicine
Tel-Aviv University, Tel-Aviv, Israel
ajacob@post.tau.ac.il

Abstract

As the pathogenesis of fibromyalgia continues to raise debate, multiple putative triggers have been implicated. The current review summarizes the available data linking fibromyalgia to either infection or vaccination. Multiple infectious agents have been associated with the development of either full-blown fibromyalgia (e.g. hepatitis C), or with symptom complexes extensively overlapping with that syndrome (e.g. chronic Lyme disease). The cases of Lyme disease, mycoplasma, hepatitis C and HIV are detailed. Despite the described associations, no evidence is available demonstrating the utility of antibiotic or anti-viral treatment in the management of fibromyalgia. Possible mechanistic links between fibromyalgia and HIV are reviewed. Associations have been described between various vaccinations and symptom complexes including fibromyalgia and chronic fatigue syndrome. The case of Gulf War syndrome, a functional multisystem entity sharing many clinical characteristics with fibromyalgia is discussed, with emphasis on the possibility of association with administration of multiple vaccinations during deployment in the Persian Gulf and the interaction with stress and trauma. Based on this example a model is proposed, wherein vaccinations function as co-triggers for the development of functional disorders including fibromyalgia, in conjunction with additional contributing factors.

<http://www.ncbi.nlm.nih.gov/pubmed/17071055>

“Based on this example
a model is proposed, wherein
vaccinations function as co-triggers
for the development of functional disorders
including fibromyalgia, in conjunction with
additional contributing factors.”

Possible immunological disorders in autism: concomitant autoimmunity and immune tolerance

Author information

Kawashti MI1, Amin OR, Roweby NG.

Microbiology Department
Faculty of Medicine For Women
Al Azhar University, Cairo, Egypt

Abstract

Autism is a pervasive developmental disorder that affect children early in their life. Immunological disorders is one of several contributing factors that have been suggested to cause autism. Thirty autistic children aged 3-6 years and thirty non-autistic psychologically-free siblings were studied. Circulating IgA and IgG autoantibodies to casein and gluten dietary proteins were detected by enzyme-immunoassays (EIA). Circulating IgG antibodies to measles, mumps and rubella vaccine (M.M.R) and cytomeglovirus were investigated by EIA. Results revealed high seropositivity for autoantibodies to casein and gluten: 83.3% and 50% respectively in autistic children as compared to 10% and 6.7% positivity in the control group. Surprisingly, circulating anti-measles, anti-mumps and anti-rubella IgG were positive in only 50%, 73.3% and 53.3% respectively as compared to 100% positivity in the control group. Anti-CMV IgG was positive in 43.3% of the autistic children as compared to 7% in the control group. It is concluded that, autoimmune response to dietary proteins and deficient immune response to measles, mumps and rubella vaccine antigens might be associated with autism, as a leading cause or a resulting event. Further research is needed to confirm these findings.

<http://www.ncbi.nlm.nih.gov/pubmed/17974154>

“It is concluded that,
autoimmune response to dietary
proteins and deficient immune response to
measles, mumps and rubella vaccine antigens
might be associated with autism, as a
leading cause or a resulting event.”

DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau

Author information

Aaby P1, Biai S, Veirum JE, Sodemann M, Lisse I,
Garly ML, Ravn H, Benn CS, Rodrigues A.
Projecto de Saúde de Bandim, Apartado 861
Bissau, Guinea-Bissau
p.aaby@bandim.org

Abstract

BACKGROUND

The sequence of routine immunisations may be important for childhood mortality. Three doses of diphtheria-tetanus-pertussis vaccine (DTP) should be given at 6, 10, and 14 weeks and measles vaccine (MV) at 9 months of age. The sequence is not always respected. We examined in-hospital mortality of children having received DTP with or after measles vaccine.

SETTING

The only paediatric ward in Bissau, Guinea-Bissau.

PARTICIPANTS

Children hospitalised during two periods in 1990-1996 and 2001-2002 who had received MV prior to hospitalisation.

MAIN OUTCOME MEASURE

The all-cause case fatality at the hospital for children aged 6-17 months.

RESULT

The case fatality was increased for children who had received DTP with or after measles vaccine compared with children who had received measles vaccine as the most recent vaccine, the ratio being 2.53 (1.37-4.67) and 1.77 (0.92-3.41) in the two periods, respectively. The combined estimate was 2.10 (1.34-3.28). These results were not explained by differences in nutritional status, number of doses of DTP or discharge policy.

CONCLUSION

Administration of DTP with, or after MV, may reduce the beneficial effect of MV.

<http://www.ncbi.nlm.nih.gov/pubmed/17092614>

“The case fatality was increased for children who had received DTP with or after measles vaccine compared with children who had received measles vaccine as the most recent vaccine, the ratio being 2.53 (1.37-4.67) and 1.77 (0.92-3.41) in the two periods, respectively.”

Effects of postnatal formaldehyde exposure
on pyramidal cell number, volume of cell layer
in hippocampus and hemisphere in the rat:
a stereological study

Author information

Sarsilmaz M1, Kaplan S, Songur A, Colakoglu S,
Aslan H, Tunc AT, Ozen OA, Turgut M, Bas O.

Department of Anatomy
Firat University School of Medicine
Elazig, Turkey

Abstract

The purpose of the present study was to determine whether exposure of neonatal rats to formaldehyde (FA) had either early or delayed effects on the numbers of pyramidal cells in the cornu ammonis (CA) of the hippocampus. Neonatal Wistar rats were exposed to 0 ppm (control group), 6 ppm and 12 ppm (high concentration group) of FA concentrations throughout the 30-day period following the birth by placing them for 6 h/day in a glass chamber containing FA vapor. Then, some of the animals from each FA-treated group were anesthetized and decapitated at the day 30, and the remaining ones were killed at the day 90. The brains were removed immediately and fixed in 10% neutral-buffered FA solution. The Cavalieri principle was used to determine the volumes of the CA and the entire cerebral hemisphere. The optical fractionator counting method was used to estimate the total number of pyramidal cells in the CA. The appearance of pyramidal cells was normal under light microscopy at both postnatal day (PND) 30 and PND 90 in all groups. There were concentration-related volume changes of CA at PND 30 and PND 90; low concentration of FA significantly increased, whereas high concentration decreased the volume of CA in comparison of the control at PND 30. Importantly, high concentration of FA at PND 90 increased the volume of CA in comparison of the low concentration but not with the control. Furthermore, low and high concentrations of FA decreased the volume of hemisphere at PND 30, whereas a reverse effect of these concentrations was observed at the hemisphere of PND 90 in comparison of the control. In both CA and cerebral hemisphere, an age-related volume decrease in both control and low/high concentration groups were found. On the other hand, there were significant age-related reductions in the total number of pyramidal cells at 90 days of age irrespective of the groups examined. Rats treated with high concentration FA were seen to have significantly fewer pyramidal cell neurons than either the animals treated with low concentration FA or control groups ($p < 0.01$). These observations indicate that pyramidal cells in the hippocampus may be vulnerable to FA exposure during the early period of life.

“These observations indicate
that pyramidal cells in the hippocampus
may be vulnerable to Formaldehyde exposure
during the early period of life.”

Primary immunization
of premature infants with gestational age <35 weeks:
cardiorespiratory complications and C-reactive protein responses
associated with administration of single and
multiple separate vaccines simultaneously

Author information

Pourcyrous M1, Korones SB, Arheart KL, Bada HS.

Department of Pediatrics
The University of Tennessee Health Science Center
Memphis, Tennessee 38163, USA
mpourcyrous@utmem.edu

Abstract

OBJECTIVE

To determine the incidence of cardiorespiratory events and abnormal C-reactive protein (CRP) level associated with administration of a single vaccine or multiple separate vaccines simultaneously.

STUDY DESIGN

Prospective observational study on 239 preterm infants at > or =2 months of age in the neonatal intensive care unit (NICU). Each infant received either a single vaccine or multiple vaccines on one day. CRP levels and cardiorespiratory manifestations were monitored for 3 days following immunization.

RESULTS

Abnormal elevation of CRP level occurred in 85% of infants administered multiple vaccines and up to 70% of those given a single vaccine. Overall, 16% of infants had vaccine-associated cardiorespiratory events within 48 hours postimmunization. In logistic regression analysis, abnormal CRP values were associated with multiple vaccines (OR, 15.77; 95% CI 5.10-48.77) and severe intraventricular hemorrhage (IVH) (OR, 2.28; 95% CI 1.02-5.13). Cardiorespiratory events were associated marginally with receipt of multiple injections (OR, 3.62; 95% CI 0.99-13.25) and significantly with gastroesophageal reflux (GER) (OR, 4.76; 95% CI 1.22-18.52).

CONCLUSION

CRP level is expected to be elevated in the 48 hours following immunization. In a minority of infants immunized, cardiorespiratory events were associated with presumed need for intervention. Underlying medical conditions and possibly multiple injections are associated with cardiorespiratory events. Precautionary monitoring following immunizations is warranted.

“In a minority of infants immunized [16%],
cardiorespiratory events were associated with
presumed need for intervention.”

Risk of Serious Neurologic Disease After Immunization of Young Children in Britain and Ireland

Author Information

Katherine N. Ward, MA, MB, BChir, PhD, FRCPatha, Naomi J. Bryant, MSc,
Nick J. Andrews, MScb, Jennifer S. Bowley, BSc, Anu Ohrling, MDa,
Christopher M. Verity, MA, BM, BCh, FRCP, FRCPC, DCHc,
Euan M. Ross, MD, FRCP, FRCPC, FFPH, DCHd,
Elizabeth Miller, BSc, MB, BS, FRCPath, FFPHb

- a. Centre for Virology (UCL Campus), Division of Infection and Immunity
Royal Free and University College Medical School, Windeyer Institute of Medical Sciences, London, UK
- b. Centre for Infections, Health Protection Agency, London, United Kingdom
- c. Child Development Centre, Addenbrooke's Hospital, Cambridge, United Kingdom
- d. Child Studies Department, King's College, Strand, London, United Kingdom

Abstract

OBJECTIVE

We sought to investigate the risk of serious neurologic disease after immunization in early childhood.

METHODS

The results of a 3-year prospective study of children (2–35 months old) in Britain and Ireland with encephalitis and/or severe illness with convulsions and fever were linked to each child's vaccine history. Cases were reported via the British Paediatric Surveillance Unit's network. The self-controlled case-series method was used to investigate associations between immunization and acute potential adverse events. The risk periods investigated were 0 to 3 and 0 to 7 days post–diphtheria, tetanus, whole cell pertussis, Haemophilus influenzae type b or meningococcal C conjugate vaccine and 6 to 11 and 15 to 35 days post–measles, mumps, rubella vaccine.

RESULTS

A total of 157 disease episodes from 155 children met the analytical case definition. There were 11 cases of herpes simplex encephalitis and 23 cases of primary human herpesvirus 6 and/or 7 infection. There was no evidence of a raised relative incidence of serious neurologic disease in any of the specified risk periods with the exception of a raised relative incidence of 5.68 in the 6–11 days after measles, mumps, rubella vaccine. Based on this relative incidence, between 3 and 6 of the 6 cases in this period were estimated to be attributable to the vaccine with a best estimate of 5. The 6 cases all had fever with convulsions lasting >30 minutes; in all but 1, there was complete recovery by discharge from hospital. Of the 5 patients who recovered, 1 had a concurrent primary human herpesvirus 6 infection and one a primary human herpesvirus 7.

CONCLUSIONS

Six to 11 days after measles, mumps, rubella vaccine there is an increased risk of fever and convulsions lasting >30 minutes. All 6 of the episodes temporally related to immunization met the criteria for complex febrile convulsions. The estimated attributable risk of serious neurological disease was similar to that previously found for measles vaccine.

“All 6 of the episodes temporally related to immunization met the criteria for complex febrile convulsions.”

Induction of specific micro RNA (miRNA) species by ROS-generating metal sulfates in primary human brain cells

Author information

Lukiw WJ1, Pogue AI.

Neuroscience Center and Department of Ophthalmology
Louisiana State University Health Sciences Center
New Orleans, LA 70112, USA
wlukiu@lsuhsc.edu

Abstract

Iron- and aluminum-sulfate together, at nanomolar concentrations, trigger the production of reactive oxygen species (ROS) in cultures of human brain cells. Previous studies have shown that following ROS induction, a family of pathogenic brain genes that promote inflammatory signalling, cellular apoptosis and brain cell death is significantly over-expressed. Notably, iron- and aluminum-sulfate induce genes in cultured human brain cells that exhibit expression patterns similar to those observed to be up-regulated in moderate- to late-stage Alzheimer's disease (AD). In this study we have extended our investigations to analyze the expression of micro RNA (miRNA) populations in iron- and aluminum-sulfate treated human neural cells in primary culture. The main finding was that these ROS-generating neurotoxic metal sulfates also up-regulate a specific set of miRNAs that includes miR-9, miR-125b and miR-128. Notably, these same miRNAs are up-regulated in AD brain. These findings further support the idea that iron- and aluminum-sulfates induce genotoxicity via a ROS-mediated up-regulation of specific regulatory elements and pathogenic genes that redirect brain cell fate towards progressive dysfunction and apoptotic cell death.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17629564>

“Iron- and aluminum-sulfate together, at nanomolar concentrations, trigger the production of reactive oxygen species (ROS) in cultures of human brain cells. Previous studies have shown that following reactive oxygen species (ROS) induction, a family of pathogenic brain genes that promote inflammatory signalling, cellular apoptosis and brain cell death is significantly over-expressed.”

Optic Neuritis and Vaccination Investigation: Failure to Consider Significant Sex Differences and Multiple Vaccine Combinations

Renata J. M. Engler, MD; Mary Klote, MD;
Michael R. Nelson, MD, PhD

Abstract

In follow-up to recent correspondence related to the study of vaccinations and subsequent optic neuritis by the Centers for Disease Control and Prevention (CDC),^{1,2} we are deeply concerned regarding the lack of consideration of sex differences in incidence of disease for the ICD-9 code 377.3, a common finding for autoimmune disorders, particularly in young adults aged 18 to 39 years. The Defense Medical Surveillance System (DMSS) demonstrates that in the population of service members of greatest concern, there is a consistent pattern, regardless of year for review, of increased disease incidence by first visit in women compared with men. This sex difference is also independent of race. The Figure was extracted from the remote access program to data contained within the DMSS offered by the Army Medical Surveillance Activity.³ Similar sex differences were identified for ICD-9 codes for optic neuritis, unspecified (377.30); optic papillitis (377.31); retrobulbar neuritis, acute (377.32); and optic neuritis, other (377.39) during the period between January 1, 1998, and December 31, 2003. It is of increasing concern in the context of medical evidence and research that sex differences are not adequately considered in both research design and data analysis. Given the mandatory nature of immunizations in the military health system and the fact that most visits involve complex and sometimes new mixtures, concern for sex-based risk differences is not a minor question and merits far more attention on the agenda of vaccine safety surveillance.

<http://archneur.jamanetwork.com/article.aspx?articleid=794738&resultClick=3>

“we are deeply concerned
regarding the lack of consideration
of sex differences in incidence of disease ...
there is a consistent pattern, regardless of year
for review, of increased disease incidence
by first visit in women compared with men ...”

FDA Science and Mission at Risk

FDA Mission Statement

“The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation’s food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.”

FINDINGS OF THE SUBCOMMITTEE

The FDA cannot fulfill its mission
because its scientific base has eroded and its scientific organizational structure is weak.

The FDA cannot fulfill its mission
because its scientific workforce does not have sufficient capacity and capability.

The FDA cannot fulfill its mission
because its information technology (IT) infrastructure is inadequate.

FDA does not have the capacity to ensure the safety of food for the nation.

The development of medical products based on “new science” cannot be adequately regulated by the FDA.

The FDA cannot provide the information infrastructure support to regulate products based on new science.

The FDA IT infrastructure is obsolete, unstable, and
lacks sufficient controls to ensure continuity of operations or to provide effective disaster recovery services.

There is insufficient capacity in modeling, risk assessment and analysis.

The FDA has experienced decreasing resources in the face of increasing responsibilities.

The FDA science agenda lacks a coherent structure and vision,
as well as effective coordination and prioritization.

The IT workforce is insufficient and suboptimally organized.

The FDA has an inadequate and ineffective program for scientist performance.

Recommendations of excellent FDA reviews are seldom followed.

The FDA has inadequate funding for professional development.

The FDA has not taken sufficient advantage of external and internal collaborations.

The FDA lacks the information science capability and information infrastructure
to fulfill its regulatory mandate.

The nation’s food supply is at risk. Crisis management in FDA’s two food safety centers, Center for Food Safety and Applied Nutrition (CFSAN) and Center for Veterinary Medicine (CVM), has drawn attention and resources away from FDA’s ability to develop the science base and infrastructure needed to efficiently support innovation in the food industry, provide effective routine surveillance, and conduct emergency outbreak investigation activities to protect the food supply.

FDA’s inability to keep up with scientific advances means that American lives are at risk. While the world of drug discovery and development has undergone revolutionary change — shifting from cellular to molecular and gene-based approaches — FDA’s evaluation methods have remained largely unchanged over the last half century. Likewise, evaluation methods have not kept pace with major advances in medical devices and use of products in combination.

The turnover rate in FDA science staff in key scientific areas is twice that of other government agencies. There are insufficient programs of measurement to determine worker performance. There is insufficient investment in professional development, which means that the workforce does not keep up with scientific advances. Finally, for various reasons, the FDA does not have sufficiently extensive collaboration with external scientists, thus limiting infusion of new knowledge and missing opportunities to leverage resources.

FDA’s failure to retain and motivate its workforce puts FDA’s mission at risk. Inadequately trained scientists are generally risk-averse, and tend to give no decision, a slow decision or, even worse, the wrong decision on regulatory approval or disapproval. During our encounters with staff and center leadership, we were struck by the near unanimity that the shortage of science staff (due to lack of resources to hire) and the inability to recruit and retain needed expertise are serious, longstanding challenges. Internal expertise and experience to provide the science capability and capacity needed in highly specialized and fast-evolving areas is disturbingly limited. The lack of a trained workforce means that the FDA is ineffective in responding to emerging fields that require individuals and work teams with multidisciplinary skills built on very complex, highly specialized, often esoteric bodies of knowledge.

The Subcommittee was extremely disturbed at the state of the FDA IT infrastructure .. the IT workforce is insufficient. The IT situation at FDA is problematic at best — and at worst it is dangerous. Many of the FDA systems reside on technology that has been in service beyond the usual life cycle. Systems fail frequently, and even email systems are unstable — most recently during an E.coli food contamination investigation. More importantly, reports of product dangers are not rapidly compared and analyzed, inspectors’ reports are still hand written and slow to work their way through the compliance system, and the system for managing imported products cannot communicate with Customs and other government systems (and often miss significant product arrivals because the system cannot even distinguish, for example, between road salt and table salt).

There are inadequate emergency backup systems in place: recent system failures have resulted in loss of FDA data. Critical data reside in large warehouses sequestered in piles and piles of paper documents. There is no backup of these records, which include valuable clinical trial data. The FDA has inadequate extramural funding programs and collaborations to accelerate the development of critical health information exchanges in order to support clinical trials and pharmacovigilance activities.

In contrast to previous reviews that warned crises would arise if funding issues were not addressed, recent events and our findings indicate that some of those crises are now realities and American lives are at risk.

Current childhood vaccine programs:

An overview

with emphasis on the Measles-Mumps-Rubella (MMR) vaccine
and of its compromising of the mucosal immune system

Harold E. Buttram, MD

Email: hbuttram1304@comcast.net

Abstract

Both common observation and official statistics confirm that there have been dramatic increases in chronic physical and mental illnesses in American children, such as autism, asthma, and allergies since the introduction of the MMR vaccine in 1978. Government health officials have denied a relationship with vaccines, but U.S. Congressional hearings on vaccine safety (1999 to Dec. 2004) revealed a total absence of vaccine safety tests that would meet current scientific standards, so that it can be assumed that many vaccine reactions are taking place unrecognized. Prior to the introduction of vaccines, the Th1 cellular immune system of the gastrointestinal and respiratory systems served as the primary defense systems with the Th2 humoral immune system in the bone marrow, serving a secondary role.

There is a school of thought that the “minor childhood diseases” of earlier times, including measles, mumps, chicken pox, and rubella, which involved the epithelial tissues of skin, respiratory, and/or gastrointestinal tracts, served a necessary purpose in challenging, strengthening, and establishing the dominance of Th1 cellular immune system during early childhood. Current vaccines against these diseases, in contrast, being directed at stimulating antibody production in the bone marrow, are bypassing the cellular immune system and thereby tending to reverse the roles of the cellular and humoral systems, with the former suffering from a lack of challenge. In addition, the cellular immune system is being further compromised by the powerfully immunosuppressive effects of the MMR vaccine. The time is overdue to totally rethink and redirect our current childhood vaccine program.

<http://www.vacinfo.org/buttram.pdf>

“Both common observation and official statistics confirm that there have been dramatic increases in chronic physical and mental illnesses in American children, such as autism, asthma, and allergies since the introduction of the MMR vaccine in 1978. Government health officials have denied a relationship with vaccines, but U.S. Congressional hearings on vaccine safety (1999 to Dec. 2004) revealed a total absence of vaccine safety tests that would meet current scientific standards, so that it can be assumed that many vaccine reactions are taking place unrecognized.”

Medical Veritas 2008

Vaccines, depression, and neurodegeneration after age 50 years: another reason to avoid the recommended vaccines

by Russell L. Blaylock, MD, CCN

There is growing evidence that a number of the psychiatric disorders are strongly related to glutamate excess. Likewise, recent studies have shown a connection between chronic inflammation and these same disorders. A compelling body of research links these two observations, glutamate excess (an excitotoxicity marker) and chronic inflammation (immune over-reactivity). It is known that systemic activation of the immune system also activates the brain's special immune system, which is regulated by the microglia. Based on results of studies of the sickness behavior response to natural infections, neuroscientists have deciphered much of the mechanism responsible for the behavioral effects associated with intense systemic immune activation, including social isolation, depression, anxiety, and a loss of appetite. Most of these symptoms are shared by the major depressive disorders. Other studies have linked neurodegeneration and a worsening of neurodegenerative diseases to systemic immune activation. This paper demonstrates the known links between: systemic immune activation, brain microglial activation, and both major depressive disorder and a worsening of neurodegenerative diseases. Because a number of vaccines are being recommended to adults, the risk of precipitating or worsening these disorders is quite real. The mechanism for this process is discussed.

http://www.vacinfo.org/man1742_1747.pdf

“This paper demonstrates the known links between: systemic immune activation, brain microglial activation, and both major depressive disorder and a worsening of neurodegenerative diseases. Because a number of vaccines are being recommended to adults, the risk of precipitating or worsening these disorders is quite real.”

“Adjuvants ... are challenging to develop and license because adjuvant compounds that stimulate strong protective immunity also frequently induce significant toxicity.”

Frontiers In Bioscience • January 2008

Rationally-designed vaccine adjuvants: separating efficacy from toxicity

Author information

Hauguel TM1, Hackett CJ.

Division of Allergy, Immunology, and Transplantation
National Institute of Allergy and Infectious Diseases
National Institutes of Health, Bethesda, Maryland 20892, USA

Abstract

Adjuvants, substances included in many vaccines in order to improve immune responses, are challenging to develop and license because adjuvant compounds that stimulate strong protective immunity also frequently induce significant toxicity. Adjuvant design and development has until recently been largely empirical; but with the current knowledge that most adjuvants act via receptors of the innate immune system, molecular-based approaches are rapidly advancing the field. Data support the concept that proinflammatory pathways induced by innate immune receptor triggering underlie many of the observed toxic effects. Importantly, the cellular signaling pathways that lead to inflammation are known, for a number of innate immune receptors, to be distinct from those that are involved in the costimulation of protective adaptive immune responses, leading to approaches for attenuating inflammatory signaling that should lead to safer and more effective vaccine adjuvants. This article addresses whether there is a clear rationale for the separation of toxicity from efficacy in the function of adjuvants based upon innate immune receptor ligands.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17981755>

“Maternal body weight was lowered at 7.5%. Number of pups born was lowered at 7.5%.

Lowered body weight was observed in male and female offspring ...”

Reproductive Toxicology • January 2008

Evaluation of developmental neurotoxicity of polysorbate 80 in rats

Author information

Ema M1, Hara H, Matsumoto M, Hirata-Koizumi M, Hirose A, Kamata E.

Division of Risk Assessment, Biological Safety Research Center
National Institute of Health Sciences, Tokyo, Japan
ema@nihs.go.jp

Abstract

The developmental neurotoxicity of polysorbate 80 (PS80) was evaluated in rats. CrI:CD(SD) rats were given drinking water containing PS80 at 0, 0.018, 0.13, 1.0, or 7.5% (0, 0.035, 0.245, 1.864, or 16.783ml/kgbw/day) on day 0 of pregnancy through day 21 after delivery. Pregnant rats were allowed to deliver spontaneously. Potential adverse effects of pre- and post-natal exposure on the development and function of the nervous system in offspring of rats given PS80 were examined. Maternal body weight was lowered at 7.5%. Number of pups born was lowered at 7.5%. There were no compound-related effects on locomotor activity of offspring on postnatal days (PNDs) 14-15, 17-18, 20-21 and 33-37. No compound-related changes were found in developmental landmarks, sexual maturation, or reflex responses. Although decreased rate of avoidance responses was noted on PNDs 23-27 in male and female offspring at 7.5%, no compound-related changes were found in performance in the conditioned avoidance response on PNDs 60-67. Histopathological examinations of the brain revealed no toxicological changes. Lowered body weight was observed in male and female offspring at 7.5%. The NOAEL in this study was considered to be 1.0% (1.864ml/mg/kgbw/day).

<http://www.ncbi.nlm.nih.gov/pubmed/17961976>

Vaccine • March 2008

**Kinetics of asthma- and allergy-associated
immune response gene expression in peripheral blood mononuclear cells
from vaccinated infants after in vitro re-stimulation with vaccine antigen**

Author information

Lahdenperä AI1, Nilsson LJ, Regnström K.

Division of Paediatrics
Department of Clinical and Experimental Medicine
Faculty of Health Sciences, Linköping University, 5818
Linköping, Sweden

Abstract

The global expression of immune response genes in infants after vaccination and their role in asthma and allergy is not clearly understood. Pharmacogenomics is ideally suited to study the involved cellular responses, since the expression of thousands of genes can be assessed simultaneously. Here, array technology was used to assess the expression kinetics of immune response genes with association to asthma and allergy in peripheral blood mononuclear cells (PBMC) of five healthy infants after vaccination with Infanrix-Polio+Hib. At 12h after in vitro re-stimulation of the PBMC with pertussis toxin (PT) antigen, 14 immune response pathways, 33 allergy-related and 66 asthma-related genes were found activated.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18336961>

“At 12h after in vitro re-stimulation
of the peripheral blood mononuclear cells
with pertussis toxin antigen,
14 immune response pathways,
33 allergy-related and 66 asthma-related
genes were found activated.”

“... Triton X-100-induced apoptosis ...”

Leukemia Research • March 2008

Release of cytochrome c from mitochondria
precedes Bax translocation/activation
in Triton X-100-induced apoptosis

Author information

Sawai H1, Domae N.

Department of Internal Medicine, Osaka Dental University
8-1 Kuzuhahanazonocho, Hirakata, Osaka 573-1121, Japan
sawai@cc.osaka-dent.ac.jp

Abstract

The precise mechanisms by which sublytic concentrations of detergents induce apoptosis remain unclear. Recent studies reported the ability of nonionic detergents such as Triton X-100 to induce conformational change of Bax to the active form in vitro. Here we investigated whether activation of Bax might play a role in Triton X-100-induced apoptosis in cells. Although Bax translocation/activation was inhibited by caspase inhibitors, cytochrome c release from mitochondria was not affected in Triton X-100-induced apoptosis in U-937 cells. These results demonstrate that translocation/activation of Bax occurs downstream of cytochrome c release and caspase activation in Triton X-100-induced apoptosis.

<http://www.ncbi.nlm.nih.gov/pubmed/17689609>

Considerable Differences
in Vaccine Immunogenicities and Efficacies
Related to the Diluent Used for
Aluminum Hydroxide Adjuvant

Author Information

Lin Lin,¹ Ashraf S. Ibrahim,^{1,2} Valentina Avanesian,¹ John E. Edwards, Jr.,^{1,2}
Yue Fu,^{1,2} Beverlie Baquir,¹ Rebecca Taub,¹ and Brad Spellberg^{1,2,*}

1. Division of Infectious Diseases

Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center
Torrance, California

2. The David Geffen School of Medicine at UCLA

Los Angeles, California

Abstract

We are developing an anticandidal vaccine using the recombinant N terminus of Als3p (rAls3p-N). We report that although more rAls3p-N was bound by aluminum hydroxide diluted in saline than by aluminum hydroxide diluted in phosphate-buffered saline (PBS), its immunogenicity and efficacy were superior in PBS. Thus, protein binding, by itself, may not predict the efficacy of some vaccines with aluminum adjuvants.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2268268/>

“Thus, protein binding, by itself,
may not predict the efficacy of some
vaccines with aluminum adjuvants.”

Modeling Neurodevelopment Outcomes and Ethylmercury Exposure from Thimerosal-Containing Vaccines

José G. Dórea*,1 and Rejane C. Marques†

*Universidade de Brasília, Brasília, DF, Brazil

†Fundação Universidade Federal de Rondônia, Porto Velho, RO, Brazil
dorea@rudah.com.br

Dear Editor,

The neurotoxic effects of ethylmercury (EtHg) accidentally consumed in Iraq were sufficient to withdraw ethylmercury-containing fungicides as seed dressing. Despite that, not only did thimerosal continue to be used in pharmaceutical preparations but also toxicological interest in EtHg-derived substances diminished considerably and was never addressed with regard to the small quantities used as a vaccine preservative. Thimerosal-containing vaccines (TCV) have no record of overt clinical neurological consequences due to EtHg, and the plausibility of subtle neurotoxic effects in children has been recognized only recently by the United States and other industrialized countries. In this context, we welcome the interesting work of Berman et al. (2008); it is clear that this assiduous study (in immunologically susceptible mice) took into consideration doses and schedules of TCV-Hg concentrations that had been used in infants in the United States. Their mice model does not, however, cover the full extent of modifying factors associated with TCV-Hg exposure in the majority of immature and newborns around the world that still have to depend on TCV.

According to Berman et al. (2008), the United States vaccination scheduled exposed a total of 125 µgHg distributed at 2, 2, and 6 months through TCV (hepatitis B and DTP). This type of vaccine is no longer used in industrialized countries but it is still used all over the world. We know that thimerosal concentrations vary among brands of vaccines and also that immunization schedules vary depending on a country's health policy; not only that but new outbreaks of disease introduce additional new vaccines (which may contain thimerosal) during the first year of life. As an example, the public health services of Brazil, like other countries, still uses several brands of hepatitis B vaccine (containing thimerosal as preservative) with concentrations ranging from 12.5 to 50 µgHg per 0.5 ml shot. Another salient difference between countries that use TCV (like Brazil) and the United States is that in the former country hepatitis B inoculation starts within the first 12–24 h after birth (Marques et al., 2007) and is administered to low-birth weight ≥ 2000 g (Ministério, da Saúde, 2006 and premature babies who are also recommended a fourth shot as an additional booster (DI/DH/CVE, 2006). In such situations, not only toxicokinetics (TK) but especially toxicodynamics (TD) of EtHg are entirely different between a 1-day-old (with different stages of immaturity and birth weight) and a 60-day-old child (as modeled).

The newborn presents several physiological degrees of immaturity in the excretory system (kidneys and bile formation) and target organ (central nervous system, CNS) that are important modi-

fiers of EtHg TK and TD. These features are inversely accentuated by gestational age and birth weight. Under such circumstances, unbound circulating EtHg in a newborn (and immature) may not be eliminated as fast as in a 2-month-old baby and thus will be readier to cross the more vulnerable blood-brain barrier (BBB). The newborn BBB increases in effectiveness with age; therefore, the free EtHg can more easily penetrate the immature CNS (Dorea, 2007). As a consequence, the smaller the body size and blood volume, the more altered the TD and TK of EtHg. Indeed, Stajich et al. (2000) showed that preterm infants do not metabolize Hg efficiently. Collectively, studies show that larger babies have significantly higher mean liver metallothionein than smaller babies (Dorea, 2007).

Factors associated with protein-binding capacity, excretion mechanisms, and enzyme activities are immature in the neonate and modulate differences in adverse effects between newborns and infants exposed to neurotoxic substances. During the period of immaturity, not only plasma albumin but also total protein concentrations decrease (Dorea, 2007). The best example in differences between neurotoxic effects is the type of albumin and competition for binding sites (due to increased circulatory concentrations of bilirubin). Albumin binding (to bilirubin) is less effective during the first postnatal days and, as a consequence, excess free bilirubin can cross the BBB at early stages of the postnatal CNS immaturity and cause brainstem abnormalities; albumin priming can be effective in attenuating effects caused by unbound bilirubin (Dorea, 2007).

We do not dispute the conclusions drawn by Berman et al. regarding Hg and the neurobiology of autism; however, we think it is possible to take their findings one step further in regards to thimerosal neurotoxicity. We contend that these findings are appropriate for U.S.-like scenarios (as intended by the authors) but are not sufficient to address the current TCV schedules in the majority of newborns and infants around the world. TCV are used worldwide in vaccination schedules that include more of these vaccines at an earlier age. Unfortunately, the differences that set newborns (especially low-birth-weights and prematures) apart from 2-month-old infants have not yet been modeled in experimental studies and remain neglected in TK and TD knowledge of TCV-EtHg exposure. We hope that studies like Berman et al. (2008) can inspire conventional toxicology to address uncertainties regarding current serial EtHg exposure in newborns and infants that have to take TCV.

Full Report

<http://toxsci.oxfordjournals.org/content/103/2/414.long>

Rheumatology International • April 2008

HBV vaccine and dermatomyositis: is there an association?

Author information

Altman A1, Szyper-Kravitz M, Shoenfeld Y.

Center for Autoimmune Diseases and Department of Medicine
Beth Sheba Tel-Hashomer, Sackler Faculty of Medicine
Tel Aviv University, Tel Aviv, Israel

Abstract

The etiology of dermatomyositis is unknown, but immune mechanisms play an important role. Several dermatological manifestations have been reported among carriers of hepatitis B surface antigen, and after vaccination with the HBV vaccine. Almost all the skin reactions described were peculiar skin eruptions suggestive of an immune complex reaction. Some authors described the occurrence of dermatomyositis after BCG and influenza vaccination. We report a case of a 6-year-old child, who was vaccinated for hepatitis B virus and developed a flu-like disease accompanied by a skin rash, which had the typical features of dermatomyositis. The association of vaccination with autoimmunity is discussed.

<http://www.ncbi.nlm.nih.gov/pubmed/18034245>

“Several dermatological manifestations have been reported among carriers of hepatitis B surface antigen, and after vaccination with the HBV vaccine. Some authors described the occurrence of dermatomyositis after BCG and influenza vaccination. The association of vaccination with autoimmunity is discussed.”

Clinical Rheumatology • May 2008

Polyglandular autoimmunity with macrophagic myofasciitis

Author information

Theeler BJ1, Simper NB, Ney JP.

Department of Neurology
Madigan Army Medical Center
9040A Fitzsimmons Dr., Tacoma
WA 98431, USA
btheeler@hotmail.com

Abstract

We report a man with chronic fatigue, multiple autoimmune disorders, and a muscle biopsy consistent with macrophagic myofasciitis. This rare and recently described muscle disorder is seen in patients exposed to vaccinations with aluminum hydroxide adjuvant. This case highlights the relationship between macrophagic myofasciitis and autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18180978>

“This rare and recently
described muscle disorder
is seen in patients exposed to
vaccinations with aluminum
hydroxide adjuvant.”

Hepatitis B triple series vaccine and developmental disability in US children aged 1–9 years

Author Information

Carolyn Gallagher & Melody Goodmana

Abstract

This study investigated the association between vaccination with the Hepatitis B triple series vaccine prior to 2000 and developmental disability in children aged 1–9 years (n = 1824), proxied by parental report that their child receives early intervention or special education services (EIS). National Health and Nutrition Examination Survey 1999–2000 data were analyzed and adjusted for survey design by Taylor Linearization using SAS version 9.1 software, with SAS callable SUDAAN version 9.0.1. The odds of receiving EIS were approximately nine times as great for vaccinated boys (n = 46) as for unvaccinated boys (n = 7), after adjustment for confounders. This study found statistically significant evidence to suggest that boys in United States who were vaccinated with the triple series Hepatitis B vaccine, during the time period in which vaccines were manufactured with thimerosal, were more susceptible to developmental disability than were unvaccinated boys.

http://www.fourteenstudies.com/pdf/hep_b.pdf

This report is also referenced [17] in
2008 United Nations Environmental Program (UNEP)
report under the subheading ‘New Evidence’

“The odds of receiving special education services were approximately nine times as great for vaccinated boys (n = 46) as for unvaccinated boys (n = 7), after adjustment for confounders. This study found statistically significant evidence to suggest that boys in United States who were vaccinated with the triple series Hepatitis B vaccine, during the time period in which vaccines were manufactured with thimerosal, were more susceptible to developmental disability than were unvaccinated boys.”

Effect of 50,000 IU vitamin A given with BCG vaccine on mortality in infants in Guinea-Bissau: randomised placebo controlled trial

Author information

Benn CS1, Diness BR, Roth A, Nante E, Fisker AB, Lisse IM, Yazdanbakhsh M, Whittle H, Rodrigues A, Aaby P.
Bandim Health Project, Statens Serum Institut
Artilleivej 5, 2300 Copenhagen S, Denmark
cb@ssi.dk

Abstract

OBJECTIVE

To investigate the effect of high dose vitamin A supplementation given with BCG vaccine at birth in an African setting with high infant mortality.

DESIGN

Randomised placebo controlled trial. Setting Bandim Health Project's demographic surveillance system in Guinea-Bissau, covering approximately 90,000 inhabitants. Participants 4345 infants due to receive BCG.

INTERVENTION

Infants were randomised to 50,000 IU vitamin A or placebo and followed until age 12 months.

MAIN OUTCOME MEASURE

Mortality rate ratios.

RESULTS

174 children died during follow-up (mortality=47/1000 person-years). Vitamin A supplementation was not significantly associated with mortality; the mortality rate ratio was 1.07 (95% confidence interval 0.79 to 1.44). The effect was 1.00 (0.65 to 1.56) during the first four months and 1.13 (0.75 to 1.68) from 4 to 12 months of age. The mortality rate ratio in boys was 0.84 (0.55 to 1.27) compared with 1.39 (0.90 to 2.14) in girls (P for interaction=0.10). An explorative analysis revealed a strong interaction between vitamin A and season of administration.

CONCLUSIONS

Vitamin A supplementation given with BCG vaccine at birth had no significant benefit in this African setting. Although little doubt exists that vitamin A supplementation reduces mortality in older children, a global recommendation of supplementation for all newborn infants may not contribute to better survival.

TRIAL REGISTRATION
Clinical trials NCT00168597.

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2432170/>

“Vitamin A supplementation given with BCG vaccine at birth had no significant benefit in this African setting.”

Status epilepticus and lymphocytic pneumonitis following hepatitis B vaccination

Author information

de Carvalho JF1, Shoenfeld Y.

Rheumatology Division
São Paulo University School of Medicine
São Paulo, Brazil

Abstract

The case reported refers to a patient who developed status epilepticus in the day of her third dose of hepatitis B vaccination and we review the literature on this subject. A 12 year-old girl, without a relevant previous history, taking no drugs, developed a seizure attack followed by unconsciousness, and eventually died after three days of her third dose of hepatitis B (HB) vaccination. Autopsy study revealed cerebral edema with congestion and herniation and diffuse interstitial type pneumonitis. There seem to be a straight forward time relationship between the third HB vaccine, the event of convulsion and the sudden death of the patient. We suggest that, in some cases, vaccination may be the triggering factor for autoimmune and neurological disturbances in genetically predisposed individuals and physicians should be aware of this possible association.

<http://www.ncbi.nlm.nih.gov/pubmed/18549949>

“A 12 year-old girl, without a relevant previous history, taking no drugs, developed a seizure attack followed by unconsciousness, and eventually died after three days of her third dose of hepatitis B (HB) vaccination. Autopsy study revealed cerebral edema with congestion and herniation and diffuse interstitial type pneumonitis. There seem to be a straight forward time relationship between the third HB vaccine, the event of convulsion and the sudden death of the patient. We suggest that, in some cases, vaccination may be the triggering factor for autoimmune and neurological disturbances in genetically predisposed individuals ...”

**Beta-tryptase and
quantitative mast-cell increase
in a sudden infant death
following hexavalent immunization**

Author information

D'Errico S1, Neri M, Riezzo I, Rossi G,
Pomara C, Turillazzi E, Fineschi V.

Department of Forensic Pathology, University of Foggia
Ospedale Colonnello D'Avanzo
Via degli Aviatori 1, 71100 Foggia, Italy

Abstract

The association between sudden infant death syndrome and immunization is frequently discussed. Serious adverse events following vaccination have generally been defined as those adverse events that result in permanent disability, hospitalization or prolongation of hospitalization, life threatening illness, congenital anomaly or death. They are generally referred to the inherent properties of the vaccine (vaccine reaction) or some error in the immunization process (programme error). The event could also be totally unrelated but only temporally linked to immunization (coincidental event). A fatal case of a 3-month-old female infant, who died within 24 h of vaccination with hexavalent vaccine is presented. Clinical data, post-mortem findings (acute pulmonary oedema, acute pulmonary emphysema), quali-quantitative data collected from immunohistochemical staining (degranulating mast cells) and laboratory analysis with a high level of beta-tryptase in serum, 43.3 microg/l, allows us to conclude that acute respiratory failure likely due to post hexavalent immunization-related shock was the cause of death.

<http://www.ncbi.nlm.nih.gov/pubmed/18538957>

“A fatal case of a 3-month-old female infant, who died within 24 h of vaccination with hexavalent vaccine is presented. Clinical data, post-mortem findings (acute pulmonary oedema, acute pulmonary emphysema), quali-quantitative data collected from immunohistochemical staining (degranulating mast cells) and laboratory analysis with a high level of beta-tryptase in serum, 43.3 microg/l, allows us to conclude that acute respiratory failure likely due to post hexavalent immunization-related shock was the cause of death.”

The Adjuvants Aluminum Hydroxide and MF59 Induce Monocyte and Granulocyte Chemoattractants and Enhance Monocyte Differentiation toward Dendritic Cells

Author Information

Anja Seubert, Elisabetta Monaci,
Mariagrazia Pizza, Derek T. O'Hagan and Andreas Wack

Novartis Vaccines, Siena, Italy

Abstract

Aluminum hydroxide (alum) and the oil-in-water emulsion MF59 are widely used, safe and effective adjuvants, yet their mechanism of action is poorly understood. We assessed the effects of alum and MF59 on human immune cells and found that both induce secretion of chemokines, such as CCL2 (MCP-1), CCL3 (MIP-1 α), CCL4 (MIP-1 β), and CXCL8 (IL-8), all involved in cell recruitment from blood into peripheral tissue. Alum appears to act mainly on macrophages and monocytes, whereas MF59 additionally targets granulocytes. Accordingly, monocytes and granulocytes migrate toward MF59-conditioned culture supernatants. In monocytes, both adjuvants lead to increased endocytosis, enhanced surface expression of MHC class II and CD86, and down-regulation of the monocyte marker CD14, which are all phenotypic changes consistent with a differentiation toward dendritic cells (DCs). When monocyte differentiation into DCs is induced by addition of cytokines, these adjuvants enhanced the acquisition of a mature DC phenotype and lead to an earlier and higher expression of MHC class II and CD86. In addition, MF59 induces further up-regulation of the maturation marker CD83 and the lymph node-homing receptor CCR7 on differentiating monocytes. Alum induces a similar but not identical pattern that clearly differs from the response to LPS. This model suggests a common adjuvant mechanism that is distinct from that mediated by danger signals. We conclude that during vaccination, adjuvants such as MF59 may increase recruitment of immune cells into the injection site, accelerate and enhance monocyte differentiation into DCs, augment Ag uptake, and facilitate migration of DCs into tissue-draining lymph nodes to prime adaptive immune responses.

Full Report: <http://www.jimmunol.org/content/180/8/5402.full>

“Aluminum hydroxide (alum) and the oil-in-water emulsion MF59 [squalene] are widely used, safe and effective adjuvants, yet their mechanism of action is poorly understood.”

Chronic fatigue syndrome with autoantibodies— the result of an augmented adjuvant effect of hepatitis-B vaccine and silicone implant

Author information

Nancy AL1, Shoenfeld Y.

Center for Autoimmune Diseases
Department of Medicine Beth Sheba Medical Center
Tel-Hashomer, Israel

Abstract

Background

Chronic fatigue syndrome (CFS) that defines by prolonged fatigue and other manifestations, was recently integrated into a spectrum of central sensitivity syndromes including several diseases as fibromyalgia. CFS etiology is multi-factorial commonly triggered by infectious agents. Vaccines, induce an immune response similarly to infections, and may trigger just like infections autoimmune diseases, CFS and fibromyalgia. Furthermore vaccines contain an adjuvant which enhances their immune stimulation.

Case Presentation

A 56-year-old woman was diagnosed with CFS accompanied by fibromyalgia, demyelination and autoantibodies. Her illness begun following the 2nd dose of hepatitis-B vaccine, and was aggravated by the 3rd vaccination. She underwent silicone breast implantation 6 years before vaccination with no adverse events. However, between the 2nd and 3rd vaccination she suffered a breast injury with local inflammation. Upon explanation of her breast implants silicone leak was observed.

Discussion

Vaccines have been reported to precede CFS mainly following exposure to multiple vaccinations (e.g. the Gulf war syndrome), or as an adverse response to the vaccine adjuvant (e.g. the macrophagic myofasciitis syndrome). Silicone is considered an adjuvant to the immune system, and may induce “the adjuvant disease”. Silicone implant, especially silicone leak relationship with autoimmunity and CFS has been the focus of considerable debates.

Conclusion

Our patient illness started following hepatitis-B vaccine, suggesting that it was caused or accelerated by vaccination. In parallel to vaccination our patient suffered from breast injury, which might represent the time of silicone leak. The exposure to the adjuvant, silicone, might have augmented her immune response to the vaccine. To the best of our knowledge this is the first case of combined adverse effect to vaccine and silicone. Vaccine safety in individuals with silicone implants requires further studies.

“... the changes induced by MF59
and alum share common features ...”

“Vaccines have been reported
to precede Chronic Fatigue Syndrome
mainly following exposure
to multiple vaccinations
(e.g. the Gulf war syndrome),
or as an adverse response
to the vaccine adjuvant
(e.g. the macrophagic
myofasciitis syndrome).”

Mumps epidemiology and immunity: the anatomy of a modern epidemic

Author information

Anderson LJ1, Seward JF.

Division of Viral Diseases
National Center for Immunization and Respiratory Diseases
Centers for Disease Control and Prevention
Atlanta, GA 30333, USA
lja2@cdc.gov

Abstract

The success of the measles, mumps, and rubella 2-dose vaccination program led public health officials in 1998 to set a goal to eliminate endemic transmission of mumps virus by 2010 in the United States. The large outbreak of mumps in the spring of 2006 has led public health officials to re-evaluate this goal and to recognize that the transmission and epidemiology of mumps in highly vaccinated populations may be different than anticipated. During 2006, a total of 6584 confirmed and probable cases of mumps were reported to the Centers for Disease Control and Prevention and most of these, 5865, occurred between January 1 and July 31. The peak of the outbreak was in April and seemed to be focused on college campuses in 9 midwestern states with Iowa having the highest attack rate. College campuses with mumps outbreaks included ones with 77% to 97% of students having had 2 doses of a mumps vaccine. Diagnosing mumps proved to be problematic in vaccinated persons (ie, laboratory tests seemed to be insensitive and some apparent mumps cases had mild nonclassic illness). The outbreak demonstrated that mumps can sometimes transmit efficiently in highly vaccinated populations and the clinical and laboratory diagnosis of mumps in vaccinated persons is more difficult than in naive persons. The reason for this mumps outbreak is not clear but probably results from multiple factors contributing to an overall increase in susceptibility and/or transmission.

<http://www.ncbi.nlm.nih.gov/pubmed/18820583>

“The outbreak demonstrated that mumps can sometimes transmit efficiently in highly vaccinated populations and the clinical and laboratory diagnosis of mumps in vaccinated persons is more difficult than in naive persons.”

Vaccine • November 2008

Vaccine immunogenetics: bedside to bench to population

Author information

Poland GA1, Ovsyannikova IG, Jacobson RM.

Mayo Vaccine Research Group
The Program in Translational Immunovirology and Biodefense
Mayo Clinic College of Medicine, Rochester, MN 55905, USA
poland.gregory@mayo.edu

Abstract

The immunogenetic basis for variations in immune response to vaccines in humans remains largely unknown. Many factors can contribute to the heterogeneity of vaccine-induced immune responses, including polymorphisms of immune response genes. It is important to identify those genes involved directly or indirectly in the generation of the immune response to vaccines. Our previous work with measles reveals the impact of immune response gene polymorphisms on measles vaccine-induced humoral and cellular immune responses. We demonstrate associations between genetic variations (single nucleotide polymorphisms, SNPs) in HLA class I and class II genes, cytokine, cell surface receptor, and toll-like receptor genes and variations in immune responses to measles vaccine. Such information may provide further understanding of genetic restrictions that influence the generation of protective immune responses to vaccines, and eventually the development of new vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/18598732>

“The immunogenetic basis for variations in immune response to vaccines in humans remains largely unknown.”

The history of vaccinations in the light of the autism epidemic

Author information

Cave SF

Cypress Integrative Medicine
Baton Rouge, Louisiana, USA

Abstract

Autism has been characterized as a behavioral disorder since it was first described by Leo Kanner in 1943. The number of autistic children has increased over the last decade. The incidence of autism was 1 in 10000 before the 1970s and has steadily increased to 1 in 150 in 2008 with a male:female predominance of 4:1. The cause of this epidemic has remained unknown, but several hypotheses have been studied. Many of these suggest an environmental trigger, such as the ethyl mercury contained in the preservative thimerosal, which has been used in vaccines since 1931. Other possible triggers associated with vaccinations are chemical toxins and live viruses. James has published studies suggesting a genetic predisposition in the families of autistic children, exposing them to a deficiency in glutathione and an inability to detoxify heavy metals. Vargas has shown autism to encompass ongoing inflammation in the brains of autistic children. The Hannah Poling vaccine decision was a landmark case. Poling's family was awarded funds for ongoing medical care of an autistic child who was found to have mitochondrial dysfunction exacerbated by vaccines that left her with autistic behavior and seizures. Several studies have emerged supporting the fact that a significant number of autistic children do have mitochondrial dysfunction. The impact that the Poling case will have on the ability of parents of autistic children to gain access to funds to enable them to properly care for their children remains to be seen.

<http://www.ncbi.nlm.nih.gov/pubmed/19043939>

“Poling’s family was awarded funds for ongoing medical care of an autistic child who was found to have mitochondrial dysfunction exacerbated by vaccines that left her with autistic behavior and seizures. Several studies have emerged supporting the fact that a significant number of autistic children do have mitochondrial dysfunction. The impact that the Poling case will have on the ability of parents of autistic children to gain access to funds to enable them to properly care for their children remains to be seen.”

Systemic polyarteritis nodosa following hepatitis B vaccination

Author information

de Carvalho JF1, Pereira RM, Shoenfeld Y.

Rheumatology Division
São Paulo University School of Medicine
São Paulo, Brazil

Abstract

The authors report a patient who developed systemic polyarteritis nodosa two months after hepatitis B vaccination and review the literature concerning this vaccination and the development of autoimmune conditions, mainly vasculitis. A 14-year-old boy who had no relevant previous history and who was not taking any drugs presented with a livedo reticularis, fever, loss of weight, testicular pain, and paresthesias two months after receiving the third dose of a hepatitis B vaccination. Inflammatory parameters (ESR and CRP) were high. The patient met the ACR diagnostic criteria for polyarteritis nodosa. He received corticosteroids and immunosuppressants and showed improvement. After reviewing the 27 cases of vasculitis after hepatitis B vaccination reported in the current literature, the authors suggest that, in some cases, vaccination may be the triggering factor for vasculitis in individuals with a genetic predisposition. Physicians should be aware of this possible association.

<http://www.ncbi.nlm.nih.gov/pubmed/19046721>

“After reviewing the 27 cases of vasculitis after hepatitis B vaccination reported in the current literature, the authors suggest that, in some cases, vaccination may be the triggering factor for vasculitis in individuals with a genetic predisposition.”

“There are currently over 100 human diseases that are considered to be autoimmune or chronic inflammatory affecting 5-10% of the world population and spanning through all medical specialties.”

Journal Of Autoimmunity • December 2008

**The autoimmunologist:
geoepidemiology, a new center of gravity,
and prime time for autoimmunity**

Author information

Shoenfeld Y1, Selmi C, Zimlichman E, Gershwin ME.

Department of Medicine B,
Center for Autoimmune Diseases, Sheba Medical Center
Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
shoenfel@post.tau.ac.il

Abstract

There are currently over 100 human diseases that are considered to be autoimmune or chronic inflammatory affecting 5-10% of the world population and spanning through all medical specialties. As a result, health care costs are enormous and the clinical management is often challenging, particularly considering the comorbidity rates and the multi-organ involvement of each condition. We herein propose the creation of a new specialist, coined the autoimmunologist, to overcome the current limitations in the diagnostic process and clinical follow-up of patients with autoimmune diseases. More importantly, we also propose the creation of regional centers of excellence in autoimmunity where clinical research and management, as well as basic research may be united and interact in ideal synergy to ultimately create real translational research and provide better health care.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18838248>

“In our study Oral Polio Virus at birth
had a sex-differential effect on mortality.”

PLoS ONE • 2008

Sex-Differential Effect on Infant Mortality of Oral Polio Vaccine Administered with BCG at Birth in Guinea-Bissau—A Natural Experiment

Christine Stabell Benn,^{1,*} Ane Bærent Fisker,²
Amabelia Rodrigues,² Henrik Ravn,¹ Erliyani Sartono,³ Hilton Whittle,⁴
Maria Yazdanbakhsh,³ and Peter Aaby²

1. Bandim Health Project, Statens Serum Institut, Copenhagen, Denmark
2. Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau
3. Department of Immunoparasitology, Leiden University Medical Centre
4. The MRC Laboratories, Fajara, The Gambia

Beverley J. Shea, Editor

Abstract

Background

The policy to provide oral polio vaccine (OPV) at birth was introduced in low-income countries to increase coverage. The effect of OPV at birth on overall child mortality was never studied. During a trial of vitamin A supplementation (VAS) at birth in Guinea-Bissau, OPV was not available during several periods. We took advantage of this “natural experiment” to test the effect on mortality of receiving OPV at birth.

Methodology

Between 2002 and 2004, the VAS trial randomised normal-birth-weight infants to 50,000 IU VAS or placebo administered with BCG. Provision of OPV at birth was not part of the trial, but we noted whether the infants received OPV or not. OPV was missing during several periods in 2004. We used Cox proportional hazards models to compute mortality rate ratios (MRR) of children who had received or not received OPV at birth.

Principal Findings

A total of 962 (22.1%) of the 4345 enrolled children did not receive OPV at birth; 179 children died within the first year of life. Missing OPV at birth was associated with a tendency for decreased mortality (adjusted MRR=0.69 (95% CI=0.46–1.03)), the effect being similar among recipients of VAS and placebo. There was a highly significant interaction between OPV at birth and sex ($p=0.006$). Not receiving OPV at birth was associated with a weak tendency for increased mortality in girls (1.14 (0.70–1.89)) but significantly decreased mortality in boys (0.35 (0.18–0.71)).

Conclusions

In our study OPV at birth had a sex-differential effect on mortality. Poliovirus is almost eradicated and OPV at birth contributes little to herd immunity. A randomised study of the effect of OPV at birth on overall mortality in both sexes is warranted.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2605256/>

Current childhood vaccine programs: An overview with emphasis on the Measles-Mumps-Rubella (MMR) vaccine and of its compromising of the mucosal immune system

Harold E. Buttram, MD
hbuttram1304@comcast.net

Abstract

Both common observation and official statistics confirm that there have been dramatic increases in chronic physical and mental illnesses in American children, such as autism, asthma, and allergies since the introduction of the MMR vaccine in 1978. Government health officials have denied a relationship with vaccines, but U.S. Congressional hearings on vaccine safety (1999 to Dec. 2004) revealed a total absence of vaccine safety tests that would meet current scientific standards, so that it can be assumed that many vaccine reactions are taking place unrecognized. Prior to the introduction of vaccines, the Th1 cellular immune system of the gastrointestinal and respiratory systems served as the primary defense systems with the Th2 humoral immune system in the bone marrow, serving a secondary role.

There is a school of thought that the “minor childhood diseases” of earlier times, including measles, mumps, chicken pox, and rubella, which involved the epithelial tissues of skin, respiratory, and/or gastrointestinal tracts, served a necessary purpose in challenging, strengthening, and establishing the dominance of Th1 cellular immune system during early childhood. Current vaccines against these diseases, in contrast, being directed at stimulating antibody production in the bone marrow, are bypassing the cellular immune system and thereby tending to reverse the roles of the cellular and humoral systems, with the former suffering from a lack of challenge. In addition, the cellular immune system is being further compromised by the powerfully immunosuppressive effects of the MMR vaccine. The time is overdue to totally rethink and redirect our current childhood vaccine program.

Concerns about increasing incidence of childhood autism and related disorders

Many years ago in our medical practice we began asking teachers if, during their teaching careers, they had observed a change in children. Without exception, they replied that there had been a dramatic change, most notably since the early 1980s. Steadily increasing numbers of children, they reported, were showing autistic-like behaviors, were restless, impulsive, less focused, less able to concentrate, and therefore less able to learn.

It has been documented that a sharp and persisting rise in the incidence of childhood autism commenced following the 1978 introduction of the MMR vaccine in the U.S.A. [1-2], a time when mercury-laced Hepatitis B and Hemophilus influenza type b vaccines were also introduced. For a number of years previously the live measles, mumps, and rubella vaccines had been administered separately with negligible increases in autism. It was only after they were combined that the incidence of autism began soaring with 1 in 150 children up to eight years age, according to U.S. multisite study in 2000 [3], as compared with 1 in 10,000 several generations ago. According to more recent information, the incidence of autism may be even higher, with 1 in 88 military children in U.S.A. having autism [4], and according to the Vaccine Autoimmune Project (VAP), one in 67 in U.S.A. and 1 in 86 in the United Kingdom having autism [5]. Considering that the incidence of autism in boys is approximately four times greater than in girls, the relative incidence of autism in boys would be even greater. Finally, as estimated by VAP, the average lifetime cost of caring for autistic children will be about \$3.2 million dollars per child.

In addition to the autism epidemic, in 2004 almost five million children were classified as learning disabled [6], which represents a three-fold increase since 1976-7 according to the Digest of Education Statistics [7].

Comparable increases have taken place in attention deficit hyperactive disorder (ADHD), with four and one half million children between ages 3 and 17 being diagnosed with this condition in 2004 [8].

In a bulletin sponsored by the American Academy of Pediatrics, January, 2004, entitled “AUTISM A.L.A.R.M.”, in addition to an announcement of the increasing prevalence of autism at that time, it was announced that 1 in 6 American children were diagnosed with a developmental disorder and/or behavioral disorder.

In a similar fashion the incidence of asthma has increased from roughly two and a half million children, ages 0-17 years in 1979 [8] to nine million children 0-17 years in 2004 [8], (roughly 12% of that age group), a time period in which this age-group population increased 114% compared to a 360% increase in asthma.

Autoimmune diseases are also increasing, including juvenile diabetes, multiple sclerosis, Guillain-Barre Syndrome, and Crohn’s inflammatory bowel disease. Based on the work of Vijendra Singh, who demonstrated marked elevations of brain antibodies in the form of myelin basic protein antibodies in autistic children [9-10], autism itself can be considered an autoimmune disorder.

Current studies implicating vaccines as primary causal agents of autism and related disorders

In what may be the most comprehensive publication to date on the pathophysiology of adverse vaccine reactions, Russell Blaylock has compiled a mass of evidence that repeated stimulation of the systemic immune system results in first priming of microglia of the developing brain, following by intense microglial reaction with each successive series of vaccinations [16]

In explanation, microglia and astrocytes are first-line-immunological responder cells located in the brain which defend against foreign infectious invaders. Normally this response, such as to a viral infection, is of limited duration and harmless to the brain. However, when the microcytes and astrocytes are overstimulated for prolonged periods, which vaccines are designed to bring about, this extended activation can be very destructive to the brain.

Because of the critical dependence of the developing brain on a timed sequence of cytokine and excitatory amino acid fluctuation, according to Blaylock, sequential vaccinations can result in alterations of this critical process that will not only result in synaptic and dendritic loss, but abnormal (nerve) pathway development. When microglia are excessively activated by vaccines, especially chronically, they secrete a number of inflammatory cytokines, free radicals, lipid peroxidation products, and the two excitotoxins, glutamate and quinolenic acid, which may become highly destructive to the brain when these cells are excessively stimulated for prolonged periods. This process was suggested as the central mechanism resulting in the pathological as well as clinical features of autism [16].

Since the U.S. Congressional Hearings on issues of vaccine safety ended in December, 2004, credible and statistically significant studies have begun appearing that: a) meet the established criteria for effective safety tests and b) without exception in my opinion, have implicated vaccines as central causal factors in today’s epidemic of autism and related disorders. Several are listed below:

- As published in the Annals of Neurology [17], Diana Vargas and colleagues examined the brains from autopsies of 11 autistic patients, ranging in ages from 5 to 44 years, in which they found the presence of extensively activated microglia and astrocytes along with elevations of cytokines and chemokines, which are immune system proteins involved in inflammatory processes. As the first study of its kind, it tends to support Blaylock’s theory

that overstimulation of the brain's microglia and astrocytes for excessively prolonged periods resulting from current vaccine programs plays a central causal role in today's epidemic of childhood autism.

- Surveys from four widely separated geographic areas have shown higher rates of asthma in fully vaccinated children as compared with those with limited or no vaccines [18-21].

- A study on primary immunization of 239 premature infants with gestational ages of less than 35 weeks was conducted by M. Pourcyrous et al. (Journal of Pediatrics [22], to determine the incidence of cardiorespiratory events and abnormal C-reactive protein (CRP) levels associated with administration of a single vaccine or multiple vaccines simultaneously at or about two months age. (CRP is a standard blood test to measure body inflammation.) CRP levels and cardiorespiratory events were monitored for three days following immunizations in a neonatal intensive care unit sponsored by the University of Tennessee. Elevations of CRP levels occurred in 70% of infants administered single vaccines and in 85% of those given multiple vaccines, 43% of which reached abnormal levels. Overall, 16% of infants had vaccine-associated cardiorespiratory events with episodes of apnea (cessation of breathing) and bradycardia. Most important, 17% of those receiving single vaccines had intraventricular brain hemorrhages, with an incidence of 24% of those receiving multiple vaccines. (This is the first study of its kind, showing that brain hemorrhages can commonly take place in vulnerable infants, now being misdiagnosed as Shaken Baby Syndrome in hospital emergency rooms.) It should be noted that each and every one of the preceding adverse manifestations could be attributed to vaccine-induced brain inflammation.

- Though long denied by health officials, the action of mercury in causing brain inflammation in autistic children tends to be confirmed by Sajdel, Sulkowska, et al. [23]. Also the first of its kind, this study compared the cerebellar levels of the oxidative stress marker, 3-nitrotyrosine (3-NT), mercury (Hg), and the antioxidant, selenium (Se) between autistic and normal children. Average cerebellar 3-NT levels were statistically elevated by 68% in autistic children, cerebellar Hg by 68%, and mercury levels relative to protective selenium by 75% in autistic cases in comparison to controls.

- In a study along similar lines to the S. Sulkowska study above, X. Ming et al. [24] reviewed their animal model of autism, showing that oxidative stress from methylmercury or valproic acid exposures in early postnatal life of mice resulted in aberrant social, cognitive, and motor behavior. They also found that Trolox, a water-soluble vitamin E derivative, was capable of attenuating a number of these adverse neurobehavioral side effects.

- A telephone survey commissioned by the nonprofit group, Generation Rescue, compared vaccinated with unvaccinated boys in nine counties of Oregon and California [25]. The survey included nearly 12,000 households with children ranging in age from 4 to 17 years, including more than 17,000 boys among whom 991 were described as being completely unvaccinated. The survey found that, compared to unvaccinated boys, vaccinated boys were 155% more likely to have a neurological disorder, 224% more likely to have ADHD, and 61% more likely to have autism. For older vaccinated boys in the 11-17 age bracket, the results were even more pronounced, with 158% more likely to have neurological disorders, 317% more likely to have ADHD, and 112% more likely to have autism.

- In October, 1998 the French government abandoned its mandatory hepatitis B vaccine program for school children after more than 15,000 law suits were filed for brain damage and autoimmune reactions including arthritis, multiple sclerosis, and lupus.

Vaccine adjuvants—their role in inducing prolonged immune response to vaccines and their potentially adverse consequences

- As reviewed by Blaylock [16], adjuvants are substances added to vaccine formulations during manufacturing that are designed to boost the overall immune system response when the vaccine is injected. These substances

include albumin, several forms of aluminum, formaldehyde, various amino acids, DNA residues, egg protein, gelatin, surfactants, monosodium glutamate(MSG), Thimerosal (50% ethyl mercury), and various antibiotics.

- Contrary to public avowals as to the removal of mercury from vaccines, at time of this writing it is still present in the USA as a preservative in the multi-dose vials of tetanus-toxoid booster vaccines, the Menomune vaccine, the JE-Vax, and the inactivated influenza vaccines, including the “bird-flu” vaccine. Also it's used in the manufacturing process of many vaccines to remove contaminants, which currently leaves trace residues of mercury in seven other vaccine formulations. Even these trace amounts are potentially toxic because of the universally recognized principle of toxicology, that combinations of toxins will increase toxicity exponentially; that is, two heavy metals will increase toxicity 10-fold, or three heavy metals increase toxicity 100-fold. In vaccines, the combinations would be mercury and aluminum. The same principle applies in other forms of toxic chemicals [26-28].

- A study that was conducted in Lima, Peru by J. Laurente and colleagues [29] should remove all doubts about the potential dangers of mercury-containing thimerosal as a vaccine additive: To determine if thimerosal administration in amounts equivalent to vaccine content produces neurotoxic effects on the encephalon in postnatal hamsters and on the experimentation animals' development, three serial thimerosal injections were given on birth days 7, 9, and 11, with controls receiving only saline injection. Test animals subsequently showed statistically significant reduction in both weight and stature compared with controls. Neurotoxic effects were also produced at encephalic (brain) level at the hippocampus, cerebral cortex, and cerebellum. On tissue slides there was decrease in neuronal density, neuronal necrosis, and axonal demyelination in test animals.

- In vaccines, virtually insoluble polymeric aluminum hydroxy compounds serve to dramatically boost and prolong the immune reaction to the vaccination by prolonged activation of the macrophagic immune sub-system in some people [30-35].

Ongoing mass (herd) immunizations – are they necessary?

- Vaccine proponents would have us believe that mass vaccine programs have been largely responsible for controlling virtually all of the former epidemics of killer childhood diseases in industrialized nations, In my opinion, with the exception of small-pox and the possible exception of the polio vaccine, the facts do not bear this out. According to the Metropolitan Life Insurance Company, from 1911 to 1935 the four leading causes of childhood deaths from infectious diseases in the USA were diphtheria, pertussis (whooping cough), scarlet fever, and measles. Yet, by 1945 the combined death rates from these causes had declined by 95%, before implementation of mass vaccine programs [39]. Other sources provided much the same pattern of information [40-41]. Furthermore, according to a report in Morbidity and Mortality Weekly Report, July 30, 1999, improvements in sanitation, water quality, hygiene, and the introduction of antibiotics have been the most important factors in control of infectious disease in the past century. Although vaccines were mentioned, they were not included among the major factors [42].

The MMR vaccine and childhood autism: a hypothetical model

- As mentioned earlier, it was only after the combination of the measles, mumps, and rubella live viruses into a single vaccine in the USA in 1978 that the incidence of childhood autism showed a sharp and dramatic increase [1-2]. Prior to that time the three viral vaccines had been in use a number of years, but given separately without significant increases in autism.

- In addition to the Blaylock model of microglial overstimulation, also undoubtedly playing a major role [16], there are two plausible explanations for increases in autism following the MMR vaccine: First, protein sequences in the measles virus have been found to have similarities to those in brain tissues [43], so that by process of mimicry, the formation of antibodies against the measles virus would tend to cross react adversely with the brain.

Second, and probably far more important, viruses are inherently immunosuppressive, in contrast to bacterial infections which stimulate the immune system, as reflected in the fact that viral infections generally lower white blood counts in contrast to bacterial infections, which raise white counts. The measles virus is exceptionally potent in this regard, being powerfully suppressive to cellular immunity [44-46], with the suppressive action of measles largely attributed to its suppression of interleukin 12, on which cellular immunity is dependent [45]. Consequently the combining of three viral vaccines into a single combination may substantially increase the immunosuppressive vital effect, bringing about, in varying degrees, an immune paralysis in the infant. Under these circumstances the measles virus may spread into various tissues of the body. As with combinations of toxic chemicals that bring exponential increases in toxicities [26-28], combinations in viral vaccines may bring exponential increases in their toxic, immunosuppressive effects.

- In support of this hypothesis, Wakefield et al. have demonstrated live measles virus in the small intestinal lymph nodes in children with the autistic-colitis syndrome, with the only possible source being from the live virus in the MMR vaccine [47].

- In his various lectures in this country, Wakefield stressed that it was only following the introduction of the MMR vaccine in the United Kingdom in 1987 that the rapid increase in childhood the colitis/autistic syndrome began to be seen. This pattern was further confirmed by checking back into the records of public health departments of the United Kingdom and finding reports of autism occurring among children contracting two such childhood diseases simultaneously, such as chicken pox and measles, or mumps and measles.

- As reviewed by Blaylock [16], a number of studies have shown that live viruses used in vaccines can enter the brain and reside there for a lifetime. One study, in which autopsied tissues from the elderly were examined for the presence of the measles virus, found that 20% of brains had live measles virus and that 45% of other organs were infested as well [48].

- As another study suggesting that active brain invasion by the measles virus in autistic children from the MMR vaccination, Bradstreet et al. [49] examined cerebrospinal fluid from three autistic children, which revealed the presence of measles virus genomic RNA.

- As to other viral vaccines, as reported by Bernard Rimland, the chicken pox vaccine is also playing a role in these cases.

- “The federal government’s Vaccine Adverse Event Reporting System (VAERS), which supposedly documents adverse reactions to vaccines, received nearly 10,000 reports involving the chickenpox vaccine between March, 1995 and December, 1999. Some of these reactions included brain inflammation, neurological damage, immune system abnormalities, seizures, and death. It is important to note, by the way, that since reporting adverse events is not mandatory, only an estimated 1 to 10% of adverse events are reported to VAERS.”[50]

- In addition, articles by Gary Goldman seriously question the efficacy and advisability of universal varicella vaccination [51,52].

- Immunosuppressive effects have also been reported from the rubella vaccine. In a study of eighteen school girls, ages 11 to 13 years by Pukhalsky et al., profound depression of interferon gamma (a key mediator of cellular immunity) was found 30 days following rubella vaccine [53].

Returning to the MMR vaccine, F. Imani and K. Kehoe found a previously unrecognized side effect by incubating the MMR vaccine with a line of human plasma cells, which resulted in increase in the expression of allergy-related IgE antibodies, and secondarily a decrease in protective IgG antibodies. Based on these findings, the authors concluded that viral vaccines may be playing a role in the increasing incidence of asthma and other allergic diseases [54].

John B. Classen, M.D., and epidemiologic studies concerning a suspected causal relationship between vaccines and the rising incidence of Insulin-Dependent Diabetes mellitus (IDDM)

- In 1998 John Classen, M.D. gave a presentation at a conference held by the American College of Medicine in which he reviewed 32 published articles, five authored by himself, indicating a causal relationship between vaccines and the rising incidence of IDDM. Nations represented in the papers included New Zealand, Canada, the United Kingdom, Denmark, Finland, Sweden, the U.S., and Holland. Single vaccines were used including haemophilus, hepatitis B, pertussis, BCG, and smallpox.

- A prototype was one conducted in Finland by Classen and reported in the British Medical Journal [58]. In this study, from all children born in Finland between October 1, 1985 and August 31, 1987, approximately 116,000 were randomized as test subjects to receive four doses of haemophilus vaccine starting at three months of age, or one dose starting at 24 months. 125,500 unvaccinated children served as controls. Each group was followed until age 10 years for development of IDDM. The incidence at seven years for those receiving four doses, those receiving one dose, and those receiving none was 261, 237, and 207 respectively with relative risks of 1.2, 1.14, and 1 for those receiving no vaccine.

- In virtually all of the reports from other countries the results were very similar, indicating a slight but consistent increase in IDDM following each of the single vaccines listed above. Classen interpreted these results as indicating that it was not the type of vaccination that mattered so much as the immunologic impact of vaccination itself. Typically there was a delay of 3 to 5 years between vaccines and onset of IDDM.

Quotations by Classen during the 1998 conference included:

“Vaccinating every child against every disease is fundamentally unsound.”

“There is a 3.78-fold increased risk of insulin-dependent diabetes mellitus in children from today’s vaccines.”

“All autoimmune diseases are increasing in incidence. General immune (over) stimulation from vaccines is a cause of autoimmunity.”

Summary and conclusions

- Over eons of time nature has evolved two major branches of the immune system, the Th1 cellular system located in the mucous membranes of the gastrointestinal and respiratory systems, and the Th2 humoral system, which involves the production of antigen-specific antibodies by plasma cells in bone marrow. Both systems are incredibly complex both in the timing of their developments and their functions. Since a large majority of infectious microorganisms enter the body through the mucous membranes, the cellular immune system has evolved as the primary immune defense system of the body, with the humoral system serving as a secondary or backup role. For these reasons, evolutionary challenges have required the cellular immune system to become more effective in dealing with infectious micro-organisms, especially intracellular viral infections [57]. This is undoubtedly the reason that vaccine-induced immunities to measles, mumps, chicken pox, and rubella, which bypass the cellular immune system, are of limited duration requiring repeated vaccinations. The natural diseases of former times, in contrast, were dealt with much more effectively by the cellular immune system, almost always conferring permanent immunity.

- The reader may well question that we have innumerable viruses passing around in the population today. Would they not serve the same purposes as measles, chicken pox, mumps, and rubella? Perhaps, except that chicken pox, mumps, rubella, and especially measles affect and challenge the epithelial tissues of the skin, respiratory (rubella),

and gastrointestinal tracts (measles, chicken pox, and mumps) in ways that few if any other viruses do.

- As reviewed above, a newborn infant comes into the world with a rudimentary immune system which requires a series of challenges to bring it to full functional capacity, a process requiring approximately three years. In earlier times these challenges were largely in the forms of the “minor childhood diseases” listed above. With time and experience it is becoming evident that, in addition to those already mentioned, another flaw in today’s vaccine programs is that the injectable vaccines, directed at stimulating antibody production in the bone marrow, are bypassing the cellular immune system, leaving it relatively unchallenged and therefore relatively weak and stunted during the critical infant/childhood period. In addition, there are the powerfully immunosuppressive effects of the MMR vaccine and other viral vaccines, to which the cellular immune system is uniquely vulnerable. These processes appear to be progressively undermining and eroding the cellular immune system, and unless discontinued or changed, may lead to an immunological collapses. Perhaps it already has for some children.

- It is or should be manifestly apparent that the humoral antibody-producing system of the bone marrow can never functionally replace the far more efficient cellular immune system.

- For this reason, in my opinion, any children’s vaccine program which does not allow the cellular (mucosal) immune system to develop unhampered in a natural way from natural challenges will be self-defeating. This would necessarily require a delay of childhood vaccines until two or three years of age. With this delay, the minor childhood viral diseases might well return, but would this be a bad thing? The dangers of chicken pox and mumps have been greatly exaggerated. Because of concerns for congenital rubella, the rubella vaccine could be delayed to later years, as the infection itself is very mild. Historically, measles did have some serious consequences including encephalitis, blindness or death in about 1 in 150 cases. However, there are other answers. Nutrition has been one of the missing links all along. In third world countries where measles has resulted in high mortality, this has usually been associated with malnutrition. One example of nutritional intervention is vitamin A therapy, authorized by the World Health Organization in developing nations, which has significantly reduced both mortality and morbidity from measles.

- A study in Afghanistan which showed significantly greater morbidity and mortality from measles in children administered aspirin and Tylenol than those not given these medications [62], so that these should be avoided with measles.

- Then too, we now have antibiotics for secondary infections associated with measles, which they did not have in the days when measles carried a small but significant rate of morbidities and mortality, much of which was from secondary infections.

- All of the above lies in the future. For today’s parents the Autism Research Institute with headquarters in San Diego, California (www.AutismResearchInstitute.com) has made the following safety recommendations in childhood vaccines:

- Never vaccinate a sick child, even if he or she just has a runny nose.
- Never give more than two vaccines simultaneously.
- Rather than the MMR vaccine, request that these viral vaccines be given separately, preferably six months apart; give measles last; and do not give any other vaccines for at least 1 year after measles. Some compounding pharmacies do provide these individual vaccines.
- Administer vitamins A, D and C before and after vaccines.
- Never allow a vaccine containing any level of the mercurial compound, Thimerosal.

At time of this writing in late 2008, 50 micrograms of Thimerosal is still present in each 0.5- mL dose of vaccine from multi-dose vials of influenza vaccines and multi-dose vials of tetanus booster vaccines, but not in single dose vials of these vaccines. A total of 17 vaccine formulations are still approved and available for use that contain some level of Thimerosal; 10 of these 17 vaccine formulations contain a preservative level of Thimerosal.

- Any overview on vaccines would be incomplete without mention of the work of the highly published immunologist, H. H. Fudenberg, and his work in developing clinical applications of transfer factor, which is a low molecular weight extract of lymphocytes, capable of enhancing or inducing cell-mediated immunity de novo (without immunizations) in an antigen specific fashion [63-64].

- Finally, in view of gross deficiencies of vaccine safety testings, as documented by the U.S. Congressional Hearings on issues of vaccine safety (1999-December, 2004), the time is long overdue for a total rethinking and redirecting of current childhood vaccine programs. Until the safety of such programs can be assured by thorough and dependable safety testing, any further mandating of childhood vaccines will remain morally and ethically untenable.

<http://www.know-vaccines.org/PDF/MMRmucosalIS.pdf>

The Safety Profile of Varicella Vaccine: A 10-Year Review

Susan A. Galea¹, Ann Sweet¹, Paul Beninger¹, Sharon P. Steinberg², Philip S. LaRussa², Anne A. Gershon² and Robert G. Sharrar¹

1. Merck Research Laboratories, Clinical Risk Management and Safety Surveillance, North Wales, PA

2. Columbia University College of Physicians and Surgeons, New York, NY

Abstract Excerpts

Reports of breakthrough varicella

There were 5054 reports of breakthrough varicella, for a reporting rate of 0.9 reports/ 10,000 doses of vaccine distributed. Fifty-one reports (1%) met the regulatory definition of “serious.”

Secondary transmission

The VZVIP confirmed 3 cases of secondary transmission of Oka VZV. The Oka VZV was present in a 30-year-old pregnant woman who developed 100 vesicular lesions 16 days after her 1-year-old son developed □30 vesicular lesions 24 days after varicella vaccination. She elected to have a therapeutic abortion, and the products of conception were negative for VZV by PCR analysis [5]. In the second report, the Oka VZV strain was also present in a 4-month-old boy who developed 25 lesions 19 days after his 1-year-old sibling developed 2 vesicular lesions 14 days after vaccination. The third case in which Oka VZV was identified occurred in a 35-year-old father who developed >100 lesions 17 days after his 1-year-old son developed 12 vesicular lesions 17 days after vaccination. In each of the 3 confirmed secondary-transmission cases, the vaccine recipient had a postvaccination rash and had close, household contact with the susceptible individual.

Additionally, there were 2 reported cases of possible secondary transmission, in which it was reported that the presence of Oka VZV was identified by an outside laboratory [6, 7]. The specimens for these cases were not analyzed through or confirmed by the VZVIP.

Neurologic AEs

Neurologic syndromes, such as encephalitis, aseptic meningitis, and cerebellar ataxia, have been reported in the postmarketing environment after administration of Varivax. There were 30 (CSF) specimens analyzed by PCR (table 1) from patients with reports of such syndromes. The reported AEs associated with these reports included encephalitis (12 patients), meningitis (5 patients), ataxia (5 patients), transverse myelitis (3 patients), seizures (3 patients), demyelinating disorder (1 patient), and hemiparesis (1 patient). The 5 meningitis reports associated with HZ listed in the “HZ” subsection above are different

from the cases of meningitis listed in this subsection and are not included here. None of the CSF specimens from these neurologic reports had Oka VZV identified by PCR analysis. Several of these reports have been described elsewhere [1, 4].

Herpes Zoster

There were 697 reports of HZ occurring 1-3509 days (median, 362 days) after vaccination in patients 13 months to 68 years of age (median age, 3.4 years). Four hundred patients (65%) for whom age was reported were <5 years of age. Table 2 compares the HZ reports in which PCR analysis identified Oka VZV and wild-type VZV strains.

The site of HZ was more likely to correlate with the site of vaccine injection in reports in which Oka VZV was identified. PCR was more likely to identify wild-type VZV than Oka VZV if the time to onset was within 42 days of vaccination. However, 2 reports in which HZ was diagnosed within 42 days of vaccination had specimens in which Oka VZV was identified. One of these reports was of a child with acute lymphocytic leukemia diagnosed 10 days after vaccination with Varivax. The child eventually developed HZ on 3 occasions: 23, 47, and 116 days after vaccination. PCR analysis of a specimen from the last episode of HZ identified Oka VZV. In the second report, Oka VZV was present in a girl 5 years of age who developed an HZ-like rash in the distribution of the second division of the trigeminal nerve (right side of face and right eye) 25 days after receiving Varivax.

Five patients developed meningitis in association with HZ. Cerebrospinal fluid (CSF) specimens from these patients were negative for VZV. The HZ rash specimens from 2 of the patients had Oka VZV identified; however, in 1 of these reports, enterovirus was identified in the CSF analyzed at the Centers for Disease Control and Prevention (CDC). A third patient had wild-type VZV identified from an HZ rash specimen. Additionally, 1 child who received Varivax at 2-3 years of age had acute lymphocytic leukemia diagnosed at 4 years of age. After treatment with 6-mercaptopurine weekly and methotrexate monthly, he was hospitalized for HZ and mild meningeal signs. A CSF specimen had Oka VZV identified. The child recovered.

Potential conflicts of interest

S.A.G., A.S., P.B., and R.G.S. are salaried employees of Merck and possess stock and stock options in the company.

A.A.G. lectures and consults on varicella-zoster virus vaccines for Merck and GlaxoSmithKline when invited and receives research support from Merck. Additionally, P.S.L., S.P.S., and A.A.G. are in a contractual relationship with Merck through the Varicella Zoster Virus Identification Program.

Full Report:

http://jid.oxfordjournals.org/content/197/Supplement_2/S165.full

Simpsonwood • Scientific Review of Vaccine Safety Datalink Information

Norcross, Georgia

Quotes from and link to transcript with a
Discussion on the following page

“...the number of dose related relationships [between mercury and autism] are linear and statistically significant. You can play with this all you want. They are linear. They are statistically significant.”

—Dr. William Weil, American Academy of Pediatrics. Simpsonwood, GA, June 7, 2000

“Forgive this personal comment, but I got called out at eight o’clock for an emergency call and my daughter-in-law delivered a son by c-section. Our first male in the line of the next generation and I do not want that grandson to get a Thimerosal containing vaccine until we know better what is going on. It will probably take a long time. In the meantime, and I know there are probably implications for this internationally, but in the meanwhile I think I want that grandson to only be given Thimerosal-free vaccines.”

—Dr. Robert Johnson, Immunologist, University of Colorado, Simpsonwood, GA, June 7, 2000

“But there is now the point at which the research results have to be handled, and even if this committee decides that there is no association and that information gets out, the work has been done and through the freedom of information that will be taken by others and will be used in other ways beyond the control of this group. And I am very concerned about that as I suspect that it is already too late to do anything regardless of any professional body and what they say ... My mandate as I sit here in this group is to make sure at the end of the day that 100,000,000 are immunized with DTP, Hepatitis B and if possible Hib, this year, next year and for many years to come, and that will have to be with thimerosal containing vaccines unless a miracle occurs and an alternative is found quickly and is tried and found to be safe.”

—Dr. John Clements, World Health Organization, Simpsonwood, GA, June 7, 2000

“We are in a bad position from the standpoint of defending any lawsuits, this will be a resource to our very busy plaintiff attorneys in this country.”

—Dr. Robert Brent, a pediatrician at the Alfred I. duPont Hospital for Children in Delaware. “

“given the sensitivity of the information, we have been able to keep it out of the hands of, let’s say, less responsible hands.”

—Dr. Bob Chen, head of vaccine safety for the CDC

the study “should not have been done at all” the results “will be taken by others and will be used in ways beyond the control of this group. The research results have to be handled.”

— Dr. John Clements, vaccines advisor at the World Health Organization

Link to Simpsonwood Document: <http://thinktwice.com/simpsonwood.pdf>

The truth behind the vaccine cover-up

Russell L. Blaylock, MD
www.russellblaylockmd.com

Abstract

On June 7-8, 2000 a secret conference was held at the Simpsonwood Conference Center in Norcross, Georgia to discuss a study examining the link between increasing doses of Thimerosal and neurodevelopmental disorders. The study was done using the Vaccine Safety Datalink (VSD) data-base, an official governmental data bank collecting patient vaccination information on the children from the health maintenance organizations (HMOs) being paid to participate. Attending were 51 scientists, representatives of pharmaceutical vaccine manufacturing companies and a representative of the World Health Organization; the public and the media were unlawfully excluded. The conclusions of this meeting were quite startling, since it confirmed a dose-response link between Thimerosal and neurodevelopmental disorders that held up to rigorous statistical analyses.

In their discussion, they make plain why the meeting was held in secret: the conclusions would have destroyed the public's confidence in the vaccine program, and more importantly, their faith in vaccine authorities. When the results of this study were published three years later in the journal Pediatrics, the "problem" had been fixed, in that by adding another set of data from a third HMO, reorganizing the criteria for inclusion and restructuring the patient groupings, a less than statistically significant link was demonstrated. In my analysis I discuss the more outrageous statements made during the meeting and how accepted experts in the field of mercury neurotoxicity were excluded from the meeting.

I was asked to write a paper on some of the newer mechanisms of vaccine damage to the nervous system, but in the interim I came across an incredible document that should blow the lid off the cover-up being engineered by the pharmaceutical companies in conjunction with powerful governmental agencies.

It all started when a friend of mine sent me a copy of a letter from Congressman David Weldon, M.D. to the director of the CDC, Dr Julie L. Gerberding, in which Congressman Weldon alludes to a study by a Doctor Thomas Verstraeten, then representing the CDC, on the connection between infant exposure to Thimerosal-containing vaccines and neurodevelopmental injury. In this shocking letter, Congressman Weldon refers to Dr. Verstraeten's study, which looked at the data from the Vaccine Safety Datalink and found a statistically significant correlation between Thimerosal exposure via vaccines and several neurodevelopmental disorders including tics, speech and language delays, and possibly ADD.

Congressman Weldon questions the CDC director as to why, following this meeting, Dr. Verstraeten published his results almost four years later in the journal Pediatrics to show just the opposite, that is, that except for tics, there was no statistically significant correlation to any neurodevelopmental problems related to Thimerosal exposure in infants. In this letter, Congressman Weldon refers to a report of the minutes of this meeting held in 2000, which exposes some incredible statements by the "experts" making up this study group. The group's purpose was to evaluate and discuss Dr. Verstraeten's interim results and data and make recommendations that would eventually lead to possible alterations in existing vaccine policy.

I contacted Congressman Weldon's legislative assistant and he kindly sent me a complete copy of this report. Now, as usual in these cases, the government did not give up this report willingly; it required a Freedom of Information Act lawsuit to pry it loose. Having read the report twice and having carefully analyzed it, I can see why

they did not want any outsiders to see it. It is a bombshell, as you shall see.

To help the reader understand the importance of this report, in this analysis I will not only describe and discuss this report, but also will frequently quote their words directly and supply the exact page number so others can see for themselves.

The official title of the meeting was the "Scientific Review of Vaccine Safety Datalink Information." This conference, held on June 7-8, 2000, at Simpsonwood Retreat Center in Norcross, Georgia, assembled 51 scientists and physicians, five of whom represented vaccine manufacturers. These included Smith Kline Beecham, Merck, Wyeth, North American Vaccine and Aventis Pasteur.

During this conference, these scientists focused on the study of the Datalink material, whose main author was Dr. Thomas Verstraeten and who identified himself as working at the National Immunization Program of the CDC. It was discovered by Congressman Weldon that Dr. Verstraeten left the CDC shortly after this conference to work for the Belgian operations of the pharmaceutical maker GlaxoSmithKline—a recurring regulated agency/regulated-industry pattern that has been given the name "a revolving door". It is also interesting to note that GlaxoSmithKline was involved in several lawsuits over complications secondary to their vaccines.

To start off the meeting, Dr. Roger Bernier, Associate Director for Science in the National Immunization Program (CDC), related some pertinent history. He stated that Congressional action in 1997 required that the FDA review mercury being used in drugs and biologics (vaccines). To meet this mandate, the FDA called for all the registered manufacturers of drugs, including vaccines, to submit the mercury information about their drug products. He notes that a group of European regulators and manufacturers met on April 1999 and acknowledged the situation but made no recommendations or changes. In other words, it was all for show.

At this point Dr. Bernier makes an incredible statement (page 12). He says, "*In the United States there was a growing recognition that cumulative exposure may exceed some of the guidelines.*" By guidelines, he is referring to guidelines for mercury exposure safety levels set by several regulatory agencies. The three guidelines were set by the ATSDR (The Agency for Toxic Substances and Disease Registry), the FDA (Food and Drug Administration), and the EPA (Environmental Protection Agency). The most consistently violated safety guideline was the mercury-in-food limit set by the EPA. He further explains that he is referring to children being exposed to Thimerosal in vaccines.

Based on this realization that they were violating safety guidelines, he says that this then "*resulted in a joint statement of the Public Health Service (PHS) and the American Academy of Pediatrics (AAP) in July of last year (1999), which stated that as a long term goal, it was desirable to remove mercury from vaccines because it was a potentially preventable source of exposure.*" (Page 12)

As an aside, one has to wonder, where was the Public Health Service and American Academy of Pediatrics during all the years of mercury use in vaccines and why didn't they know that, number one, they were exceeding regulatory safety levels and secondly, why weren't they aware of the extensive literature showing deleterious effects on the developing nervous system of babies? As we shall see, even these "experts" seem to be cloudy on the mercury literature.

Dr. Bernier notes that in August 1999 a public workshop was held in the Lister Auditorium in Bethesda by the National Vaccine Advisory Group and the Interagency Working Group on Vaccines to consider Thimerosal risk in vaccine use. And based on what was discussed in that conference, Merck, one manufacturer of a U.S.-licensed hepatitis B vaccine (HepB) moved to license a "no Thimerosal" formulation for young children but kept making and distributing its Thimerosal-preserved HepB formulation into the mid 2000s while GlaxoSmithKline,

the other U.S.-licensed HepB maker apparently moved to license a reduced-Thimerosal formulation; apparently, neither firm moved to recall the existing Thimerosal-preserved doses. It is interesting to note that the media took very little interest in what was learned at that meeting and it may have been a secret meeting—probably because it was also a meeting that was not, as required by law, announced publicly. As we shall see, there is a reason why they struggle to keep the contents of all these meetings secret from the public.

Dr. Bernier then notes on page 13 that on October 1999 the Advisory Committee on Immunization Practices (ACIP) “*looked this situation over again and did not express a preference for any of the vaccines that were Thimerosal free.*” In this discussion he further notes that the ACIP concluded that the Thimerosal-containing vaccines could be used but the “long-term goal” is to try to remove Thimerosal as soon as possible.

Now, we need to stop and think about what has transpired. We have an important group here, the ACIP that essentially plays a role in vaccine policy affecting tens of millions of children every year. And, we have evidence from the Thimerosal meeting in 1999 that the potential for serious injury to the infant’s brain is so serious that a recommendation for removal becomes policy. In addition, they are all fully aware that tiny babies are receiving mercury doses that exceed even EPA safety limits for adults, yet all they can say is that we must “*try to remove Thimerosal as soon as possible.*” Do they not worry about the tens of millions of babies who will continue receiving Thimerosal-containing vaccines until they can get around to stopping the use of Thimerosal?

It should also be noted that it is a misnomer to say “removal of Thimerosal” since they are not removing anything. They just plan to stop adding it to future vaccines once they use up existing stocks, which entails millions of doses. And incredibly, the government allows them to do it. Even more incredibly, the American Academy of Pediatrics and the American Academy of Family Practice similarly endorse this insane policy. In fact, they specifically state that children should continue to receive the Thimerosal-containing vaccines until new Thimerosal-free vaccines can be manufactured at the will of the manufacturers. It was disclosed that Thimerosal was in all influenza, HepB and DPT vaccines, as well as most DtaP vaccines .

Had vaccine safety been their primary concern, as it should be, the most obvious solution was to recommend only single-dose vials, which require no preservative, coupled with a ban on the use of any mercury compound in the manufacture of all drugs. So, why didn’t they make this or at least a “no Thimerosal” recommendation? “*Oh,*” they exclaim, “*it would add to the cost of the vaccine.*” Of course, we are only talking about a few dollars per vaccine at most, certainly worth the health of your child’s brain and future. They could use some of the hundreds of millions of dollars they waste on vaccine promotion every year to cover the cost for the poor. Yet, that would cut into some fat-cat’s profit and we can’t have that.

As they begin to concentrate on the problem at hand we first begin to learn that the greatest problem with the meeting is that they know virtually nothing about what they are doing. On page 15, for example, they admit that there is very little pharmacokinetic data on ethylmercury, the form of mercury in Thimerosal. In fact, they say there is no data on excretion and the data on toxicity is sparse; yet it is recognized to cause hypersensitivity, neurological problems, and even death, and it is known to easily pass the blood-brain barrier and the placental barrier.

Therefore, what they are admitting is that we have a form of mercury that has been used in vaccines since the 1930s and no one has bothered to study the effects on biological systems, especially the brains of infants. Their defense throughout this conference is “*we just don’t know the effects of ethylmercury.*” As a solution, they resort to studies on methylmercury because there are thousands of studies on this form of mercury. The major source of this form is seafood consumption.

It takes them awhile to get the two forms of mercury straight, since for several pages of the report they say methylmercury is in Thimerosal rather than ethylmercury. They can be forgiven for this. On page 16, Dr. Johnson, an immunologist and pediatrician at the University of Colorado School of Medicine and the National Jewish Center

for Immunology and Respiratory Medicine, notes that he would like to see the incorporation of wide margins of safety, that is 3 to 10-fold margins of safety to “*account for data uncertainties.*” What he means is that there are so many things we do not know about this toxin that we had better use very wide margins of safety. For most substances the FDA uses a 100-fold margin of safety.

The reason for this, which they do not mention, is that in a society of hundreds of millions of people, there are groups of people who are much more sensitive to the toxin than others. For instance, the elderly, the chronically ill, the nutritionally deficient, small babies, premature babies, those on certain medications and those with inborn defects in detoxification, just to name a few. In fact, premature babies and low birth weight babies were excluded from the main study since (1) some had the highest mercury levels, (2) these would be hard to study, and (3) they had the most developmental problems possibly related to the mercury. In other words, including these babies might endanger their claims of safety.

It should also be noted that all participants at this conference ignored the differences in total mercury exposure among infants and small children living in different geographical areas. For example, a child’s mother who had dental amalgams, who regularly eats high-methylmercury-containing seafood and lives in an area with high atmospheric mercury levels will have much higher total mercury exposure than one exposed to little dietary, dental, and environmental mercury.

Also on page 16, Dr. Johnson makes an incredible statement, one that defines the problem we have in this country with the promoters of these vaccines. He states, “*As an aside, we found a cultural difference between vaccinologist and environmental health people in that many of us in the vaccine arena have never thought about uncertainty factors before. We tend to be relatively concrete in our thinking.*” Then he says, “*One of the big cultural events in that meeting ... was when Dr. Clarkson repetitively pointed out to us that we just didn’t get it about uncertainty, and he was actually quite right.*”

This is an incredible admission. First, what is a “vaccinologist”? Do you go to school to learn to be one? How many years of residency training are required to be a “vaccinologist”? Are there board exams? It’s an ill-defined term used to describe people who are obsessed with vaccines, not that they actually study the effects of the vaccines, as we shall see throughout this meeting. Most important is the admission by Dr. Johnson that he and his fellow “vaccinologists” are so blinded by their obsession with forcing vaccines on society that they never even considered that there might be factors involved that could greatly affect human health, the so-called “uncertainties”. Further, he admits that he and his fellow “vaccinologists” like to think in concrete terms; that is, they are very narrow in their thinking and wear blinders that prevent them from seeing the numerous problems occurring with large numbers of vaccinations in infants and children. Their goal in life is to vaccinate as many people as possible with an ever-growing number of vaccines.

On page 17 his “concrete thinking” once again takes over. He refers to the Bethesda meeting on Thimerosal safety issues and says, “*there was no evidence of a problem, only a theoretical concern that young infants’ developing brains were being exposed to an organomercurial.*” Of course, as I shall point out later, it is a lot more than a “theoretical concern”. He then continues by saying, “*We agree that while there was no evidence of a problem, the increasing number of vaccine injections given to infants, was increasing the theoretical mercury exposure risk.*”

It’s hard to conceive of a true scientist not seeing the incredible irony of these statements. The medical literature abounds with studies on the deleterious effects of mercury on numerous enzymes, mitochondrial energy production, synaptic function, dendritic function, neurotubule dissolution and excitotoxicity—yet he sees only a “theoretical risk” associated with an ever increasing addition of Thimerosal-containing vaccines. It is also important to note that these geniuses never even saw a problem in the first place, it was pressure from outside scientists, parents of affected children, and groups representing them that pointed out the problem. They were, in essence, reacting to pressure from outside the “vaccinologist club” and, therefore, had not discovered internally that a problem even “might” exist.

In fact, if these outside groups had not become involved, these “vaccinologists” would have continued to add more and more mercury-containing vaccines to the list of required vaccines. Only when the problem became so obvious, that is of epidemic proportion and the legal profession became involved, would they have even noticed there was a problem. This is a recurring theme in the government’s regulatory agencies, as witnessed with fluoride, aspartame, MSG, dioxin and pesticides issues.

It is also interesting that Dr. Johnson did admit that the greatest risk was among low birth weight infants and premature infants. Now why would that be if there existed such a large margin of safety with mercury used in vaccines? Could just a few pounds of body weight make such a dramatic difference? In fact, it does, but it also means that normal birth weight children, especially those near the low range of normal birth weight, are also in greater danger. It also would mean that children receiving doses of mercury higher than the 75 ug in this study would be at high risk as well because their dose, based on body weight, would be comparable to that of the low birth weight child receiving the lower dose. This is never even considered by these “vaccinologist” experts who decide policy for your children.

Now this next statement should shock everyone, but especially the poor who might believe that these “vaccinologist” experts have their best interest in mind. Dr. Johnson says on page 17, *“We agree that it would be desirable to remove mercury from U.S. licensed vaccines, but we did not agree that this was a universal recommendation that we would make because of the issue concerning preservatives for delivering vaccines to other countries, particularly developing countries, in the absence of hard data that implied that there was in fact a problem.”*

So, here you have it. The data is convincing enough that the American Academy of Pediatrics and the American Academy of Family Practice, as well as the regulatory agencies and the CDC, all recommend its removal as quickly as possible because of concerns of adverse effects of mercury on brain development, but not for the children in the developing countries. I thought the whole idea of child health programs in the United States directed toward the developing world was to give poor children a better chance in an increasingly competitive world. This policy being advocated would increase the neurodevelopmental problems seen in poor children of developing countries and of this country, impairing their ability to learn and develop competitive minds. Remember, there was a representative of the World Health Organization (WHO), Dr. John Clements, serving on this panel of “experts” who apparently never challenged this statement made by Dr. Johnson.

It also needs to be appreciated that children in developing countries are at a much greater risk of complications from vaccinations and from mercury toxicity than children in developed countries. This is because of poor nutrition, concomitant parasitic and bacterial infections, and a high incidence of low birth weight in these children. We are now witnessing a disaster in African countries caused by the use of older live virus polio vaccines that has now produced an epidemic of vaccine related polio, that is, polio caused by the vaccine itself. In fact, in some African countries, polio was not seen until the vaccine was introduced.

The WHO and the “vaccinologist experts” from this country now justify a continued polio vaccination program with this dangerous vaccine on the basis that now that they have created the epidemic of polio, they cannot stop the program. In a recent article it was pointed out that this is the most deranged reasoning, since more vaccines will mean more vaccine-related cases of polio. But then, “vaccinologists” have difficulty with these “uncertainties”. (Jacob JT. A developing country perspective on vaccine-associated paralytic poliomyelitis. Bulletin WHO 2004; 82:53-58. See commentary by D.M. Salisbury at the end of the article.)

Then Dr. Johnson again emphasizes the philosophy that the health of children is secondary to “the program” when he says, *“We saw some compelling data that delaying the birth dose of HepB vaccine would lead to significant disease burden as a consequence of missed opportunity to immunize.”* This implies that our children would be endangered from the risk of hepatitis B should the vaccine program stop vaccinating newborns with the HepB vaccine.

In fact, this statement is not based on any risk to U.S. children at all and he makes that plain when he states, “that the potential impact on countries that have 10% to 15% newborn hepatitis B exposure risk was very distressing to consider.” (page 18) In other words the risk is not to normal U.S. children but to children in developing countries. In fact, hepatitis B is not a risk until the teenage years and after in this country. The only at-risk children are those born to drug abusing parents, to mothers infected with hepatitis B, or to HIV infected parents.

Infectious disease authorities know that 90% of people infected with this virus either have a mild infection and recover or have no symptoms at all. Even pregnant women infected with the virus have only a 20% chance of transmitting the virus to their babies. According to statistics, the United States has one of the lowest rates of hepatitis B infection in the world, with only 53 cases of the infection being reported in children among 3.9 million births. In fact, there were three times as many serious complications from the vaccine as there were children who contracted the disease. The real reason for vaccinating the newborns is to capture them before they can escape the vaccinologists’ vaccine program.

This is a tactic often used to scare mothers into having their children vaccinated. For example, vaccinologists say that if children are not vaccinated against measles, millions of children could die during a measles epidemic. They know this is nonsense. What they are using are examples taken from developing countries with poor nutrition and poor immune function in which such epidemic death can occur. In the United States we would not see this because of better nutrition, better health facilities and better sanitation. In fact, most deaths seen during measles outbreaks in the United States occur in children in whom vaccination was contraindicated, when the vaccine did not work or in children with chronic, immune-suppressing diseases.

In fact, most studies show that children catching the measles or other childhood diseases have been either fully immunized or partially immunized. The big secret among “vaccinologists” is that anywhere from 20 to 50% of children are not resistant to the diseases for which they have been vaccinated.

Also on page 18, Dr. Johnson tells the committee that it was Dr. Walter Orenstein who *“asked the most provocative question which introduced a great deal of discussion. That was, should we try to seek neurodevelopmental outcomes from children exposed to varying doses of mercury by utilizing the Vaccine Safety Datalink data from one or more sites.”* (page 18)

I take from this no one had ever even thought of looking at the data that had just been sitting there all these years unreviewed. Children could have been dropping like flies or suffering from terrible neurodevelopmental defects caused by the vaccine program and no one in the government would have known. In fact, that is exactly what the data suggested was happening, at least as regards neurodevelopmental delays.

We should also appreciate that the government sponsored two conferences on the possible role of metals, aluminum and mercury, being used in vaccines, without any change in vaccine policy occurring after the meetings. These meetings were held a year before this year’s 2000 meeting and before any examination of the data which was being held tightly by the CDC (which was denied to other independent, highly qualified researchers). I will talk more about what was discussed in the aluminum conference later. It is very important and is only briefly referred to in this conference for a very good reason. If the public knew what was discussed at the aluminum meeting no one would ever get a vaccination using the presently manufactured types of vaccines again.

Despite what was discussed in the aluminum meeting and the scientific literature on the neurotoxicity of aluminum, Dr. Johnson makes the following remark; *“Aluminum salts have a very wide margin of safety. Aluminum and mercury are often simultaneously administered to infants, both at the same site and at different sites.”* Also on page 20, he states, *“However, we also learned that there is absolutely no data, including animal data, about the potential for synergy, additively or antagonism, all of which can occur in binary metal mixtures...”*

It is important here to appreciate a frequently used deception by those who are trying to defend an indefensible practice. They use the very same language just quoted, that is, that there is no data to show, etc., etc. They intend it to convey the idea that the issue has been looked at and studied thoroughly and no toxicity was found. In truth, it means that no one has looked at this possibility and there have been no studies that would give us an answer one way or the other.

In fact, we know that aluminum is a significant neurotoxin and that it shares many common mechanisms with mercury as a neurotoxin. For example, they are both toxic to neuronal neurotubules, interfere with antioxidant enzymes, poison DNA repair enzymes, interfere with mitochondrial energy production, block the glutamate reuptake proteins (GLT-1 and GLAST), bind to DNA and interfere with neuronal membrane function. Toxins that share toxic mechanisms are almost always additive and frequently synergistic in their toxicity. So, Dr. Johnson's statement is sheer nonsense.

A significant number of studies have shown that both of these metals play a significant role in all of the neurodegenerative disorders. It is also important to remember, both of these metals accumulate in the brain and spinal cord. This makes them accumulative toxins and therefore much more dangerous than rapidly excreted toxins.

To jump ahead, on page 23 Dr. Tom Sinks, Associate Director for Science at the National Center for Environmental Health at the CDC and the Acting Division Director for Division of Birth Defects, Developmental Disabilities and Health, asks, "*I wonder is there a particular health outcome that is related to aluminum salts that may have anything that we are looking at today?*" Dr. Martin Meyers, Acting Director of the National Vaccine Program Office, answers, "*No, I don't believe there are any particular health concerns that were raised.*" This is after an aluminum conference held the previous year that did, indeed, find significant health concerns and extensive scientific literature showing aluminum to be of great concern.

On page 24 Dr. William Weil, a pediatrician representing the Committee on Environmental Health of the American Academy of Pediatrics, brings some sense to the discussion by reminding them that, "*there are just a host of neurodevelopmental data that would suggest that we've got a serious problem. The earlier we go, the more serious the problem.*" Here he means that the further back you go during the child's brain development, the more likely the damage to the infant. I must give him credit; at least he briefly recognized that a significant amount of brain development does take place later—that is after birth. He also reminds his colleagues that aluminum produced severe dementia and death in dialysis cases. He concludes by saying, "*To think there isn't some possible problem here is unreal.*" (page 25)

Not to let it end there, Dr. Meyers adds, "*We held the aluminum meeting in conjunction with the metal ions in biology and medicine meeting, we were quick to point out that in the absence of data we didn't know about additive or inhibitory activities.*" Once again we see the "no data" ploy. There is abundant data on the deleterious effects of aluminum on the brain, a significant portion of which came out in that very meeting.

Dr. Johnson also quotes Dr. Thomas Clarkson, who identifies himself as associated with the mercury program at the University of Rochester, as saying that delaying the HepB vaccine for 6 months or so would not affect the mercury burden (page 20). He makes the correct conclusion when he says, "*I would have thought that the difference was in the timing. That is you are protecting the first six months of the developing central nervous system.*" Hallelujah, for a brief moment I thought that they had stumbled on one of the most basic concepts in neurotoxicology. Then Dr. Meyers dashed my hopes by saying that single, separated doses would not affect blood levels at all. At this juncture, we need a little enlightenment. It is important to appreciate that mercury is a fat soluble metal. That is, it is stored in the body's fat. The brain contains 60% fat and therefore is a common site for mercury storage. Now, they establish in this discussion that about half of methylmercury is excreted over several months when ingested. A recent study found that ethylmercury has a half-life of 7 days.

A significant proportion of the mercury will enter the brain (it has been shown to easily pass through the blood-brain barrier) where it is stored in the phospholipids (fats). It should also be appreciated that when cleared from the blood, the ethylmercury enters the bowel, where it is re-circulated many times over—each time depositing more mercury in the child's brain.

With each new vaccine dose, and remember, at the time of this conference, these children were receiving as many as 36 doses of these vaccines by age 2 years, many of which contained mercury—another increment of mercury is added to the brain storage depot. This is why we call mercury an accumulative poison. They never once, not once, mention this vital fact throughout the entire conference. Not once. Moreover, they do so for a good reason; it gives the unwary, those not trained in neuroscience, assurance that all that matters here is blood levels.

In fact, on page 163, Dr. Robert Brent, a developmental biologist and pediatrician at Thomas Jefferson University and Dupont Hospital for Children, says that we don't have data showing accumulation and "*that with the multiple exposures you get an increasing level, and we don't know whether that is true or not.*" He redeems himself somewhat by pointing out that some of the damage is irreversible and with each dose more irreversible damage occurs and in that way it is accumulative.

On page 21 Dr. Thomas Clarkson makes the incredible statement implying that he knows of no studies that show exposure to mercury after birth or at six months would have deleterious effects. Dr. Isabelle Rapin, a neurologist for children at Albert Einstein College of Medicine, follows up by saying that "*I am not an expert on mercury in infancy*" but she knows it can affect the nerves (peripheral nervous system). So, here is one of our experts admitting that she knows little about the effects of mercury on the infant. My question is: Why is she here? Dr. Rapin is a neurologist for children at Albert Einstein College of Medicine who stated that she has a keen interest in developmental disorders, in particular those involving language and autism, yet she knows little about the effects of mercury on the infant brain.

This conference is concerned with the effects of mercury in the form of Thimerosal on infant brain development, yet throughout this conference our experts, especially the "vaccinologists", seem to know little about mercury except limited literature that shows no toxic effects except at very high levels. None of the well known experts were invited, such as Dr. Michael Aschner from Bowman Grey School of Medicine or Dr. Boyd Haley, who has done extensive work on the toxic effects of low concentrations of mercury on the CNS (Central Nervous System). They were not invited because they would be harmful to the true objective of this meeting, and that was to exonerate mercury in vaccines.

Several times throughout this conference, Dr. Brent reminds everyone that the most sensitive period for the developing brain is during the early stages of pregnancy. In fact, he pinpoints the 8th to 18th week as the period of neuromaturation. In fact, the most rapid period of brain maturation, synaptic development and brain pathway development, is during the last three months of pregnancy continuing until two years after birth. This is often referred to as the "brain growth spurt". This is also not mentioned once in this conference, again because if mothers knew that their child's brain was busy developing for up to two years after birth, they would be less likely to accept this safety of mercury nonsense these "vaccinologists" proclaim.

The brain develops over 100 trillion synaptic connections and tens of trillions of dendritic connections during this highly sensitive period. Both dendrites and synapses are very sensitive, even to very low doses of mercury and other toxins. It has also been shown that subtoxic doses of mercury can block the glutamate transport proteins that play such a vital role in protecting the brain against excitotoxicity. Compelling studies indicate that damage to this protective system plays a major role in most of the neurodegenerative diseases and abnormal brain development as well.

Recent studies have shown that glutamate accumulates in the brains of autistic children, yet these experts seem to be unconcerned about a substance (mercury) that is very powerful in triggering brain excitotoxicity.

It is also interesting to see how many times Dr. Brent emphasizes that we do not know the threshold for mercury toxicity for the developing brain. Again, that is not true. We do know and the Journal of Neurotoxicology states that anything above 10µg (micrograms) is neurotoxic. The WHO in fact states that there is no safe level of mercury.

On page 164 Dr. Robert Davis, Associate Professor of Pediatrics and Epidemiology at the University of Washington, makes a very important observation. He points out that in a population like the United States you have individuals with varying levels of mercury from other causes (diet, living near coal-burning facilities, etc.) and by vaccinating everyone you raise those with the highest levels even higher and bring those with median levels into a category of higher levels. The “vaccinologists” with their problem of “concrete thinking” cannot seem to appreciate the fact that not everyone is the same. That is, they fail to see these “uncertainties”.

To further emphasize this point, let’s consider a farming family that lives within three miles of a coal-burning electrical plant. Since they also live near the ocean they eat seafood daily. The fertilizers, pesticides and herbicides used on the crops contain appreciable levels of mercury. The coal-burning electrical plant emits high levels of mercury in the air they breathe daily and the seafood they consume has levels of mercury higher than EPA safety standards. This means that any babies born to these people will have very high mercury levels.

Once born, they are given numerous vaccines containing even more mercury, thereby adding significantly to their already high mercury burden. Are these “vaccinologists” trying to convince us that these children don’t matter and that they are to be sacrificed at the altar of “vaccine policy”?

Recent studies by neurotoxicologists have observed that as our ability to detect subtle toxic effects improves, especially on behavior and other neurological functions, we lower the level of acceptable exposure. In fact, Dr. Sinks brings up that exact point, using lead as an example. He notes that as our neurobehavioral testing improved, we lowered the acceptable dose considerably and continue to do so. Dr. Johnson had the audacity to add, “*The smarter we get, the lower the threshold.*” Yet, neither he, nor the other participants seem to be getting any smarter concerning this issue.

Dr. Robert Chen, Chief of Vaccine Safety and Development at the National Immunization Program at the CDC, then reveals why they refuse to act on this issue. He says, “*the issue is that it is impossible, unethical to leave kids unimmunized, so you will never, ever resolve that issue. So then we have to refer back from that.*” (page 169) In essence, immunization of the kids takes precedence over safety concerns with the vaccines. If the problem of vaccine toxicity cannot be solved, he seems to be saying, then we must accept that some kids will be harmed by the vaccines. In fact, we are now seeing that the harm from the vaccines exceeds the benefit of disease prevention.

Dr. Brent makes the statement that he knows of no known genetic susceptibility data on mercury and therefore assumes there is a fixed threshold of toxicity. That is, that everyone is susceptible to the same dose of mercury and there are no genetically hypersensitive groups of people. In fact, a recent study found just such a genetic susceptibility in mice. In this study researchers found that mice susceptible to autoimmunity developed neurotoxic effects to their hippocampus, including excitotoxicity, not seen in other strains of mice. They even hypothesize that the same may be true in humans, since familial autoimmunity increases the likelihood of autism in offspring. (Hornig M, Chian D, Lipkin WI. Neurotoxic effects of postnatal Thimerosal are mouse strain dependent. Mol Psychiatry 2004 Sep.;9(9):833–45).

For the next quotation you need a little discussion to be able to appreciate the meaning. They are discussing the fact that in Dr. Verstraeten’s study frightening correlations were found between the higher doses of Thimerosal

and problems with neurodevelopment, including ADD and autism. The problem with the study was that there were so few children that had been administered Thimerosal-free vaccines, that a true control group could not be used. Instead they had to use children getting 12.5µg of mercury as the control and some even wanted to use the control dose as 37.5µg. So the controls had mercury levels that could indeed cause neurodevelopmental problems. Even with this basic flaw, a strong positive correlation was found between the dose of mercury given and these neurodevelopmental problems.

It was proposed that a group of children receiving non-Thimerosal vaccines be compared to those who had Thimerosal. In fact, we later learn that a large group of children could have been used as a Thimerosal-free control. It seems that for two years before this conference, the Bethesda Naval Hospital had been using unlicensed reduced-Thimerosal vaccines in place of the U.S.-licensed Thimerosal-preserved vaccines to immunize their outpatient children. Unfortunately, in general, these children were too young for the symptoms of neurodevelopmental-regressive autism to be manifest when Verstraeten began his studies in the late 1990s.

So, now to the quote: Dr. Braun responds to the idea of starting a new study using such Thimerosal-free controls by saying, “*Sure we will have the answer in five years. The question is what can we do now with the data we have?*” (page 170) Well, we have the answer to that, they simply covered this study up, declared that Thimerosal is of no concern and continued the unaltered policy. That is, they can suggest that the pharmaceutical manufacturers of vaccines remove the Thimerosal but not make it mandatory or examine the vaccines to make sure they have removed it.

Let us take a small peek at just how much we can trust the pharmaceutical manufacturers to do the right thing. Several reports of major violations of vaccine manufacturing policy have been cited by the regulatory agencies. This includes obtaining plasma donations without taking adequate histories on donors as to disease exposures and previous health problems, poor record keeping on these donors, improper procedures, and improper handling of specimens.

That these are not minor violations is emphasized by the discovery that a woman with variant Mad Cow Disease was allowed to give plasma to be used in vaccines in England. In fact, it was learned only after the contaminated plasma was pooled and used to make millions of doses of vaccines that her disease was discovered. British health officials told the millions of vaccinated not to worry, since the “experts” have no idea if it will really spread the disease.

Contamination of vaccines is a major concern in this country as well, as these regulatory violations make plain. It is also important to note that no fines were given, just warnings.

Conclusions by the study group

At the end of the conference, a poll was taken asking two questions. One was, Do you think that there is sufficient data to make a causal connection between the use of Thimerosal-containing vaccines and neurodevelopmental delays? Second, do you think further study is called for based on this study?

First, let us see some of the comments on the question of doing further studies. Dr. Paul Stehr-Green, Associate Professor of Epidemiology at the University of Washington School of Public Health and Community Medicine, who voted yes, gave as his reason, “*The implications are so profound these should be examined further.*” (page 180) Meanwhile, Dr. Brent interjects his concern that the lawyers will get hold of this information and begin filing lawsuits. He says, “*They want business and this could potentially be a lot of business.*” (page 191)

Dr. Loren Koller, Pathologist and Immunotoxicologist at the College of Veterinary Medicine, Oregon State University, is to be congratulated for recognizing more is involved in the vaccine effects than just ethylmercury (page

192). He mentions aluminum and even the viral agents beings used as other possibilities. This is especially important in the face of Dr. R. K. Gherardi's identification of macrophagic myofasciitis, a condition causing profound weakness and multiple neurological syndromes, one of which closely resembled multiple sclerosis.

Both human studies and animal studies have shown a strong causal relationship to the aluminum hydroxide or aluminum phosphate used as vaccine adjuvants. More than 200 cases have been identified [1000s across the globe since this report was written] in European countries and the United States and have been described as an "emerging condition".

Here are some of the neurological problems seen with the use of aluminum hydroxide and aluminum phosphate in vaccines. In two children aged 3 and 5 years, doctors at the All Children's Hospital in St. Petersburg, Florida described chronic intestinal pseudo-obstruction, urinary retention, and other findings indicative of a generalized loss of autonomic nervous system function (diffuse dysautonomia). The 3-year old had developmental delay and hypotonia (loss of muscle tone). A biopsy of the children's vaccine injection site disclosed elevated aluminum levels.

In a study of some 92 patients suffering from this emerging syndrome, eight developed a full-blown demyelinating Central Nervous System disorder (i.e., multiple sclerosis) [Authier FJ, Cherin P, et al. Central nervous system disease in patients with macrophagic myofasciitis. *Brain* 2001;124:974–83]. This included sensory and motor symptoms, visual loss, bladder dysfunction, cerebellar signs (loss of balance and coordination) and cognitive (thinking) and behavioral disorders.

Dr. Gherardi, the French physician who first described the condition in 1998, has collected over 200 proven cases. One third of these developed an autoimmune disease such as multiple sclerosis. Of critical importance is his finding that even in the absence of obvious autoimmune disease there is evidence of chronic immune stimulation caused by the injected aluminum, known to be a very powerful immune adjuvant.

The reason this is so important is that there is overwhelming evidence that chronic immune activation in the brain (activation of microglial cells in the brain) is a major cause of damage in numerous degenerative brain disorders, from multiple sclerosis to the classic neurodegenerative diseases (Alzheimer's disease, Parkinson's and ALS). In fact, I have presented evidence that chronic immune activation of CNS microglia is a major cause of autism, attention deficit disorder and Gulf War Syndrome.

Dr. Gherardi emphasizes that once the aluminum is injected into the muscle, the immune activation persists for years. In addition, we must consider the effect of the aluminum that travels to the brain itself. Numerous studies have shown harmful effects when aluminum accumulates in the brain. A growing amount of evidence points to high brain aluminum levels as a major contributor to Alzheimer's disease and possibly Parkinson's disease and ALS (Lou Gehrig's disease). This may also explain the 10X increase in Alzheimer's disease in those receiving the flu vaccine 5 years in a row. (Dr. Hugh Fudenberg, in press, *Journal of Clinical Investigation*). It is also interesting to note that a recent study found that aluminum phosphate produced a 3X elevation in blood levels of aluminum, as did aluminum hydroxide (Flarend RE, Hem SL, et al. In vivo absorption of aluminum-containing vaccine adjuvants using ²⁶Al. *Vaccine* 1997 Aug.-Sept.;15:1314–8).

Of course, in this conference, our illustrious experts tell us that there is "no data showing an additive or synergistic effect between mercury and aluminum."

Dr. Rapin expressed her concern over public opinion when this information eventually gets out. She says (page 197), they are going to be captured by the public and we had better make sure that "(a) we counsel them carefully and (b) that we pursue this because of the very important public health and public implications of the data." Dr. Johnson adds, "the stakes are very high..." From this, how can one conclude anything other than the fact

that at least these scientists were extremely concerned by what was discovered by this study examining the Vaccine Safety Datalink material? They were obviously terrified that the information would leak out to the public. Stamped in bold letters at the top of each page of the study were the words: "DO NOT COPY OR RELEASE" and "CONFIDENTIAL".

This is not the wording one would expect on a clinical study of vaccine safety; rather you would expect it on top-secret NSA or CIA files. Why was this information being kept secret? The answer is obvious—it might endanger the vaccine program and indict the federal regulatory agencies for ignoring this danger for so many years. Our society is littered with millions of children who have been harmed in one degree or another by this vaccine policy. In addition, let us not forget the millions of parents who have had to watch helplessly as their children have been destroyed by this devastating vaccine program.

Dr. Bernier on page 198 says, "the negative findings need to be pinned down and published." Why was he so insistent that the "negative findings" be published? Because he said, "other less responsible parties will treat this as a signal." By that he means, a signal of a problem with Thimerosal-containing vaccines. From this, I assume he wants a paper that says only that nothing was found by the study. As we shall see, he gets his wish.

In addition, on page 198, Dr. Rapin notes that a study in California found a 300X increase in autism following the introduction of certain vaccines. She quickly attributes this to better physician recognition. Two things are critical to note at this point. She makes this assertion on better physician recognition without any data at all, just her wishful thinking. If someone pointing out the dangers of vaccines were to do that, she would scream "junk science". Second, Dr. Weil on page 207, attacks this reasoning when he says, "the number of dose related relationships are linear and statistically significant. You can play with this all you want. They are linear. They are statistically significant." In other words, how can you argue with results that show a strong dose/response relationship between the dose of mercury and neurodevelopmental outcomes? The higher the mercury levels in the children the greater the number of neurological problems. He continues by saying that the increase in neurobehavioral problems is probably real. He tells them that he works in a school system with special education programs and "I have to say the number of kids getting help in special education is growing nationally and state by state at a rate not seen before. So there is some kind of increase. We can argue about what it is due to." (page 207)

Dr. Johnson seems to be impressed by the findings as well. He says on page 199, "This association leads me to favor a recommendation that infants up to two years old not be immunized with Thimerosal-containing vaccines if suitable alternative preparations are available." Incredibly, he quickly adds, "I do not believe the diagnosis justifies compensation in the Vaccine Compensation Program at this point." It is interesting to note that one of our experts in attendance is Dr. Vito Caserta, the Chief Officer for the Vaccine Injury Compensation Program.

At this point Dr. Johnson tells the group of his concerns for his own grandchild. He says, (page 200) "Forgive this personal comment, but I got called out at eight o'clock for an emergency call and my daughter-in-law delivered a son by C-section. Our first male in the line of the next generation and I do not want that grandson to get a Thimerosal-containing vaccine until we know better what is going on. It will probably take a long time. In the meantime, and I know there are probably implications for this internationally, but in the meanwhile I think I want that grandson to only be given Thimerosal-free vaccines."

So, we have a scientist sitting on this panel which will eventually make policy concerning all of the children in this country, as well as other countries, who is terrified about his new grandson getting a Thimerosal-containing vaccine but he is not concerned enough about your child to speak out and try to stop this insanity. He allows a cover-up to take place after this meeting adjourns and remains silent.

It is also interesting to note that he feels the answers will be a long time coming, but in the mean time, his grandson will be protected. The American Academy of Pediatrics, The American Academy of Family Practice, the AMA,

CDC and every other organization will endorse these vaccines and proclaim them to be safe as spring water, but Dr. Johnson and some of the others will keep their silence.

It is only during the last day of the conference that we learn that most of the objections concerning the positive relationship between Thimerosal-containing vaccines and ADD and ADHD were bogus. For example, Dr. Rapin on page 200 notes that all children in the study were below age 6 and that ADD and ADHD are very difficult to diagnose in pre-schoolers. She also notes that some children were followed for only a short period.

Dr. Stein adds that in fact the average age for diagnosis of ADHD was 4 years and 1 month, a very difficult diagnosis to make with the guidelines, as published by the American Academy of Pediatrics, limiting diagnosis to 6 to 12 year olds. Of course, he was implying that too many were diagnosed as ADHD. Yet, a recent study found that the famous Denmark study that led to the announcement by the Institute of Medicine that there was no relationship between autism and the MMR vaccine, used the same tactic. They cut off the age of follow-up at age six.

It is known that many cases appear after this age group, especially with ADD and ADHD. In fact, most learning problems appear as the child is called on to handle more involved intellectual material. Therefore, the chances are that they failed to diagnose a number of cases by stopping the study too early.

Several of the participants tried to imply that autism was a genetic disorder and therefore could have nothing to do with vaccines. Dr. Weil put that to rest with this comment, *"We don't see that kind of genetic change in 30 years."* In other words, how can we suddenly see a 300% increase in a genetically related disorder over such a short period? It is also known that there are two forms of autism, one that is apparent at birth and one that develops later in childhood. The former has not changed in incidence since statistics have been kept; the other is epidemic.

One interesting exchange, which involves two studies in children born to mothers consuming high intakes of mercury-contaminated fish, ends up providing their justification for the view that mercury is of no danger to children vaccinated with vaccines containing Thimerosal. One study in the journal *Neurotoxicology*, examined children living in the Republic of Seychelles. This study examined the effect of prenatal exposure to mercury through the mother's consumption of fish high in methylmercury.

A battery of developmental milestone tests were done and no adverse effects were reported in the study done by Dr. Clarkson and co-workers, the very same person in this conference. He never mentions that a follow-up study of these same children did find a positive correlation between methylmercury exposure and poor performance on a memory test. In a subsequent study of children living on the Faroe Islands exposed to methylmercury, researchers also found impairments of neurodevelopment. This experiment was done by scientists from Japan.

Throughout the remainder of this discussion, Dr. Clarkson and others refer to these two studies. When they are reminded that the Faroe study did find neurological injury to the children, they counter by saying that this was prenatal exposure to mercury and not exposure following birth as would be seen with vaccination. The idea being that prenatally the brain is undergoing neural formation and development making it more vulnerable. As I have mentioned, this rapid brain growth and development continues for two years after birth and even at age 6 years the brain is only 80% formed.

Dr. Clarkson keeps referring to the Seychelles study which demonstrated that the children reached normal neurodevelopmental milestones as shown by a number of tests. Dr Weil points out on page 216 that this tells us little about these children's future brain function. He says, *"I have taken a lot of histories of kids who are in trouble in school. The history is that developmental milestones were normal or advanced and they can't read at second grade, they can't write at third grade, they can't do math in the fourth grade and it has no relationship as far as I can tell to the history we get of the developmental milestones. So I think this is a very crude measure of neurodevelopment."*

In other words, both of these studies tell us nothing about the actual development of these children's brain function except that they reached the most basic of milestones. To put this another way, your child may be able to stack blocks, recognize shapes and have basic language skills, but later in life she/he could be significantly impaired when it came to higher math, more advanced language skills (comprehension) and ability to compete in a very competitive intellectual environment, like college or advanced schooling. The future of such children would be limited to the more mundane and intellectually limited jobs.

Postnatal brain development, that is from birth to age six or seven, involves the fine tuning of synaptic connections, dendritic development and pathway refinement, all of which prepare the brain for more complex thinking. These brain elements are very sensitive to toxins and excessive immune stimulation during this period. This fact is never mentioned at the conference.

In addition, it must be remembered that the children in these two studies were exposed only to methylmercury and not the combined neurotoxic effect of mercury, aluminum and excessive and chronic activation of the brain's immune system (microglia). This is what makes it so incredible, that several of these "vaccinologists" and so-called experts would express doubt about the "biological plausibility" of Thimerosal or any vaccine component causing neurodevelopmental problems. The medical literature is exploding with such studies. The biological plausibility is very powerful.

Mercury, for example, even in low concentrations, is known to impair energy production by mitochondrial enzymes. The brain has one of the highest metabolic rates of any organ and impairment of its energy supply, especially during development, can have devastating consequences. In addition, mercury, even in lower concentrations, is known to damage DNA and impair DNA repair enzymes, which again plays a vital role in brain development. Mercury is known to impair neurotubule stability, even in very low concentrations. Neurotubules are absolutely essential to normal brain cell function. Mercury activates microglial cells, which increases excitotoxicity and brain free radical production as well as lipid peroxidation, central mechanisms in brain injury. In addition, even in doses below that which can cause obvious cell injury, mercury impairs the glutamate transport system, which in turn triggers excitotoxicity, a central mechanism in autism and other neurological disorders. Ironically, aluminum also paralyzes this system.

On page 228, we see another admission that the government has had no interest in demonstrating the safety of Thimerosal-containing vaccines despite over 2000 articles showing harmful effects of mercury. Here we see a reference to the fact that the FDA *"has a wonderful facility in Arkansas with hundreds of thousands of animals"* available for any study needed to supply these answers on safety. The big question to be asked is – So, why has the government ignored the need for research to answer these questions concerning Thimerosal safety? You will recall in the beginning the participants of this conference complained that there were just so few studies or no studies concerning this "problem".

Again, on page 229 Dr. Brent rails about the lawsuit problem. He tells the others that he has been involved in three lawsuits related to vaccine injuries leading to birth defects and concluded, *"If you want to see junk science, look at those cases..."* He then complains about the type of scientists testifying in these cases. He adds, *"But the fact is those scientist are out there in the United States."* In essence, he labels anyone who opposes the "official policy" on vaccines as a junk scientists. We have seen in the discussion who the "junk scientists" really are.

Knowing that what they have found can cause them a great deal of problems he adds, *"The medical/legal findings in this study, causal or not, are horrendous.... If an allegation was made that a child's neurobehavioral findings were caused by Thimerosal-containing vaccines, you could readily find a junk scientist who will support the claim with a reasonable degree of certainty."* On page 229 he then admits that they are in a bad position because they have no data for their defense. Now, who are the junk scientists?

Is a “real scientist” one who has no data, just wishful thinking and a “feeling” that everything will be all right? Are real scientists the ones who omit recognized experts on the problem in question during a conference because it might endanger the “program”? Are they the ones who make statements that they don’t want their grandson to get Thimerosal-containing vaccines until the problem is worked out, but then tell millions of parents that the vaccines are perfectly safe for their children and grandchildren?

Dr. Meyers on page 231 put it this way, “My own concern, and a couple of you said it, there is an association between vaccines and outcomes that worries both parents and pediatricians.” He sites other possible connections to vaccine-related neurobehavioral and neurodevelopmental problems including the number of vaccines being given, the types of antigens being used, and other vaccine additives.

Dr. Caserta tells the group that he attended the aluminum conference the previous year and learned that metals could often act differently in biological systems when existing as an ion. This is interesting in the face of the finding that fluoride when combined to aluminum forms a compound that can destroy numerous hippocampal neurons at a concentration of 0.5 ppm in drinking water. It seems that aluminum readily combines with fluoride to form this toxic compound. With over 60% of communities having fluoridated drinking water this becomes a major concern.

It has also been learned that fluoroaluminum compounds mimic the phosphate and can activate G-proteins. G-proteins play a major role in numerous biological systems, including endocrine, neurotransmitters, and as cellular second messengers. Some of the glutamate receptors are operated by a G- protein mechanism.

Over the next ten to fifteen pages, they discuss how to control this information so that it will not get out and if it does how to control the damage. On page 248 Dr. Clements has this to say: “*But there is now the point at which the research results have to be handled, and even if this committee decides that there is no association and that information gets out, the work has been done and through the freedom of information that will be taken by others and will be used in other ways beyond the control of this group. And I am very concerned about that as I suspect that it is already too late to do anything regardless of any professional body and what they say.*”

In other words, he wants this information kept not only from the public but also from other scientists and pediatricians until they can be properly counseled. In the next statement he spills the beans as to why he is determined that no outsider get hold of this damaging information. He says, “*My mandate as I sit here in this group is to make sure at the end of the day that 100,000,000 are immunized with DTP, Hepatitis B and if possible Hib, this year, next year, and for many years to come, and that will have to be with Thimerosal-containing vaccines unless a miracle occurs and an alternative is found quickly and is tried and found to be safe.*”

This is one of the most shocking statements I have ever heard. In essence, he is saying, I don’t care if the vaccines are found to be harmful and destroying the development of children’s brains, these vaccines will be given now and forever. His only concern, by his own admission, is to protect the vaccine program even if it is not safe. Dr. Brent refers to this as an “*eloquent statement.*”

On page 253, we again see that these scientists have a double standard when it comes to their children and grandchildren. Dr. Rapin raises the point about a loss of an IQ point caused by Thimerosal exposure. She says, “*Can we measure the IQ that accurately, that this one little point is relevant?*” Then she answers her own question by saying, “*Even in my grandchildren, one IQ point I am going to fight about.*” Yet, they are saying in unison, in essence—“To hell with your children”—to the rest of America.

It is also interesting that they bring up the history of lead as a neurobehavioral toxin. Dr. Weil noted that the neurotoxicologists and regulatory agencies have lowered the acceptable level from 10 to 5µg. In fact, some feel that even lower levels are neurotoxic to the developing brain. Before the toxicologists began to look at lead as a brain

toxin in children most “experts” assumed it was not toxic even at very high levels. Again, it shows that “experts” can be wrong and it is the public who pays the price.

Dr. Chen on page 256 expresses his concern about this information reaching the public. He remarks, “*We have been privileged so far that given the sensitivity of information, we have been able to manage to keep it out of, let’s say, less responsible hands...*” Dr. Bernier agrees and notes, “*This information has been held fairly tightly.*” Later he calls it “*embargoed information*” and “*very highly protected information.*”

That they knew the implications of what they had discovered was illustrated by Dr. Chen’s statement on page 258. He says, “*I think overall there was this aura that we were engaged in something as important as anything else we have ever done. So I think that this was another element to this that made this a special meeting.*” You may remember, Dr. Weil emphasized that the data analysis left no doubt that there was a strong correlation between neurodevelopmental problems and exposure to Thimerosal-containing vaccines. So if they understood the importance of this finding and this was the most important thing they have ever dealt with, why was this being kept from the public? In fact, it gets even worse.

Just so you will not doubt my statement that this audience of experts was not objective, I give you the words of Dr. Walter Orenstein, Director of the National Immunization Program at the CDC, on page 259. He tells the group, “*I have seen him (Verstraeten) in audience after audience deal with exceedingly skeptical individuals...*” “Exceedingly skeptical individuals” does that sound like objective scientists who wanted to look at the data with a clear mind, or were they scientists who were convinced before the meeting was held that there was no danger to children from Thimerosal or any other vaccine component?

In one of the closing remarks (page 257) Dr. Bernier says, “*the other thing I was struck by was the science,*” meaning the science expressed by the attendees of the meeting. Then Dr. Orenstein adds, “*I would also like to thank Roger Bernier who pulled off this meeting in rather short notice...*” Here is a meeting that has been called one of the most important they have ever dealt with and we learn that it was “pulled off” on short notice. In addition, we were told that the results of this meeting would lead to eventual vaccine policy. He then has the nerve to add: “*In a sense this meeting addresses some of the concerns we had last summer when we were trying to make policy in the absence of a careful scientific review. I think this time we have gotten it straight.*”

Well, I hate to be the one to break the news, but he didn’t get it straight. There was little or no science in this meeting; rather it was composed of a lot of haggling and nit picking over epidemiological methodology and statistical minutia in an effort to discredit the data, all without success. In fact, the so-called mercury experts admitted they had to do some quick homework to refresh their memories and learn something about the subject.

Conclusions

This top secret meeting was held to discuss a study done by Dr. Thomas Verstraeten and his co-workers using Vaccine Safety Datalink data as a project collaboration between the CDC’s National Immunization Program (NIP) and four HMOs. The study examined the records of 110,000 children. Within the limits of the data, they did a very thorough study and found the following:

1. Exposure to Thimerosal-containing vaccines at one month was associated significantly with the misery and unhappiness disorder that was dose related. That is, the higher the child’s exposure to Thimerosal the higher the incidence of the disorder. This disorder is characterized by a baby that cries uncontrollably and is fretful more so than that seen in normal babies.
2. A nearly significant increased risk of ADD with 12.5µg exposure at one month.

3. With exposure at 3 months, they found an increasing risk of neurodevelopmental disorders, including speech disorders, with increasing exposure to Thimerosal. This was statistically significant.

It is important to remember that the control group was not children without Thimerosal exposure but, rather, those at 12.5µg exposure. This means that there is a significant likelihood that even more neurodevelopmental problems would have been seen had they used a real control population. No one disagreed that these findings were significant and troubling. Yet, when the final study was published in the journal *Pediatrics*, Dr. Verstraeten and co-workers reported that no consistent associations were found between Thimerosal-containing vaccine exposure and neurodevelopmental problems. In addition, he lists himself as an employee of the CDC, not disclosing the fact that at the time the article was accepted, he worked for GlaxoSmithKline, a vaccine manufacturing company.

So how did they do this bit of prestidigitation? They simply added another HMO to the data: the Harvard Pilgrimage. (Additionally there were other manipulations, e.g., altering inclusion criteria, discarding children receiving the highest total dose, splitting children into separate groups, using only one HMO's data in some cases, expressing effects ratios in terms of per dose of mercury.) Congressman Dave Weldon noted in his letter to the CDC Director that this HMO had been in receivership by the state of Massachusetts because its records were in shambles. Yet, this study was able to make the embarrassing data from Dr. Verstraeten's previous study disappear. Attempts by Congressman Weldon to force the CDC to release the data to an independent researcher, Dr. Mark Geier, a researcher with impeccable credentials and widely published in peer-reviewed journals, have failed and the CDC now claims that the original data-sets Verstraeten et al. used have been "lost".

It is obvious that a massive cover-up is in progress, as we have seen with so many other scandals, such as fluoride, food-based excitotoxins, pesticides, aluminum, and now vaccines. I would caution those critical of the present vaccine policy not to put all their eggs in one basket, that is, with Thimerosal as being the main culprit. There is no question that it plays a significant role, but there are other factors that are also critical, including aluminum, fluoroaluminum complexes, and chronic immune activation of brain microglia. I believe that repeated, closely spaced, sequential vaccinations given during the most active period of brain development is the major cause of autism.

In fact, excessive, chronic microglial activation can explain many of the effects of excessive vaccine exposure as I point out in two recently published articles. One property of both aluminum and mercury is microglial activation. With chronic microglial activation, large concentrations of excitotoxins are released as well as neurotoxic cytokines. These have been shown to destroy synaptic connections, dendrites and cause abnormal pathway development in the developing brain as well as in the adult brain.

In essence, too many vaccines are being given to children during the brain's most rapid growth period. Known toxic metals are being used in vaccines, interfering with brain metabolism and antioxidant enzymes, damaging DNA and DNA repair enzymes and triggering excitotoxicity. Removing the mercury will help but will not solve the problem because overactivation of the brain's immune system will cause varying degrees of neurological damage to the highly-vulnerable developing brain.

Full Report With References:

www.vacinfo.org/man1714_1726.pdf

DNA Repair Modulates The Vulnerability Of The Developing Brain To Alkylating Agents

Author Information

- G.E. Kisby,*¹ A. Olivas,¹ T. Park,¹ M. Churchwell,²
D. Doerge,² L. D. Samson,³ S.L. Gerson,⁴ and M.S. Turker¹
1. Center for Research on Occupational and Environmental Toxicology (CROET)
Oregon Health Sciences University, Portland, OR 97201
 2. NCTR, Jefferson, AR
 3. Biological Engineering Division, Center for Environmental Health Sciences
Massachusetts Institute of Technology, Cambridge, MA 02139
 4. Case Western Reserve University, Case Comprehensive Cancer Center
10900 Euclid Avenue, Cleveland, OH 44106

Abstract

Neurons of the developing brain are especially vulnerable to environmental agents that damage DNA (i.e., genotoxicants), but the mechanism is poorly understood. The focus of the present study is to demonstrate that DNA damage plays a key role in disrupting neurodevelopment. To examine this hypothesis, we compared the cytotoxic and DNA damaging properties of the methylating agents methylazoxymethanol (MAM) and dimethyl sulfate (DMS) and the mono- and bifunctional alkylating agents chloroethylamine (CEA) and nitrogen mustard (HN2), in granule cell neurons derived from the cerebellum of neonatal wild type mice and three transgenic DNA repair strains. Wild type cerebellar neurons were significantly more sensitive to the alkylating agents DMS and HN2 than neuronal cultures treated with MAM or the half-mustard CEA. Parallel studies with neuronal cultures from mice deficient in alkylguanine DNA glycosylase (Aag^{-/-}) or O6-methylguanine methyltransferase (Mgmt^{-/-}), revealed significant differences in the sensitivity of neurons to all four genotoxicants. Mgmt^{-/-} neurons were more sensitive to MAM and HN2 than the other genotoxicants and wild type neurons treated with either alkylating agent. In contrast, Aag^{-/-} neurons were for the most part significantly less sensitive than wild type or Mgmt^{-/-} neurons to MAM and HN2. Aag^{-/-} neurons were also significantly less sensitive than wild type neurons treated with either DMS or CEA. Granule cell development and motor function were also more severely disturbed by MAM and HN2 in Mgmt^{-/-} mice than in comparably treated wild type mice. In contrast, cerebellar development and motor function were well preserved in MAM treated Aag^{-/-} or MGMT overexpressing (MgmtTg⁺) mice, even as compared with wild type mice suggesting that AAG protein increases MAM toxicity, whereas MGMT protein decreases toxicity. Surprisingly, neuronal development and motor function were severely disturbed in MgmtTg⁺ mice treated with HN2. Collectively, these in vitro and in vivo studies demonstrate that the type of DNA lesion and the efficiency of DNA repair are two important factors that determine the vulnerability of the developing brain to long-term injury by a genotoxicant.

“Neurons of the developing brain are especially vulnerable to environmental agents that damage DNA (i.e., genotoxicants), but the mechanism is poorly understood. Collectively, these in vitro and in vivo studies demonstrate that the type of DNA lesion and the efficiency of DNA repair are two important factors that determine the vulnerability of the developing brain to long-term injury by a genotoxicant.”

“Of these 1162 cases, 1105 were considered to be related to the vaccination ...”

European Journal of Pediatrics • January 2009

Discolored leg syndrome after vaccination—descriptive epidemiology

Jeanet M. Kemmeren , Patricia E. Vermeer-de Bondt, Nicoline A. T. van der Maas

Abstract

Discoloration of the leg following vaccination is a relatively unknown entity. We carried out a study of discolored leg syndrome (DLS) during a 10-year consecutive period with the objective of characterizing DLS in infants following vaccination received in the Dutch National Vaccination Program as well as its occurrence and association with different vaccines. Discolored leg syndrome was defined as an even or patchy red, blue or purple discoloration of the leg(s) and/or leg petechiae with or without swelling. All reports of adverse events following immunization that were made to the passive surveillance system between 1994 and 2003 were included—a total of 1162 identified cases. Red, blue, purple discoloration and isolated petechiae were reported in 39, 19, 27 and 14% of these cases, respectively. Of these 1162 cases, 1105 were considered to be related to the vaccination, based on a predefined risk window with symptom onset after vaccination (48 h for discolorations and 2 weeks for petechiae). Of the 1105 cases, about 50% occurred after DTP-IPV+Hib1 vaccinations, and 30% occurred after DTP-IPV+Hib2 vaccinations. Discolored leg syndrome was frequently accompanied by fierce crying (78%). The median time interval between vaccination and the occurrence of DLS was 3.8 ± 46.7 h, and the median duration was short (2 ± 61.7 h). Advancing the vaccination schedule from 3 to 2 months of age caused a small increase in DLS. Discolored leg syndrome manifested mainly after the first and/or second vaccination. In addition to dose, the occurrence of DLS may be slightly age-dependent and self-limiting. The pathophysiology is unknown but may be the result of a vasomotor reaction. Future studies should elucidate the recurrence rate, identify risk factors and assess late outcomes.

<http://link.springer.com/article/10.1007%2Fs00431-008-0707-0>

“... Triton X-100 (TX)-induced apoptosis.”

Biochemical And Biophysical Research Communications • January 2009

Differential roles for Bak in Triton X-100- and deoxycholate-induced apoptosis

Author information

Sawai H1, Domae N.

Department of Internal Medicine, Osaka Dental University
8-1 Kuzuhahanazonocho, Hirakata, Osaka 573-1121, Japan

Abstract

We recently reported that Bax activation occurs downstream of caspase activation in Triton X-100 (TX)-induced apoptosis. Here, Bak was found to be activated in TX-induced apoptosis. Although z-VAD-fmk completely suppressed Bax activation, it only partially attenuated TX-induced Bak activation. Moreover, activation of both Bak and Bax was detected in apoptosis induced by deoxycholate, a physiological detergent in bile. z-VAD-fmk completely suppressed deoxycholate-induced Bak as well as Bax activation. Furthermore, Bak siRNA attenuated TX- but not deoxycholate-induced caspase activation. These results suggest that Bak activation may occur upstream of caspase activation in TX- but not deoxycholate-induced apoptosis and that the mechanism of TX-induced apoptosis may differ from that of deoxycholate-induced apoptosis at least with regard to the role for Bak.

<http://www.ncbi.nlm.nih.gov/pubmed/19041633>

Elevated immune response in the brain of autistic patients

Author information

Li X1, Chauhan A, Sheikh AM, Patil S,
Chauhan V, Li XM, Ji L, Brown T, Malik M.

Abstract

This study determined immune activities in the brain of ASD patients and matched normal subjects by examining cytokines in the brain tissue. Our results showed that proinflammatory cytokines (TNF-alpha, IL-6 and GM-CSF), Th1 cytokine (IFN-gamma) and chemokine (IL-8) were significantly increased in the brains of ASD patients compared with the controls. However the Th2 cytokines (IL-4, IL-5 and IL-10) showed no significant difference. The Th1/Th2 ratio was also significantly increased in ASD patients.

Conclusion

ASD patients displayed an increased innate and adaptive immune response through the Th1 pathway, suggesting that localized brain inflammation and autoimmune disorder may be involved in the pathogenesis of ASD.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2770268/>

“ASD patients displayed an increased innate and adaptive immune response through the Th1 pathway, suggesting that localized brain inflammation and autoimmune disorder may be involved in the pathogenesis of ASD.”

“... these occurrences support an association between receipt of aluminium adjuvant and sterile abscesses in susceptible patients.”

BMJ Case Reports • March 2009

Findings that shed new light on the possible pathogenesis of a disease or an adverse effect

Recurrent sterile abscesses following aluminium adjuvant-containing vaccines

Author Information

Nicola P Klein¹, Kathryn M Edwards³, Robert C Sparks³, Cornelia L Dekker²,
on behalf of the Clinical Immunization Safety Assessment (CISA) Network

1. Kaiser Permanente Vaccine Study Center, 16th Floor, One Kaiser Plaza, Oakland, California 94612, USA
2. Stanford University School of Medicine, Division of Pediatric Infectious Diseases, 300 Pasteur Drive, Stanford, California, USA
3. Vanderbilt University Medical Center, Vanderbilt Vaccine Research Program, Department of Pediatrics
1211 Medical Center Drive, Nashville, Tennessee 37232, USA

Nicola Klein, Nicola.Klein@kp.org

Summary

Abscess formation following immunisation is a previously reported complication, generally associated with microbial contamination of the vaccine. Less commonly, such abscesses have been sterile. Here we describe two children evaluated in the Center for Disease Control and Prevention (CDC)-funded Clinical Immunization Safety Assessment (CISA) network who developed recurrent sterile abscesses after administration of vaccines containing aluminium adjuvant, either individually or in combination. Although the abscesses healed without sequelae, these occurrences support an association between receipt of aluminium adjuvant and sterile abscesses in susceptible patients. For patients with similar symptoms, clinicians may wish to choose a vaccine formulation containing the least amount of aluminium adjuvant.

<http://casereports.bmj.com/content/2009/bcr.09.2008.0951.long>

Formaldehyde exposure and leukemia: a new meta-analysis and potential mechanisms

Author information

Zhang L1, Steinmaus C, Eastmond DA, Xin XK, Smith MT.

School of Public Health
50 University Hall
University of California
Berkeley, CA 94720-7356, USA
luoping@berkeley.edu

Abstract

Formaldehyde is an economically important chemical, to which more than 2 million U.S. workers are occupationally exposed. Substantially more people are exposed to formaldehyde environmentally, as it is generated by automobile engines, is a component of tobacco smoke and is released from household products, including furniture, particleboard, plywood, and carpeting. The International Agency for Research on Cancer (IARC) recently classified formaldehyde as a human carcinogen that causes nasopharyngeal cancer and also concluded that there is “strong but not sufficient evidence for a causal association between leukemia and occupational exposure to formaldehyde”. Here, we review the epidemiological studies published to date on formaldehyde-exposed workers and professionals in relation to lymphohematopoietic malignances. In a new meta-analysis of these studies, focusing on occupations known to have high formaldehyde exposure, we show that summary relative risks (RRs) were elevated in 15 studies of leukemia (RR=1.54; confidence interval (CI), 1.18-2.00) with the highest relative risks seen in the six studies of myeloid leukemia (RR=1.90; 95% CI, 1.31-2.76). The biological plausibility of this observed association is discussed and potential mechanisms proposed. We hypothesize that formaldehyde may act on bone marrow directly or, alternatively, may cause leukemia by damaging the hematopoietic stem or early progenitor cells that are located in the circulating blood or nasal passages, which then travel to the bone marrow and become leukemic stem cells. To test these hypotheses, we recommend that future studies apply biomarkers validated for other chemical leukemogens to the study of formaldehyde.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=18674636>

“formaldehyde may act on bone marrow directly or, alternatively, may cause leukemia by damaging the hematopoietic stem or early progenitor cells that are located in the circulating blood or nasal passages, which then travel to the bone marrow and become leukemic stem cells.”

Vaccination alone or
in combination with pyridostigmine
promotes and prolongs activation of
stress-activated kinases induced by s
tress in the mouse brain

Author information

Wang D1, Perides G, Liu YF.

¹Department of Pharmacology
Boston University School of Medicine
Massachusetts 02118, USA

Abstract

Gulf war illnesses (GWI) are currently affecting thousands of veterans. To date, the molecular mechanisms underlying the pathogenesis of these illnesses remain unknown. During Gulf war I, military personnel were exposed to multiple stressors, one or more vaccines, pyridostigmine (PY), and other chemicals. In our previous studies, we found that stress induces activation of mitogen activated protein-kinase kinase 4 (MKK4) and c-Jun-N-terminal kinase (JNK) in the mouse brain (Liu et al. 2004). Our working hypothesis is that stress, vaccination, and PY may synergistically induce activation of MKK4 and JNK in the brain, leading to over-activation of these kinases and neurological injuries. To test our hypothesis, we examined the effect of key-hole limpet hemocyanin (KLH) immunization alone or in combination with PY on activation of MKK4 and JNK induced by stress. We found that KLH immunization alone had a small effect on MKK4 or JNK activity but it significantly enhanced and prolonged activation of these kinases induced by stress, from a few hours to several days. Additionally, KLH immunization caused activation of p38MAPK. PY treatment further enhanced and prolonged activation of these kinases induced by stress in combination with KLH immunization and triggered activation of caspase-3. Our current studies suggest that stress, vaccination, and PY may synergistically act on multiple stress-activated kinases in the brain to cause neurological impairments in GWI.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=15857404>

Full Report: <http://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.2005.03093.x/full>

“Gulf war illnesses (GWI) are currently affecting thousands of veterans. Our current studies suggest that stress, vaccination, and pyridostigmine may synergistically act on multiple stress-activated kinases in the brain to cause neurological impairments in Gulf war illnesses.”

Correspondence (letter to the editor):
Long Term Side Effects Due to
Vaccination And Pharmacovigilance

Maurice Pich,* Arno Köster,* and Andreas Klement, Dr.

Institut für Allgemeinmedizin
Martin-Luther-Universität Halle-Wittenberg
06112 Halle/Saale, Germany

We thank the authors for their clear overview of vaccine sceptics' common objections, which are helpful for everyday clinical practice.

Most vaccinations and vaccination advice in Germany are given by general practitioners and pediatricians. Appropriate and responsible advice includes providing information to those about to receive the vaccine and their parents, about rare but possible side effects. These include the possible occurrence of Guillain-Barré syndromes after flu vaccinations (1), for example; the possible association between recombinant hepatitis B vaccine and multiple sclerosis (2), which is still under discussion in current publications; and the unexplained possible association of multiple vaccinations with neurodegenerative disorders in connection with aluminum hydroxide, which to date is the most common vaccine adjuvant in use (3).

Long term side effects due to vaccination can be detected to a sufficiently high quality standard only by means of long term, active pharmacovigilance conducted through independent and sufficiently equipped monitoring systems. To assess the long term safety of vaccines, passive post-vaccination observation by notification of vaccination complications by primary care physicians is not enough: possible causal associations with developing disorders—for example, neurodegenerative disorders—are difficult to state in individual cases years after the vaccine was given.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2689587/>

“... the possible occurrence of Guillain-Barré syndromes after flu vaccinations, for example; the possible association between recombinant hepatitis B vaccine and multiple sclerosis, which is still under discussion in current publications; and the unexplained possible association of multiple vaccinations with neurodegenerative disorders in connection with aluminum hydroxide, which to date is the most common vaccine adjuvant in use ...”

JEM spotlight:
metal speciation related to
neurotoxicity in humans

Author information

Michalke B1, Halbach S, Nischwitz V.

Helmholtz Zentrum München
Institute of Ecological Chemistry, 85764
Neuherberg, Germany
bernhard.michalke@helmholtz-muenchen.de

Abstract

Improved living conditions have led to a steady increase in the life expectancy of humans in most countries. However, this is accompanied by an increased probability of suffering from neurodegenerative diseases like Alzheimer's disease or Parkinson's disease. Unfortunately, the therapeutic possibilities for curing these diseases are very limited up to now. Many studies indicate that a variety of environmental factors contribute to the initiation and promotion of neurodegenerative diseases. For example, the role of metal exposure and disturbance of metal homeostasis in the brain is discussed in this respect. However, most studies focus on the neurological and toxicological aspects but not on a detailed characterisation of the species of the involved metals. Therefore, this review summarizes the neurotoxic effects of selected metals on humans and focuses on contributions from trace element speciation analysis with relevance to neuroscientific research. In spite of the advance in instrumentation and methodology of speciation analysis there are few applications for matrices like cerebrospinal fluid which is due to limited access to these samples and analytical challenges caused by matrix interferences, low concentrations and limited stability of many trace element species of interest. The most relevant neurotoxic metals aluminium, lead, manganese and mercury are reviewed in detail while further metals like cadmium, arsenic, bismuth and tin are briefly discussed. Current results indicate that knowledge on trace element speciation can contribute to a better understanding of the transport of metals across the neural barriers and potentially of their role in diseased human brains.

<http://www.ncbi.nlm.nih.gov/pubmed/19436852>

“The most relevant neurotoxic metals aluminium, lead, manganese and mercury are reviewed in detail while further metals like cadmium, arsenic, bismuth and tin are briefly discussed. Current results indicate that knowledge on trace element speciation can contribute to a better understanding of the transport of metals across the neural barriers and potentially of their role in diseased human brains.”

Re: Determinants Of The Incidence Of Childhood Asthma: A Two-Stage Case-Control Study

Author Information

José G. Dórea

Faculty of Health Sciences
Universidade de Brasilia
70919-970 Brasilia, Brazil
dorea@rudah.com.br

Abstract

In a recent article, Martel et al. (1) took into consideration 47 variables that could influence children's asthma incidence but missed one that has been significantly researched—vaccines. The Quebec, Canada, children enrolled in the study were born between 1990 and 2002. During this time, Canada underwent major changes in types of vaccines and the calendar of immunization for infants and children: Thimerosal was withdrawn from infants' vaccines, some of the vaccines were combined, some new vaccines were introduced, and still others underwent changes in their starting date and subsequent calendar; this without counting parental preference for administration of multiple shots at a single clinical visit.

Some vaccines can contain thimerosal, which is a recognized sensitizer in children (2); additionally, a polymorphism in the glutathione S-transferase gene can alter its metabolism in children. Indeed, glutathione S-transferase M1 deficiency was found to be significantly more frequent among patients who had been sensitized to thimerosal (3). Thyssen et al. (4) speculated that the decrease in allergy in the general population of Denmark could be due to thimerosal's no longer being used as a vaccine preservative in that country. Although contact allergy due to thimerosal is not a contraindication for receipt of vaccines, these reactions are expected to be fewer in the future because of changes in current vaccine formulations (5).

Fombonne et al. (6) have described changes in vaccine formulations and schedules taking place in Canada from 1985 to 2006. The measles-mumps-rubella vaccines were officially incorporated in 1976 and were recommended for use at age 1 year in Quebec; as of 1996, 2 doses of measles-mumps-rubella vaccine were being given at ages 12 and 18 months. A combined diphtheria-tetanus-pertussis vaccine was recommended at ages 2, 4, 6, and 18 months and ages 4–6 years; this vaccine contained 50 µg of thimerosal and was used from 1985 to 1987. In 1988, a Haemophilus influenzae type b vaccine (which also contained thimerosal) was added to the schedule at 18 months of age. As of 1992,

the H. influenzae type b vaccines were also administered at ages 2, 4, 6, and 18 months. The poliomyelitis vaccine was administered separately at ages 2, 4, and 18 months and ages 4–6 years from 1987 to 1995. With the exception of the measles-mumps-rubella and poliomyelitis vaccines, all of the vaccines contained 50 µg of thimerosal. Estimated cumulative exposure to thimerosal was 200 µg by age 2 years until 1988; it then increased to 250 µg by 1990. Therefore, as of 1992, cumulative exposure to thimerosal by age 2 years reached 400 µg (6).

Because of mass immunization against meningococcal disease (occurring in 1993), there was additional exposure to thimerosal. Following Fombonne et al.'s (6) reasoning, there could have been different cumulative thimerosal exposures of 300 µg in children born between March 1990 and December 1991 and 450 µg in children born between January 1992 and September 1992. However, both the poliomyelitis and H. influenzae type b vaccines were combined with the diphtheria-pertussis (cellular)-tetanus vaccine in a thimerosal-free formulation in 1996; this pentavaccine was administered at ages 2, 4, 6, and 18 months, with a poliomyelitis-pertussis (cellular)-tetanus booster (thimerosal-free) being given at ages 4–6 years. In 1998, the cellular pertussis vaccine was replaced by the acellular vaccine in the pentavaccine. From 1996 onward, all immunizations were thimerosal-free. Nevertheless, there is 1 additional challenge that has been overlooked (or is difficult to track) by almost all epidemiologic studies that have addressed the issue of vaccines and asthma: multiple applications of different vaccines at a single immunization visit (7).

A study carried out in Canada indicated a negative association between delay in administration of the first dose of diphtheria-pertussis-tetanus vaccine and the development of asthma; a greater association was shown with delays in the first 3 doses (8). De Serres et al. (9) also reported oculorespiratory syndrome as an adverse event that occurred with influenza vaccines used in Canada (2000–2003).

“Thyssen et al. speculated that the decrease in allergy in the general population of Denmark could be due to thimerosal's no longer being used as a vaccine preservative in that country.”

Toxic additives in medication for preterm infants

Author information

Whittaker A1, Currie AE, Turner MA,
Field DJ, Mulla H, Pandya HC.
Department of Infection
Immunity & Inflammation, University of Leicester Robert Kilpatrick Clinical Sciences Building
Leicester Royal Infirmary, Leicester LE2 7LX, UK
hp28@le.ac.uk

Abstract

BACKGROUND

Little is known about exposure of preterm infants to excipients during routine clinical care.

OBJECTIVE

To document excipient exposure in vulnerable preterm babies in a single centre, taking into account chronic lung disease (CLD) as a marker of illness severity.

DESIGN

Excipient exposure after treatment with eight oral liquid medications was determined by retrospectively analysing the drug charts of infants admitted to a neonatal unit.

SETTING

The Leicester Neonatal Service.

PARTICIPANTS

38 infants born between June 2005 and July 2006 who were less than 30 weeks' gestation and 1500 g in weight at birth and managed in Leicester to discharge.

RESULTS

The 38 infants represented 53% of the eligible target group; 7/38 infants had CLD. During their in-patient stay, infants were exposed to over 20 excipients including ethanol and propylene glycol, chemicals associated with neurotoxicity. Infants with CLD were exposed to higher concentrations of these toxins. Infants were also exposed to high concentrations of sorbitol, with some infants being exposed to concentrations in excess of recommended guidelines for maximum exposure in adults.

CONCLUSIONS

Preterm infants are commonly exposed to excipients, some of which are potentially toxic. Strategies aimed at reducing excipient load in preterm infants are urgently required.

“Preterm infants
are commonly exposed
to excipients, some of which
are potentially toxic.”

What is regressive autism and why does it occur?
Is it the consequence of multi-systemic dysfunction
affecting the elimination of heavy metals and
the ability to regulate neural temperature?

Graham E. Ewing, Director

Montague Healthcare
Mulberry House, 6 Vine Farm Close
Cotgrave, Nottingham NG12 3TU, United Kingdom

Abstract

There is a compelling argument that the occurrence of regressive autism is attributable to genetic and chromosomal abnormalities, arising from the overuse of vaccines, which subsequently affects the stability and function of the autonomic nervous system and physiological systems. That sense perception is linked to the autonomic nervous system and the function of the physiological systems enables us to examine the significance of autistic symptoms from a systemic perspective. Failure of the excretory system influences elimination of heavy metals and facilitates their accumulation and subsequent manifestation as neurotoxins: the long-term consequences of which would lead to neurodegeneration, cognitive and developmental problems. It may also influence regulation of neural hyperthermia. This article explores the issues and concludes that sensory dysfunction and systemic failure, manifested as autism, is the inevitable consequence arising from subtle DNA alteration and consequently from the overuse of vaccines.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3364648/>

“This article explores the issues and concludes that sensory dysfunction and systemic failure, manifested as autism, is the inevitable consequence arising from subtle DNA alteration and consequently from the overuse of vaccines.”

Macrophagic myofasciitis plus (distinct types of muscular dystrophy)

Author information

Müller HD1, Landeghem FK,
Schmidt PF, Sommer C, Goebel HH.

Department of Neuropathology
University Medical Center of the Johannes Gutenberg University Mainz
Mainz, Germany
mueller@neuropatho.klinik.uni-mainz.de

Abstract

Macrophagic myofasciitis (MMF) is a well-known lesion following vaccination with aluminium-containing vaccines. It has abundantly been reported in adults and several times in children, often in single patients or in rather small cohorts. Only few of these published reports on children have shown distinct myopathology of another neuromuscular disease except for MMF. Indications for biopsy often were nondescript clinical features in children, such as hypotonia or delay in motor development but, apparently, never that of suspected MMF. Thus, in previous reports as well as in our two patients, encountering MMF in the biopsied tissue specimens was coincidental. Our two unrelated patients with MMF also had two separate types of muscular dystrophy, a merosinopathy and dystrophinopathy, showing a combination of myopathologically well-defined neuromuscular diseases, muscular dystrophies and MMF. Detecting such a combination of two separate conditions may, in the future, be rare when non-invasive techniques, e. g., genetic, will have replaced muscle biopsy in ascertaining hereditary neuromuscular conditions, especially in children.

<http://www.ncbi.nlm.nih.gov/pubmed/20135575>

“Macrophagic myofasciitis (MMF) is a well-known lesion following vaccination with aluminium-containing vaccines. It has **abundantly** been reported in adults and several times in children, often in single patients or in rather small cohorts. Our two unrelated patients with MMF also had two separate types of muscular dystrophy, a merosinopathy and dystrophinopathy, showing a combination of myopathologically well-defined neuromuscular diseases, muscular dystrophies and MMF.”

Bordetella pertussis strains with increased toxin production associated with pertussis resurgence

Author information

Mooi FR1, van Loo IH, van Gent M, He Q, Bart MJ, Heuvelman KJ, de Greeff SC, Diavatopoulos D, Teunis P, Nagelkerke N, Mertsola J.

National Institute for Public Health and the Environment
Bilthoven, the Netherlands
frits.mooi@rivm.nl

Abstract

Before childhood vaccination was introduced in the 1940s, pertussis was a major cause of infant death worldwide. Widespread vaccination of children succeeded in reducing illness and death. In the 1990s, a resurgence of pertussis was observed in a number of countries with highly vaccinated populations, and pertussis has become the most prevalent vaccine-preventable disease in industrialized countries. We present evidence that in the Netherlands the dramatic increase in pertussis is temporally associated with the emergence of *Bordetella pertussis* strains carrying a novel allele for the pertussis toxin promoter, which confers increased pertussis toxin (Ptx) production. Epidemiologic data suggest that these strains are more virulent in humans. We discuss changes in the ecology of *B. pertussis* that may have driven this adaptation. Our results underline the importance of Ptx in transmission, suggest that vaccination may select for increased virulence, and indicate ways to control pertussis more effectively.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19751581>

“We present evidence that in the Netherlands the dramatic increase in pertussis is temporally associated with the emergence of *Bordetella pertussis* strains carrying a novel allele for the pertussis toxin promoter, which confers increased pertussis toxin (Ptx) production. Epidemiologic data suggest that these strains are more virulent in humans.”

Breastfeeding is an essential complement to vaccination

Author information

Dòrea JG.

Department of Nutrition
Universidade de Brasília
70919-970 Brasília, DF, Brazil
dorea@rudah.com.br

Abstract

AIM:

This article explores the role of breastfeeding in different aspects of vaccination in the first 6 months when infants are still developing: (1) pain management; (2) immunomodulation of infants' vaccine responses; (3) metabolism of thimerosal.

METHODS:

Major databases were searched for studies that addressed outcomes of related issues.

RESULTS:

Studies reveal that breastfeeding can: (1) help mothers and infants to cope with the stressful situations that accompany parenteral vaccines; (2) improve response to vaccines in the still maturing immunologic and enterohepatic systems of infants; (3) influence physiologic parameters that can change metabolism of ethylmercury derived from some vaccines.

CONCLUSION:

Health promotion that supports vaccinations should also emphasize early initiation and maintenance of exclusive breastfeeding up until 6 months for maximum protection of the infants with a possible beneficial effect on the vaccine response. Paediatric professionals should inform mothers of the proven benefits of breastfeeding and its importance in complementing vaccination and lowering stress and the risk of untoward reactions on susceptible infants.

<http://www.ncbi.nlm.nih.gov/pubmed/19594471>

“Health promotion that supports vaccinations should also emphasize early initiation and maintenance of exclusive breastfeeding up until 6 months for maximum protection of the infants with a possible beneficial effect on the vaccine response.”

“This study demonstrates
a significant positive association between
the severity of autism and the
relative body burden of toxic metals.”

Journal Of Toxicology • August 2009

The Severity of Autism Is Associated with Toxic Metal Body Burden and Red Blood Cell Glutathione Levels

J. B. Adams,^{1,*} M. Baral,² E. Geis,³ J. Mitchell,¹ J. Ingram,³ A. Hensley,³ I. Zappia,³ S. Newmark,⁴ E.
Gehn,³ R. A. Rubin,⁵ K. Mitchell,³ J. Bradstreet,^{2, 6} and J. M. El-Dahr⁷

1. Division of Basic Medical Sciences, Southwest College of Naturopathic Medicine, Tempe, AZ 85282, USA
 2. Department of Pediatric Medicine, Southwest College of Naturopathic Medicine, Tempe, AZ 85282, USA
 3. Autism Research Institute, San Diego, CA 92116-2599, USA
 4. Center for Integrative Pediatric Medicine, Tucson, AZ 85711, USA
 5. Department of Mathematics, Whittier College, Whittier, CA 90601-4413, USA
 6. International Child Development Resource Center, Phoenix, AZ, USA
 7. Department of Pediatrics, Tulane University School of Medicine, New Orleans, LA 70112, USA
- *J. B. Adams: Email: jade.usa@smada.mij

Abstract

This study investigated the relationship of children's autism symptoms with their toxic metal body burden and red blood cell (RBC) glutathione levels. In children ages 3–8 years, the severity of autism was assessed using four tools: ADOS, PDD-BI, ATEC, and SAS. Toxic metal body burden was assessed by measuring urinary excretion of toxic metals, both before and after oral dimercaptosuccinic acid (DMSA). Multiple positive correlations were found between the severity of autism and the urinary excretion of toxic metals. Variations in the severity of autism measurements could be explained, in part, by regression analyses of urinary excretion of toxic metals before and after DMSA and the level of RBC glutathione (adjusted R² of 0.22–0.45, P < .005 in all cases). This study demonstrates a significant positive association between the severity of autism and the relative body burden of toxic metals.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2809421/>

“... vaccination is depicted as playing an important role in Chronic Fatigue Syndrome onset.”

Annals Of The New York Academy Of Science • September 2009

Infection, vaccination, and autoantibodies in chronic fatigue syndrome, cause or coincidence?

Author information

Ortega-Hernandez OD1, Shoenfeld Y.

Department of Internal Medicine B and Research for Autoimmune Diseases
Sheba Medical Center, Tel Hashomer, Israel

Abstract

Chronic fatigue syndrome (CFS) is a heterogeneous syndrome of unknown etiology and pathophysiology. CFS patients complain about disabling fatigue, depression, difficulty with memory, and concomitant skeletal and muscular pain. Interestingly enough, there is certain overlap between CFS symptoms, autoimmune rheumatic disease, and infectious diseases. Certain neuroendocrine-immune abnormalities have also been described, and autoantibodies commonly described in some autoimmune diseases have been found in CFS patients as well. An increasing number of autoantibodies, mainly directed against other nuclear cell components, have been illustrated. Likewise, an association between some infectious agents, antibody production, and later CFS onset has been reported. Similarly, vaccination is depicted as playing an important role in CFS onset. Recently, a case report pointed toward a causal association between silicone breast linkage, hepatitis B virus vaccination, and CFS onset in a previously healthy woman. Such findings suggest that there is a likely deregulation of the immune system influenced by specific agents (infections, vaccination, and products, such as silicone). Evidence suggests that CFS is a complex disease in which several risk factors might interact to cause its full expression. Thus, although different alterations have been found in CFS patients, undoubtedly the main feature is central nervous system involvement with immunological alterations. Therefore, a new term neuro-psycho-immunology must be quoted. New studies based on this concept are needed in order to investigate syndromes, such as CFS, in which immunological alterations are thought to be associated with concomitant psychological and health disturbances.

<http://www.ncbi.nlm.nih.gov/pubmed/19758205>

Lupus • November 2009

Transverse myelitis and vaccines: a multi-analysis

Author information

Agmon-Levin N1, Kivity S,
Szyper-Kravitz M, Shoenfeld Y.

Center for Autoimmune Diseases
Sheba Medical Center
Tel-Hashomer, Israel

Abstract

Transverse myelitis is a rare clinical syndrome in which an immune-mediated process causes neural injury to the spinal cord. The pathogenesis of transverse myelitis is mostly of an autoimmune nature, triggered by various environmental factors, including vaccination. Our aim here was to search for and analyze reported cases of transverse myelitis following vaccination. A systematic review of PubMed, EMBASE and DynaMed for all English-language journals published between 1970 and 2009 was performed, utilizing the key words transverse myelitis, myelitis, vaccines, post-vaccination, vaccination and autoimmunity. We have disclosed 37 reported cases of transverse myelitis associated with different vaccines including those against hepatitis B virus, measles-mumps-rubella, diphtheria-tetanus-pertussis and others, given to infants, children and adults. In most of these reported cases the temporal association was between several days and 3 months, although a longer time frame of up to several years was also suggested. Although vaccines harbor a major contribution to public health in the modern era, in rare cases they may be associated with autoimmune phenomena such as transverse myelitis. The associations of different vaccines with a single autoimmune phenomenon allude to the idea that a common denominator of these vaccines, such as an adjuvant, might trigger this syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/19880568>

“We have disclosed 37 reported cases of transverse myelitis associated with different vaccines including those against hepatitis B virus, measles-mumps-rubella, diphtheria-tetanus-pertussis and others, given to infants, children and adults. Although vaccines harbor a major contribution to public health in the modern era, in rare cases they may be associated with autoimmune phenomena such as transverse myelitis. The associations of different vaccines with a single autoimmune phenomenon allude to the idea that a common denominator of these vaccines, such as an adjuvant, might trigger this syndrome.”

Ten cases of systemic lupus erythematosus related to hepatitis B vaccine

Author information

Agmon-Levin N1, Zafrir Y, Paz Z,
Shilton T, Zandman-Goddard G, Shoenfeld Y.

Center for Autoimmune Diseases
Sheba Medical Center, Tel-Hashomer, Israel

Abstract

The objective of this article is to identify common and atypical features of systemic lupus erythematosus diagnosed following hepatitis B vaccination. We analyzed retrospectively the medical records of 10 systemic lupus erythematosus patients from different centers, who developed the disease following hepatitis B vaccination and determined the prevalence of different manifestations and the time association to vaccination. In this case series, 80% of the patients were female, mean age 35 +/- 9 years, of which 20% received one inoculation, 20% received two doses and 60% received all three inoculations. The mean latency period from the first hepatitis B virus immunization and onset of autoimmune symptoms was 56.3 days. All patients were diagnosed with systemic lupus erythematosus, according to the American College of Rheumatology revised criteria within 1 year. The prevalence of some systemic lupus erythematosus manifestations was typical and included involvement of the joints (100%), skin (80%), muscles (60%) and photosensitivity (30%). Other symptoms differed in this unique group of systemic lupus erythematosus patients such as low rate of kidney and hematologic involvement, and a relatively high rate of hepatitis (20%). Neurological (80%) and pulmonary (70%) symptoms were also common in this group. Data from this case-series, and previously documented cases in the literature could only show a temporal relation between hepatitis B vaccination and the appearance of systemic lupus erythematosus. Systemic lupus erythematosus related to vaccine may differ from idiopathic systemic lupus erythematosus in its clinical presentation and may resemble drug-induced systemic lupus erythematosus. Thus, physicians should be alerted to this potential association, its possible long latency period and unique presentations, and be encouraged to report and analyze these cases.

<http://www.ncbi.nlm.nih.gov/pubmed/19880567>

“Other symptoms differed in this unique group of systemic lupus erythematosus patients such as low rate of kidney and hematologic involvement, and a relatively high rate of hepatitis (20%). Neurological (80%) and pulmonary (70%) symptoms were also common in this group. Systemic lupus erythematosus related to vaccine may differ from idiopathic systemic lupus erythematosus in its clinical presentation and may resemble drug-induced systemic lupus erythematosus.”

“Owing to the adverse effects exerted by adjuvants, there is no doubt that safer adjuvants need to be developed and incorporated into future vaccines.”

Lupus • November 2009

Adjuvants and autoimmunity

Author information

Israeli E1, Agmon-Levin N,
Blank M, Shoenfeld Y.

Center for Autoimmune Diseases
Sheba Medical Center
Tel-Hashomer, Israel

Abstract

Some adjuvants may exert adverse effects upon injection or, on the other hand, may not trigger a full immunological reaction. The mechanisms underlying adjuvant adverse effects are under renewed scrutiny because of the enormous implications for vaccine development. In the search for new and safer adjuvants, several new adjuvants were developed by pharmaceutical companies utilizing new immunological and chemical innovations. The ability of the immune system to recognize molecules that are broadly shared by pathogens is, in part, due to the presence of special immune receptors called toll-like receptors (TLRs) that are expressed on leukocyte membranes. The very fact that TLR activation leads to adaptive immune responses to foreign entities explains why so many adjuvants used today in vaccinations are developed to mimic TLR ligands. Alongside their supportive role, adjuvants were found to inflict by themselves an illness of autoimmune nature, defined as ‘the adjuvant diseases’. The debatable question of silicone as an adjuvant and connective tissue diseases, as well as the Gulf War syndrome and macrophagic myofasciitis which followed multiple injections of aluminium-based vaccines, are presented here. Owing to the adverse effects exerted by adjuvants, there is no doubt that safer adjuvants need to be developed and incorporated into future vaccines. Other needs in light of new vaccine technologies are adjuvants suitable for use with mucosally delivered vaccines, DNA vaccines, cancer and autoimmunity vaccines. In particular, there is demand for safe and non-toxic adjuvants able to stimulate cellular (Th1) immunity. More adjuvants were approved to date besides alum for human vaccines, including MF59 in some viral vaccines, MPL, AS04, AS01B and AS02A against viral and parasitic infections, virosomes for HBV, HPV and HAV, and cholera toxin for cholera. Perhaps future adjuvants occupying other putative receptors will be employed to bypass the TLR signaling pathway completely in order to circumvent common side effects of adjuvant-activated TLRs such as local inflammation and the general malaise felt because of the costly whole-body immune response to antigen.

<http://www.ncbi.nlm.nih.gov/pubmed/19880572>

National Reviews In Rheumatology • November 2009

Vaccines and autoimmunity

Author information

Agmon-Levin N1, Paz Z, Israeli E, Shoenfeld Y.

Center for Autoimmune Diseases and Department of Medicine B
Sheba Medical Center, Sheba Medical Center, Tel-Hashomer 52621, Israel

Abstract

Vaccines have been used for over 200 years and are the most effective way of preventing the morbidity and mortality associated with infections. Like other drugs, vaccines can cause adverse events, but unlike conventional medicines, which are prescribed to people who are ill, vaccines are administered to healthy individuals, thus increasing the concern over adverse reactions. Most side effects attributed to vaccines are mild, acute and transient; however, rare reactions such as hypersensitivity, induction of infection, and autoimmunity do occur and can be severe and even fatal. The rarity and subacute presentation of post-vaccination autoimmune phenomena means that ascertaining causality between these events can be difficult. Moreover, the latency period between vaccination and autoimmunity ranges from days to years. In this article, on the basis of published evidence and our own experience, we discuss the various aspects of the causal and temporal interactions between vaccines and autoimmune phenomena, as well as the possible mechanisms by which different components of vaccines might induce autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/19865091>

“Most side effects attributed to vaccines are mild, acute and transient; however, rare reactions such as hypersensitivity, induction of infection, and autoimmunity do occur and can be severe and even fatal. Moreover, the latency period between vaccination and autoimmunity ranges from days to years.”

Vaccination of healthy subjects and autoantibodies: from mice through dogs to humans

Author information

Toplak N1, Avcin T.

1. Department of Allergology
Rheumatology and Clinical Immunology
University Children's Hospital
University Medical Centre Ljubljana, Slovenia
natasa.toplak@kclj.si

Abstract

Vaccination against pathogenic microorganisms is one of the major achievements of modern medicine, but due to an increasing number of reports of adverse reactions the vaccination procedure has induced also considerable debate. It is well known that certain infections are involved in triggering the production of autoantibodies, which could lead to autoimmune adverse reactions in genetically predisposed subjects. Based on these findings it was assumed that vaccinations might induce similar autoimmune reactions. At present there is no clear-cut evidence that vaccinations are associated with overt autoimmune diseases but it has been demonstrated that in genetically predisposed persons vaccination can trigger the production of autoantibodies and autoimmune adverse reactions. The first studies investigating the production of autoantibodies following vaccination were done in dogs and mice. Several studies investigated the production of autoantibodies following vaccination in patients with autoimmune diseases, but there are only limited data on the autoimmune responses after vaccinations in apparently healthy humans. This review summarizes current evidence on the vaccination-induced autoantibodies in apparently healthy subjects including studies in animals and humans.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19880566>

“due to an increasing number of reports of adverse reactions the vaccination procedure has induced also considerable debate ... it has been demonstrated that in genetically predisposed persons vaccination can trigger the production of autoantibodies and autoimmune adverse reactions.”

Vaccines as a trigger for myopathies

Author information

Orbach H1, Tanay A.

Department of Medicine B
Wolfson Medical Center, Holon, Israel
orbach@wolfson.health.gov.il

Abstract

Vaccines are considered to be among the greatest medical discoveries, credited with the virtual eradication of some diseases and the consequent improved survival and quality of life of the at-risk population. With that, vaccines are among the environmental factors implicated as triggers for the development of inflammatory myopathies. The sporadic reports on vaccine-induced inflammatory myopathies include cases of hepatitis B virus, bacillus Calmette-Guérin, tetanus, influenza, smallpox, polio, diphtheria, diphtheria-pertussis-tetanus, combination of diphtheria with scarlet fever and diphtheria-pertussis-tetanus with polio vaccines. However, a significant increase in the incidence of dermatomyositis or polymyositis after any massive vaccination campaign has not been reported in the literature. In study patients with inflammatory myopathies, no recent immunization was recorded in any of the patients. Moreover, after the 1976 mass flu vaccination, no increase in the incidence of inflammatory myopathies was observed. Although rare, macrophagic myofasciitis has been reported following vaccination and is attributed to the aluminium hydroxide used as an adjuvant in some vaccines. Prospective multicenter studies are needed to identify potential environmental factors, including vaccines, as potential triggers for inflammatory myopathies.

<http://www.ncbi.nlm.nih.gov/pubmed/19880571>

“... macrophagic myofasciitis
has been reported following vaccination
and is attributed to the aluminium hydroxide
used as an adjuvant in some vaccines.”

Self-organized criticality theory of autoimmunity

Author information

Tsumiyama K1, Miyazaki Y, Shiozawa S.

Department of Biophysics
Kobe University Graduate School of Health Science
Kobe, Japan

Abstract

BACKGROUND

The cause of autoimmunity, which is unknown, is investigated from a different angle, i.e., the defect in immune ‘system’, to explain the cause of autoimmunity.

METHODOLOGY/PRINCIPAL FINDINGS

Repeated immunization with antigen causes systemic autoimmunity in mice otherwise not prone to spontaneous autoimmune diseases. Overstimulation of CD4(+) T cells led to the development of autoantibody-inducing CD4(+) T (aiCD4(+) T) cell which had undergone T cell receptor (TCR) revision and was capable of inducing autoantibodies. The aiCD4(+) T cell was induced by de novo TCR revision but not by cross-reaction, and subsequently overstimulated CD8(+) T cells, driving them to become antigen-specific cytotoxic T lymphocytes (CTL). These CTLs could be further matured by antigen cross-presentation, after which they caused autoimmune tissue injury akin to systemic lupus erythematosus (SLE).

CONCLUSIONS/SIGNIFICANCE

Systemic autoimmunity appears to be the inevitable consequence of overstimulating the host’s immune ‘system’ by repeated immunization with antigen, to the levels that surpass system’s self-organized criticality.

<http://www.ncbi.nlm.nih.gov/pubmed/20046868>

“Systemic autoimmunity appears to be the inevitable consequence of over-stimulating the host’s immune ‘system’ by repeated immunization with antigen, to the levels that surpass system’s self-organized criticality.”

Bordetella pertussis and vaccination: the persistence of a genetically monomorphic pathogen

Author information

Mooi FR.

Lab for Infectious Diseases and Screening
Netherlands Centre for Infectious Diseases Control
Natl Institute for Public Health and the Environment
RIVM, PO Box 1, 3720 BA Bilthoven, Netherlands
frits.mooi@rivm.nl

Abstract

Before childhood vaccination was introduced in the 1950s, pertussis or whooping cough was a major cause of infant death worldwide. Widespread vaccination of children was successful in significantly reducing morbidity and mortality. However, despite vaccination, pertussis has persisted and, in the 1990s, resurged in a number of countries with highly vaccinated populations. Indeed, pertussis has become the most prevalent vaccine-preventable disease in developed countries with estimated infection frequencies of 1-6%. Recently vaccinated children are well protected against pertussis disease and its increase is mainly seen in adolescents and adults in which disease symptoms are often mild. The etiologic agent of pertussis, *Bordetella pertussis*, is extremely monomorphic and its ability to persist in the face of intensive vaccination is intriguing. Numerous studies have shown that *B. pertussis* populations changed after the introduction of vaccination suggesting adaptation. These adaptations did not involve the acquisition of novel genes but small genetic changes, mainly SNPs, and occurred in successive steps in a period of 40 years. The earliest adaptations resulted in antigenic divergence with vaccine strains. More recently, strains emerged with increased pertussis toxin (Ptx) production. Here I argue that the resurgence of pertussis is the compound effect of pathogen adaptation and waning immunity. I propose that the removal by vaccination of naïve infants as the major source for transmission was the crucial event which has driven the changes in *B. pertussis* populations. This has selected for strains which are more efficiently transmitted by primed hosts in which immunity has waned. The adaptation of *B. pertussis* to primed hosts involved delaying an effective immune response by antigenic divergence with vaccine strains and by increasing immune suppression through higher levels of Ptx production. Higher levels of Ptx may also benefit transmission by enhancing clinical symptoms. The study of *B. pertussis* populations has not only increased our understanding of pathogen evolution, but also suggests way to improve pertussis vaccines, underlining the public health significance of population-based studies of pathogens.

<http://www.ncbi.nlm.nih.gov/pubmed/19879977>

“despite vaccination,
pertussis has persisted and, in the 1990s,
resurged in a number of countries with highly vaccinated
populations. Here I argue that the resurgence of pertussis
is the compound effect of pathogen adaptation
and waning immunity.”

[resurgence is not a result of the unvaccinated]

Revisiting the possibility of serious adverse events
from the whole cell pertussis vaccine:
were metabolically vulnerable children at risk?

Author information

Wilson K1, Potter B, Manuel D, Keelan J, Chakraborty P.

Department of Medicine, Ottawa Hospital Research Institute
University of Ottawa, Ottawa, Canada
kwilson@ohri.ca

Abstract

In the early 1980's concerns about the safety of the whole cell pertussis vaccine in the United States resulted in declining vaccination rates and the withdrawal of multiple vaccine providers from the market. While the possibility of inflammation and febrile reactions to the vaccine were acknowledged by public health authorities, parents also claimed the vaccine was associated with sudden infant death syndrome and encephalopathy. Epidemiological studies examining this question, however, consistently failed to identify an association. We argue that these reactions may have occurred in metabolically vulnerable children, specifically those with defects in fatty acid oxidation. In these children the combination of anorexia and fever that could be caused by the vaccine may have resulted in hypoglycemic episodes and possibly death. We believe that this association was not detected because these conditions were not recognized at the time and because these conditions are uncommon. Nevertheless, at a population level, enough events could have occurred to cause concern amongst parents.

<http://www.ncbi.nlm.nih.gov/pubmed/19660877>

“We argue that these reactions may have occurred in metabolically vulnerable children, specifically those with defects in fatty acid oxidation. In these children the combination of anorexia and fever that could be caused by the vaccine may have resulted in hypoglycemic episodes and possibly death. We believe that this association was not detected because these conditions were not recognized at the time and because these conditions are uncommon. Nevertheless, at a population level, enough events could have occurred to cause concern amongst parents.”

**Sibling Transmission
of Vaccine-Derived Rotavirus (RotaTeq)
Associated With Rotavirus Gastroenteritis**

Daniel C. Payne, Kathryn M. Edwards,
Michael D. Bowen, Erin Keckley, Jody Peters,
Mathew D. Esona, Elizabeth N. Teel, Diane Kent,
Umesh D. Parashar, Jon R. Gentsch

Abstract

Although rotavirus vaccines are known to be shed in stools, transmission of vaccine-derived virus to unvaccinated contacts resulting in symptomatic rotavirus gastroenteritis has not been reported to our knowledge. We document here the occurrence of vaccine-derived rotavirus (RotaTeq [Merck and Co, Whitehouse Station, NJ]) transmission from a vaccinated infant to an older, unvaccinated sibling, resulting in symptomatic rotavirus gastroenteritis that required emergency department care. Results of our investigation suggest that reassortment between vaccine component strains of genotypes P7[5]G1 and P1A[8]G6 occurred during replication either in the vaccinated infant or in the older sibling, raising the possibility that this reassortment may have increased the virulence of the vaccine-derived virus. Both children remain healthy 11 months after this event and are without underlying medical conditions.

<http://pediatrics.aappublications.org/content/125/2/e438>

“Although rotavirus vaccines are known to be shed in stools, transmission of vaccine-derived virus to unvaccinated contacts resulting in symptomatic rotavirus gastroenteritis has not been reported to our knowledge.

We document here the occurrence of vaccine-derived rotavirus (RotaTeq, Merck and Co, Whitehouse Station, NJ) transmission from a vaccinated infant to an older, unvaccinated sibling, resulting in symptomatic rotavirus gastroenteritis that required emergency department care.”

Vaccines and autoimmune diseases of the adult

Author information

Orbach H1, Agmon-Levin N, Zandman-Goddard G.

Department of Medicine B
Wolfson Medical Center
Holon, Israel

Abstract

Infectious agents contribute to the environmental factors involved in the development of autoimmune diseases possibly through molecular mimicry mechanisms. Hence, it is feasible that vaccinations may also contribute to the mosaic of autoimmunity. Evidence for the association of vaccinations and the development of these diseases is presented in this review. Infrequently reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barré syndrome, and vasculitis. In addition, we will discuss macrophagic myofasciitis, aluminum containing vaccines, and the recent evidence for autoimmunity following the use of human papillomavirus vaccine.

<http://www.ncbi.nlm.nih.gov/pubmed/20193633>

“Hence, it is feasible that vaccinations may also contribute to the mosaic of autoimmunity. Evidence for the association of vaccinations and the development of these diseases is presented in this review. In addition, we will discuss macrophagic myofasciitis, aluminum containing vaccines, and the recent evidence for autoimmunity following the use of human papillomavirus vaccine.”

Full Report

<http://www.discoverymedicine.com/Hedi-Orbach/2010/02/04/vaccines-and-autoimmune-diseases-of-the-adult/>

Vaccines and Autoimmune Diseases of the Adult

Author: Hedi Orbach

Specialty: Immunology, Rheumatology, Microbiology, Infectious Diseases
Institution: Department of Medicine B, Wolfson Medical Center

Author: Nancy Agmon-Levin

Specialty: Immunology, Rheumatology, Microbiology, Infectious Diseases
Institution: Center for Autoimmune Diseases, Sheba Medical Center

Author: Gisele Zandman-Goddard

Specialty: Immunology, Rheumatology, Microbiology, Infectious Diseases
Institution: Department of Medicine C, Wolfson Medical Center

Abstract

Infectious agents contribute to the environmental factors involved in the development of autoimmune diseases possibly through molecular mimicry mechanisms. Hence, it is feasible that vaccinations may also contribute to the mosaic of autoimmunity. Evidence for the association of vaccinations and the development of these diseases is presented in this review. Infrequently reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barré syndrome, and vasculitis. In addition, we will discuss macrophagic myofasciitis, aluminum containing vaccines, and the recent evidence for autoimmunity following human papilloma virus vaccine.

Introduction

Systemic and organ-specific autoimmune diseases are known to develop following infectious triggers. Recently we have suggested that certain autoimmune diseases like systemic lupus erythematosus (SLE) may result due to specific viral agents. Furthermore, the spectrum of disease may be influenced by a certain microbial agent in the genetically predisposed individual (Zandman-Goddard et al., 2009).

Vaccines are a prototypic source for natural immune stimulation, but may be involved in pathogenic disease in the setting of aberrant immune system function. Possibly, the burden on the immune system resulting from simultaneous multiple vaccines and even the different types of vaccines may also be an overwhelming challenge in the autoimmune prone individual (Shoenfeld et al., 2008). In this review, we discuss the evidence for the development of autoimmune diseases following infections and vaccinations.

While vaccinations are generally safe, warranted and have virtually eradicated endemic diseases and probably lessened morbidity and mortality, a question arises regarding the evaluation of possible autoimmune phenomena in vaccinated individuals.

Reported post-vaccination autoimmune diseases in the adult include SLE, rheumatoid arthritis (RA), inflammatory myopathies, multiple sclerosis (MS), Guillain-Barré syndrome (GBS), and vasculitis. Evidence for the association of vaccinations and the development of these diseases is presented in this review. In addition, we will discuss macrophagic myofasciitis, post aluminum containing vaccines and the recent support for autoimmunity following human papilloma virus vaccine.

<http://www.discoverymedicine.com/Hedi-Orbach/2010/02/04/vaccines-and-autoimmune-diseases-of-the-adult/>

“Vaccines are a prototypic source for natural immune stimulation, but may be involved in pathogenic disease in the setting of aberrant immune system function.

Possibly, the burden on the immune system resulting from simultaneous multiple vaccines and even the different types of vaccines may also be an overwhelming challenge in the autoimmune prone individual (Shoenfeld et al., 2008).

Reported post-vaccination autoimmune diseases in the adult include SLE, rheumatoid arthritis (RA), inflammatory myopathies, multiple sclerosis (MS), Guillain-Barré syndrome (GBS), and vasculitis.

Evidence for the association of vaccinations and the development of these diseases is presented in this review. In addition, we will discuss macrophagic myofasciitis, post aluminum containing vaccines and the recent support for autoimmunity following human papilloma virus vaccine.”

Effect of revaccination with BCG in early childhood on mortality: randomised trial in Guinea-Bissau

Adam Edvin Roth, clinician,^{1,2}
Christine Stabell Benn, senior researcher,³
Henrik Ravn, senior statistician,³
Amabelia Rodrigues, research director,¹
Ida Maria Lisse, senior registrar,⁴
Maria Yazdanbakhsh, professor,⁵
Hilton Whittle, professor,⁶ and
Peter Aaby, professor^{1,3}

1. Bandim Health Project, Indepth Network, Apartado 861, Bissau, Guinea-Bissau
2. Department of Medical Microbiology, Lund University, 205 02 Malmö, Sweden
3. Bandim Health Project, Danish Epidemiology Science Centre, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark
4. Department of Pathology, Herlev University Hospital, 2730 Herlev, Denmark
5. Department of Parasitology, Leiden University, Netherlands
6. MRC Laboratories, Fajara, POB 273, Gambia

Abstract

Objective

To determine whether BCG revaccination at 19 months of age reduces overall child mortality.

Design

Randomised trial, with follow-up to age 5.

Setting

A health project in Bissau, Guinea-Bissau, which maintains a health and demographic surveillance system in an urban area with 90,000 inhabitants.

Participants

2871 children aged 19 months to 5 years with low or no reactivity to tuberculin and who were not severely sick on the day of enrolment.

Intervention

BCG vaccination or no vaccination (control).

Main outcome measure

Hazard ratios for mortality.

Results

77 children died during follow-up. Compared with controls, the BCG revaccinated children had a hazard ratio of 1.20 (95% confidence interval 0.77 to 1.89). Two hundred and fifty children were admitted to hospital for the first time between enrolment and the end of the study, with an incidence rate ratio for BCG revaccinated children versus controls of 1.04 (0.81 to 1.33). The trial was stopped prematurely because of a cluster of deaths in the BCG arm of the study. This increase in mortality occurred at a time when many children had received missing vaccinations or vitamin A or iron supplementation; the hazard ratio for BCG revaccinated children compared with controls was 2.69 (1.05 to 6.88) in the period after these campaigns. Throughout the trial, the effect of BCG revaccination on mortality was significantly different ($P=0.006$) in children who had received diphtheria-tetanus-pertussis (DTP) booster vaccination before enrolment (hazard ratio 0.36, 0.13 to 0.99) and children who had not received the booster before enrolment (1.78, 1.04 to 3.04).

Conclusions

There was no overall beneficial effect of being revaccinated with BCG. The effect of BCG revaccination on mortality might depend on other health interventions.

“77 of 2871 children died during follow-up”

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2839082/>

“77 children died

during follow-up.

Two hundred and fifty children

were admitted to hospital

for the first time.

There was no overall

beneficial effect of

being revaccinated

with BCG.”

Hepatitis B vaccine and uveitis: an emerging hypothesis suggested by review of 32 case reports

Author information

Fraunfelder FW1, Suhler EB, Fraunfelder FT.

Casey Eye Institute
Portland, Oregon 97239, USA
fraunfel@ohsu.edu

Abstract

OBJECTIVE

To report a possible association between hepatitis B vaccine and uveitis.

METHODS

Spontaneous reports from the National Registry of Drug-Induced Ocular Side Effects, the World Health Organization, and the Food and Drug Administration were collected on hepatitis B vaccine associated with uveitis between 1982 and 2009. In addition, we performed a Medline literature search using the keywords of uveitis, iritis, or vitritis, in combination with vaccines and hepatitis B vaccine. Data garnered from the spontaneous reports included age, gender, adverse drug reaction, temporal association of uveitis with vaccine doses, concomitant drugs, other systemic disease, recovery, and recurrence after repeat dosage.

RESULTS

Thirty-two case reports of uveitis occurring after hepatitis B vaccine were reported to the spontaneous reporting databases. The mean age of the patients was 29 years (1-57 years), with 8 male and 24 female patients. The mean number of days until uveitis was reported after vaccination was 3 days (1-15 days). The uveitis was reported to occur after the first vaccination in 15 patients, after the second vaccination in 3 patients, and after the third vaccination in 3 patients; the duration of time to occurrence of uveitis was not reported for 9 patients. One patient had recurrent uveitis after both the second and third doses of vaccine. One patient had recurrent uveitis after the first and second doses of vaccine.

CONCLUSION

Hepatitis B vaccine may have a possible association with the development of uveitis in some patients. Immune complex deposition and adjuvant effects are potential pathogenic mechanisms.

“Hepatitis B vaccine
may have a possible association
with the development of uveitis
in some patients. Immune complex
deposition and adjuvant effects are
potential pathogenic mechanisms.”

Induction of metallothionein in mouse cerebellum and cerebrum with low-dose thimerosal injection

Author information

Minami T1, Miyata E,
Sakamoto Y, Yamazaki H, Ichida S.

Department of Life Sciences
Kinki University, Higashi-osaka
Osaka, Japan
minamita@life.kindai.ac.jp

Abstract

Thimerosal, an ethyl mercury compound, is used worldwide as a vaccine preservative. We previously observed that the mercury concentration in mouse brains did not increase with the clinical dose of thimerosal injection, but the concentration increased in the brain after the injection of thimerosal with lipopolysaccharide, even if a low dose of thimerosal was administered. Thimerosal may penetrate the brain, but is undetectable when a clinical dose of thimerosal is injected; therefore, the induction of metallothionein (MT) messenger RNA (mRNA) and protein was observed in the cerebellum and cerebrum of mice after thimerosal injection, as MT is an inducible protein. MT-1 mRNA was expressed at 6 and 9 h in both the cerebrum and cerebellum, but MT-1 mRNA expression in the cerebellum was three times higher than that in the cerebrum after the injection of 12 microg/kg thimerosal. MT-2 mRNA was not expressed until 24 h in both organs. MT-3 mRNA was expressed in the cerebellum from 6 to 15 h after the injection, but not in the cerebrum until 24 h. MT-1 and MT-3 mRNAs were expressed in the cerebellum in a dose-dependent manner. Furthermore, MT-1 protein was detected from 6 to 72 h in the cerebellum after 12 microg/kg of thimerosal was injected and peaked at 10 h. MT-2 was detected in the cerebellum only at 10 h. In the cerebrum, little MT-1 protein was detected at 10 and 24 h, and there were no peaks of MT-2 protein in the cerebrum. In conclusion, MT-1 and MT-3 mRNAs but not MT-2 mRNA are easily expressed in the cerebellum rather than in the cerebrum by the injection of low-dose thimerosal. It is thought that the cerebellum is a sensitive organ against thimerosal. As a result of the present findings, in combination with the brain pathology observed in patients diagnosed with autism, the present study helps to support the possible biological plausibility for how low-dose exposure to mercury from thimerosal-containing vaccines may be associated with autism.

<http://www.ncbi.nlm.nih.gov/pubmed/19357975>

“It is thought that the cerebellum is a sensitive organ against thimerosal. As a result of the present findings, in combination with the brain pathology observed in patients diagnosed with autism, the present study helps to support the possible biological plausibility for how low-dose exposure to mercury from thimerosal containing vaccines may be associated with autism.”

Sex differences in the evaluation and diagnosis of autism spectrum disorders among children

Author information

Giarelli E1, Wiggins LD, Rice CE,
Levy SE, Kirby RS, Pinto-Martin J, Mandell D.

University of Pennsylvania School of Nursing, Philadelphia, 19104, USA
giarelli@nursing.upenn.edu

Abstract

BACKGROUND

One of the most consistent features of the autism spectrum disorders (ASDs) is the predominance among males, with approximately four males to every female. We sought to examine sex differences among children who met case definition for ASD in a large, population-based cohort with respect to age at first developmental evaluation, age of diagnosis, influence of cognitive impairment on these outcomes, and sex-specific behavioral characteristics.

METHODS

We conducted a secondary analysis of data collected for a population-based study of the prevalence of ASD. The sample comprised 2,568 children born in 1994 who met the case definition of ASD as established by the Autism and Developmental Disabilities Monitoring (ADDM) Network for ASD surveillance. Children who had a history of developmental disability and behavioral features consistent with the DSM-IV-TR criteria for autistic disorder, Asperger's disorder, and Pervasive Developmental Disorder-Not Otherwise Specified in existing evaluation records were classified as ASD cases via two paths: streamlined and non-streamlined. Streamlined reviews were conducted if there was an ASD diagnosis documented in the records. Data were collected in 13 sites across the United States through the ADDM Network, funded by the Centers for Disease Control and Prevention.

RESULTS

Males constituted 81% of the sample. There were no differences by sex in average age at first evaluation or average age of diagnosis among those with an existing documented chart diagnosis of an ASD. Girls were less likely than boys to have a documented diagnosis (odds ratio [OR] = 0.76, $p = .004$). This analysis was adjusted for cognitive impairment status. In the logistic model, with the interaction term for sex and cognitive impairment, girls with IQ of 70 or less were less likely than boys with IQ of 70 or less to have a documented diagnosis (OR = 0.70, 95% confidence interval [CI] = 0.50-0.97, $p = .035$). Boys with IQ greater than 70 were less likely than boys with IQ of 70 or less to have a documented diagnosis (OR = 0.60, 95% CI = 0.49-0.74, $p < .001$). This finding (less likely to have a documented diagnosis) was also true for girls with IQ greater than 70 (OR = 0.45, 95% CI = 0.32-0.66, $p < .001$). Girls were more likely to have notations of seizure-like behavior ($p < .001$). Boys were more likely to have notations of hyperactivity or a short attention span and aggressive behavior ($p < .01$).

CONCLUSIONS

Girls, especially those without cognitive impairment, may be formally identified at a later age than boys. This may delay referral for early intervention. Community education efforts should alert clinicians and parents to the potential of ASDs in boys and girls.

“One of the most consistent features of the autism spectrum disorders (ASDs) is the predominance among males, with approximately four males to every female. We sought to examine sex differences among children who met case definition for ASD ...”

Oral polio vaccine influences the immune response to BCG vaccination A natural experiment

Author information

Sartono E1, Lisse IM, Terveer EM, van de Sande PJ,
Whittle H, Fisker AB, Roth A, Aaby P, Yazdanbakhsh M, Benn CS.

Department of Parasitology, Leiden University Medical Center
Leiden, The Netherlands
E.Sartono@lumc.nl

Abstract

BACKGROUND

Oral polio vaccine (OPV) is recommended to be given at birth together with BCG vaccine. While we were conducting two trials including low-birth-weight (LBW) and normal-birth-weight (NBW) infants in Guinea-Bissau, OPV was not available during some periods and therefore some infants did not receive OPV at birth, but only BCG. We investigated the effect of OPV given simultaneously with BCG at birth on the immune response to BCG vaccine.

METHODS AND FINDINGS

We compared the *in vitro* and the *in vivo* response to PPD in the infants who received OPV and BCG with that of infants who received BCG only. At age 6 weeks, the *in vitro* cytokine response to purified protein derivate (PPD) of *M. Tuberculosis* was reduced in LBW and NBW infants who had received OPV with BCG. In a pooled analysis receiving OPV with BCG at birth was associated with significantly lower IL-13 ($p = 0.041$) and IFN-gamma ($p = 0.004$) and a tendency for lower IL-10 ($p = 0.054$) in response to PPD. Furthermore, OPV was associated with reduced *in vivo* response to PPD at age 2 months, the prevalence ratio (PR) of having a PPD reaction being 0.75 (0.58-0.98), $p = 0.033$, and with a tendency for reduced likelihood of having a BCG scar (0.95 (0.91-1.00), $p = 0.057$). Among children with a scar, OPV was associated with reduced scar size, the regression coefficient being -0.24 (-0.43-0.05), $p = 0.012$.

CONCLUSIONS

This study is the first to address the consequences for the immune response to BCG of simultaneous administration with OPV. Worryingly, the results indicate that the common practice in low-income countries of administering OPV together with BCG at birth may down-regulate the response to BCG vaccine.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2873948/>

“Worryingly, the results indicate that the common practice in low-income countries of administering Oral polio vaccine together with Bacille Calmette-Guerin [BCG - tuberculosis] vaccine at birth may down-regulate the response to Bacille Calmette-Guerin [BCG - tuberculosis] vaccine.”

The relative toxicity of compounds used as preservatives in vaccines and biologics

Author information

Geier DA1, Jordan SK, Geier MR.

CoMeD, Inc., Silver Spring, MD, USA

Abstract

BACKGROUND

In vaccines/biologics, preservatives are used to prevent microbial growth.

MATERIAL/METHODS

The present study examined: (1) the comparative toxicities of commonly used preservatives in US licensed vaccines to human neurons; and (2) the relative toxicity index of these compounds to human neurons in comparison to bacterial cells.

RESULTS

Using human neuroblastoma cells, the relative cytotoxicity of the levels of the compounds commonly used as preservative in US licensed vaccines was found to be phenol < 2-phenoxyethanol < benzethonium chloride < Thimerosal. The observed relative toxicity indices (human neuroblastoma cells/bacterial cells) were 2-phenoxyethanol (4.6-fold) < phenol (12.2-fold) < Thimerosal (>330-fold). In addition, for the compounds tested, except for 2-phenoxyethanol, the concentrations necessary to induce significant killing of bacterial cells were significantly higher than those routinely present in US licensed vaccine/biological preparations.

CONCLUSIONS

None of the compounds commonly used as preservatives in US licensed vaccine/biological preparations can be considered an ideal preservative, and their ability to fully comply with the requirements of the US Code of Federal Regulations (CFR) for preservatives is in doubt. Future formulations of US licensed vaccines/biologics should be produced in aseptic manufacturing plants as single dose preparations, eliminating the need for preservatives and an unnecessary risk to patients.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20424565>

“None of the compounds commonly used as preservatives in US licensed vaccine/biological preparations can be considered an ideal preservative, and their ability to fully comply with the requirements of the US Code of Federal Regulations (CFR) for preservatives is in doubt.”

Ramifications of adverse events in children in Australia

Author information

Peter Collignon,
infectious diseases physician and microbiologist¹
Peter Doshi, program in history, anthropology, science,
technology and society²
Tom Jefferson, coordinator³

1. School of Clinical Medicine, Australian National University
PO Box 11, Woden, ACT 2607, Australia
2. Massachusetts Institute of Technology
Cambridge, MA 02139, USA
3. Cochrane Vaccines Field, Rome, Italy
peter.collignon@act.gov.au

Many serious adverse reactions to this year's seasonal influenza vaccine have occurred across Australia, and its use remains suspended in children aged 5 years and under.^{1 2 3} Data released on 1 June 2010 show that 1 in every 110 young children vaccinated with the CSL vaccine had a febrile seizure.³

A previous H1N1 vaccine study published earlier this year showed that a large proportion of children developed fevers after vaccination: between three and six in every 10 children under 3 years, depending on dose.⁴ The study was, however, underpowered to detect febrile convulsions at the current rates in Australia because it included only 162 children under 3 years.

Fever is the most important risk factor for febrile convulsions. The vaccine manufacturer CSL, which sponsored the trial, and Australia's regulatory body, the Therapeutic Goods Administration, which used these data in approving the vaccine for children, were presumably aware of these important findings.⁴ But the authors did not discuss the high incidence of fever associated with vaccination,⁴ and most data were reported without comment in the online only supplementary tables.⁴

The many children with adverse effects and the subsequent suspension of the vaccine challenge the assumption that regulators are ensuring the safety and efficacy of all marketed therapeutics. Influenza vaccine is said to have "an established record of safety in all age groups."² However, published data on the effects of vaccinating young children against influenza are comparatively few.⁵ Some manufacturers have even withheld data from public scrutiny amid general indifference.^{2 5}

Last winter the likelihood that a child without risk factors would die from swine flu was less than one in a million.² When such a high proportion of children develop moderate to severe febrile reactions to the influenza vaccine, more harm than good seems likely from vaccinating them.

Report available for purchase. I accessed this report using a 14-day free trial:

<http://www.bmj.com/content/340/bmj.c2994.long>

"... the likelihood that a child without risk factors would die from swine flu was less than one in a million. When such a high proportion of children develop moderate to severe febrile reactions to the influenza vaccine, more harm than good seems likely from vaccinating them."

BMJ • June 2010

Australian government says healthy under 5s should not be given seasonal flu jab

Moynihan R.

<http://www.ncbi.nlm.nih.gov/pubmed/20530085>

Prophylactic HPV vaccines: current knowledge of impact on gynecologic premalignancies

Author information

Harper DM1, Williams KB.

University of Missouri-Kansas City School of Medicine
7900 Lee's Summit Road, Kansas City, Missouri 64139, USA
diane.m.harper@gmail.com

Abstract

Approaches for cervical cancer prevention are changing. Screening still remains the most effective method for cervical cancer prevention. Guidelines are moving to an older group of women to be screened less frequently with combinations of technologies that include biomarkers and cytology. HPV vaccination is an appropriate option for this older group of women as well, should the woman not wish to make her decision about vaccination until 21 years of age, the age of screening. Parents making decisions about HPV vaccination for their young adolescent daughters need to be fully informed that only continued screening prevents cervical cancer. HPV vaccination reduces the possibility of their daughter having an abnormal Pap test by 10% if the vaccines have not waned by the time the young adolescent becomes sexually active. HPV vaccine efficacy must last at least 15 years to contribute to the prevention of cervical cancers. At this time, protection against cervical intraepithelial neoplasia grade 2/3 (CIN 2/3) is 5 years for Gardasil and 8.4 years for Cervarix. The value of the current protection HPV vaccines offer will be viewed differently by different women. Physicians' ethical duties are to provide full explanation of the risks and benefits of adding HPV vaccination to the ongoing screening programs, and to support women in their personal choice for cervical cancer prevention.

<http://www.ncbi.nlm.nih.gov/pubmed/20670593>

“Screening still remains the most effective method for cervical cancer prevention. HPV vaccination reduces the possibility of their daughter having an abnormal Pap test by 10% if the vaccines have not waned by the time the young adolescent becomes sexually active.”

The toxic effects of formaldehyde on the nervous system

Author information

Songur A1, Ozen OA, Sarsilmaz M.

Department of Anatomy, School of Medicine
University of Kocatepe, Afyonkarahisar, Turkey
asongur55@yahoo.com

Abstract

Formaldehyde (FA) is found in the polluted atmosphere of cities, domestic air (e.g., paint, insulating materials, chipboard and plywood, fabrics, furniture, paper), and cigarette smoke, etc.; therefore, everyone and particularly susceptible children may be exposed to FA. FA is also widely used in industrial and medical settings and as a sterilizing agent, disinfectant, and preservative. Therefore, employees may be highly exposed to it in these settings. Of particular concern to the authors are anatomists and medical students, who can be highly exposed to formaldehyde vapor during dissection sessions. Formaldehyde is toxic over a range of doses; chances of exposure and subsequent harmful effects are increased as (room) temperature increases, because of FA's volatility. Many studies have been conducted to evaluate the effects of FA during systemic and respiratory exposures in rats. This review compiles that literature and emphasizes the neurotoxic effects of FA on neuronal morphology, behavior, and biochemical parameters. The review includes the results of some of the authors' work related to FA neurotoxicity, and such neurotoxic effects from FA exposure were experimentally demonstrated. Moreover, the effectiveness of some antioxidants such as melatonin, fish omega-3, and CAPE was observed in the treatment of the harmful effects of FA. Despite the harmful effects from FA exposure, it is commonly used in Turkey and elsewhere in dissection laboratories. Consequently, all anatomists must know and understand the effects of this toxic agent on organisms and the environment, and take precautions to avoid unnecessary exposure. The reviewed studies have indicated that FA has neurotoxic characteristics and systemic toxic effects. It is hypothesized that inhalation of FA, during the early postnatal period, is linked to some neurological diseases that occur in adults. Although complete prevention is impossible for laboratory workers and members of industries utilizing FA, certain precautions can be taken to decrease and/or prevent the toxic effects of FA.

“The reviewed studies have indicated that Formaldehyde has neurotoxic characteristics and systemic toxic effects.”

Journal Of Toxicology And Environmental Health Part A • 2010

Hepatitis B vaccination of male neonates and autism diagnosis NHIS 1997-2002

Author information

Gallagher CM1, Goodman MS.

PhD Program in Population Health and Clinical Outcomes Research
Stony Brook University Medical Center
State University of New York at Stony Brook
Stony Brook, New York, USA
cmgallagher@notes.cc.sunysb.edu

Abstract

Universal hepatitis B vaccination was recommended for U.S. newborns in 1991; however, safety findings are mixed. The association between hepatitis B vaccination of male neonates and parental report of autism diagnosis was determined. This cross-sectional study used weighted probability samples obtained from National Health Interview Survey 1997-2002 data sets. Vaccination status was determined from the vaccination record. Logistic regression was used to estimate the odds for autism diagnosis associated with neonatal hepatitis B vaccination among boys age 3-17 years, born before 1999, adjusted for race, maternal education, and two-parent household. Boys vaccinated as neonates had threefold greater odds for autism diagnosis compared to boys never vaccinated or vaccinated after the first month of life. Non-Hispanic white boys were 64% less likely to have autism diagnosis relative to nonwhite boys. Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period. Nonwhite boys bore a greater risk.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21058170>

“Findings suggest that U.S. male neonates vaccinated with the hepatitis B vaccine prior to 1999 (from vaccination record) had a threefold higher risk for parental report of autism diagnosis compared to boys not vaccinated as neonates during that same time period. Nonwhite boys bore a greater risk.”

Influence of pediatric vaccines on amygdala growth and opioid ligand binding in rhesus macaque infants: A pilot study

Author information

Hewitson L1, Lopresti BJ, Stott C, Mason NS, Tomko J.

¹Department of Obstetrics and Gynecology
University of Pittsburgh School of Medicine
Pittsburgh, PA, USA
lch1@pitt.edu

Abstract

This longitudinal, case-control pilot study examined amygdala growth in rhesus macaque infants receiving the complete US childhood vaccine schedule (1994-1999). Longitudinal structural and functional neuroimaging was undertaken to examine central effects of the vaccine regimen on the developing brain. Vaccine-exposed and saline-injected control infants underwent MRI and PET imaging at approximately 4 and 6 months of age, representing two specific timeframes within the vaccination schedule. Volumetric analyses showed that exposed animals did not undergo the maturational changes over time in amygdala volume that was observed in unexposed animals. After controlling for left amygdala volume, the binding of the opioid antagonist [(11)C]diprenorphine (DPN) in exposed animals remained relatively constant over time, compared with unexposed animals, in which a significant decrease in [(11)C]DPN binding occurred. These results suggest that maturational changes in amygdala volume and the binding capacity of [(11)C]DPN in the amygdala was significantly altered in infant macaques receiving the vaccine schedule. The macaque infant is a relevant animal model in which to investigate specific environmental exposures and structural/functional neuroimaging during neurodevelopment.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20628439>

“This longitudinal, case-control pilot study examined amygdala growth in rhesus macaque infants receiving the complete US childhood vaccine schedule (1994-1999). These results suggest that maturational changes in amygdala volume and the binding capacity of [(11)C]DPN in the amygdala was significantly altered in infant macaques receiving the vaccine schedule.”

“The decrease in the collapse pressure of the monolayer film caused by coated nanoparticles, in vitro, was associated with an acute pulmonary toxicity in vivo.”

American Association Of Pharmaceutical Sciences • September 2010

Pulmonary Toxicity of Polysorbate-80-coated Inhalable Nanoparticles; In vitro and In vivo Evaluation

M. H. D. Kamal Al-Hallak, Shirzad Azarmi, Chris Sun, Patrick Lai,
Elmar J. Prenner, Wilson H. Roa, and Raimar Löbenberg

Faculty of Pharmacy and Pharmaceutical Sciences, 3126 Dentistry/Pharmacy Centre
University of Alberta, Edmonton, Alberta T6G 2N8 Canada

Faculty of Pharmacy and Pharmaceutical Sciences, Damascus University, Damascus, Syria

Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran

Department of Biological Sciences, University of Calgary, Calgary, Alberta Canada

Cross Cancer Institute, University of Alberta, Edmonton, Alberta Canada

CONCLUSION

The presented in vitro model for studying the surface pressure-area isotherms is an early screening tool to assess the biophysical compatibility of selected drug carriers with lung surfactant films. The decrease in the collapse pressure of the monolayer film caused by coated NPs, in vitro, was associated with an acute pulmonary toxicity in vivo. This in vivo toxicity was not observed when uncoated nanoparticles were used. Therefore, the dosage from toxicity of colloidal carriers intended for pulmonary delivery is mainly determined by their final composition rather than their individual components. More investigations are required to set different cut-off points for the collapse pressure to correlate them with different stages of pulmonary toxicity in vivo. The outcomes of this study should not be generalized for all surfactants or bi-block polymers. Other surfactants with different hydrophilic-lipophilic properties might interact differently with lung surfactant films. This method may be useful to establish upper deposition limits for inhalable dry powders.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2895437/>

Triton X-100 concentration
effects on membrane permeability
of a single HeLa cell by
scanning electrochemical microscopy (SECM)

Author information

Koley D1, Bard AJ.

Center for Electrochemistry
Department of Chemistry and Biochemistry
University of Texas at Austin
1 University Station, A5300
Austin, TX 78712-0165, USA

Abstract

Changes in HeLa cell morphology, membrane permeability, and viability caused by the presence of Triton X-100 (TX100), a nonionic surfactant, were studied by scanning electrochemical microscopy (SECM). No change in membrane permeability was found at concentrations of 0.15 mM or lower during an experimental period of 30 to 60 min. Permeability of the cell membrane to the otherwise impermeable, highly charged hydrophilic molecule ferrocyanide was seen starting at concentrations of TX100 of about 0.17 mM. This concentration level of TX100 did not affect cell viability. Based on a simulation model, the membrane permeability for ferrocyanide molecules passing through the live cell membrane was $6.5 \pm 2.0 \times 10^{-6}$ m/s. Cells underwent irreversible permeabilization of the membrane and structural collapse when the TX100 concentration reached the critical micelle concentration (CMC), in the range of 0.19 to 0.20 mM. The impermeability of ferrocyanide molecules in the absence of surfactant was also used to determine the height and diameter of a single living cell with the aid of the approach curve and probe scan methods in SECM.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20837548>

“Permeability of the cell membrane to the otherwise impermeable, highly charged hydrophilic molecule ferrocyanide was seen starting at concentrations of TX100 of about 0.17 mM. Cells underwent irreversible permeabilization of the membrane and structural collapse when the TX100 concentration reached the critical micelle concentration (CMC), in the range of 0.19 to 0.20 mM.”

Triton X-100 concentration effects on membrane permeability of a single HeLa cell by scanning electrochemical microscopy (SECM)

Dipankar Koley and Allen J. Bard¹

Center for Electrochemistry
Department of Chemistry and Biochemistry
University of Texas at Austin, 1 University Station
A5300, Austin, TX 78712-0165

ABSTRACT

Changes in HeLa cell morphology, membrane permeability, and viability caused by the presence of Triton X-100 (TX100), a nonionic surfactant, were studied by scanning electrochemical microscopy (SECM). No change in membrane permeability was found at concentrations of 0.15 mM or lower during an experimental period of 30 to 60 min. Permeability of the cell membrane to the otherwise impermeable, highly charged hydrophilic molecule ferrocyanide was seen starting at concentrations of TX100 of about 0.17 mM. This concentration level of TX100 did not affect cell viability. Based on a simulation model, the membrane permeability for ferrocyanide molecules passing through the live cell membrane was $6.5 \pm 2.0 \times 10^{-6}$ m/s. Cells underwent irreversible permeabilization of the membrane and structural collapse when the TX100 concentration reached the critical micelle concentration (CMC), in the range of 0.19 to 0.20 mM. The impermeability of ferrocyanide molecules in the absence of surfactant was also used to determine the height and diameter of a single living cell with the aid of the approach curve and probe scan methods in SECM.

DISCUSSION

When the concentration of TX100 is below the CMC range (i.e. 0.17 mM and less) the surfactant may act as a permeabilizing agent depending on the dose and duration of exposure to cells. This is a good range for transfection of the cell with an added agent, but prolonged exposure to cells even at these low concentrations can lead to some cell death. When concentrations of TX100 in the CMC range, > 0.18 mM, are used, the cell membrane disintegrated causing a collapse of the entire cell structure and cell death within a few minutes.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2947864/>

“When concentrations of TX100 in the CMC range, > 0.18 mM, are used, the cell membrane disintegrated causing a collapse of the entire cell structure and cell death within a few minutes.”

Polysorbate-80 modified neurotoxin nanoparticle with its transport and cytotoxicity against blood-brain barrier

Author information

Zhao YM1, Xia AX, Wei YH, Ruan YP, Li FZ.

College of Pharmaceutical Science
Zhejiang Chinese Medical University
Hangzhou 310053, China

Abstract

This study was aimed at the transport across blood-brain barrier (BBB) of polysorbate-80 modified neurotoxin loaded polybutyl-cyanoacrylate nanoparticle (P-80-NT-NP) and its cytotoxicity. An in vitro model of BBB using rat brain microvascular endothelial cells (rBMECs) was established. The cytotoxicity of P-80-NT-NP was measured by the MTT assays, where neurotoxin (NT), nanoparticle (NP), neurotoxin nanoparticle (NT-NP) as control, and the permeability of P-80-NT-NP was determined by using of Millicell insert coculture with rBMECs and fluorescence spectrophotometry. MTT results showed that NT, NP, NT-NP and P-80-NT-NP were avirulent to rBMECs when the concentration of NT was lower than 200 ng x mL(-1). But the cytotoxicity of NP, NT-NP and P-80-NT-NP would be augmented accordingly as concentration increased ($P < 0.01$), causing obvious reductions of cell survival rate, with no significant difference between them ($P > 0.05$). When the concentration of NT was 150 ng x mL(-1), the permeability on rBMECs of P-80-NT-NP and NT-NP were both significantly higher than that of NT ($P < 0.01$), and the permeability of P-80-NT-NP was greater than that of NT-NP ($P < 0.05$). In conclusion, polysorbate-80 modified neurotoxin nanoparticles can transport across the BBB, while concentration of NT is greater than 200 ng x mL(-1), P-80-NT-NP has a little cytotoxicity against rBMECs.

<http://www.ncbi.nlm.nih.gov/pubmed/21348312>

“... polysorbate-80 modified
neurotoxin nanoparticles
can transport across the Blood Brain Barrier ...”

Diphtheria-tetanus-pertussis vaccine
administered simultaneously with measles vaccine
is associated with increased morbidity and poor growth in girls
A randomised trial from Guinea-Bissau

Author information

Agergaard J1, Nante E, Poulstrup G, Nielsen J, Flanagan KL, Østergaard L, Benn CS, Aaby P.
Bandim Health Project, Indepth Network, Apartado 861, 1004 Bissau Codex, Guinea-Bissau
heja@dadlnet.dk

Abstract

BACKGROUND

Combined vaccination with diphtheria-tetanus-pertussis (DTP) and measles vaccine (MV) has been associated with increased mortality in observational studies. Among children missing MV and a dose of DTP and oral polio vaccine (OPV), we conducted a randomised trial of providing MV+DTP+OPV simultaneously, as currently recommended, or MV+OPV only, and examined the effect on morbidity and growth. We hypothesised that the MV+OPV group would experience less morbidity and grow better. Due to previous observations of sex differences in the non-specific effects of vaccinations, we analysed all data stratified by sex.

METHODS

At the Bandim Health Project in Guinea-Bissau, 568 children who were due to receive MV and who were missing either DTP3 or DTP booster were enrolled in the study. A subgroup of 332 children was followed intensively to register adverse events and infections in the first month after vaccination. A subgroup of 276 children was followed every third month for a year to monitor growth. All children were followed for one year for infectious diseases, consultations, and hospitalisations.

RESULTS

As expected, adverse events were more common in the MV+DTP+OPV group; diarrhoea and use of medication

were increased among girls but not among boys (both $p=0.02$, test of interaction between DTP and sex). Febrile disease with vesicular rash, as well as consultations and hospitalisations tended to be more common in the MV+DTP+OPV group than in the MV+OPV group; the hazard ratio (HR) for febrile disease with vesicular rash was 1.86 (1.00; 3.47). The strongest tendencies for more febrile diseases and hospitalisations in the MV+DTP+OPV group were found in girls. Overall, growth did not differ by randomisation group. However, results differed by sex. Girls in the MV+DTP+OPV group had a consistent pattern of worse z-scores for weight, height, and mid-upper-arm-circumference (MUAC) than girls in the MV+OPV group. The effect was opposite for boys, with boys in the MV+OPV group faring worse than those in the MV+DTP+OPV group, the interaction test for sex and DTP being significant for weight at 6 and 9 months, for MUAC at 12 months and for weight-for-height at 3 and 9 months after randomisation.

CONCLUSION

This is the first randomised trial of the non-specific effects of DTP and supports that these effects may be sex-differential and of clinical and anthropometric importance. Combined vaccination with DTP+MV+OPV may be detrimental for girls.

<http://www.ncbi.nlm.nih.gov/pubmed/21093496>

“This is the first randomised trial of the non-specific effects of DTP and supports that these effects may be sex-differential and of clinical and anthropometric importance. Combined vaccination with DTP+MV+OPV may be detrimental for girls.”

Protegen: a web-based protective antigen database and analysis system

Author information

Yang B1, Sayers S, Xiang Z, He Y.

Unit for Laboratory Animal Medicine
University of Michigan Medical School
Center for Computational Medicine and Bioinformatics
University of Michigan, Ann Arbor, MI 48109

Abstract

Protective antigens are specifically targeted by the acquired immune response of the host and are able to induce protection in the host against infectious and non-infectious diseases. Protective antigens play important roles in vaccine development, as biological markers for disease diagnosis, and for analysis of fundamental host immunity against diseases. Protegen is a web-based central database and analysis system that curates, stores and analyzes protective antigens. Basic antigen information and experimental evidence are curated from peer-reviewed articles. More detailed gene/protein information (e.g. DNA and protein sequences, and COG classification) are automatically extracted from existing databases using internally developed scripts. Bioinformatics programs are also applied to compute different antigen features, such as protein weight and pI, and subcellular localizations of bacterial proteins. Presently, 590 protective antigens have been curated against over 100 infectious diseases caused by pathogens and non-infectious diseases (including cancers and allergies). A user-friendly web query and visualization interface is developed for interactive protective antigen search. A customized BLAST sequence similarity search is also developed for analysis of new sequences provided by the users. To support data exchange, the information of protective antigens is stored in the Vaccine Ontology (VO) in OWL format and can also be exported to FASTA and Excel files. Protegen is publically available at <http://www.violinet.org/protegen>.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3013795/>

“Protegen is a web-based central database and analysis system that curates, stores and analyzes protective antigens. Presently, 590 protective antigens have been curated against over 100 infectious diseases caused by pathogens and non-infectious diseases (including cancers and allergies).”

Journal Of Autoimmunity • February 2011

**Autoimmune or auto-inflammatory syndrome
induced by adjuvants (ASIA):
old truths and a new syndrome?**

Author information

Meroni PL1.

Division of Rheumatology, Istituto G. Pini, Milan, Italy
pierluigi.meroni@unimi.it

Abstract

There has been considerable interest in the role of environmental factors and the induction of autoimmunity and the ways by which they facilitate loss of tolerance. Clearly both genetic and environmental factors are incriminated, as evidenced by the lack of concordance in identical twins and the relatively recent identification of the shared epitope in rheumatoid arthritis. In this issue a new syndrome called 'Asia'-autoimmune/auto-inflammatory syndrome induced by adjuvants has been proposed. It is an intriguing issue and one that is likely to be provocative and lead to further biologic and molecular investigations.

<http://www.ncbi.nlm.nih.gov/pubmed/21051205>

“In this issue a new syndrome called
'Asia'-autoimmune/auto-inflammatory syndrome
induced by adjuvants has been proposed. It is an
intriguing issue and one that is likely to be
provocative and lead to further biologic
and molecular investigations.”

**‘ASIA’
autoimmune/inflammatory syndrome
induced by adjuvants**

Author information

Shoenfeld Y1, Agmon-Levin N.

The Zabłudowicz Center for Autoimmune Diseases
Department of Medicine B’ Sheba Medical Center
Tel-Hashomer, Israel
shoenfel@post.tau.ac.il

Abstract

The role of various environmental factors in the pathogenesis of immune mediated diseases is well established. Of which, factors entailing an immune adjuvant activity such as infectious agents, silicone, aluminium salts and others were associated with defined and non-defined immune mediated diseases both in animal models and in humans. In recent years, four conditions: siliconosis, the Gulf war syndrome (GWS), the macrophagic myofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant. Furthermore, these four diseases share a similar complex of signs and symptoms which further support a common denominator. Thus, we review herein the current data regarding the role of adjuvants in the pathogenesis of immune mediated diseases as well as the amassed data regarding each of these four conditions. Relating to the current knowledge we would like to suggest to include these comparable conditions under a common syndrome entitled ASIA, “Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants”.

<http://www.ncbi.nlm.nih.gov/pubmed/20708902>

“Relating to the current knowledge
we would like to suggest to include these
comparable conditions under a common syndrome
entitled ASIA, “Autoimmune (Auto-inflammatory)
Syndrome Induced by Adjuvants”.”

“By means of a study including 300 unexplained sudden unexpected deaths (uSUD),
a 16-fold risk increase [in death] after the 4th dose could be detected with a power of at least 90 per cent.
A general 2-fold risk increase after vaccination could be detected with a power of 80 per cent.”

Statistics In Medicine • March 2011

A modified self-controlled case series method to examine association between multidose vaccinations and death

Author information

Kuhnert R1, Hecker H, Poethko-Müller C, Schlaud M,
Vennemann M, Whitaker HJ, Farrington CP.

Robert Koch-Institute
Division for Health of Children and Adolescents
Prevention Concepts, Postfach 650261
13353 Berlin, Germany
KuhnertR@rki.de

Abstract

The self-controlled case series method (SCCS) was developed to analyze the association between a time-varying exposure and an outcome event. We consider penta- or hexavalent vaccination as the exposure and unexplained sudden unexpected death (uSUD) as the event. The special situation of multiple exposures and a terminal event requires adaptation of the standard SCCS method. This paper proposes a new adaptation, in which observation periods are truncated according to the vaccination schedule. The new method exploits known minimum spacings between successive vaccine doses. Its advantage is that it is very much simpler to apply than the method for censored, perturbed or curtailed post-event exposures recently introduced. This paper presents a comparison of these two SCCS methods by simulation studies and an application to a real data set. In the simulation studies, the age distribution and the assumed vaccination schedule were based on real data. Only small differences between the two SCCS methods were observed, although 50 per cent of cases could not be included in the analysis with the SCCS method with truncated observation periods. By means of a study including 300 uSUD, a 16-fold risk increase after the 4th dose could be detected with a power of at least 90 per cent. A general 2-fold risk increase after vaccination could be detected with a power of 80 per cent. Reanalysis of data from cases of the German case-control study on sudden infant death (GeSID) resulted in slightly higher point estimates using the SCCS methods than the odds ratio obtained by the case-control analysis.

<http://www.ncbi.nlm.nih.gov/pubmed/21337361>

Genotoxicity biomarkers in occupational exposure to formaldehyde the case of histopathology laboratories

Author information

Ladeira C1, Viegas S, Carolino E, Prista J, Gomes MC, Brito M.

Escola Superior de Tecnologia da Saúde de Lisboa
Instituto Politécnico de Lisboa, Portugal
carina.ladeira@estesl.ipl.pt

Abstract

Formaldehyde, classified by the IARC as carcinogenic in humans and experimental animals, is a chemical agent that is widely used in histopathology laboratories. The exposure to this substance is epidemiologically linked to cancer and to nuclear changes detected by the cytokinesis-block micronucleus test (CBMN). This method is extensively used in molecular epidemiology, since it provides information on several biomarkers of genotoxicity, such as micronuclei (MN), which are biomarkers of chromosomes breakage or loss, nucleoplasmic bridges (NPB), common biomarkers of chromosome rearrangement, poor repair and/or telomere fusion, and nuclear buds (NBUD), biomarkers of elimination of amplified DNA. The aim of this study is to compare the frequency of genotoxicity biomarkers, provided by the CBMN assay in peripheral lymphocytes and the MN test in buccal cells, between individuals occupationally exposed and non-exposed to formaldehyde and other environmental factors, namely tobacco and alcohol consumption. The sample comprised two groups: 56 individuals occupationally exposed to formaldehyde (cases) and 85 unexposed individuals (controls), from whom both peripheral blood and exfoliated epithelial cells of the oral mucosa were collected in order to measure the genetic endpoints proposed in this study. The mean level of TWA(8h) was 0.16 ± 0.11 ppm (< detection limit until 0.51 ppm) and the mean of ceiling values was 1.14 ± 0.74 ppm (0.18-2.93 ppm). All genotoxicity biomarkers showed significant increases in exposed workers in comparison with controls (Mann-Whitney test, $p < 0.002$) and the analysis of confounding factors showed that there were no differences between genders. As for age, only the mean MN frequency in lymphocytes was found significantly higher in elderly people among the exposed groups ($p = 0.006$), and there was also evidence of an interaction between age and gender with regards to that biomarker in those exposed. Smoking habits did not influence the frequency of the biomarkers, whereas alcohol consumption only influenced the MN frequency in lymphocytes in controls ($p = 0.011$), with drinkers showing higher mean values. These results provide evidence of the association between occupational exposure to formaldehyde and the presence of genotoxicity biomarkers.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21256246>

“These results provide evidence of the association between occupational exposure to formaldehyde and the presence of genotoxicity biomarkers.”

Vaccination, consent and multidose vials

Mark R Diamond, PhD, Research Psychologist
Angela O'Brien-Malone, PhD, Research Psychologist

School of Psychology, University of Tasmania, Hobart, TAS
Correspondence: diamondm@utas.edu.au

Abstract

- Multidose vials (MDVs) for injectable therapeutic agents, including vaccines, pose a risk of infection to injected patients as a result of contamination of the vials.
- The Australian Government Department of Health and Ageing (DoHA) distributed the vaccine against pandemic (H1N1) 2009 influenza in MDVs. The distribution was accompanied by consent forms.
- The consent forms provided an inadequate basis for a discussion with patients about the risks associated with the use of MDVs.
- The High Court of Australia has previously held that medical practitioners who fail to explain the material risks of medical procedures to their patients might be held liable in negligence for any adverse sequelae of the procedures, even if the risks are very low.
- Medical practitioners, nurses, medical indemnity insurers and the DoHA should prepare now for the probable future use of MDVs by developing a consent form that would provide a solid foundation for a discussion of material risks with patients seeking vaccination.

Full Report

https://www.mja.com.au/system/files/issues/194_08_180411/dia10882_fm.pdf

“The consent forms provided an inadequate basis for a discussion with patients about the risks associated with the use of Multi-dose Vials.”

Revisiting the Sham: Is It all Smoke and Mirrors?

Author information

Horn B1, Balk J, Gold JI.

Eastern Center for Complementary Medicine, PC
Los Angeles, California, USA

Abstract

The misuse of sham controls in examining the efficacy or effectiveness of Complementary and Alternative Medicine has created numerous problems. The theoretical justification for incorporating a sham is questionable. The sham does not improve our control of bias and leads to relativistic data that, in most instances, has no appropriate interpretation with regards to treatment efficacy. Even the concept of a sham or placebo control in an efficacy trial is inherently paradoxical. Therefore, it is prudent to re-examine how we view sham controls in the context of medical research. Extreme caution should be used in giving weight to any sham-controlled study claiming to establish efficacy or safety.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3137704/>

Formaldehyde induces neurotoxicity to PC12 cells involving inhibition of paraoxonase-1 expression and activity

Tang XQ1, Ren YK, Chen RQ,
Zhuang YY, Fang HR, Xu JH, Wang CY, Hu B.

Author information

Department of Physiology, Medical College
University of South China, Hengyang, Hunan, China

Abstract

1. Formaldehyde (FA) has been found to cause toxicity to neurons. However, its neurotoxic mechanisms have not yet been clarified. Increasing evidence has shown that oxidative damage is one of the most critical effects of formaldehyde exposure. Paraoxonase-1 (PON-1) is a pivotal endogenous anti-oxidant. Thus, we hypothesized that FA-mediated downregulation of PON1 is associated with its neurotoxicity.
2. In the present work, we used PC12 cells to study the neurotoxicity of FA and explore whether PON-1 is implicated in FA-induced neurotoxicity.
3. We found that FA has potent cytotoxic and apoptotic effects on PC12 cells. FA induces an accumulation of intracellular reactive oxygen species along with downregulation of Bcl-2 expression, as well as increased cytochrome c release. FA significantly suppressed the expression and activity of PON-1 in PC12 cells. Furthermore, H(2)S, an endogenous anti-oxidant gas, antagonizes FA-induced cytotoxicity as well as 2-hydroxyquinoline, a specific inhibitor of PON-1, which also induces cytotoxicity to PC12 cells.
4. The results of the present study provide, for the first time, evidence that the inhibitory effect on PON-1 expression and activity is involved in the neurotoxicity of FA, and suggest a promising role of PON-1 as a novel therapeutic strategy for FA-mediated toxicity.

<http://www.ncbi.nlm.nih.gov/pubmed/21261675>

“The results of the present study provide, for the first time, evidence that the inhibitory effect on Paraoxonase-1 expression and activity is involved in the neurotoxicity of Formaldehyde ...”

British Journal of Dermatology • May 2011

**Biologic-induced urticaria due to polysorbate 80:
usefulness of prick test**

L. Pérez-Pérez, J. García-Gavín, B. Piñeiro and A. Zulaica

Department of Dermatology
University Complex Hospital of Vigo
C/ Porriño 5, 36209 Vigo (Pontevedra), Spain

Report Available For Purchase Only:

<http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2011.10220.x/abstract>

Genetic drift evolution under vaccination pressure among H5N1 Egyptian isolates

Author information

Abdel-Moneim AS1, Afifi MA, El-Kady MF.

Department of Virology
Faculty of Veterinary Medicine
Beni-Suef University, Beni-Suef, Egypt
asa@bsu.edu.eg

Abstract

Background

The highly pathogenic H5N1 is a major avian pathogen that intensively affects the poultry industry in Egypt even in spite of the adoption of vaccination strategy. Antigenic drift is among the strategies the influenza virus uses to escape the immune system that might develop due to the pressure of extensive vaccination. H5N1 mutates in an intensified manner and is considered a potential candidate for the possible next pandemic with all the catastrophic consequences such an eventuality will entail.

Methods

H5N1 was isolated from the pooled organ samples of four different affected flocks in specific pathogen free embryonated chicken eggs (SPF-ECE). A reverse transcriptase polymerase chain reaction (RT-PCR) was performed to the haemagglutinin and neuraminidase. Sequencing of the full length haemagglutinin was performed. Sequence analyses of the isolated strains were performed and compared to all available H5N1 from Egyptian human and avian strains in the flu database. Changes in the different amino acid that may be related to virus virulence, receptor affinity and epitope configuration were assigned and matched with all available Egyptian strains in the flu database.

Results

One out of the four strains was found to be related to the B2 Egyptian lineage, 2 were related to A1 lineage and the 4th was related to A2 lineage. Comparing data obtained from the current study by other available Egyptian H5N1 sequences remarkably demonstrates that amino acid changes in the immune escape variants are remarkably restricted to a limited number of locations on the HA molecule during antigenic drift. Molecular diversity in the HA gene, in relevance to different epitopes, were not found to follow a regular trend, suggesting abrupt cumulative sequence mutations. However a number of amino acids were found to be subjected to high mutation pressure.

Conclusion

The current data provides a comprehensive view of HA gene evolution among H5N1 subtype viruses in Egypt. Egyptian H5N1-AIVs are constantly undergoing genetic changes and reveal a complex pattern of drifts. These findings raise the concerns about the value of using influenza vaccines in correlation with the development of antigenic drift in influenza epidemics.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3146449/>

“The current data provides a comprehensive view of HA gene evolution among H5N1 subtype viruses in Egypt. Egyptian H5N1-AIVs are constantly undergoing genetic changes and reveal a complex pattern of drifts. These findings raise the concerns about the value of using influenza vaccines in correlation with the development of antigenic drift in influenza epidemics.”

Immunoexcitotoxicity
as a central mechanism in chronic traumatic encephalopathy
—A unifying hypothesis

Russell L. Blaylock* and Joseph Maroon1

Theoretical Neurosciences, LLC Visiting Professor of Biology
Belhaven University, Jackson, MS 315 Rolling Meadows Rd
Ridgeland, MS 39157, USA

2. Department of Neurosurgery, Heindl Scholar in Neuroscience
University of Pittsburgh Medical Center
Team Neurosurgeon, The Pittsburgh Steelers, USA

Abstract

Some individuals suffering from mild traumatic brain injuries, especially repetitive mild concussions, are thought to develop a slowly progressive encephalopathy characterized by a number of the neuropathological elements shared with various neurodegenerative diseases. A central pathological mechanism explaining the development of progressive neurodegeneration in this subset of individuals has not been elucidated. Yet, a large number of studies indicate that a process called immunoexcitotoxicity may be playing a central role in many neurodegenerative diseases including chronic traumatic encephalopathy (CTE). The term immunoexcitotoxicity was first coined by the lead author to explain the evolving pathological and neurodevelopmental changes in autism and the Gulf War Syndrome, but it can be applied to a number of neurodegenerative disorders. The interaction between immune receptors within the central nervous system (CNS) and excitatory glutamate receptors trigger a series of events, such as extensive reactive oxygen species/reactive nitrogen species generation, accumulation of lipid peroxidation products, and prostaglandin activation, which then leads to dendritic retraction, synaptic injury, damage to microtubules, and mitochondrial suppression. In this paper, we discuss the mechanism of immunoexcitotoxicity and its link to each of the pathophysiological and neurochemical events previously described with CTE, with special emphasis on the observed accumulation of hyperphosphorylated tau.

[Although this report discusses traumatic brain injury the data discussed fits in perfectly with and coincides with vaccine-induced brain injury and is included for that reason]

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157093/>

Vaccine • August 2011

Pandemic influenza H1N1 2009 infection in Victoria, Australia: no evidence for harm or benefit following receipt of seasonal influenza vaccine in 2009

Author information

Kelly HA1, Grant KA, Fielding JE, Carville KS, Looker CO, Tran T, Jacoby P.

Victorian Infectious Diseases Reference Laboratory
Melbourne, Victoria, Australia
heath.kelly@mh.org.au

Abstract

Conflicting findings regarding the level of protection offered by seasonal influenza vaccination against pandemic influenza H1N1 have been reported. We performed a test-negative case control study using sentinel patients from general practices in Victoria to estimate seasonal influenza vaccine effectiveness against laboratory proven infection with pandemic influenza. Cases were defined as patients with an influenza-like illness who tested positive for influenza while controls had an influenza-like illness but tested negative. We found no evidence of significant protection from seasonal vaccine against pandemic influenza virus infection in any age group. Age-stratified point estimates, adjusted for pandemic phase, ranged from 44% in persons aged less than 5 years to -103% (odds ratio=2.03) in persons aged 50-64 years. Vaccine effectiveness, adjusted for age group and pandemic phase, was 3% (95% CI -48 to 37) for all patients. Our study confirms the results from our previous interim report, and other studies, that failed to demonstrate benefit or harm from receipt of seasonal influenza vaccine in patients with confirmed infection with pandemic influenza H1N1 2009.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=21473950>

“Our study confirms the results from our previous interim report, and other studies, that failed to demonstrate benefit or harm from receipt of seasonal influenza vaccine ...”

Stability of the non-ionic surfactant polysorbate 80 investigated by HPLC-MS and charged aerosol detector

Author information

Christiansen A1, Backensfeld T, Kühn S, Weitschies W.

Analytical Development
Bayer Schering Pharma AG
Berlin, Germany

Abstract

An analytical method using HPLC coupled with a charged aerosol detector (CAD) and a mass selective detector (MSD) was developed to characterize the non-ionic surfactant polysorbate 80 (PS 80). The molecular structure and heterogeneous composition due to isomers and various lengths of PEG-chains make it difficult to develop sensitive and specific analytical methods. Hence, there is only limited knowledge about the stability and purity of this compound. Polysorbate 80 does not possess any chromophore, thus UV detection is not applicable. Therefore, CAD and MSD have been used for determination. The aim of this study was to characterize polysorbate 80 and to examine its stability at pH 1.0 and 37 degrees C simulating harsh gastric conditions. It was shown that this surfactant is liable to degradation under these conditions. Within 8 h monoesters of PS 80 were hydrolyzed to an extent of 9.5% (+/- 3.0%), whereas incubation in water did not result in any detectable degradation. Furthermore, we demonstrated that HPLC-MS is a suitable technique to investigate ethoxylated compounds like polysorbates.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22026121>

“The aim of this study was to characterize polysorbate 80 and to examine its stability at pH 1.0 and 37 degrees C simulating harsh gastric conditions. It was shown that this surfactant is liable to degradation under these conditions.”

Infant mortality rates regressed against number of vaccine doses routinely given: Is there a biochemical or synergistic toxicity?

Neil Z Miller and Gary S Goldman

Neil Z Miller
PO Box 9638, Santa Fe, NM 87504, USA
neilzmillier@gmail.com

Abstract

The infant mortality rate (IMR) is one of the most important indicators of the socio-economic well-being and public health conditions of a country. The US childhood immunization schedule specifies 26 vaccine doses for infants aged less than 1 year—the most in the world—yet 33 nations have lower IMRs. Using linear regression, the immunization schedules of these 34 nations were examined and a correlation coefficient of $r = 0.70$ ($p < 0.0001$) was found between IMRs and the number of vaccine doses routinely given to infants. Nations were also grouped into five different vaccine dose ranges: 12–14, 15–17, 18–20, 21–23, and 24–26. The mean IMRs of all nations within each group were then calculated. Linear regression analysis of unweighted mean IMRs showed a high statistically significant correlation between increasing number of vaccine doses and increasing infant mortality rates, with $r = 0.992$ ($p = 0.0009$). Using the Tukey-Kramer test, statistically significant differences in mean IMRs were found between nations giving 12–14 vaccine doses and those giving 21–23, and 24–26 doses. A closer inspection of correlations between vaccine doses, biochemical or synergistic toxicity, and IMRs is essential.

Conclusion

The US childhood immunization schedule requires 26 vaccine doses for infants aged less than 1 year, the most in the world, yet 33 nations have better IMRs. Using linear regression, the immunization schedules of these 34 nations were examined and a correlation coefficient of 0.70 ($p < 0.0001$) was found between IMRs and the number of vaccine doses routinely given to infants. When nations were grouped into five different vaccine dose ranges (12–14, 15–17, 18–20, 21–23, and 24–26), 98.3% of the total variance in IMR was explained by the unweighted linear regression model. These findings demonstrate a counter-intuitive relationship: nations that require more vaccine doses tend to have higher infant mortality rates.

Efforts to reduce the relatively high US IMR have been elusive. Finding ways to lower preterm birth rates should be a high priority. However, preventing premature births is just a partial solution to reduce infant deaths. A closer inspection of correlations between vaccine doses, biochemical or synergistic toxicity, and IMRs, is essential. All nations—rich and poor, advanced and developing—have an obligation to determine whether their immunization schedules are achieving their desired goals.

“These findings demonstrate
a counter-intuitive relationship:
nations that require more vaccine doses
tend to have higher infant mortality rates.”

Immune enhancement by novel vaccine adjuvants in autoimmune-prone NZB/W F1 mice: relative efficacy and safety

Author information

Aachoui Y1, Ghosh SK.
Department of Biology
Indiana State University
Terre Haute, IN 47809, USA

Abstract

BACKGROUND

Vaccines have profoundly impacted global health although concerns persist about their potential role in autoimmune or other adverse reactions. To address these concerns, vaccine components like immunogens and adjuvants require critical evaluation not only in healthy subjects but also in those genetically averse to vaccine constituents. Evaluation in autoimmune-prone animal models of adjuvants is therefore important in vaccine development. The objective here was to assess the effectiveness of experimental adjuvants: two phytol-derived immunostimulants PHIS-01 (phytanol) and PHIS-03 (phytanil mannose), and a new commercial adjuvant from porcine small intestinal submucosa (SIS-H), relative to a standard adjuvant alum. Phytol derivatives are hydrophobic, oil-in water diterpenoids, while alum is hydrophilic, and SIS is essentially a biodegradable and collagenous protein cocktail derived from extracellular matrices.

RESULTS

We studied phthalate -specific and cross-reactive anti-DNA antibody responses, and parameters associated with the onset of autoimmune disorders. We determined antibody isotype and cytokine/chemokine milieu induced by the above experimental adjuvants relative to alum. Our results indicated that the phytol-derived adjuvant PHIS-01 exceeded alum in enhancing anti-phthalate antibody without much cross reactivity with ds-DNA. Relatively, SIS and PHIS-03 proved less robust, but they were also less inflammatory. Interestingly, these adjuvants facilitated isotype switching of anti-hapten, but not of anti-DNA response. The current study reaffirms our earlier reports on adjuvanticity of phytol compounds and SIS-H in non autoimmune-prone BALB/c and C57BL/6 mice. These adjuvants are as effective as alum also in autoimmune-prone NZB/WF1 mice, and they have little deleterious effects.

CONCLUSION

Although all adjuvants tested impacted cytokine/chemokine milieu in favor of Th1/Th2 balance, the phytol compounds fared better in reducing the onset of autoimmune syndromes. However, SIS is least inflammatory among the adjuvants evaluated.

“Evaluation in autoimmune-prone animal models of adjuvants is therefore important in vaccine development.”

Postvaccination Miller Fisher Syndrome

Ashkan Shoamanesh, MD;
Kristine Chapman, MD;
Anthony Traboulsee, MD

Abstract

Background

Although postvaccination Guillain-Barré syndrome is commonly reported, there have only been 2 previously reported cases of postvaccination Miller Fisher syndrome, and none in association with the novel influenza A(H1N1) vaccine.

Objective

To describe a case of Miller Fisher syndrome following receipt of the seasonal influenza and novel influenza A(H1N1) vaccine.

Design

Case report and literature review.

Setting

Vancouver General Hospital.

Patient

A 77-year-old Chinese woman.

Results

The patient presented with ophthalmoplegia, ataxia, areflexia, and a sensory neuropathy within 2 weeks of immunization. Findings of parainfectious evaluation were unremarkable. Treatment with 2 courses of intravenous immunoglobulin led to clinical improvement. Her presentation and natural history of disease were similar to the 2 previously published cases.

Conclusions

We present the third case of postvaccination Miller Fisher syndrome in the literature and the first associated with the novel influenza A(H1N1) vaccine. The benefits of the development of vaccines and the ensuing modern immunization programs are overwhelmingly without question. Nevertheless, there is a growing public concern surrounding the potential for postvaccination adverse events, a sentiment that has dwelled since their nascence.¹ In view of the recent novel influenza A(H1N1) pandemic and scramble toward developing new vaccines for mass worldwide immunization campaigns, a better understanding of these potential adverse events is vital. We present a case of Miller Fisher syndrome (MFS) following seasonal influenza and novel influenza A(H1N1) vaccination, as well as a review of the literature on postvaccination MFS.

“We present the third case of postvaccination Miller Fisher syndrome in the literature and the first associated with the novel influenza A(H1N1) vaccine.”

Macrophagic myofasciitis a vaccine (alum) autoimmune-related disease

Author information

Israeli E1, Agmon-Levin N, Blank M, Shoenfeld Y.

Center for Autoimmune Diseases
Sheba Medical Center
Tel-Hashomer, Israel

Abstract

Macrophagic myofasciitis (MMF) is an immune-mediated condition first reported in 1998. MMF is characterized by post-vaccination systemic manifestations as well as local-stereotyped and immunologically active lesion in the site of inoculation (deltoid muscle). MMF systemic symptoms included myalgias, arthralgias, marked asthenia, muscle weakness, chronic fatigue, and fever. Recently, studies demonstrated that the local lesion is due to persistence for years at site of injection of an aluminum (Al(OH)₃) adjuvant commonly used in human vaccines. Time elapsed from last immunization with an Al(OH)₃-containing vaccine to muscle biopsy range from 3 months to 8 years; in rare cases, MMF may be diagnosed even 10 years post-vaccination. The discrepancy between the wide applications of aluminum hydroxide-containing vaccines and the very limited number of MMF cases reported may be resolved by observations suggesting that aluminum-containing vaccinations may trigger MMF in genetically susceptible subjects carrying the HLA-DRB1*01. Thus, MMF may be defined as an emerging novel condition that may be triggered by exposure to alum-containing vaccines, in patients with a specific genetic background, and this temporal association may be exhibited from a few months up to 10 years.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20882368>

“MMF may be defined as an emerging novel condition that may be triggered by exposure to alum-containing vaccines ... and this temporal association may be exhibited from a few months up to 10 years.”

The common immunogenic etiology
of chronic fatigue syndrome:
from infections to vaccines via adjuvants
to the ASIA syndrome

Author information

Rosenblum H1, Shoenfeld Y, Amital H.

Department of Medicine B
Sheba Medical Center
Sackler Faculty of Medicine
Tel Aviv University, Ramat Aviv
Tel-Hashomer 52621, Israel

Abstract

Chronic fatigue syndrome (CFS) is characterized by unexplained fatigue that lasts for at least 6 months with a constellation of other symptoms. Most cases start suddenly, and are usually accompanied by a flu-like illness. It is a symptom-based diagnosis of exclusion, the pathogenesis of which is unknown. Studies have examined and hypothesized about the possible biomedical and epidemiologic characteristics of the disease, including genetic predisposition, infections, endocrine abnormalities, and immune dysfunction and psychological and psychosocial factors. Recently, the AISA (autoimmune/inflammatory syndrome induced by adjuvants) syndrome was recognized, indicating the possible contribution of adjuvants and vaccines to the development of autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/22054760>

“Recently, the AISA
(autoimmune/inflammatory syndrome induced by adjuvants)
syndrome was recognized, indicating the possible contribution
of adjuvants and vaccines to the development of autoimmunity.”

**Hypothesis:
conjugate vaccines
may predispose children
to autism spectrum disorders**

Author information

Richmand BJ1.
brichmand@gmail.com

Abstract

The first conjugate vaccine was approved for use in the US in 1988 to protect infants and young children against the capsular bacteria *Haemophilus influenzae* type b (Hib). Since its introduction in the US, this vaccine has been approved in most developed countries, including Denmark and Israel where the vaccine was added to their national vaccine programs in 1993 and 1994, respectively. There have been marked increases in the reported prevalence of autism spectrum disorders (ASDs) among children in the US beginning with birth cohorts in the late 1980s and in Denmark and Israel starting approximately 4-5 years later. Although these increases may partly reflect ascertainment biases, an exogenous trigger could explain a significant portion of the reported increases in ASDs. It is hypothesized here that the introduction of the Hib conjugate vaccine in the US in 1988 and its subsequent introduction in Denmark and Israel could explain a substantial portion of the initial increases in ASDs in those countries. The continuation of the trend toward increased rates of ASDs could be further explained by increased usage of the vaccine, a change in 1990 in the recommended age of vaccination in the US from 15 to 2 months, increased immunogenicity of the vaccine through changes in its carrier protein, and the subsequent introduction of the conjugate vaccine for *Streptococcus pneumoniae*. Although conjugate vaccines have been highly effective in protecting infants and young children from the significant morbidity and mortality caused by Hib and *S. pneumoniae*, the potential effects of conjugate vaccines on neural development merit close examination. Conjugate vaccines fundamentally change the manner in which the immune systems of infants and young children function by deviating their immune responses to the targeted carbohydrate antigens from a state of hypo-responsiveness to a robust B2 B cell mediated response. This period of hypo-responsiveness to carbohydrate antigens coincides with the intense myelination process in infants and young children, and conjugate vaccines may have disrupted evolutionary forces that favored early brain development over the need to protect infants and young children from capsular bacteria.

“This period of hypo-responsiveness to carbohydrate antigens coincides with the intense myelination process in infants and young children, and conjugate vaccines may have disrupted evolutionary forces that favored early brain development over the need to protect infants and young children from capsular bacteria.”

Reumatismo • 2011

‘ASIA’ -
Autoimmune/inflammatory syndrome
induced by adjuvants: even and odd

Author information

Perricone C1, Alessandri C, Valesini G.

Reumatologia
Dipartimento di Medicina Interna e Specialità Mediche
Sapienza Università di Roma, Viale del Policlinico 155
Rome, Italy
carlo.perricone@gmail.com

Abstract

Recently, Shoenfeld and Agmon-Levin described a potential new syndrome, namely ASIA - autoimmune/inflammatory syndrome induced by adjuvants, that comprises four medical conditions: siliconosis, the Gulf war syndrome, the macrophagic myofasciitis syndrome and post-vaccination phenomena, characterized by hyperactive immune responses accompanied by a similar complex of signs and symptoms. Most relevantly, these conditions share a linkage represented by adjuvants. This common soil may possibly induce autoimmune or auto-inflammatory diseases in humans as it was demonstrated in different animal models. Reconsidering under a unified umbrella this apparently detached condition is not only intriguing, but also provocative, and may help in unraveling novel pathogenetic mechanisms, preventive measures, and therapeutic targets.

<http://www.ncbi.nlm.nih.gov/pubmed/21776441>

“This common soil
may possibly induce autoimmune or
auto-inflammatory diseases in humans as it was
demonstrated in different animal models.”

Public Health Report • 2011

Highlights of Historical Events Leading to National Surveillance of Vaccination Coverage in the United States

Author Information

Philip J. Smith, PhD,^a David Wood, MD, MPH,^b and Paul M. Darden, MD^c

^aCenters for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases, Atlanta, GA

^bUniversity of Florida, College of Medicine
Community Pediatrics, Jacksonville, FL

^cUniversity of Oklahoma Health Sciences Center
General & Community Pediatrics, Oklahoma City, OK

Abstract

The articles published in this special supplement of Public Health Reports provide examples of only some of the current efforts in the United States for evaluating vaccination coverage. So, how did we get here? The history of vaccination and assessment of vaccination coverage in the U.S. has its roots in the pre-Revolutionary War era. In many cases, development of vaccines, and attention devoted to the assessment of vaccination coverage, has grown from the impact of infectious disease on major world events such as wars. The purpose of this commentary is to provide a brief overview of the key historical events in the U.S. that influenced the development of vaccines and the efforts to track vaccination coverage, which laid the foundation for contemporary vaccination assessment efforts.

Full Report • Recommended Reading

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3113425/>

“The history of vaccination
and assessment of vaccination coverage
in the U.S. has its roots in the
pre-Revolutionary War era.”

Serum Vaccine Antibody Concentrations in Children Exposed to Perfluorinated Compounds

Philippe Grandjean, MD, DMSc; Elisabeth Wreford Andersen, PhD;
Esben Budtz-Jørgensen, PhD; Flemming Nielsen, PhD; Kåre Mølbak, MD, DMSc;
Pal Weihe, MD; Carsten Heilmann, MD, DMSc

Abstract

Context

Perfluorinated compounds (PFCs) have emerged as important food contaminants. They cause immune suppression in a rodent model at serum concentrations similar to those occurring in the US population, but adverse health effects of PFC exposure are poorly understood.

Objective

To determine whether PFC exposure is associated with antibody response to childhood vaccinations.

Design, Setting, and Participants

Prospective study of a birth cohort from the National Hospital in the Faroe Islands. A total of 656 consecutive singleton births were recruited during 1997-2000, and 587 participated in follow-up through 2008.

Main Outcome Measures

Serum antibody concentrations against tetanus and diphtheria toxoids at ages 5 and 7 years.

Results

Similar to results of prior studies in the United States, the PFCs with the highest serum concentrations were perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA). Among PFCs in maternal pregnancy serum, PFOS showed the strongest negative correlations with antibody concentrations at age 5 years, for which a 2-fold greater concentration of exposure was associated with a difference of -39% (95% CI, -55% to -23%) in the diphtheria antibody concentration. PFCs in the child's serum at age 5 years showed uniformly negative associations with antibody levels, especially at age 7 years, except that the tetanus antibody level following PFOS exposure was not statistically significant. In a structural equation model, a 2-fold greater concentration of major PFCs in child serum was associated with a difference of -49% (95% CI, -67% to -31%) in the overall antibody concentration. A 2-fold increase in PFOS and PFOA concentrations at age 5 years was associated with odds ratios between 2.38 (95% CI, 0.89 to 6.35) and 4.20 (95% CI, 1.54 to 11.44) for falling below a clinically protective level of 0.1 IU/mL for tetanus and diphtheria antibodies at age 7 years.

Conclusion

Elevated exposures to PFCs were associated with reduced humoral immune response to routine childhood immunizations in children aged 5 and 7 years.

“Elevated exposures to PFCs were associated with reduced humoral immune response to routine childhood immunizations in children aged 5 and 7 years.”

Diphtheria, pertussis (whooping cough),
and tetanus vaccine induced recurrent seizures
and acute encephalopathy in a pediatric patient:
Possibly due to pertussis fraction

Author information

Patel MK1, Patel TK, Tripathi CB.

Department of Pharmacology
Government Medical College
Bhavnagar, Gujarat, India

Abstract

A 5-month-old male patient developed recurrent seizures and acute encephalopathy possibly due to first dose of diphtheria, pertussis (whooping cough), and tetanus (DPT) vaccine used for routine immunization. Postreaction computed tomography (CT) scan of brain, magnetic resonance imaging (MRI) of brain, and electroencephalogram were normal. Pertussis fraction of DPT vaccine is responsible for this reaction. It is suggested that acellular pertussis vaccine should be used instead of whole cell vaccine because it is associated with lower frequency of neurological complications, such as seizures, encephalopathy, and hypotensive episodes. However, acellular pertussis-containing vaccines are currently not affordable in most developing countries.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3284047/>

“It is suggested that acellular pertussis vaccine should be used instead of whole cell vaccine because it is associated with lower frequency of neurological complications, such as seizures, encephalopathy, and hypotensive episodes.”

**Influenza vaccination
can induce new-onset anticardiolipins
but not B2-glycoprotein-I antibodies
among patients with systemic lupus erythematosus**

Author information

Vista ES1, Crowe SR, Thompson LF,
Air GM, Robertson JM, Guthridge JM, James JA.

1. Oklahoma Medical Research Foundation, Oklahoma City, OK 73104,
USA

Abstract

BACKGROUND

Antiphospholipid syndrome is characterized by autoantibodies against cardiolipins (aCL), lupus anticoagulant, and independent B2-glycoprotein (B2GPI). Controversy exists as to whether vaccination triggers the development of antiphospholipid antibodies (aPL) in patients with systemic lupus erythematosus (SLE).

METHODS

Patients with SLE (101) and matched controls (101) were enrolled from 2005-2009 and received seasonal influenza vaccinations. Sera were tested by ELISA for aCL at baseline, 2, 6, and 12 weeks after vaccination. Vaccine responses were ranked according to an overall anti-influenza antibody response index. Individuals with positive aCL were further tested for B2GPI antibodies.

RESULTS

Patients with SLE and healthy controls can develop new-onset aCL post vaccination, although at rates which do not differ between patients and controls (12/101 cases and 7/101 controls, OR 1.81, $p = 0.34$). New-onset moderate aCL are slightly enriched in African American SLE patients (5/36 cases; $p = 0.094$). The optical density measurements for aCL reactivity in patients were significantly higher than baseline at 2 weeks ($p < 0.05$), 6 weeks ($p < 0.05$), and 12 weeks ($p < 0.05$) post vaccination. No new B2GPI antibodies were detected among patients with new aCL reactivity. Vaccine response was not different between patients with and without new-onset aCL reactivity ($p = 0.43$).

CONCLUSIONS

This study shows transient increases in aCL, but not anti-B2GPI responses, after influenza vaccination.

“Controversy exists
as to whether vaccination
triggers the development of
antiphospholipid antibodies (aPL)
in patients with systemic lupus
erythematosus (SLE). This study
shows transient increases in aCL,
but not anti-B2GPI responses,
after influenza vaccination.”

Autoimmune response following influenza vaccination in patients with autoimmune inflammatory rheumatic disease

Author information

Perdan-Pirkmajer K1, Thallinger GG, Snoj N,

1. University Medical Centre Ljubljana
Department of Rheumatology
Ljubljana, Slovenia

Abstract

Vaccines have undoubtedly brought overwhelming benefits to mankind and are considered safe and effective. Nevertheless, they can occasionally stimulate autoantibody production or even a recently defined syndrome known as autoimmune/inflammatory syndrome induced by adjuvants (ASIA). There is scarce data regarding autoimmune response after seasonal/influenza A (H1N1) vaccine in patients with autoimmune inflammatory rheumatic disease (AIRD). The objective of our study was therefore to determine autoimmune response in a large group of AIRD patients vaccinated against seasonal and/or H1N1 influenza. We conducted a prospective cohort study with a 6-month follow-up. Two-hundred and eighteen patients with AIRD (50 vaccinated against seasonal influenza, six against H1N1, 104 against both, 58 non-vaccinated controls) and 41 apparently healthy controls (nine vaccinated against seasonal influenza, three against H1N1, 18 against both, 11 non-vaccinated controls) were included. Blood samples were taken and screened for autoantibodies [antinuclear antibody (ANA), anti-extractable nuclear antigen (anti-ENA), anticardiolipin (aCL) IgG/IgM antibodies, anti-beta 2-glycoprotein I (anti-β2GPI)] at inclusion in the study, before each vaccination, 1 month after the last vaccination and 6 months after inclusion. For non-vaccinated participants (patients and healthy controls) blood samples were taken at the time of inclusion in the study and 6 months later. We report that after the administration of seasonal/H1N1 vaccine there were mostly transient changes in autoantibody production in AIRD patients and in healthy participants. However, a small subset of patients, especially ANA-positive patients, had a tendency towards anti-ENA development. Although no convincing differences between the seasonal and H1N1 vaccines were observed, our results imply that there might be a slight tendency of the H1N1 vaccine towards aCL induction. Although seasonal and H1N1 vaccines are safe and effective, they also have the potential to induce autoantibodies in selected AIRD patients and healthy adults. Follow-up of such individuals is proposed and further research is needed.

“they [vaccines] can
occasionally stimulate
autoantibody production
or even a recently defined
syndrome known as
autoimmune/inflammatory
syndrome induced by
adjuvants (ASIA).”

Aluminum as an adjuvant in Crohn's disease induction

Author information

Lerner A.

Pediatric Gastroenterology and Nutrition Unit
Carmel Medical Center, Haifa, Israel
lerner_aaron@clalit.org.il

Abstract

Alum (AlK(SO₄)(₂)) is an adjuvant commonly utilized in vaccines, and is a ubiquitous element used extensively in contemporary life. Food, air, water, waste, the earth's surface, and pharmaceuticals all represent pathways of aluminum (Al) exposure. Crohn's disease (CD) is a chronic relapsing intestinal inflammation in genetically susceptible individuals and is caused by yet unidentified environmental factors. Al is a potential factor for the induction of inflammation in CD, and its immune activities share many characteristics with the immune pathology of CD: many luminal bacterial or dietary compounds can be adsorbed to the metal surface and induce Th1 profile cytokines, shared cytokines/chemokines, co-stimulatory molecules, and intracellular pathways and stress-related molecular expression enhancement, affecting intestinal microbiota, trans-mural granuloma formation, and colitis induction in an animal CD model. The inflammasome plays a central role in Al mode of action and in CD pathophysiology. It is suggested that Al adjuvant activity can fit between the aberrations of innate and adaptive immune responses occurring in CD. The CD mucosa is confronted with numerous inappropriate bacterial components adsorbed on the Al compound surface, constituting a pro-inflammatory supra-adjuvant. Al fits the diagnostic criteria of the newly described autoimmune/inflammatory syndrome induced by adjuvants. If a cause and effect relationship can be established, the consequences will greatly impact public health and CD prevention and management.

<http://www.ncbi.nlm.nih.gov/pubmed/22235058>

“The inflammasome plays a central role in Aluminum mode of action and in Crohn's Disease (CD) pathophysiology. It is suggested that Aluminum adjuvant activity can fit between the aberrations of innate and adaptive immune responses occurring in Crohn's Disease. The CD mucosa is confronted with numerous inappropriate bacterial components adsorbed on the Aluminum compound surface, constituting a pro-inflammatory supra-adjuvant. Aluminum fits the diagnostic criteria ...”

Adjuvant immunization induces high levels of pathogenic antiphospholipid antibodies in genetically prone mice: another facet of the ASIA syndrome

Author information

Katzav A1, Kivity S, Blank M, Shoenfeld Y, Chapman J.

Department of Neurology and Sagol Center for Neurosciences
Sheba Medical Center, affiliated to the Sackler Faculty of Medicine
Tel Aviv University, Tel Aviv, Israel
avivakatzav@gmail.com

Abstract

Adjuvants may induce autoimmune diseases in susceptible individuals, a phenomenon recently defined as autoimmune/inflammatory syndrome induced by adjuvants (ASIA). Patients with both antiphospholipid antibodies (aPL) and the genetic coagulopathy factor V Leiden (FVL) are frequently found. We therefore evaluated whether adjuvant can induce aPL in heterozygous FVL mice. aPL were measured in naïve mice and at 1 and 5 months after immunization with either complete or incomplete Freund's adjuvant (CFA, IFA) in FVL and control C57/B6 background mice. We defined antibody levels 3 SD above the mean of C57/B6 mice immunized with adjuvant as positive (specificity of 99%). For B(2)GPI-dependent aPL, 28.6% (6/21) of FVL mice 5 months after immunization with adjuvant (both IFA and CFA) were positive compared with 4.8% (1/22) of FVL mice 1 month after adjuvant and 0% of naïve FVL and C57/B6 mice (0/16, $p < 0.001$). aPL levels correlated with behavioral hyperactivity in the staircase test. FVL mice immunized with adjuvant did not develop B(2)GPI-independent aPL. We hypothesize that the FVL aPL association is not a coincidence, but that chronic coagulation defects combined with external inflammatory stimuli analogous to adjuvant may induce aPL and also antiphospholipid syndrome, thus supporting the notion of ASIA.

<http://www.ncbi.nlm.nih.gov/pubmed/22235055>

“Adjuvants may induce
autoimmune diseases in susceptible individuals,
a phenomenon recently defined as autoimmune/
inflammatory syndrome induced by adjuvants (ASIA).”

Autoimmunity following hepatitis B vaccine
as part of the spectrum of ‘Autoimmune (Auto-inflammatory) Syndrome
induced by Adjuvants’ (ASIA):
analysis of 93 cases

Author information

Zafirir Y1, Agmon-Levin N, Paz Z, Shilton T, Shoenfeld Y.
The Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel

Abstract

OBJECTIVES

In this study we analyzed the clinical and demographic manifestations among patients diagnosed with immune/autoimmune-mediated diseases post-hepatitis B vaccination. We aimed to find common denominators for all patients, regardless of different diagnosed diseases, as well as the correlation to the criteria of Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants (ASIA).

PATIENTS AND METHODS

We have retrospectively analyzed the medical records of 114 patients, from different centers in the USA, diagnosed with immune-mediated diseases following immunization with hepatitis-B vaccine (HBVv). All patients in this cohort sought legal consultation. Of these, 93/114 patients diagnosed with disease before applying for legal consultation were included in the study. All medical records were evaluated for demographics, medical history, number of vaccine doses, peri-immunization adverse events and clinical manifestations of diseases. In addition, available blood tests, imaging results, treatments and outcomes were recorded. Signs and symptoms of the different immune-mediated diseases were grouped according to the organ or system involved. ASIA criteria were applied to all patients.

RESULTS

The mean age of 93 patients was 26.5 ± 15 years; 69.2% were female and 21% were considered autoimmune susceptible. The mean latency period from the last dose of HBVv and onset of symptoms was 43.2 days. Of note, 47% of patients continued with the immunization program despite experiencing adverse events. Manifestations that were commonly reported included neuro-psychiatric (70%), fatigue (42%) mucocutaneous (30%), musculoskeletal (59%) and gastrointestinal (50%) complaints. Elevated titers of autoantibodies were documented in 80% of sera tested. In this cohort 80/93 patients (86%), comprising 57/59 (96%) adults and 23/34 (68%) children, fulfilled the required criteria for ASIA.

CONCLUSIONS

Common clinical characteristics were observed among 93 patients diagnosed with immune-mediated conditions post-HBVv, suggesting a common denominator in these diseases. In addition, risk factors such as history of autoimmune diseases and the appearance of adverse event(s) during immunization may serve to predict the risk of post-immunization diseases. The ASIA criteria were found to be very useful among adults with post-vaccination events. The application of the ASIA criteria to pediatric populations requires further study.

“Manifestations that were commonly reported included neuro-psychiatric (70%), fatigue (42%) mucocutaneous (30%), musculoskeletal (59%) and gastrointestinal (50%) complaints.”

Macrophagic myofasciitis: characterization and pathophysiology

Author information

Gherardi RK1, Authier FJ.

1. AP-HP, Hôpital H. Mondor, France

Abstract

Aluminium oxyhydroxide (alum), a nanocrystalline compound forming agglomerates, has been used in vaccines for its immunological adjuvant effect since 1927. Alum is the most commonly used adjuvant in human and veterinary vaccines, but the mechanisms by which it stimulates immune responses remain incompletely understood. Although generally well tolerated, alum may occasionally cause disabling health problems in presumably susceptible individuals. A small proportion of vaccinated people present with delayed onset of diffuse myalgia, chronic fatigue and cognitive dysfunction, and exhibit very long-term persistence of alum-loaded macrophages at the site of previous intramuscular (i.m.) immunization, forming a granulomatous lesion called macrophagic myofasciitis (MMF). Clinical symptoms associated with MMF are paradigmatic of the recently delineated ‘autoimmune/inflammatory syndrome induced by adjuvants’ (ASIA). The stereotyped cognitive dysfunction is reminiscent of cognitive deficits described in foundry workers exposed to inhaled Al particles. Alum safety concerns will largely depend on whether the compound remains localized at the site of injection or diffuses and accumulates in distant organs. Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22235051>

“Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain.”

Gulf War syndrome
as a part of the
autoimmune (autoinflammatory) syndrome
induced by adjuvant (ASIA)

Author information

Israeli E.

1. The Zabłudowicz Center for Autoimmune Diseases
Chaim Sheba Medical Center, Tel-Hashomer, Israel
eitanister@gmail.com

Abstract

Gulf War syndrome (GWS) is a multi-symptom condition comprising a variety of signs and symptoms described in the literature, which not been fully resolved. The various symptoms of the condition include muscle fatigue and tiredness, malaise, myalgia, impaired cognition, ataxia, diarrhoea, bladder dysfunction, sweating disturbances, headaches, fever, arthralgia, skin rashes, and gastrointestinal and sleep disturbances. In addition, excessive chemical sensitivity and odour intolerance is reported. The aetiology of the condition is unclear, but many reviews and epidemiological analyses suggest association with pyridostigmine bromide (PB), certain vaccination regimes, a variety of possible chemical exposures, including smoke from oil-well fires or depleted uranium from shells, as well as physical and psychological stress. Recently, Shoenfeld et al. suggested that four conditions--siliconosis, macrophagic myofasciitis (MMF), GWS and post-vaccination phenomena--that share clinical and pathogenic resemblances, may be incorporated into common syndrome called 'Autoimmune (Autoinflammatory) Syndrome induced by Adjuvants' (ASIA). Symptoms and signs of the four conditions described by Shoenfeld et al. show that at least eight out of ten main symptoms are in correlation in all four conditions. Namely, myalgia, arthralgias, chronic fatigue, neurological cognitive impairment, gastrointestinal symptoms, respiratory symptoms, skin manifestations and appearance of autoantibodies. Regardless of the aetiology of GWS, be it exposure to environmental factors or chemical drugs, vaccinations or the adjuvants in them, GWS fits well with the definition of ASIA and is included as part of 'Shoenfeld's syndrome'.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22235052>

“Recently, Shoenfeld et al. suggested that four conditions—siliconosis, macrophagic myofasciitis (MMF), GWS and post-vaccination phenomena—that share clinical and pathogenic resemblances, may be incorporated into common syndrome called ‘Autoimmune (Autoinflammatory) Syndrome induced by Adjuvants’ (ASIA). Symptoms and signs of the four conditions described by Shoenfeld et al. show that at least eight out of ten main symptoms are in correlation in all four conditions. Namely, myalgia, arthralgias, chronic fatigue, neurological cognitive impairment, gastrointestinal symptoms, respiratory symptoms, skin manifestations and appearance of autoantibodies.”

Vaccine model of antiphospholipid syndrome induced by tetanus vaccine

Institute of Virology, Vaccines and Sera-Torlak
Department of Research and Development, Belgrade, Serbia
ljiljana.dimitrijevic@gmail.com

Abstract

Successful induction of antiphospholipid syndrome (APS) in two different non-autoimmune prone mouse strains, BALB/c and C57BL/6, was achieved by tetanus toxoid (TTd) hyperimmunization using different adjuvants (glycerol or aluminium hydroxide), and different adjuvant pretreatments (glycerol or Complete Freund's Adjuvant (CFA)). APS had different manifestations of reproductive pathology in BALB/c and C57BL/6 mice: fetal resorption (as a consequence of extreme T-cell activation obtained in the course of pretreatment), and lowering of fecundity (as a consequence of polyclonal B-cell stimulation), respectively. In BALB/c mice fetal resorption coincided with glycerol and CFA pretreatments, while in C57BL/6 mice lowering of fecundity was most obvious in CFA-pretreated mice immunized with TTd in aluminium hydroxide. Both molecular mimicry and polyclonal B-cell activation occur in APS induction, with molecular mimicry effects being dominant in BALB/c mice, and polyclonal cell activation being dominant in C57BL/6 mice. Confirmation of molecular mimicry effects, which in the condition of T-cell stimulation generated fetal resorptions in the BALB/c strain, was achieved by passive infusion of monoclonal antibody (MoAb) T-26 specific for TTd and anti- $\alpha(2)$ -glycoprotein I obtained after TTd hyperimmunization. High polyclonal B-cell activation in C57BL/6 mice prevented fetal resorption but induced fecundity lowering, as was the case in passive administration of MoAb T-26 in this mouse strain. Passive infusion of anti-idiotypic MoAb Y7 into C57BL/6 mice induced fetal resorptions and confirmed the above suggestion on the protective role of polyclonal B-cell stimulation in fetal resorptions.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22235053>

“Successful induction of antiphospholipid syndrome (APS) in two different non-autoimmune prone mouse strains ... was achieved by tetanus toxoid (TTd) hyperimmunization using different adjuvants (glycerol or aluminium hydroxide), and different adjuvant pretreatments (glycerol or Complete Freund's Adjuvant (CFA)).”

Oily adjuvants and autoimmunity: now time for reconsideration?

Author information

Whitehouse M.

School of Medicine, Griffith University
Gold Coast, Queensland, Australia
whitehousemd@spin.net.au

Abstract

Immunologists have relied heavily on oil-based adjuvants to generate antibodies or induce auto-allergic responses in experimental animals. These are rarely used today for human vaccination because of their persistent irritancies and propensity to cause ulcers at sites of injection. However oily materials with adjuvant properties abound in our modern environment, both personal and extraneous. Their inadvertent impact as cryptotoxins may contribute to the rising incidence of auto-allergic diseases in recent times. Experimentally, the potential adjuvanticity of various oils, fats and other lipids can be evaluated by their ability (or otherwise) to induce auto-allergic disease(s) in rats and mice with, or even without, the addition of a mycobacterial immunostimulant. Genetic factors have been recognized that determine an animal's susceptibility or resistance to these oil-induced immunopathies. So it may be profitable to further characterize these factors, first in animals and then perhaps in human populations, to help find ways to enhance natural resistance to those adjuvant-active oils that may be widely distributed in the personal environment, notably mineral oil(s). (The six tables in this article summarize some relevant facts and a few conjectures.) A caveat: This review is restricted to the adjuvant properties of some oils in the personal environment. It does not cover the mechanisms of adjuvanticity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22235056>

“Immunologists have relied heavily on oil-based adjuvants to generate antibodies or induce auto-allergic responses in experimental animals. These are rarely used today for human vaccination because of their persistent irritancies and propensity to cause ulcers at sites of injection. However oily materials with adjuvant properties abound in our modern environment, both personal and extraneous. Their inadvertent impact as cryptotoxins may contribute to the rising incidence of auto-allergic diseases in recent times.”

Induction of the 'ASIA' syndrome in NZB/NZWF1 mice after injection of complete Freund's adjuvant (CFA)

Author information

Bassi N1, Luisetto R, Del Prete D,
Ghirardello A, Ceol M, Rizzo S, Iaccarino L,
Gatto M, Valente ML, Punzi L, Doria A.

Division of Rheumatology
Department of Clinical and Experimental Medicine
University of Padova, Italy

Abstract

Adjuvants, commonly used in vaccines, may be responsible for inducing autoimmunity and autoimmune diseases, both in humans and mice. The so-called 'ASIA' (Autoimmune/inflammatory Syndrome Induced by Adjuvants) syndrome has been recently described, which is caused by the exposure to a component reproducing the effect of adjuvants. The aim of our study was to evaluate the effect of injection of complete Freund's adjuvant (CFA) in NZB/NZWF1 mice, a lupus-prone murine model. We injected 10 NZB/NZWF1 mice with CFA/PBS and 10 with PBS, three times, 3 weeks apart, and followed-up until natural death. CFA-injected mice developed both anti-double-stranded DNA and proteinuria earlier and at higher levels than the control group. Proteinuria-free survival rate and survival rate were significantly lower in CFA-treated mice than in the control mice ($p = 0.002$ and $p = 0.001$, respectively). Histological analyses showed a more severe glomerulonephritis in CFA-injected mice compared with the control mice. In addition, lymphoid hyperplasia in spleen and lungs, myocarditis, and vasculitis were observed in the former, but not in the latter group. In conclusion, the injection of CFA in NZB/NZWF1 mice accelerated autoimmune manifestations resembling 'ASIA' syndrome in humans.

<http://www.ncbi.nlm.nih.gov/pubmed/22235054>

“... lymphoid hyperplasia in spleen and lungs, myocarditis, and vasculitis were observed in the former, but not in the latter group. In conclusion, the injection of Complete Freund's Adjuvant (CFA) [a vaccine ingredient] in NZB/NZWF1 mice accelerated autoimmune manifestations resembling 'ASIA' syndrome in humans.”

[complete Freund's adjuvant is used in some vaccines]

“The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate. The evidence of adverse events following immunisation with the MMR vaccine cannot be separated from its role in preventing the target diseases.”

Cochrane Database Of Systematic Reviews • February 2012

Vaccines for measles, mumps and rubella in children

Author information

Demicheli V1, Rivetti A, Debalini MG, Di Pietrantonj C.
Servizio Regionale di Riferimento per l'Epidemiologia, SSEpi-SeREMI - Cochrane Vaccines Field, Azienda Sanitaria Locale ASL AL, Alessandria, Italy
vdemicheli@aslal.it

Abstract

BACKGROUND

Mumps, measles and rubella (MMR) are serious diseases that can lead to potentially fatal illness, disability and death. However, public debate over the safety of the trivalent MMR vaccine and the resultant drop in vaccination coverage in several countries persists, despite its almost universal use and accepted effectiveness.

OBJECTIVES

To assess the effectiveness and adverse effects associated with the MMR vaccine in children up to 15 years of age.

SEARCH METHODS

For this update we searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2011, Issue 2), which includes the Cochrane Acute Respiratory Infections Group's Specialised Register, PubMed (July 2004 to May week 2, 2011) and Embase.com (July 2004 to May 2011).

SELECTION CRITERIA

We used comparative prospective or retrospective trials assessing the effects of the MMR vaccine compared to placebo, do nothing or a combination of measles, mumps and rubella antigens on healthy individuals up to 15 years of age.

DATA COLLECTION AND ANALYSIS

Two review authors independently extracted data and assessed methodological quality of the included studies. One review author arbitrated in case of disagreement.

MAIN RESULTS

We included five randomised controlled trials (RCTs), one controlled clinical trial (CCT), 27 cohort studies, 17 case-control studies, five time-series trials, one case cross-over trial, two ecological studies, six self controlled case series studies involving in all about 14,700,000 children and assessing effectiveness and safety of MMR vaccine. Based on the available evidence, one MMR vaccine dose is at least 95% effective in preventing clinical measles and 92% effective in preventing secondary cases among household contacts. Effectiveness of at least one dose of MMR in preventing clinical mumps in children is estimated to be between 69% and 81% for the vaccine prepared with Jeryl Lynn mumps strain and between 70% and 75% for the vaccine containing the Urabe strain. Vaccination with MMR containing the Urabe strain has demonstrated to be 73% effective in preventing secondary mumps cases. Effectiveness of Jeryl Lynn containing MMR in preventing laboratory-confirmed mumps cases in children and adolescents was estimated to be between 64% to 66% for one dose and 83% to 88% for two vaccine doses. We did not identify any studies assessing the effectiveness of MMR in preventing rubella. The highest risk of association with aseptic meningitis was observed within the third week after immunisation with Urabe-containing MMR (risk ratio (RR) 14.28; 95% confidence interval (CI) from 7.93 to 25.71) and within the third (RR 22.5; 95% CI 11.8 to 42.9) or fifth (RR 15.6; 95% CI 10.3 to 24.2) weeks after immunisation with the vaccine prepared with the Leningrad-Zagreb strain. A significant risk of association with febrile seizures and MMR exposure during the two previous weeks (RR 1.10; 95% CI 1.05 to 1.15) was assessed in one large person-time cohort study involving 537,171 children aged between three months and five year of age. Increased risk of febrile seizure has also been observed in children aged between 12 to 23 months (relative incidence (RI) 4.09; 95% CI 3.1 to 5.33) and children aged 12 to 35 months (RI 5.68; 95% CI 2.31 to 13.97) within six to 11 days after exposure to MMR vaccine. An increased risk of thrombocytopenic purpura within six weeks after MMR immunisation in children aged 12 to 23 months was assessed in one case-control study (RR 6.3; 95% CI 1.3 to 30.1) and in one small self controlled case series (incidence rate ratio (IRR) 5.38; 95% CI 2.72 to 10.62). Increased risk of thrombocytopenic purpura within six weeks after MMR exposure was also assessed in one other case-control study involving 2311 children and adolescents between one month and 18 years (odds ratio (OR) 2.4; 95% CI 1.2 to 4.7). Exposure to the MMR vaccine was unlikely to be associated with autism, asthma, leukaemia, hay fever, type 1 diabetes, gait disturbance, Crohn's disease, demyelinating diseases, bacterial or viral infections.

AUTHORS' CONCLUSIONS

The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate. The evidence of adverse events following immunisation with the MMR vaccine cannot be separated from its role in preventing the target diseases.

<http://www.ncbi.nlm.nih.gov/pubmed/22336803>

“Herein, we report 10 cases of previously healthy subjects who developed GCA/PMR within 3 months of influenza vaccination (Inf-V). A Medline search uncovered an additional 11 isolated cases of GCA/PMR occurring after influenza vaccination Inf-V.”

[GCA stands for giant cell arteritis and PMR stands for polymyalgia rheumatica]

Lupus • February 2012

**Giant cell arteritis and polymyalgia rheumatica
after influenza vaccination:
report of 10 cases and review of the literature**

Author information

Soriano A1, Verrecchia E, Marinaro A, Giovinale M, Fonnesu C, Landolfi R, Manna R.

Clinical Autoimmunity Unit
Catholic University of the Sacred Heart
Rome, Italy

Abstract

Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are inflammatory rheumatic diseases common in people over the age of 50 years. Herein, we report 10 cases of previously healthy subjects who developed GCA/PMR within 3 months of influenza vaccination (Inf-V). A Medline search uncovered additional 11 isolated cases of GCA/PMR occurring after Inf-V. We discuss the role of individual susceptibility, the potential function of immune adjuvants as triggers of autoimmunity post-vaccination, and the correlation of our observation with the ‘ASIA’ syndrome, i.e. autoimmune/inflammatory syndrome induced by adjuvants and including post-vaccination phenomena.

<http://www.ncbi.nlm.nih.gov/pubmed/22235046>

The spectrum of ASIA: 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants'

N Agmon-Levin, GRV Hughes, Y Shoenfeld¹

1. The Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel
2. Head, Lupus Research Unit, The Rayne Institute, St. Thomas' Hospital, London, UK
3. Sackler Faculty of Medicine, Incumbent of the Laura Schwarz-Kip, Chair for Research of Autoimmune Diseases, Tel-Aviv University, Israel
Yehuda Shoenfeld, MD, FRCP, Zabludowicz Center for Autoimmune Diseases
Chaim Sheba Medical Center, Tel-Hashomer 52621, Israel
shoenfel@post.tau.ac.il

Abstract

Physicians are often puzzled by enigmatic medical conditions or the abrupt appearance of an immune-mediated disease. Such a story was recently presented to us by a young Sheikh. A Saudi Sheikh, who suffered at the age of 27 from joint pains, rash and serological evidence of anti-Ro antibodies, was diagnosed with probable systemic lupus erythematosus (SLE) at that time. He was treated with Plaquenil for a year, but as no signs of SLE were apparent, treatment was stopped and he remained disease free for the next 12 years. At the age of 39 years, 2 weeks after immunization with the flu vaccine, his disease reemerged. This time he presented with severe arthritis and pericarditis, which required treatment with high doses of steroids.

This patient's story illustrates the acceleration of an autoimmune or immune-mediated condition following exposure to external stimuli. During the past year a new syndrome was introduced and termed ASIA, 'Autoimmune (Auto-inflammatory) Syndrome induced by Adjuvants'.¹ This syndrome assembles a spectrum of immune-mediated diseases triggered by an adjuvant stimulus.^{2 – 4} The use of medical adjuvants has become common practice and substances such as aluminum adjuvant are added to most human and animal vaccines, while the adjuvant silicone is extensively used for breast implants and cosmetic procedures. Furthermore, 'hidden adjuvants' such as infectious material or house molds have also been associated with different immune mediated conditions.^{1,5} The adjuvant effect has been recognized for years, and is broadly utilized to enhance desired antigen-specific immune responses.⁶ This effect is accomplished via mechanisms that impinge on both the innate and adaptive immune systems.^{6 – 9} Formerly, adjuvants were thought to pose little or no independent threat. Alas, studies of animal models and humans demonstrated the ability of some of them to inflict autoimmunity and immune-mediated diseases by themselves.^{2,10,11} Intriguingly, although exposure is common, adjuvant disease is relatively rare. It has been suggested that for a clinically overt adjuvant disease additional risk factors are required such as genetic susceptibilities or the co-exposure to other environmental factors.¹

This special issue of Lupus is dedicated to ASIA and contains diverse articles from different geographical areas which provide a broad view of the clinical manifestations as well as the mechanisms related to the adjuvant effect.

Disordered porphyrin metabolism: a potential biological marker for autism risk assessment

Author information

Heyer NJ1, Echeverria D, Woods JS.

Battelle Centers for Public Health Research and Evaluation
Seattle, Washington, USA

Abstract

Autism (AUT) is a complex neurodevelopmental disorder that, together with Asperger's syndrome and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS), comprises the expanded classification of autistic spectrum disorder (ASD). The heterogeneity of ASD underlies the need to identify biomarkers or clinical features that can be employed to identify meaningful subtypes of ASD, define specific etiologies, and inform intervention and treatment options. Previous studies have shown that disordered porphyrin metabolism, manifested principally as significantly elevated urinary concentrations of pentacarboxyl (penta) and coproporphyrins, is commonly observed among some children with ASD. Here, we extend these observations by specifically evaluating penta and coproporphyrins as biological indicators of ASD among 76 male children comprising 30 with validated AUT, 14 with PDD-NOS, and 32 neurotypical (NT) controls. ASD children (AUT and PDD-NOS) had higher mean urinary penta ($P < 0.006$) and copro ($P < 0.006$) concentrations compared with same-aged NT children, each characterized by a number of extreme values. Using Receiver Operating Characteristic curve analysis, we evaluated the sensitivity and specificity of penta, copro, and their combined Z-scores in ASD detection. The penta sensitivity was 30% for AUT and 36% for PDD-NOS, with 94% specificity. The copro sensitivity was 33% and 14%, respectively, with 94% specificity. The combined Z-score measure had 33% and 21% sensitivity for AUT and PDD-NOS, respectively, with 100% specificity. These findings demonstrate that porphyrin measures are strong predictors of both AUT and PDD-NOS, and support the potential clinical utility of urinary porphyrin measures for identifying a subgroup of ASD subjects in whom disordered porphyrin metabolism may be a salient characteristic.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3329579/>

“These findings demonstrate that porphyrin measures are strong predictors of both AUT and PDD-NOS, and support the potential clinical utility of urinary porphyrin measures for identifying a subgroup of ASD subjects in whom disordered porphyrin metabolism may be a salient characteristic.”

“Given all this, supporting the ‘one-size fits all’ vaccination program is neither reasonable nor ethical.”

Vaccine • March 2012

Vaccination: Why the ‘one size fits all’ vaccination argument does not fit all!

By Lucija Tomljenovic, PhD

Imagine the next time you went to Walmart, Target or Sears that due to scientific research and government regulation your retailer only stocked one size of clothing – regardless of whether you are male or female, child or adult, and with no sensitivity to your cultural or ethnic background. Would you be happy? Would you accept it? Would you wear the clothes? The answer is clearly NO! What if the clothing manufacturer used a highly toxic dye in the clothing fabric and knew this dye could cause serious skin reactions in some people but they failed to declare this? Would that be acceptable to you? Yet that is exactly what the current approach to vaccines worldwide is – one size fits all and some “collateral damage” is acceptable for the sake of the alleged “greater good”.

In the case of vaccines, the good news is that even those in the scientific community who are strong proponents of vaccinations, are coming to question the scientific legitimacy of “one-size fits all” vaccination practices. [1]

For example, Gregory Poland MD, Editor in Chief of the journal *Vaccine* and co-author of “The age-old struggle against the anti-vaccinationists” [2] and colleagues rightly ask whether:

...with the advances coming from the new biology of the 21st century. It is time to consider how might new genetic and molecular biology information inform vaccinology practices of the future? [1]

In light of this question Poland et al. conclude that “one-size fits all” approach for all vaccines and all persons should be abandoned. According to Poland, this conclusion applies to both vaccine efficacy, as well as safety.[1]

Regarding the safety, the widely held view that serious vaccine-related adverse reactions are rare needs revision, as current worldwide vaccination policies indeed operate on a “one-size fits all” assumption. This assumption persists despite the fact that historically, vaccine trials routinely exclude vulnerable individuals with a variety of pre-existing conditions (i.e., premature birth, personal or family history of developmental delay or neurologic disorders including epilepsy/seizures, hypersensitivity to vaccine constituents etc...). [3-7]

Because of such selection bias at the very base level of research, the occurrence of serious adverse reactions resulting from vaccinations is considerably underestimated.

Worse yet, such an outcome should be of concern to all who vaccinate in view of the documented scientific evidence describing cases of permanent neurodevelopmental disabilities and deaths following vaccination in children with underlying genetic/mitochondrial disorders and other susceptibilities, such as a family history of auto-immune diseases (i.e., asthma, diabetes, multiple sclerosis, etc...), allergies, or a compromised immune system. [8-10]

Poland’s along with the other scientists’ current data therefore have far broader implications for understanding vaccines, not only in terms of efficacy and the desired immune response, but also in terms of safety for those susceptible to adverse health outcomes and excluded from clinical trials --- but not from receipt!

Vulnerable individuals, both male and female, will neither have the same antibody response nor the same level of tolerance to serious adverse reactions as non-vulnerable individuals. [1, 11]

Before one considers vaccinating their child according to the current ‘one size fits all’ vaccination program, one should think about the fact that we all have a different genetic history, personal health history, current health status, nutritional status and exposures to level of environmental toxins – all of which may impact how an individual, or their child will respond to a vaccine. Given all this, supporting the ‘one-size fits all’ vaccination program is neither reasonable nor ethical.

References:

1. Poland, G.A., I.G. Ovsyannikova, and R.M. Jacobson, Vaccine immunogenetics: bedside to bench to population. *Vaccine*, 2008. 26(49): p. 6183-8.
2. Poland, G.A. and R.M. Jacobson, The age-old struggle against the antivaccinationists. *N Engl J Med*, 2011. 364(2): p. 97-9.
3. Kovel, A., et al., Safety and immunogenicity of acellular diphtheria-tetanus-pertussis and *Haemophilus conjugate* vaccines given in combination or at separate injection sites. *J Pediatr*, 1992. 120(1): p. 84-7.
4. Kaplan, S.L., et al., Immunogenicity and safety of *Haemophilus influenzae* type b-tetanus protein conjugate vaccine alone or mixed with diphtheria-tetanus-pertussis vaccine in infants. *J Pediatr*, 1994. 124(2): p. 323-7.
5. Li, G., et al., Safety and immunogenicity of a diphtheria, tetanus, acellular pertussis and *Haemophilus influenzae* Type b combination vaccine compared with separate administration of licensed equivalent vaccines in Chinese infants and toddlers for primary and booster immunization. *Vaccine*, 2010. 28(25): p. 4215-23.
6. Shinefield, H., et al., Evaluation of a quadrivalent measles, mumps, rubella and varicella vaccine in healthy children. *Pediatr Infect Dis J*, 2005. 24(8): p. 665-9.
7. Velu, V., et al., Comparative efficacy of two dosages of recombinant hepatitis B vaccine in healthy adolescents in India. *Pediatr Infect Dis J*, 2007. 26(11): p. 1038-41.
8. Poling, J.S., et al., Developmental regression and mitochondrial dysfunction in a child with autism. *J Child Neurol*, 2006. 21(2): p. 170-2.
9. Yang, Y., et al., Acute metabolic crisis induced by vaccination in seven Chinese patients. *Pediatr Neurol*, 2006. 35(2): p. 114-8.
10. Ottaviani, G., A.M. Lavezzi, and L. Maturri, Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination: another pathology in suspected SIDS? *Virchows Arch*, 2006. 448(1): p. 100-4.
11. Thomas, C. and M. Moridani, Interindividual variations in the efficacy and toxicity of vaccines. *Toxicology*, 2009. 278(2): p. 204-10.

<http://www.ncbi.nlm.nih.gov/pubmed/22119595>

“103 vaccine adjuvants have been curated in Vaxjo.

Among these adjuvants, 98 have been used in 384 vaccines stored in VIOLIN against over 81 pathogens, cancers, or allergies. All these vaccine adjuvants are categorized and analyzed based on adjuvant types, pathogens used, and vaccine types.”

Journal Of Biomedicine & Biotechnology • March 2012

**Vaxjo:
a web-based vaccine adjuvant database
and its application for analysis of vaccine adjuvants
and their uses in vaccine development**

Sayers S., Ulysses G., Xiang Z., He Y.

Unit for Laboratory Animal Medicine
University of Michigan Medical School
Ann Arbor, MI 48109 USA

Abstract

Vaccine adjuvants are compounds that enhance host immune responses to co-administered antigens in vaccines. Vaxjo is a web-based central database and analysis system that curates, stores, and analyzes vaccine adjuvants and their usages in vaccine development. Basic information of a vaccine adjuvant stored in Vaxjo includes adjuvant name, components, structure, appearance, storage, preparation, function, safety, and vaccines that use this adjuvant. Reliable references are curated and cited. Bioinformatics scripts are developed and used to link vaccine adjuvants to different adjuvanted vaccines stored in the general VIOLIN vaccine database. Presently, 103 vaccine adjuvants have been curated in Vaxjo. Among these adjuvants, 98 have been used in 384 vaccines stored in VIOLIN against over 81 pathogens, cancers, or allergies. All these vaccine adjuvants are categorized and analyzed based on adjuvant types, pathogens used, and vaccine types. As a use case study of vaccine adjuvants in infectious disease vaccines, the adjuvants used in Brucella vaccines are specifically analyzed. A user-friendly web query and visualization interface is developed for interactive vaccine adjuvant search. To support data exchange, the information of vaccine adjuvants is stored in the Vaccine Ontology (VO) in the Web Ontology Language (OWL) format.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22505817>

AS03 adjuvanted AH1N1 vaccine associated with an abrupt increase in the incidence of childhood narcolepsy in Finland

Author information

Nohynek H1, Jokinen J, Partinen M, Vaarala O, Kirjavainen T, Sundman J, Himanen SL, Hublin C, Julkunen I, Olsén P, Saarenpää-Heikkilä O, Kilpi T.
Department of Vaccines and Immune Protection
National Institute for Health and Welfare, Helsinki, Finland
hanna.nohynek@thl.fi

Abstract

BACKGROUND

Narcolepsy is a chronic sleep disorder with strong genetic predisposition causing excessive daytime sleepiness and cataplexy. A sudden increase in childhood narcolepsy was observed in Finland soon after pandemic influenza epidemic and vaccination with AS03-adjuvanted Pandemrix. No increase was observed in other age groups.

METHODS

Retrospective cohort study. From January 1, 2009 to December 31, 2010 we retrospectively followed the cohort of all children living in Finland and born from January 1991 through December 2005. Vaccination data of the whole population was obtained from primary health care databases. All new cases with assigned ICD-10 code of narcolepsy were identified and the medical records reviewed by two experts to classify the diagnosis of narcolepsy according to the Brighton collaboration criteria. Onset of narcolepsy was defined as the first documented contact to health care because of excessive daytime sleepiness. The primary follow-up period was restricted to August 15, 2010, the day before media attention on post-vaccination narcolepsy started.

FINDINGS

Vaccination coverage in the cohort was 75%. Of the 67 confirmed cases of narcolepsy, 46 vaccinated and 7 unvaccinated were included in the primary analysis. The incidence of narcolepsy was 9.0 in the vaccinated as compared to 0.7/100,000 person years in the unvaccinated individuals, the rate ratio being 12.7 (95% confidence interval 6.1-30.8). The vaccine-attributable risk of developing narcolepsy was 1:16,000 vaccinated 4 to 19-year-olds (95% confidence interval 1:13,000-1:21,000).

CONCLUSIONS

Pandemrix vaccine contributed to the onset of narcolepsy among those 4 to 19 years old during the pandemic influenza in 2009-2010 in Finland. Further studies are needed to determine whether this observation exists in other populations and to elucidate potential underlying immunological mechanism. The role of the adjuvant in particular warrants further research before drawing conclusions about the use of adjuvanted pandemic vaccines in the future.

<http://www.ncbi.nlm.nih.gov/pubmed/22470453>

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3314666/>

“Pandemrix vaccine

contributed to the onset of narcolepsy

among those 4 to 19 years old during the

pandemic influenza in 2009-2010 in Finland.

The role of the adjuvant in particular warrants

further research before drawing conclusions about

the use of adjuvanted pandemic vaccines in the future.”

Guillain-Barré syndrome a classical autoimmune disease triggered by infection or vaccination

Author information

Israeli E1, Agmon-Levin N,
Blank M, Chapman J, Shoenfeld Y.

The Chaim Zabludowicz Center for Autoimmune Diseases
Sheba Medical Center, Tel-Hashomer, Tel-Aviv, Israel

Abstract

Guillain-Barré syndrome (GBS) is a rare autoimmune disorder, the incidence of which is estimated to be 0.6-4/100,000 person/year worldwide. Often, GBS occurs a few days or weeks after the patient has had symptoms of a respiratory or gastrointestinal microbial infection. The disorder is sub-acute developing over the course of hours or days up to 3 to 4 weeks. About a third of all cases of Guillain-Barré syndrome are preceded by *Campylobacter jejuni* infection. *C. jejuni* strains isolated from GBS patients have a lipooligosaccharide (LOS) with a GM1-like structure. Molecular mimicry between LOS and the peripheral nerves as a cause of GBS was demonstrated in animal models of human GBS. Following the “swine flu” virus vaccine program in the USA in 1976, an increase in incidence of GBS was observed and the calculated relative risk was 6.2. Later studies have found that influenza vaccines contained structures that can induce anti-GM1 (ganglioside) antibodies after inoculation into mice. More recent information has suggested that the occurrence of GBS after currently used influenza and other vaccines is rare. GBS involves genetic and environmental factors, may be triggered by infections or vaccinations, and predisposition can be predicted by analyzing some of these factors.

<http://www.ncbi.nlm.nih.gov/pubmed/20890797>

“ Guillain-Barré syndrome involves genetic and environmental factors, may be triggered by infections or vaccinations, and predisposition can be predicted by analyzing some of these factors.”

In vitro induction of apoptosis, necrosis and genotoxicity by cosmetic preservatives: application of flow cytometry as a complementary analysis by NRU

Author information

Carvalho CM1, Menezes PF, Letenski GC, Praes CE, Feferman IH, Lorencini M.

Grupo Boticário
Research and Innovation Department
Biomolecular Research Laboratory
Av. Rui Barbosa no. 3450, 83.065-260
São José dos Pinhais, PR- Brazil
camilamc@grupoboticario.com.br

Abstract

Preservatives are used in cosmetics to prevent microbial contamination; however, some preservatives are not free of allergenic and cytotoxic potential. Allergenicity and cytotoxicity potential values are major aspects of preservative safety, which determine limitations and maximum concentration dose in a cosmetic product. The purpose of this study was to investigate and compare the in vitro apoptosis, necrosis and genotoxicity-inducing potential of five different types of preservatives: Phenoxyethanol (PE), Propylparaben (PP), Methylparaben (MP), Benzyl Alcohol (BA) and Ethylhexyl Glycerine (EG). In vitro experiments were carried out on human dermal fibroblasts by a quantitative flow cytometry method, using specific cell markers (Annexin V, Propidium Iodide and H2AX). We compared the resulting cell viability by means of neutral red uptake (NRU) and established the IC(50). Our results showed that PE, PP, MP and BA have similar cytotoxic mechanisms (high apoptosis and necrosis levels only at the test concentration of 1%), whereas EG showed only an apoptosis pathway. For genotoxicity, both parabens yielded the highest values. Results obtained by flow cytometry for necrosis were comparable to those produced by NRU; however, NRU does not distinguish apoptosis from necrosis. We propose that flow cytometry is a more sophisticated methodology for understanding the cytotoxic mechanisms of cosmetic preservatives and can be used to complement the NRU.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22118339>

“Our results showed that
Phenoxyethanol [a vaccine ingredient] ...
have similar cytotoxic mechanisms
(high apoptosis and necrosis levels only
at the test concentration of 1%) ...”

Dermatitis • May 2012

Hypersensitivity reactions to vaccine constituents: a case series and review of the literature

Author information

Leventhal JS1, Berger EM, Brauer JA, Cohen DE.

Ronald O. Perelman Department of Dermatology
New York University School of Medicine, NY, USA

Abstract

Vaccines are composed of immunogens, preservatives, adjuvants, antibiotics, and manufacturing by-products. Components of vaccines may rarely elicit adverse reactions in susceptible individuals, thus raising concerns regarding vaccine safety. In this report, we add to the medical literature 3 cases of cutaneous delayed-type hypersensitivity to the vaccine preservative aluminum. We provide a review of major constituents in vaccines that have elicited immediate-type or delayed-type hypersensitivity reactions and describe their clinical manifestations. We include a table of the Food and Drug Administration-approved vaccines, which lists the quantities of major components including ovalbumin (egg protein), gelatin, aluminum, neomycin, 2-phenoxyethanol, thimerosal, and formaldehyde. Our goals were to inform physicians on the variety of hypersensitivity reactions to common vaccines and to provide information on the choice of vaccines in patients with suspected hypersensitivity.

<http://www.ncbi.nlm.nih.gov/pubmed/22653170>

“Our goals were to inform physicians on the variety of hypersensitivity reactions to common vaccines and to provide information on the choice of vaccines in patients with suspected hypersensitivity.”

Hypersensitivity reaction to human papillomavirus vaccine due to polysorbate 80

Author information

Badiu I1, Geuna M, Heffler E, Rolla G.

Allergy and Clinical Immunology
University of Torino and AO Ordine Mauriziano
Torino, Italy

Abstract

A 17-year-old girl reported generalised urticaria, eyelid angioedema, rhino-conjunctivitis, dyspnoea and wheezing 1 h after third intramuscular administration of quadrivalent human papilloma virus vaccine (Gardasil). She was treated with antihistamine, and corticosteroids with prompt relief of rhinitis and dyspnoea, while urticaria and angioedema lasted 24 h. Intradermal test with Gardasil, which contains polysorbate 80 (PS80), resulted positive, while skin tests with the bivalent vaccine were negative. Prick test performed with PS80 resulted positive in the patient and negative in ten healthy controls. The CD203 basophil activation test result was negative for PS80 at all the tested dilutions and specific IgE was not found. As flu vaccine was recommended, the authors skin tested two flu vaccine, one containing PS80 (Fluarix, GSK), which resulted positive and another flu vaccine with no adjuvant or preservative (Vaxigrip, Sanofi Pasteur MSD), which gave negative results. The patient then received Vaxigrip without adverse reactions.

Full Report:

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3351639/>

“... the authors skin tested two flu vaccine, one containing PS80 (Fluarix, GSK), which resulted positive and another flu vaccine with no adjuvant or preservative (Vaxigrip, Sanofi Pasteur MSD), which gave negative results.”

“With herd immunity to whooping cough,
DTP is associated with higher mortality for girls.”

BMJ Open • May 2012

Testing the hypothesis that diphtheria–tetanus–pertussis vaccine has negative non-specific and sex-differential effects on child survival in high-mortality countries

Author Information

Peter Aaby,^{1,2} Christine Benn,^{1,2} Jens Nielsen,^{1,2} Ida Maria
Lisse,^{1,2} Amabelia Rodrigues,^{1,2} and Henrik Ravn^{1,2}

1. Bandim Health Project, INDEPTH Network,
Statens Serum Institut, Bissau, Guinea-Bissau
2. Research Centre for Vitamins and Vaccines (CVIVA), Bandim
Health Project, Statens Serum Institut, Copenhagen, Denmark

Abstract

Background

Measles vaccines (MV) have sex-differential effects on mortality not explained by protection against measles infection.

Objective

The authors examined whether whole-cell diphtheria–tetanus–pertussis (DTP) vaccine has sex-differential and non-specific effects.

Data sources and eligibility

Following previous reviews and a new search, the effect of DTP on mortality up to the next vaccination was assessed in all studies where DTP was given after BCG or DTP was given after MV and there was prospective follow-up after ascertainment of vaccination status.

Setting

High-mortality countries in Africa and Asia.

Methods

The initial observation of negative effect of DTP generated six hypotheses, which were examined in all available studies and two randomised trials reducing the time of exposure to DTP.

Main outcome

Consistency between studies.

Results

In the first study, DTP had negative effects on survival in contrast to the beneficial effects of BCG and MV. This pattern was repeated in the six other studies available. Second, the two ‘natural experiments’ found significantly higher mortality for DTP-vaccinated compared with DTP-unvaccinated children. Third, the female–male mortality ratio was increased after DTP in all nine studies; in contrast, the ratio was decreased after BCG and MV in all studies. Fourth, the increased female mortality associated with high-titre measles vaccine was found only among children who had received DTP after high-titre measles vaccine. Fifth, in six randomised trials of early MV, female but not male mortality was increased if DTP was likely to be given after MV. Sixth, the mortality rate declined markedly for girls but not for boys when DTP-vaccinated children received MV. The authors reduced exposure to DTP as most recent vaccination by administering a live vaccine (MV and BCG) shortly after DTP. Both trials reduced child mortality.

Conclusions

These observations are incompatible with DTP merely protecting against the targeted diseases. With herd immunity to whooping cough, DTP is associated with higher mortality for girls. Randomised studies of DTP are warranted to measure the true impact on survival.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3364456/>

Hepatitis B vaccine induces apoptotic death in Hepa1-6 cells

Author information

Hamza H1, Cao J, Li X, Li C, Zhu M, Zhao S.

Key Lab of Agricultural Animal Genetics
Breeding, and Reproduction of Ministry of Education
College of Animal Science and Technology
Huazhong Agricultural University, Wuhan
People's Republic of China
Heyam68_hamza@yahoo.com

Abstract

Vaccines can have adverse side-effects, and these are predominantly associated with the inclusion of chemical additives such as aluminum hydroxide adjuvant. The objective of this study was to establish an in vitro model system amenable to mechanistic investigations of cytotoxicity induced by hepatitis B vaccine, and to investigate the mechanisms of vaccine-induced cell death. The mouse liver hepatoma cell line Hepa1-6 was treated with two doses of adjuvanted (aluminium hydroxide) hepatitis B vaccine (0.5 and 1 µg protein per ml) and cell integrity was measured after 24, 48 and 72 h. Hepatitis B vaccine exposure increased cell apoptosis as detected by flow cytometry and TUNEL assay. Vaccine exposure was accompanied by significant increases in the levels of activated caspase 3, a key effector caspase in the apoptosis cascade. Early transcriptional events were detected by qRT-PCR. We report that hepatitis B vaccine exposure resulted in significant upregulation of the key genes encoding caspase 7, caspase 9, Inhibitor caspase-activated DNase (ICAD), Rho-associated coiled-coil containing protein kinase 1 (ROCK-1), and Apoptotic protease activating factor 1 (Apaf-1). Upregulation of cleaved caspase 3,7 were detected by western blot in addition to Apaf-1 and caspase 9 expressions argues that cell death takes place via the intrinsic apoptotic pathway in which release of cytochrome c from the mitochondria triggers the assembly of a caspase activation complex. We conclude that exposure of Hepa1-6 cells to a low dose of adjuvanted hepatitis B vaccine leads to loss of mitochondrial integrity, apoptosis induction, and cell death, apoptosis effect was observed also in C2C12 mouse myoblast cell line after treated with low dose of vaccine (0.3, 0.1, 0.05 µg/ml). In addition In vivo apoptotic effect of hepatitis B vaccine was observed in mouse liver.

<http://www.ncbi.nlm.nih.gov/pubmed/22249285>

“We conclude that exposure of Hepa1-6 cells to a low dose of adjuvanted hepatitis B vaccine leads to loss of mitochondrial integrity, apoptosis induction, and cell death, apoptosis effect was observed also in C2C12 mouse myoblast cell line after treated with low dose of vaccine (0.3, 0.1, 0.05 µg/ml). In addition In vivo apoptotic effect of hepatitis B vaccine was observed in mouse liver.”

“We will discuss the possible mechanisms which pertain to ASIA (Shoenfeld syndrome).”

Lupus • June 2012

**When APS (Hughes syndrome)
met the autoimmune/inflammatory syndrome induced by adjuvants
(ASIA)**

Blank M1, Israeli E, Shoenfeld Y.

Zabludowitz Center for Autoimmune Diseases
Sheba Medical Center affiliated to Sackler Faculty of Medicine
Tel-Aviv University, Israel

Abstract

Vaccination of healthy individuals is the most effective approach to protect the public from infections and prevent the spread of many infectious diseases all over the globe. Licensed vaccines are mostly safe, but in rare cases they may be associated with humoral response to self-antigens due to molecular mimicry, epitope spread, bystander activation or polyclonal triggering. Moreover, the clinical picture of autoimmune conditions following post-vaccination is rarer. Nevertheless, anecdotal case reports on the flare of autoimmune response with clinical manifestations were reported. Herein, we discuss this topic in relation to post-vaccination-induced antiphospholipid antibodies following tetanus toxoid vaccine, HBV and influenza associated in rare cases with antiphospholipid syndrome clinical manifestations. We will discuss the possible mechanisms which pertain to ASIA (Shoenfeld syndrome). Therefore, these all strengthen the importance of ASIA and should be kept in mind during clinical work and research.

Full Report

<http://lup.sagepub.com/content/21/7/711.long>

Neurotoxic metal coexposures and neurodevelopment

José G. Dórea

Faculty of Health Sciences, Universidade de Brasília, Brasília, Brazil
E-mail: dorea@rudah.com.br

Abstract

Claus Henn et al. (2012) addressed a “real world scenario” of exposure to multiple neurotoxic metals in their unique and interesting study. They investigated manganese–lead coexposure and its association with neurodevelopmental deficiencies in Mexican children. Their rationale was that neurodevelopmental deficiencies of both metals together could be more severe than expected based on effects of exposure to each metal alone. Indeed, they observed a synergism between manganese and lead. Given the early age of the subjects (12 and 24 months of age), I suggest that some confounders not included in their model deserve consideration in regard to this study.

Claus Henn et al. (2012) collected information on duration of breast-feeding, but it seems that in their statistical analyses, they adjusted only for sex, gestational age, hemoglobin, maternal IQ (intelligence quotient), and maternal education. Other confounders, such as thimerosal (a compound containing ethylmercury that is used as a preservative in some vaccines) and breast-feeding, may influence neurodevelopment outcomes. In countries such as Mexico, children 12–24 months of age may be immunized with thimerosal-containing vaccines (TCVs) (WHO 2011). Because of opposite effects on the central nervous system, the combination of breast-feeding and ethylmercury may influence neurodevelopmental outcomes. Kramer et al. (2008) showed that children who were exclusively breast-fed had improved cognitive development. Indeed, Kostial et al. (1978) demonstrated that infant rats fed cow’s milk diets absorbed more lead and manganese, which are associated with a higher relative retention of mercury in the brain.

Blood levels of lead and manganese are indicators of ongoing exposure; however, ethylmercury has a short half-life and thus is unlikely to be concurrently measured

in blood (Dórea et al. 2011). Nevertheless we can ascertain exposure from vaccination cards (Dórea et al. 2012; Marques et al. 2009). Following participants in the National Immunization Program of Mexico, the amount of ethylmercury from routine immunizations against hepatitis B (three doses), DTP (diphtheria, tetanus, and pertussis, three doses), and influenza can be estimated from records on vaccination cards. Additionally, during pregnancy, Mexican mothers may receive tetanus toxoid (TT) vaccines and other products, such as anti-RhoD immune globulins (given to Rh-negative mothers) that may contain thimerosal (Marques et al. 2009). These sources of prenatal and postnatal ethylmercury exposure should be considered significant sources of an additional neurotoxic coexposure—organic mercury.

Claus Henn et al. (2012) realized that information on the association of neurodevelopment and coexposure to multiple chemicals is limited; the scientific literature is even more scarce for the specific exposure to small amounts of ethylmercury derived from TCVs (Oken and Bellinger 2008), which are largely used in nonindustrialized countries. However, recent work has suggested that when studies with young children are properly adjusted for exposure to TCVs, subtle neurodevelopmental effects can be demonstrated (Dórea et al. 2012; Marques et al. 2009; Mrozek-Budzyn 2011a, 2011b). Therefore, the potential for interaction of ethylmercury, manganese, and lead provides an opportunity to expand our knowledge.

Factors related to maternal neurotoxic exposure and neurodevelopment (e.g., breast-feeding) are significant in studies of children’s exposure to ethylmercury (Marques et al. 2009). The study design used by Claus Henn et al. (2012) could provide further information on this timely issue and also provide direction for future studies of contaminants and confounders that affect neurodevelopment.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3385458/>

“Claus Henn et al. (2012) realized that information on the association of neurodevelopment and coexposure to multiple chemicals is limited; the scientific literature is even more scarce for the specific exposure to small amounts of ethyl mercury derived from Thimerosal containing vaccines, which are largely used in nonindustrialized countries.”

A case of multiple sclerosis improvement following removal of heavy metal intoxication: lessons learnt from Matteo's case

Author information

Fulgenzi A1, Zanella SG, Mariani MM, Vietti D, Ferrero ME.

Dipartimento di Morfologia Umana e Scienze Biomediche Città Studi
Università degli Studi di Milano, Via L. Mangiagalli, 31, 20133 Milan, Italy
alessandro.fulgenzi@unimi.it

Abstract

Multiple sclerosis (MS) is a chronic progressive disease of the central nervous system (CNS) provoking disability and neurological symptoms. The exact causes of MS are unknown, even if it is characterized by focal inflammatory lesions in CNS accompanied by autoimmune reaction against myelin. Indeed, many drugs able to modulate the immune response of patients have been used to treat MS. More recently, toxic metals have been proposed as possible causes of neurodegenerative diseases. The objective of this study is to investigate in vivo the impact of heavy metal intoxication in MS progression. We studied the case of a patient affected by MS, who has been unsuccessfully treated for some years with current therapies. We examined his levels of toxic heavy metals in the urine, following intravenous "challenge" with the chelating agent calcium disodium ethylene diamine tetraacetic acid (EDTA). The patient displayed elevated levels of aluminium, lead and mercury in the urine. Indeed, he was subjected to treatment with EDTA twice a month. Under treatment, the patient revealed in time improved symptoms suggestive of MS remission. The clinical data correlated with the reduction of heavy metal levels in the urine to normal range values. Our case report suggests that levels of toxic metals can be tested in patients affected by neurodegenerative diseases as MS.

<http://www.ncbi.nlm.nih.gov/pubmed/22438029/>

“More recently, toxic metals have been proposed as possible causes of neurodegenerative diseases.”

“Being protected against influenza, trivalent inactivated influenza vaccine recipients may lack temporary non-specific immunity that protected against other respiratory viruses.”

Clinical Infectious Disease • June 2012

Increased risk of noninfluenza respiratory virus infections associated with receipt of inactivated influenza vaccine

Author information

Cowling BJ1, Fang VJ, Nishiura H, Chan KH, Ng S, Ip DK, Chiu SS, Leung GM, Peiris JS.

School of Public Health, Li Ka Shing Faculty of Medicine,
The University of Hong Kong, Pokfulam, Hong Kong SAR, China
bcowling@hku.hk

Abstract

We randomized 115 children to trivalent inactivated influenza vaccine (TIV) or placebo. Over the following 9 months, TIV recipients had an increased risk of virologically-confirmed non-influenza infections (relative risk: 4.40; 95% confidence interval: 1.31-14.8). Being protected against influenza, TIV recipients may lack temporary non-specific immunity that protected against other respiratory viruses.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/>

Comparative study on pseudoanaphylactoid reactions induced by medicinal tween 80 and injectable tween 80

Author information

Wang Y1, Li C, Yi Y, Qin L, Zhao Y,
Li G, Cong X, Cao S, Liang A.

Capital Medical University
School of Traditional Chinese Medicine
Beijing 100069, China
wangyunting0@sina.com

Abstract

OBJECTIVE

To investigate the safety of different level of tween 80 by comparing the degree of pseudoanaphylactoid reactions (PR) induced by medicinal tween 80 and injectable tween 80.

METHOD

The analysis of vascular permeability of the mice ears: ICR mouse were divided into different test groups, the mice were intravenously injected with solutions of medicinal tween 80 and injectable tween 80 with 0.2%, 1% and 5% concentration, positive control Compound 48/80 and 5% glucose injection. All test substances were mixed with 0.4% Evans blue. The reaction and vascular permeability of the ears were observed and measured 30 min after injection. The analysis of vascular permeability of the rat's skin: the rats were intravenous injected with 0.6% Evans blue normal saline solution first, 10 minutes later, the same substances were intradermal administered into the back of rats. The rats were sacrificed and the diameter of locus ceruleus and the content of Evans blue leak out were measured 20 min after injection.

RESULT

Medicinal tween 80 and injectable tween 80 with 5% concentration caused obvious vascular hyper permeability in ICR mice, but the degree of vascular hyperpermeability caused by injectable tween 80 was lighter than by medicinal tween 80. Other tween 80 didn't cause obvious vascular hyper permeability in the ears of mouse. The solution of different concentration of tween 80 caused obvious locus ceruleus reaction in rat's back. As for the content Evans blue leak out, there was no statistical significance between each group except positive control Compound 48/80 group.

CONCLUSION

Tween 80 can cause obvious vascular hyper permeability and the effect is dose dependent, which indicated that tween 80 can cause PR. On the other hand, injectable tween 80 is more security than medicinal tween 80, the dosage of tween 80 should be still controlled strictly so that to decrease the incidence of PR.

“Tween 80 can cause obvious vascular hyper permeability and the effect is dose dependent, which indicated that Tween 80 can cause PR [pseudoanaphylactoid reactions].

Infections and vaccines in the etiology of antiphospholipid syndrome

Author information

Cruz-Tapias P1, Blank M, Anaya JM, Shoenfeld Y.

Zabludowitz Center for Autoimmune Diseases
Sheba Medical Center affiliated to Sackler Faculty of Medicine
Tel-Aviv University, Israel

Abstract

PURPOSE OF REVIEW

To present scientific evidence supporting the infectious origin for the antiphospholipid syndrome (APS) by molecular mimicry between pathogens, infection and vaccination with β 2-glycoprotein I (β 2-GPI) molecule.

RECENT FINDINGS

APS is characterized by the presence of pathogenic autoantibodies against β 2-GPI. The infection etiology of APS was well established. Likewise, a link between vaccination such as tetanus toxoid may trigger antibodies targeting tetanus toxoid and β 2-GPI, due to molecular mimicry between the two molecules. During the years, the pathogenic potential of anti-tetanus toxoid antibodies cross reactive with β 2-GPI were found to be pathogenic in animal models, inducing experimental APS.

SUMMARY

Accumulated evidence supports that the presence of anti- β 2-GPI antibodies is associated with a history of infections and the main mechanism to explain this correlation is molecular mimicry. The relationship between tetanus toxoid vaccination and APS reveals a novel view on the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA).

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22617823>

“The relationship between tetanus toxoid vaccination and Anti-Phospholipid Syndrome reveals a novel view on the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA).

Blood • July 2012

The significance of autoantibodies against β 2-glycoprotein I

Author information

de Groot PG1, Urbanus RT.

Department of Clinical Chemistry and Haematology
University Medical Center, Heidelberglaan 100
Utrecht, The Netherlands
ph.g.degroot@umcutrecht.nl

Abstract

The antiphospholipid syndrome (APS) is defined by the persistent presence of antiphospholipid antibodies in patients with a history of thrombosis and/or pregnancy morbidity, including fetal loss. APS is an autoimmune disease with a confusing name because the pathologic auto-antibodies are shown to be directed against the plasma protein β (2)-glycoprotein I and not against phospholipids. In fact, auto-antibodies that recognize phospholipids themselves are not associated with thrombosis but with infectious diseases. One of the intriguing questions is why autoantibodies against β (2)-glycoprotein I are so commonly found in both patients and the healthy. Several potential mechanisms have been suggested to explain the increased thrombotic risk in patients with these autoantibodies. In this overview, we will summarize our knowledge on the etiology of the autoantibodies, and we will discuss the evidence that identify autoantibodies against β (2)-glycoprotein I as the culprit of APS.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22553312>

“... we will summarize our knowledge on the etiology of the autoantibodies, and we will discuss the evidence that identify autoantibodies against β (2)-glycoprotein I as the culprit of Antiphospholipid Syndrome.”

Fragrance material review on 2-phenoxyethanol

Author information

Scognamiglio J1, Jones L, Letizia CS, Api AM.

Research Institute for Fragrance Materials Inc.
50 Tice Boulevard, Woodcliff Lake, NJ 07677, USA
jscognamiglio@rifm.org

Abstract

A toxicologic and dermatologic review of 2-phenoxyethanol when used as a fragrance ingredient is presented. 2-Phenoxyethanol is a member of the fragrance structural group Aryl Alkyl Alcohols and is a primary alcohol. The AAAs are a structurally diverse class of fragrance ingredients that includes primary, secondary, and tertiary alkyl alcohols covalently bonded to an aryl (Ar) group, which may be either a substituted or unsubstituted benzene ring. The common structural element for the AAA fragrance ingredients is an alcohol group -C-(R1)(R2)OH and generically the AAA fragrances can be represented as an Ar-C-(R1)(R2)OH or Ar-Alkyl-C-(R1)(R2)OH group. This review contains a detailed summary of all available toxicology and dermatology papers that are related to this individual fragrance ingredient and is not intended as a stand-alone document. Available data for 2-phenoxyethanol were evaluated then summarized and includes physical properties, acute toxicity, skin irritation, mucous membrane (eye) irritation, skin sensitization, elicitation, phototoxicity, photoallergy, toxicokinetics, repeated dose, and reproductive toxicity data. A safety assessment of the entire Aryl Alkyl Alcohols will be published simultaneously with this document; please refer to Belsito et al. (2012) for an overall assessment of the safe use of this material and all Aryl Alkyl Alcohols in fragrances.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22036980>

Editors Note: 2-Phenoxyethanol MSDS States:

This substance is toxic to kidneys, nervous system, liver.

Link for 2-Phenoxyethanol MSDS

<http://www.sciencelab.com/msds.php?msdsid=9926486>

“Available data for 2-phenoxyethanol

[a vaccine ingredient used in some vaccines]

were evaluated then summarized and

includes physical properties, acute toxicity,

skin irritation, mucous membrane (eye) irritation,

skin sensitization, elicitation, phototoxicity,

photoallergy, toxicokinetics, repeated dose,

and reproductive toxicity data.”

Relative trends in hospitalizations and mortality among infants by the number of vaccine doses and age, based on the Vaccine Adverse Event Reporting System (VAERS) 1990-2010

Author information

Goldman GS1, Miller NZ.

Computer Scientist
Pearblossom, CA 93553, USA
gsgoldman@roadrunner.com

Abstract

In this study, the Vaccine Adverse Event Reporting System (VAERS) database, 1990-2010, was investigated; cases that specified either hospitalization or death were identified among 38,801 reports of infants. Based on the types of vaccines reported, the actual number of vaccine doses administered, from 1 to 8, was summed for each case. Linear regression analysis of hospitalization rates as a function of (a) the number of reported vaccine doses and (b) patient age yielded a linear relationship with $r(2) = 0.91$ and $r(2) = 0.95$, respectively. The hospitalization rate increased linearly from 11.0% (107 of 969) for 2 doses to 23.5% (661 of 2817) for 8 doses and decreased linearly from 20.1% (154 of 765) for children aged <0.1 year to 10.7% (86 of 801) for children aged 0.9 year. The rate ratio (RR) of the mortality rate for 5-8 vaccine doses to 1-4 vaccine doses is 1.5 (95% confidence interval (CI), 1.4-1.7), indicating a statistically significant increase from 3.6% (95% CI, 3.2-3.9%) deaths associated with 1-4 vaccine doses to 5.5% (95% CI, 5.2-5.7%) associated with 5-8 vaccine doses. The male-to-female mortality RR was 1.4 (95% CI, 1.3-1.5). Our findings show a positive correlation between the number of vaccine doses administered and the percentage of hospitalizations and deaths. Since vaccines are given to millions of infants annually, it is imperative that health authorities have scientific data from synergistic toxicity studies on all combinations of vaccines that infants might receive. Finding ways to increase vaccine safety should be the highest priority.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3547435/>

“Our findings show a positive correlation between the number of vaccine doses administered and the percentage of hospitalizations and deaths.

Since vaccines are given to millions of infants annually, it is imperative that health authorities have scientific data from synergistic toxicity studies on all combinations of vaccines that infants might receive.”

[complex and unknown synergies]

“Despite widespread pertussis immunization in childhood, there are an estimated 50 million cases and 300,000 deaths due to pertussis globally each year.”

Expert Review Of Vaccines • November 2012

Re-emergence of pertussis: what are the solutions?

Author information

Libster R1, Edwards KM.
Vanderbilt University School of Medicine
Department of Pediatrics, Vanderbilt Vaccine Research Program
Nashville, TN, USA

Abstract

Whooping cough, due to *Bordetella pertussis* and *Bordetella parapertussis*, is an important cause of childhood morbidity and mortality. Despite widespread pertussis immunization in childhood, there are an estimated 50 million cases and 300,000 deaths due to pertussis globally each year. Infants who are too young to be vaccinated, children who are partially vaccinated and fully-vaccinated persons with waning immunity are especially vulnerable to disease. Since pertussis is one of the vaccine-preventable diseases on the rise, additional vaccine approaches are needed. These approaches include vaccination of newborns, additional booster doses for older adolescents and adults, and immunization of pregnant women with existing vaccines. Innovative new vaccines are also being studied. Each of these options will be discussed and their potential impact on pertussis control assessed.

<http://www.ncbi.nlm.nih.gov/pubmed/23249233>

Breast-feeding and responses to infant vaccines: constitutional and environmental factors

Author information

Dórea JG

Department of Nutrition
Universidade de Brasília
Brasília, Brazil
dorea@rudah.com.br

Abstract

Neonates and nursing infants are special with regard to immune development and vulnerability to infectious diseases. Although breast-feeding is essential to modulate and prime immune defenses, vaccines (an interventional prophylaxis) are crucial to prevent and control infectious diseases. During nursing, the type of feeding influences infants' natural defenses (including gut colonization) and their response to vaccines, both through cell-mediated immunity and specific antibody production. Given the variety and combination of vaccine components (antigens and excipients, preservative thimerosal, and aluminum adjuvants) and route of administration, there is a need to examine the role of infant feeding practices in intended and nonintended outcomes of vaccination. Maternal factors related to milk constituents (nutrients and pollutants) and feeding practices can affect response to vaccines. Collectively, studies that compared type of feeding (or used breast-feeding-adjusted statistical models) showed significant influence on some vaccines taken during infancy. Nurslings deprived of the full benefit of breast-feeding could have altered immune responses affecting vaccine outcome. In the absence of studies elucidating neurodevelopment (including excitotoxicity) and immunotoxicity issues, vaccination practices should promote and support breast-feeding.

<http://www.ncbi.nlm.nih.gov/pubmed/22773284>

“Maternal factors related to milk constituents (nutrients and pollutants) and feeding practices can affect response to vaccines. Collectively, studies that compared type of feeding (or used breast-feeding-adjusted statistical models) showed significant influence on some vaccines taken during infancy. Nurslings deprived of the full benefit of breast-feeding could have altered immune responses affecting vaccine outcome.”

Comparison of Shedding Characteristics of Seasonal Influenza Virus (Sub)Types and Influenza A(H1N1)pdm09 Germany, 2007–2011

Conclusion

Asymptomatic/subclinical infections occur infrequently, but may be associated with substantial amounts of viral shedding. Presymptomatic shedding may arise in one third of cases, and shedding characteristics appear to be independent of (seasonal or pandemic) (sub)type, age, antiviral therapy or vaccination; however the power to find moderate differences was limited.

In summary, our study addresses several important questions on clinical manifestation, duration of infectiousness, viral shedding patterns, including shedding before symptom onset and in asymptomatic/subclinical patients, as well as the effect of vaccination and antiviral therapy on viral shedding. Important single results include the finding that children do not seem to be infected asymptotically, that shedding one day before symptom onset may occur in one third of influenza patients, that asymptomatic/subclinical influenza patients occur rarely, but viral load (and probably infectiousness) may be substantial, and vaccinated influenza patients do not show different shedding patterns compared to non-vaccinated cases with ILI. Overall results do not show marked differences between seasonal influenza (sub)types and influenza A(H1N1)pdm09.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3519848/>

“Asymptomatic/subclinical infections occur infrequently, but may be associated with substantial amounts of viral shedding. Presymptomatic shedding may arise in one third of cases, and shedding characteristics appear to be independent of (seasonal or pandemic) (sub)type, age, antiviral therapy or vaccination...”

“The effectiveness of influenza vaccines is still controversial ...”

Vaccine • December 2012

Adjuvants in influenza vaccines

Author information

Tetsutani K1, Ishii KJ.

Laboratory of Adjuvant Innovation
National Institute of Biomedical Innovation
Japan

Abstract

The effectiveness of influenza vaccines is still controversial, and the role of adjuvants in such vaccines is briefly reviewed in this paper. Inactivated whole virus vaccines may include components that function as adjuvants, meaning that additive adjuvants are often not required. MF59 and AS03 showed higher adjuvanticity than aluminum salts in several clinical studies. Recent research has suggested that immune cell recruitment is the main mechanism underlying adjuvant actions in general, and that aluminum salts induce this recruitment via inflammation at the injected site. The aspect of how oil-based adjuvants, such as MF59 and AS03, recruit immune cells remains to be clarified.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23084848>

Detection of human papillomavirus (HPV) L1 gene DNA possibly bound to particulate aluminum adjuvant in the HPV vaccine Gardasil

Author information

Lee SH1.
Milford Hospital and Milford Molecular Laboratory
2044 Bridgeport Avenue, Milford, CT 06460, USA
shlee01@snet.net

Abstract

Medical practitioners in nine countries submitted samples of Gardasil (Merck & Co.) to be tested for the presence of human papillomavirus (HPV) DNA because they suspected that residual recombinant HPV DNA left in the vaccine might have been a contributing factor leading to some of the unexplained post-vaccination side effects. A total of 16 packages of Gardasil were received from Australia, Bulgaria, France, India, New Zealand, Poland, Russia, Spain and the United States. A nested polymerase chain reaction (PCR) method using the MY09/MY11 degenerate primers for initial amplification and the GP5/GP6-based nested PCR primers for the second amplification were used to prepare the template for direct automated cycle DNA sequencing of a hypervariable segment of the HPV L1 gene which is used for manufacturing of the HPV L1 capsid protein by a DNA recombinant technology in vaccine production. Detection of HPV DNA and HPV genotyping of all positive samples were finally validated by BLAST (Basic Local Alignment Search Tool) analysis of a 45-60 bases sequence of the computer-generated electropherogram. The results showed that all 16 Gardasil samples, each with a different lot number, contained fragments of HPV-11 DNA, or HPV-18 DNA, or a DNA fragment mixture from both genotypes. The detected HPV DNA was found to be firmly bound to the insoluble, proteinase-resistant fraction, presumably of amorphous aluminum hydroxyphosphate sulfate (AAHS) nanoparticles used as adjuvant. The clinical significance of these residual HPV DNA fragments bound to a particulate mineral-based adjuvant is uncertain after intramuscular injection, and requires further investigation for vaccination safety.

<http://www.ncbi.nlm.nih.gov/pubmed/23078778>

“Medical practitioners in nine countries submitted samples of Gardasil (Merck & Co.) to be tested for the presence of human papillomavirus (HPV) DNA because they suspected that residual recombinant HPV DNA left in the vaccine might have been a contributing factor leading to some of the unexplained post-vaccination side effects. A total of 16 packages of Gardasil were received from Australia, Bulgaria, France, India, New Zealand, Poland, Russia, Spain and the United States.

The results showed that all 16 Gardasil samples, each with a different lot number, contained fragments of HPV-11 DNA, or HPV-18 DNA, or a DNA fragment mixture from both genotypes. The detected HPV DNA was found to be firmly bound to the insoluble, proteinase-resistant fraction, presumably of amorphous aluminum hydroxyphosphate sulfate (AAHS) nanoparticles used as adjuvant. The clinical significance of these residual HPV DNA fragments bound to a particulate mineral-based adjuvant is uncertain after intramuscular injection ...”

**Autoimmunity
in connection with a metal implant:
a case of autoimmune/autoinflammatory
syndrome induced by adjuvants**

Author information

Loyo E1, Jara LJ2, López PD3, Puig AC3.

1. Director, Rheumatology and Clinical Immunology Department
Hospital Regional Universitario José Ma. Cabral y Báez
Santiago, Dominican Republic
2. Hospital de Especialidades “Dr. Antonio Fraga Mouret”
Centro Médico Nacional La Raza, IMSS, Mexico, DF Mexico
3. Pontificia Universidad Católica Madre y Maestra
Santiago, Dominican Republic

Abstract

Autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA) has been recently proposed by Shoenfeld and Agmon-Levin as a new entity that comprises several conditions: the macrophagic-myofasciitis syndrome, the Gulf War syndrome, silicosis and post-vaccination phenomena, autoimmunity related to infectious fragments, hormones, aluminum, silicone, squalene oil, and pristane. We report the case of a 23-year-old woman who developed serial episodes of high fever, extreme fatigue, transient thrombocytopenia, multiple cervical adenopathies, hepatosplenomegaly, anemia, neutropenia, severe proteinuria and urine sediment abnormalities, elevated serum ferritin levels, and transient low positive antinuclear antibodies 1 year after she had a nickel-titanium chin implant for cosmetic reasons. The clinical picture simulated a variety of probable diseases: systemic lupus erythematosus, Kikuchi-Fujimoto syndrome, adult onset Still's disease, antiphospholipid syndrome, and hemophagocytic syndrome, among others, so she underwent an extensive medical investigation including two lymph node biopsies. She received treatment accordingly with steroids, methotrexate, and mofetil mycophenolate, with initial improvement of her symptoms, which recurred every time the dose was reduced. Two and a half years later the patient decided to retire the chin implant and afterwards all her systemic symptoms have disappeared. She remains in good health, without recurrence of any symptom and off medications until today. Albeit this patient fulfills proposed major ASIA criteria, to our knowledge it would be the first description of systemic features of autoinflammation in connection with a metal implant.

<http://www.ncbi.nlm.nih.gov/pubmed/26000140>

“We report the case of a 23-year-old woman who developed serial episodes of high fever, extreme fatigue, transient thrombocytopenia, multiple cervical adenopathies, hepatosplenomegaly, anemia, neutropenia, severe proteinuria and urine sediment abnormalities, elevated serum ferritin levels, and transient low positive antinuclear antibodies 1 year after she had a nickel-titanium chin implant for cosmetic reasons.

Two and a half years later the patient decided to retire the chin implant and afterwards all her systemic symptoms have disappeared.”

Comparison of Shedding Characteristics of Seasonal Influenza Virus (Sub)Types and Influenza A(H1N1) Germany, 2007–2011

Thorsten Suess, Cornelius Remschmidt, Susanne B. Schink, Brunhilde Schweiger, Alla Heider, Jeanette Milde, Andreas Nitsche, Kati Schroeder, Joerg Doellinger, Christian Braun, Walter Haas, Gérard Krause, Udo Buchhol

Abstract

Background

Influenza viral shedding studies provide fundamental information for preventive strategies and modelling exercises. We conducted a prospective household study to investigate viral shedding in seasonal and pandemic influenza between 2007 and 2011 in Berlin and Munich, Germany.

Methods

Study physicians recruited index patients and their household members. Serial nasal specimens were obtained from all household members over at least eight days and tested quantitatively by qRT-PCR for the influenza virus (sub)type of the index patient. A subset of samples was also tested by viral culture. Symptoms were recorded daily.

Results

We recruited 122 index patients and 320 household contacts, of which 67 became secondary household cases. Among all 189 influenza cases, 12 were infected with seasonal/prepandemic influenza A(H1N1), 19 with A(H3N2), 60 with influenza B, and 98 with A(H1N1)pdm09. Nine (14%) of 65 non-vaccinated secondary cases were asymptomatic/subclinical (0 (0%) of 21 children, 9 (21%) of 44 adults; $p=0.03$). Viral load among patients with influenza-like illness (ILI) peaked on illness days 1, 2 or 3 for all (sub)types and declined steadily until days 7–9. Clinical symptom scores roughly paralleled viral shedding dynamics. On the first day prior to symptom onset 30% (12/40) of specimens were positive. Viral load in 6 asymptomatic/subclinical patients was similar to that in ILI-patients. Duration of infectiousness as measured by viral culture lasted approximately until illness days 4–6. Viral load did not seem to be influenced by antiviral therapy, age or vaccination status.

Conclusion

Asymptomatic/subclinical infections occur infrequently, but may be associated with substantial amounts of viral shedding. Presymptomatic shedding may arise in one third of cases, and shedding characteristics appear to be independent of (seasonal or pandemic) (sub)type, age, antiviral therapy or vaccination; however the power to find moderate differences was limited.

Full Report

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0051653>

“Asymptomatic/subclinical infections occur infrequently, but may be associated with substantial amounts of viral shedding. Presymptomatic shedding may arise in one third of cases, and shedding characteristics appear to be independent of (seasonal or pandemic) (sub)type, age, antiviral therapy or vaccination ...”

Persistent swelling after flushing of an abscess with Octenisept

Author information

Bauer B1, Majic M, Rauthe S, Bröcker EB, Kerstan A.

Klinik und Poliklinik für Dermatologie
Venerologie und Allergologie
Universitätsklinikum Würzburg
Josef-Schneider-Straße 2, 97080
Würzburg, Deutschland
Bauer_B1@klinik.uni-wuerzburg.de

Abstract

We report the case of a long-lasting cutaneous side effect after inappropriate use of Octenisept® solution (containing octenidine and phenoxyethanol). Following lavage of an abscess in the inguinal region, a painful erythematous induration mimicking cellulitis persisted for several months. Manual lymphatic drainage considerably improved the symptoms. Octenisept® shows considerable tissue toxicity in vivo including - but not restricted to - blood vessel damage. Deterioration of endothelial cells followed by oedema and continued tissue damage can be seen histologically. Despite the fact that there is a circular letter issued by the manufacturer as well as a boxed warning on the bottles, the awareness to avoid this misuse of Octenisept® is still lacking.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22101779>

“Octenisept® solution

(containing octenidine and phenoxyethanol) ...

shows considerable tissue toxicity in vivo including -
but not restricted to - blood vessel damage.

Deterioration of endothelial cells followed by
oedema and continued tissue damage can
be seen histologically.”

[phenoxyethanol is a vaccine ingredient]

Breast-Feeding and Responses to Infant Vaccines: Constitutional and Environmental Factors

José G. Dórea

Department of Nutrition
Universidade de Brasília
Brasília, Brazil

Abstract

Neonates and nursing infants are special with regard to immune development and vulnerability to infectious diseases. Although breast-feeding is essential to modulate and prime immune defenses, vaccines (an interventional prophylaxis) are crucial to prevent and control infectious diseases. During nursing, the type of feeding influences infants' natural defenses (including gut colonization) and their response to vaccines, both through cell-mediated immunity and specific antibody production. Given the variety and combination of vaccine components (antigens and excipients, preservative thimerosal, and aluminum adjuvants) and route of administration, there is a need to examine the role of infant feeding practices in intended and nonintended outcomes of vaccination. Maternal factors related to milk constituents (nutrients and pollutants) and feeding practices can affect response to vaccines. Collectively, studies that compared type of feeding (or used breast-feeding-adjusted statistical models) showed significant influence on some vaccines taken during infancy. Nurslings deprived of the full benefit of breast-feeding could have altered immune responses affecting vaccine outcome. In the absence of studies elucidating neurodevelopment (including excitotoxicity) and immunotoxicity issues, vaccination practices should promote and support breast-feeding.

<https://www.thieme-connect.com/DOI/DOI?10.1055/s-0032-1316442>

“Nurslings deprived of the full benefit of breast-feeding could have altered immune responses affecting vaccine outcome.”

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) 2013: Unveiling the pathogenic, clinical and diagnostic aspects

Carlo Perricone a, b, Serena Colafrancesco a, b, Roei D. Mazor a,
Alessandra Soriano a, c, Nancy Agmon-Levina, Yehuda Shoenfelda,d,*

a. The Zabłudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel

b. Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche, Sapienza Università di Roma, Rome, Italy

c. Department of Clinical Medicine and Rheumatology, University Campus Bio-Medico of Rome, Italy

d. Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases, Sackler Faculty of Medicine Tel-Aviv University

Abstract

In 2011 a new syndrome termed ‘ASIA Autoimmune/Inflammatory Syndrome Induced by Adjuvants’ was defined pointing to summarize for the first time the spectrum of immune-mediated diseases triggered by an adjuvant stimulus such as chronic exposure to silicone, tetramethylpentadecane, pristane, aluminum and other adjuvants, as well as infectious components, that also may have an adjuvant effect. All these environmental factors have been found to induce autoimmunity by themselves both in animal models and in humans: for instance, silicone was associated with siliconosis, aluminum hydroxide with post- vaccination phenomena and macrophagic myofasciitis syndrome. Several mechanisms have been hypothesized to be involved in the onset of adjuvant-induced autoimmunity; a genetic favorable background plays a key role in the appearance of such vaccine-related diseases and also justifies the rarity of these phenomena. This paper will focus on protean facets which are part of ASIA, focusing on the roles and mechanisms of action of different adjuvants which lead to the autoimmune/inflammatory response. The data herein illustrate the critical role of environmental factors in the induction of autoimmunity. Indeed, it is the interplay of genetic susceptibility and environment that is the major player for the initiation of breach of tolerance.

Final remarks

Despite the huge amount of money invested in studying vaccines, there are few observational studies and virtually no randomized clinical trials documenting the effect on mortality of any of the existing vaccines. One recent paper found an increased hospitalization rate with the increase of the number of vaccine doses and a mortality rate ratio for 5×10^8 vaccine doses to 1×10^4 vaccine doses of 1.5, indicating a statistically significant increase of deaths associated with higher vaccine doses. Since vaccines are given to millions of infants annually, it is imperative that health authorities have scientific data from synergistic toxicity studies on all combinations of vaccines that infants might receive to improve vaccine safety [194].

Moreover, from one side the non-specific beneficial effects of vaccines on survival can be underestimated, on the other side the negative effect of other vaccines may not be captured by current studies [195]. As a matter of fact, in case of vaccine-associated autoimmune phenomena latency periods between the vaccine administration and the appearance of clinical symptoms can be longer (months or years after vaccination) than the time interval commonly established in most vaccine risk assessment studies [196].

Full Report

<http://www.2ndchance.info/onesize4all-Perricone2013.pdf>

“Despite the huge amount of money invested in studying vaccines, there are few observational studies and virtually no randomized clinical trials documenting the effect on mortality of any of the existing vaccines.

One recent paper found an increased hospitalization rate with the increase of the number of vaccine doses and a mortality rate ratio for 5×10^8 vaccine doses to 1×10^4 vaccine doses of 1.5, indicating a statistically significant increase of deaths associated with higher vaccine doses.”

A novel mechanism of formaldehyde neurotoxicity: inhibition of hydrogen sulfide generation by promoting overproduction of nitric oxide

Author information

Tang XQ1, Fang HR, Zhou CF,
Zhuang YY, Zhang P, Gu HF, Hu B.

Department of Physiology, Medical College
University of South China, Hengyang
Hunan, PR China
txq01001@gmail.com

Abstract

BACKGROUND

Formaldehyde (FA) induces neurotoxicity by overproduction of intracellular reactive oxygen species (ROS). Increasing studies have shown that hydrogen sulfide (H₂S), an endogenous gastransmitter, protects nerve cells against oxidative stress by its antioxidant effect. It has been shown that overproduction of nitric oxide (NO) inhibits the activity of cystathionine-beta-synthase (CBS), the predominant H₂S-generating enzyme in the central nervous system.

OBJECTIVE

We hypothesize that FA-caused neurotoxicity involves the deficiency of this endogenous protective antioxidant gas, which results from excessive generation of NO. The aim of this study is to evaluate whether FA disturbs H₂S synthesis in PC12 cells, and whether this disturbance is associated with overproduction of NO.

PRINCIPAL FINDINGS

We showed that exposure of PC12 cells to FA causes reduction of viability, inhibition of CBS expression, decrease of endogenous H₂S production, and NO production. CBS silencing deteriorates FA-induced decreases in endogenous H₂S generation, neurotoxicity, and intracellular ROS accumulation in PC12 cells; while ADMA, a specific inhibitor of NOS significantly attenuates FA-induced decreases in endogenous H₂S generation, neurotoxicity, and intracellular ROS accumulation in PC12 cells.

CONCLUSION/SIGNIFICANCE

Our data indicate that FA induces neurotoxicity by inhibiting the generation of H₂S through excess of NO and suggest that strategies to manipulate endogenous H₂S could open a suitable novel therapeutic avenue for FA-induced neurotoxicity.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3554621/>

“Our data indicate that
Formaldehyde induces neurotoxicity
by inhibiting the generation of hydrogen sulfide
through excess of nitric oxide ...”

Altered immune pathway activity under exercise challenge in Gulf War Illness: an exploratory analysis

Author information

Broderick G1, Ben-Hamo R, Vashishtha S, Efroni S,
Nathanson L, Barnes Z, Fletcher MA, Klimas N.

Department of Medicine, University of Alberta
Edmonton, Canada
gordon.broderick@ualberta.ca

Abstract

Though potentially linked to the basic physiology of stress response we still have no clear understanding of Gulf War Illness (GWI), a debilitating illness presenting with a complex constellation of immune, endocrine and neurological symptoms. Here we compared male GWI (n=20) with healthy veterans (n=22) and subjects with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) (n=7). Blood was drawn during a Graded eExercise Test (GXT) prior to exercise, at peak effort (VO₂ max) and 4-h post exercise. Affymetrix HG U133 plus 2.0 microarray gene expression profiling in peripheral blood mononuclear cells (PBMCs) was used to estimate activation of over 500 documented pathways. This was cast against ELISA-based measurement of 16 cytokines in plasma and flow cytometric assessment of lymphocyte populations and cytotoxicity. A 2-way ANOVA corrected for multiple comparisons (q statistic <0.05) indicated significant increases in neuroendocrine-immune signaling and inflammatory activity in GWI, with decreased apoptotic signaling. Conversely, cell cycle progression and immune signaling were broadly subdued in CFS. Partial correlation networks linking pathways with symptom severity via changes in immune cell abundance, function and signaling were constructed. Central to these were changes in IL-10 and CD2⁺ cell abundance and their link to two pathway clusters. The first consisted of pathways supporting neuronal development and migration whereas the second was related to androgen-mediated activation of NF- κ B. These exploratory results suggest an over-expression of known exercise response mechanisms as well as illness-specific changes that may involve an overlapping stress-potentiated neuro-inflammatory response.

<http://www.ncbi.nlm.nih.gov/pubmed/23201588>

“These exploratory results suggest an over-expression of known exercise response mechanisms as well as illness-specific changes that may involve an overlapping stress-potentiated neuro-inflammatory response.”

Vaccine adverse events reported
during the first ten years (1998-2008)
after introduction in the state of Rondonia, Brazil

Author information

Cunha MP1, Dórea JG, Marques RC, Leão RS.

Department of Nursing
Fundação Universidade Federal de Rondônia
76801-974 Porto Velho, RO, Brazil

Abstract

Despite good safety records, vaccines given to young children can cause adverse events. We investigated the reported adverse events following immunization (AEFI) of vaccines given to children of less than seven years of age during the first ten years (1998 to 2008) in the state of Rondonia, Brazil. We worked with the events related to BCG (Bacillus Calmett-Guérin), HB (hepatitis B), DTwP/Hib (diphtheria-tetanus-pertussis+Hemophilus influenza b), DTP (diphtheria-tetanus-pertussis), MMR (mumps, measles, rubella), and YF (yellow fever) vaccines because they were part of the recommended scheme. The number of doses of vaccines given was 3,231,567 with an average of AEFI of 57.2/year during the studied period. DTwP/Hib was responsible for 298 (57.8%), DTP 114 (22.9%), HB 31 (6%), MMR 28 (5.4%), BCG 24 (4.7%), and YF 20 (3.9%) of the reported AEFI. The combination of the AEFI for DTwP/Hib vaccines showed the highest number of systemic (61.4%) and local events (33.8%). Young children (≤ 1 -year old) were more susceptible to AEFI occurring in the 6 hours (54.2%) following vaccine uptake. This study suggests significant differences in reactogenicity of vaccines and that despite limitations of the AEFI Brazilian registry system we cannot ignore underreporting and should use the system to expand our understanding of adverse events and effects.

“This study suggests significant
differences in reactogenicity of vaccines ...”

The meaning of aluminium exposure on human health and aluminium-related diseases

Crisponi G, Fanni D, Gerosa C, Nemolato S,
Nurchi VM, Crespo-Alonso M, Lachowicz JI, Faa G.

Abstract

The aim of this review is to attempt to answer extremely important questions related to aluminium-related diseases. Starting from an overview on the main sources of aluminium exposure in everyday life, the principal aspects of aluminium metabolism in humans have been taken into consideration in an attempt to enlighten the main metabolic pathways utilised by trivalent metal ions in different organs. The second part of this review is focused on the available evidence concerning the pathogenetic consequences of aluminium overload in human health, with particular attention to its putative role in bone and neurodegenerative human diseases.

<http://www.ncbi.nlm.nih.gov/pubmed/25436567>

“ The second part of this review is focused on the available evidence concerning the pathogenetic consequences of aluminium overload in human health, with particular attention to its putative role in bone and neurodegenerative human diseases.”

Vaccine Adverse Events Reported during the First Ten Years (1998–2008) after Introduction in the State of Rondonia, Brazil

Author Information

Mônica P. L. Cunha, 1 José G. Dórea, 2 ,*
Rejane C. Marques, 3 and Renata S. Leão 4

1Department of Nursing, Fundação Universidade Federal de Rondônia
76801-974 Porto Velho, RO, Brazil

2Faculty of Health Sciences, Universidade de Brasília
70919-970 Brasília, DF, Brazil

3Universidade Federal do Rio de Janeiro, Campus Macaé
27971-550 Rio de Janeiro, RJ, Brazil

4Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro
21941-902 Rio de Janeiro, RJ, Brazil

Abstract

Despite good safety records, vaccines given to young children can cause adverse events. We investigated the reported adverse events following immunization (AEFI) of vaccines given to children of less than seven years of age during the first ten years (1998 to 2008) in the state of Rondonia, Brazil. We worked with the events related to BCG (Bacillus Calmett-Guérin), HB (hepatitis B), DTwP/Hib (diphtheria-tetanus-pertussis+Hemophilus influenza b), DTP (diphtheria-tetanus-pertussis), MMR (mumps, measles, rubella), and YF (yellow fever) vaccines because they were part of the recommended scheme. The number of doses of vaccines given was 3,231,567 with an average of AEFI of 57.2/year during the studied period. DTwP/Hib was responsible for 298 (57.8%), DTP 114 (22.9%), HB 31 (6%), MMR 28 (5.4%), BCG 24 (4.7%), and YF 20 (3.9%) of the reported AEFI. The combination of the AEFI for DTwP/Hib vaccines showed the highest number of systemic (61.4%) and local events (33.8%). Young children (≤ 1 -year old) were more susceptible to AEFI occurring in the 6 hours (54.2%) following vaccine uptake. This study suggests significant differences in reactogenicity of vaccines and that despite limitations of the AEFI Brazilian registry system we cannot ignore underreporting and should use the system to expand our understanding of adverse events and effects.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3586457/>

“... despite limitations of
the AEFI Brazilian registry system
we cannot ignore underreporting ...”

Are the Currently Existing Anti-Human Papillomavirus Vaccines Appropriate for the Developing World?

Author Information

LJ van Bogaert

Department Of Histopathology
National Health Laboratory, Service and University of Limpopo
Polokwane, South Africa

Abstract

Cervical cancer prevention is expected to be achieved by vaccination of girls 2-3 years before sexual debut, and cervical smear cytology follow-up. The existing human papillomavirus (HPV) vaccines target the low-risk 6 and 11, and the high-risk 16 and 18 subtypes, the most common agents of ano-genital pre-invasive and invasive lesions. We conducted the review by searching PubMed using the terms “HPV,” “HPV subtypes,” “developing world,” and “HPV-vaccine” to retrieve articles published between 2000 and 2011. We focused on studies that were relevant to the developing world. The proposed vaccination policy is currently unachievable in the developing world because of the cost of the vaccine, the lack of adequate cytology and follow-up infrastructures. Moreover, the subtypes of HPV involved in cervical pathology, their associations, and natural history (clearance and persistence rates) differ from the industrialized world. Therefore, the current bivalent and quadrivalent anti-HPV vaccines are unlikely to achieve their target in the developing world. It follows from published data that there is an obligation of the pharmaceutical industry and of the public-health policy makers not to embark on mass vaccination campaigns without thorough information and investigation of the local relevance.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3793430/>

“The proposed vaccination policy is currently unachievable in the developing world because of the cost of the vaccine, the lack of adequate cytology and follow-up infrastructures. Moreover, the subtypes of HPV involved in cervical pathology, their associations, and natural history (clearance and persistence rates) differ from the industrialized world.”

EMBO Reports • March 2013

**Scientific dissent and public policy.
Is targeting dissent a reasonable way
to protect sound policy decisions?**

Author information

de Melo-Martín IJ, Intemann K.

Division of Medical Ethics
Department of Public Health
Weill Cornell Medical College, New York, USA
imd2001@med.cornell.edu

The temptation to silence dissenters whose non-mainstream views negatively affect public policies is powerful. However, silencing dissent, no matter how scientifically unsound it might be, can cause the public to mistrust science in general. Dissent is crucial for the advancement of science. Disagreement is at the heart of peer review and is important for uncovering unjustified assumptions, flawed methodologies and problematic reasoning.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3589084>

“Dissent is crucial
for the advancement of science.
Disagreement is at the heart
of peer review and is important
for uncovering unjustified
assumptions, flawed
methodologies and
problematic reasoning.”

**Review of the United States universal varicella vaccination program:
Herpes zoster incidence rates, cost-effectiveness, and vaccine efficacy
based primarily on the Antelope Valley Varicella
Active Surveillance Project data**

Author information

Goldman GS1, King PG.

Abstract

In a cooperative agreement starting January 1995, prior to the FDA's licensure of the varicella vaccine on March 17, the Centers for Disease Control and Prevention (CDC) funded the Los Angeles Department of Health Services' Antelope Valley Varicella Active Surveillance Project (AV-VASP). Since only varicella case reports were gathered, baseline incidence data for herpes zoster (HZ) or shingles was lacking. Varicella case reports decreased 72%, from 2834 in 1995 to 836 in 2000 at which time approximately 50% of children under 10 years of age had been vaccinated. Starting in 2000, HZ surveillance was added to the project. By 2002, notable increases in HZ incidence rates were reported among both children and adults with a prior history of natural varicella. However, CDC authorities still claimed that no increase in HZ had occurred in any US surveillance site. The basic assumptions inherent to the varicella cost-benefit analysis ignored the significance of exogenous boosting caused by those shedding wild-type VZV. Also ignored was the morbidity associated with even rare serious events following varicella vaccination as well as the morbidity from increasing cases of HZ among adults. Vaccine efficacy declined below 80% in 2001. By 2006, because 20% of vaccinees were experiencing breakthrough varicella and vaccine-induced protection was waning, the CDC recommended a booster dose for children and, in 2007, a shingles vaccination was approved for adults aged 60 years and older. In the prelicensure era, 95% of adults experienced natural chickenpox (usually as children)-these cases were usually benign and resulted in long-term immunity. Varicella vaccination is less effective than the natural immunity that existed in prevaccine communities. Universal varicella vaccination has not proven to be cost-effective as increased HZ morbidity has disproportionately offset cost savings associated with reductions in varicella disease. Universal varicella vaccination has failed to provide long-term protection from VZV disease.

<http://www.ncbi.nlm.nih.gov/pubmed/22659447>

“In the prelicensure era, 95% of adults experienced natural chickenpox (usually as children)-these cases were usually benign and resulted in long-term immunity.

Varicella vaccination is less effective than the natural immunity that existed in prevaccine communities.

Universal varicella vaccination has not proven to be cost-effective as increased HZ morbidity has disproportionately offset cost savings associated with reductions in varicella disease. Universal varicella vaccination has failed to provide long-term protection from VZV disease.”

Vaccine delivery using nanoparticles

Anthony E. Gregory,^{1,*} Richard Titball,¹ and Diane Williamson²

1. College of Life and Environmental Sciences, University of Exeter, Exeter, UK
2. DSTL Porton Down, Salisbury, Wiltshire, SP4 0QJ, UK

Abstract

Vaccination has had a major impact on the control of infectious diseases. However, there are still many infectious diseases for which the development of an effective vaccine has been elusive. In many cases the failure to devise vaccines is a consequence of the inability of vaccine candidates to evoke appropriate immune responses. This is especially true where cellular immunity is required for protective immunity and this problem is compounded by the move toward devising sub-unit vaccines. Over the past decade nanoscale size (<1000 nm) materials such as virus-like particles, liposomes, ISCOMs, polymeric, and non-degradable nanospheres have received attention as potential delivery vehicles for vaccine antigens which can both stabilize vaccine antigens and act as adjuvants. Importantly, some of these nanoparticles (NPs) are able to enter antigen-presenting cells by different pathways, thereby modulating the immune response to the antigen. This may be critical for the induction of protective Th1-type immune responses to intracellular pathogens. Their properties also make them suitable for the delivery of antigens at mucosal surfaces and for intradermal administration. In this review we compare the utilities of different NP systems for the delivery of sub-unit vaccines and evaluate the potential of these delivery systems for the development of new vaccines against a range of pathogens.

Many of the NP delivery systems mentioned in this review are capable of eliciting both cellular and humoral immune responses. However, an efficient and protective vaccine is likely to induce a combination of both responses and should be tailored to the pathogen in question accordingly. Whilst these delivery vehicles may present as an exciting prospect for future vaccination strategies, it is also worth noting their potential drawbacks, particularly those associated with cytotoxicity. Since NPs have a relatively short history in medicine they do not have a longstanding safety profile in human use. It is therefore essential that further research is carried out in NP toxicity to fully address these questions if they are to be accepted as an alternative method for the delivery of novel vaccines and are licensed more widely for human use.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3607064/>

“Whilst these delivery vehicles may present as an exciting prospect for future vaccination strategies, it is also worth noting their potential drawbacks, particularly those associated with cytotoxicity.”

“This is the new wind blowing within the branches of autoimmunity ...”

BMC Medicine • April 2013

Novel pebbles in the mosaic of autoimmunity

Perricone C, Agmon-Levin N, Shoenfeld Y.

Abstract

Almost 25 years ago, the concept of the ‘mosaic of autoimmunity’ was introduced to the scientific community, and since then this concept has continuously evolved, with new pebbles being added regularly. We are now looking at an era in which the players of autoimmunity have changed names and roles. In this issue of BMC Medicine, several aspects of autoimmunity have been addressed, suggesting that we are now at the forefront of autoimmunity science. Within the environmental factors generating autoimmunity are now included unsuspected molecules such as vitamin D and aluminum. Some adjuvants such as aluminum are recognized as causal factors in the development of the autoimmune response. An entirely new syndrome, the autoimmune/inflammatory syndrome induced by adjuvants (ASIA), has been recently described. This is the new wind blowing within the branches of autoimmunity, adding knowledge to physicians for helping patients with autoimmune disease.

<http://www.ncbi.nlm.nih.gov/pubmed/23557479>

Genetic characterization of HA gene of low pathogenic H9N2 influenza viruses isolated in Israel during 2006-2012 periods

Author information

Davidson I1, Shkoda I, Golender N, Perk S,
Lapin K, Khinich Y, Panshin A.

Kimron Veterinary Institute
P.O. Box 12, 50250 Beit Dagan, Israel
davidsoni@int.gov.il

Abstract

H9N2 influenza viruses are isolated in Israel since 2000 and became endemic. From November 2006 to the beginning of 2012, many H9N2 viruses were identified, all belonged to the Asian G1-like lineage represented by A/qu/Hong Kong/G1/97 (H9N2). In the present study, 66 isolates were selected for their hemagglutinin gene characterization. Most H9N2 isolates were distributed between two main groups, identified as the 4th and 5th introductions. The 5th introduction, was represented by a compact cluster containing viruses isolated in 2011-2012; the 4th introduction was subdivided into two subgroups, A and B, each containing at least two clusters, which can be identified as A-1, A-2, B-1, and B2, respectively. Genetic analysis of the deduced HA proteins of viruses, belonging to the 4th and 5th introductions, revealed amino acid variations in 79 out of 542 positions. All isolates had typical low pathogenicity motifs at the hemagglutinin (HA) cleavage site. Most viruses had leucine at position 216 in a receptor binding pocket that enables the virus to bind successfully with the cellular receptors intrinsic to mammals, including humans. It was shown that the differences between the HA proteins of viruses used for vaccine production and local field isolates increased in parallel with the duration and intensity of vaccine use, illustrating the genetic diversity of the H9N2 viruses in Israel.

<http://www.ncbi.nlm.nih.gov/pubmed/23271448>

“... the differences between the HA proteins of viruses used for vaccine production and local field isolates increased in parallel with the duration and intensity of vaccine use, illustrating the genetic diversity of the H9N2 viruses in Israel.”

How aluminum, an intracellular ROS generator promotes hepatic and neurological diseases: the metabolic tale

Author information

Han S1, Lemire J, Appanna VP,
Auger C, Castonguay Z, Appanna VD.

Department of Chemistry and Biochemistry
Laurentian University, Sudbury
Ontario, P3E 2C6, Canada

Abstract

Metal pollutants are a global health risk due to their ability to contribute to a variety of diseases. Aluminum (Al), a ubiquitous environmental contaminant is implicated in anemia, osteomalacia, hepatic disorder, and neurological disorder. In this review, we outline how this intracellular generator of reactive oxygen species (ROS) triggers a metabolic shift towards lipogenesis in astrocytes and hepatocytes. This Al-evoked phenomenon is coupled to diminished mitochondrial activity, anerobiosis, and the channeling of α -ketoacids towards anti-oxidant defense. The resulting metabolic reconfiguration leads to fat accumulation and a reduction in ATP synthesis, characteristics that are common to numerous medical disorders. Hence, the ability of Al toxicity to create an oxidative environment promotes dysfunctional metabolic processes in astrocytes and hepatocytes. These molecular events triggered by Al-induced ROS production are the potential mediators of brain and liver disorders.

<http://www.ncbi.nlm.nih.gov/pubmed/23463459>

“The resulting metabolic reconfiguration leads to fat accumulation and a reduction in ATP synthesis, characteristics that are common to numerous medical disorders.

Hence, the ability of Al toxicity to create an oxidative environment promotes dysfunctional metabolic processes in astrocytes and hepatocytes. These molecular events triggered by Al-induced ROS production are the potential mediators of brain and liver disorders.”

“The incidence of narcolepsy was 25 times higher after the vaccination compared with the time period before. The children in the postvaccination group had a lower age at onset and a more sudden onset than that generally seen.”

Neurology • April 2013

Increased childhood incidence of narcolepsy in western Sweden after H1N1 influenza vaccination

Author information

Szakács A1, Darin N, Hallböök T.

Department of Children
County Hospital, Halmstad, Sweden

Abstract

OBJECTIVES

To assess the incidence of narcolepsy between January 2000 and December 2010 in children in western Sweden and its relationship to the Pandemrix vaccination, and to compare the clinical and laboratory features of these children.

METHODS

The children were identified from all local and regional pediatric hospitals, child rehabilitation centers, outpatient pediatric clinics, and regional departments of neurophysiology. Data collection was performed with the aid of a standardized data collection form, from medical records and telephone interviews with patients and parents. The laboratory and investigational data were carefully scrutinized.

RESULTS

We identified 37 children with narcolepsy. Nine of them had onset of symptoms before the H1N1 vaccination and 28 had onset of symptoms in relationship to the vaccination. The median age at onset was 10 years. All patients in the postvaccination group were positive for human leukocyte antigen (HLA)-DQB1*0602. Nineteen patients in the postvaccination group, compared with one in the prevaccination group, had a clinical onset that could be dated within 12 weeks.

CONCLUSION

Pandemrix vaccination is a precipitating factor for narcolepsy, especially in combination with HLA-DQB1*0602. The incidence of narcolepsy was 25 times higher after the vaccination compared with the time period before. The children in the postvaccination group had a lower age at onset and a more sudden onset than that generally seen.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23486871>

Autoimmune/inflammatory syndrome induced by adjuvants (Shoenfeld's syndrome): clinical and immunological spectrum

Author information

Vera-Lastra OI, Medina G, Cruz-Dominguez Mdel P, Jara LJ, Shoenfeld Y.

Hospital de Especialidades Centro Médico La Raza
Instituto Mexicano del Seguro Social
Mexico City, Mexico

Abstract

An adjuvant is a substance that enhances the antigen-specific immune response, induces the release of inflammatory cytokines, and interacts with Toll-like receptors and the NALP3 inflammasome. The immunological consequence of these actions is to stimulate the innate and adaptive immune response. The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes postvaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis. This syndrome is characterized by nonspecific and specific manifestations of autoimmune disease. The main substances associated with ASIA are squalene (Gulf War syndrome), aluminum hydroxide (postvaccination phenomena, macrophagic myofasciitis) and silicone with siliconosis. Mineral oil, guaiacol and iodine gadital are also associated with ASIA. The following review describes the wide clinical spectrum and pathogenesis of ASIA including defined autoimmune diseases and nonspecific autoimmune manifestations, as well as the outlook of future research in this field.

<http://www.ncbi.nlm.nih.gov/pubmed/23557271>

“The activation of the immune system by adjuvants, a desirable effect, could trigger manifestations of autoimmunity or autoimmune disease. Recently, a new syndrome was introduced, autoimmune/inflammatory syndrome induced by adjuvants (ASIA), that includes postvaccination phenomena, macrophagic myofasciitis, Gulf War syndrome and siliconosis.”

Altered response to A(H1N1)pnd09 vaccination in pregnant women: a single blinded randomized controlled trial

Author information

Bischoff AL1, Følsgaard NV, Carson CG, Stokholm J,
Pedersen L, Holmberg M, Bisgaard A, Birch S, Tsai TF, Bisgaard H.
Copenhagen Prospective Studies on Asthma in Childhood (COPSAC)
Health Sciences, University of Copenhagen, Copenhagen University Hospital
Gentofte, Denmark

Abstract

BACKGROUND

Pregnant women were suspected to be at particular risk when H1N1pnd09 influenza became pandemic in 2009. Our primary objective was to compare the immune responses conferred by MF59®-adjuvanted vaccine (Focetria®) in H1N1pnd09-naïve pregnant and non-pregnant women. The secondary aims were to compare influences of dose and adjuvant on the immune response.

METHODS

The study was nested in the Copenhagen Prospective Studies on Asthma in Childhood (COPSAC2010) pregnancy cohort in 2009-2010 and conducted as a single-blinded block-randomised [1:1:1] controlled clinical trial in pregnant women after gestational week 20: (1) 7.5 µg H1N1pnd09 antigen with MF59-adjuvant (Pa7.5 µg); (2) 3.75 µg antigen half MF59-adjuvanted (Pa3.75 µg); (3) 15 µg antigen unadjuvanted (P15 µg); and in non-pregnant women receiving (4) 7.5 µg antigen full adjuvanted (NPa7.5 µg). Blood samples were collected at baseline, 3 weeks, 3 and 10 months after vaccination, adverse events were recorded prospectively.

RESULTS

58 pregnant women were allocated to Pa7.5 µg and 149 non-pregnant women were recruited to NPa7.5 µg. The sero-conversion rate was significantly increased in non-pregnant (NPa7.5 µg) compared with pregnant (Pa7.5 µg) women (OR=2.48 [1.03-5.95], p=0.04) and geometric mean titers trended towards being higher, but this difference was not statistically significant (ratio 1.27 [0.85-1.93], p=0.23). The significant titer increase rate showed no difference between pregnant (Pa7.5 µg) and non-pregnant (NPa7.5 µg) groups (OR=0.49 [0.13-1.85], p=0.29).

CONCLUSION

Our study suggests the immune response to the 7.5 µg MF59-adjuvanted Focetria® H1N1pnd09 vaccine in pregnant women may be diminished compared with non-pregnant women.

“Our study suggests
the immune response
to the 7.5 µg MF59-adjuvanted Focetria®
H1N1pnd09 vaccine in pregnant women
may be diminished compared
with non-pregnant women.”

“Prevalence of CD and UC increased 2-fold to 3-fold among VA users between 1998 and 2009.”

Inflammatory Bowel Diseases • April 2013

The incidence and prevalence of inflammatory bowel disease among U.S. veterans: A national cohort study

Hou, J.K.^{ab}, Kramer, J.R.^{ab}, Richardson, P.^{ab}, Mei, M.^{ab}, El-Serag, H.B.^{ab}

- a. Houston VA HSR and D Center of Excellence, Houston, TX, United States
- b. Department of Medicine, Baylor College of Medicine, Houston, TX, United States

Abstract

Background: Temporal trends in incidence and prevalence of Crohn’s disease (CD) and ulcerative colitis (UC) in the United States have been reported only in regional populations. The Veterans Affairs (VA) health care system encompasses a national network of clinical care facilities. The aim of this study was to identify temporal trends in the incidence and prevalence of CD and UC among VA users using national VA data sets. **Methods:** Veterans with CD and UC were identified during fiscal years 1998 to 2009 in the national VA outpatient and inpatient files. Incident and prevalent cases were identified by diagnosis code, and age-standardized and gender-standardized annual prevalence and incidence rates were estimated using the VA 1998 population as the standard population. **Results:** The total of unique incident cases were 16,842 and 26,272 for CD and UC, respectively; 94% were men. The average annual age-standardized and gender-standardized incidence rate of CD was 33 per 100,000 VA users (range, 27-40), whereas the average for UC was 50 per 100,000 VA users (range, 36-65). In 2009, the age-standardized and gender-standardized point prevalence rate of CD was 287 per 100,000 VA users, whereas the point prevalence of UC was 413 per 100,000 VA users. **Conclusions:** Prevalence of CD and UC increased 2-fold to 3-fold among VA users between 1998 and 2009. The incidence of UC decreased among VA users from 1998 to 2004 but has remained stable from 2005 to 2009. The incidence of CD has remained stable during the observed time period.

<http://www.ncbi.nlm.nih.gov/pubmed/23448789>

Influenza vaccine effectiveness in the community and the household

Author information

Ohmit SE1, Petrie JG, Malosh RE
Cowling BJ, Thompson MG, Shay DK, Monto AS.
Department of Epidemiology
University of Michigan School of Public Health
Ann Arbor, MI, USA
sohmit@umich.edu

Abstract

Background

There is a recognized need to determine influenza vaccine effectiveness on an annual basis and a long history of studying respiratory illnesses in households.

Methods

We recruited 328 households with 1441 members, including 839 children, and followed them during the 2010-2011 influenza season. Specimens were collected from subjects with reported acute respiratory illnesses and tested by real-time reverse transcriptase polymerase chain reaction. Receipt of influenza vaccine was defined based on documented evidence of vaccination in medical records or an immunization registry. The effectiveness of 2010-2011 influenza vaccination in preventing laboratory-confirmed influenza was estimated using Cox proportional hazards models adjusted for age and presence of high-risk condition, and stratified by prior season (2009-2010) vaccination status.

Results

Influenza was identified in 78 (24%) households and 125 (9%) individuals; the infection risk was 8.5% in the vaccinated and 8.9% in the unvaccinated ($P = .83$). Adjusted vaccine effectiveness in preventing community-acquired influenza was 31% (95% confidence interval [CI], -7% to 55%). In vaccinated subjects with no evidence of prior season vaccination, significant protection (62% [95%

CI, 17%-82%]) against community-acquired influenza was demonstrated. Substantially lower effectiveness was noted among subjects who were vaccinated in both the current and prior season. There was no evidence that vaccination prevented household transmission once influenza was introduced; adults were at particular risk despite vaccination.

Influenza Vaccine Effectiveness (From Full Report Linked Below)

Adjusted vaccine effectiveness in preventing community-acquired influenza was 31% (95% confidence interval [CI], -7 to 55); point estimates were lowest in young children and modestly higher in adults. Stratified analyses indicated substantial differences in vaccine effectiveness based on whether or not seasonal influenza vaccine had been received the prior season (interaction term: $P = .014$). Among subjects with documented evidence of prior season vaccination, estimates of current season vaccine effectiveness were low overall and in each of the age groups examined. In contrast, for those subjects without evidence of prior season vaccine receipt, effectiveness estimates were higher for all age groups and statistically significant overall (62% [95% CI, 17%-82%]).

In adjusted analyses for all ages combined, effectiveness estimates were highest against influenza type B (48% [95% CI, -5% to 75%]), and lower for A (pH1N1) (26% [95% CI, -68% to 67%]) and A (H3N2) (10% [95% CI, -74% to 54%]). In analyses stratified by prior season vaccination status, estimates were substantially higher for those subjects without evidence of prior season vaccine receipt.

Conclusions

Vaccine effectiveness estimates were lower than those demonstrated in other observational studies carried out during the same season. The unexpected findings of lower effectiveness with repeated vaccination and no protection given household exposure require further study.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23413420>

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3693492/>

“Influenza was identified in 78 (24%) households and 125 (9%) individuals; the infection risk was 8.5% in the vaccinated and 8.9% in the unvaccinated ($P = .83$). Adjusted vaccine effectiveness in preventing community-acquired influenza was 31% (95% confidence interval [CI], -7% to 55%).

In vaccinated subjects with no evidence of prior season vaccination, significant protection (62% [95% CI, 17%-82%]) against community-acquired influenza was demonstrated. Substantially lower effectiveness was noted among subjects who were vaccinated in both the current and prior season. There was no evidence that vaccination prevented household transmission once influenza was introduced; adults were at particular risk despite vaccination.”

Comparison of VAERS fetal-loss reports
during three consecutive influenza seasons:
was there a synergistic fetal toxicity associated
with the two-vaccine 2009/2010 season?

Author information

Goldman GS

Independent Computer Scientist
Pearblossom, CA 93553, USA
gsgoldman@roadrunner.com

Abstract

The aim of this study was to compare the number of inactivated-influenza vaccine-related spontaneous abortion and stillbirth (SB) reports in the Vaccine Adverse Event Reporting System (VAERS) database during three consecutive flu seasons beginning 2008/2009 and assess the relative fetal death reports associated with the two-vaccine 2009/2010 season. The VAERS database was searched for reports of fetal demise following administration of the influenza vaccine/vaccines to pregnant women. Utilization of an independent surveillance survey and VAERS, two-source capture-recapture analysis estimated the reporting completeness in the 2009/2010 flu season. Capture-recapture demonstrated that the VAERS database captured about 13.2% of the total 1321 (95% confidence interval (CI): 815-2795) estimated reports, yielding an ascertainment-corrected rate of 590 fetal-loss reports per million pregnant women vaccinated (or 1 per 1695). The unadjusted fetal-loss report rates for the three consecutive influenza seasons beginning 2008/2009 were 6.8 (95% CI: 0.1-13.1), 77.8 (95% CI: 66.3-89.4), and 12.6 (95% CI: 7.2-18.0) cases per million pregnant women vaccinated, respectively. The observed reporting bias was too low to explain the magnitude increase in fetal-demise reporting rates in the VAERS database relative to the reported annual trends. Thus, a synergistic fetal toxicity likely resulted from the administration of both the pandemic (A-H1N1) and seasonal influenza vaccines during the 2009/2010 season.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3888271/>

“Thus, a synergistic fetal toxicity likely resulted from the administration of both the pandemic (A-H1N1) and seasonal influenza vaccines during the 2009/2010 season.”

“While young infants represent the major target population for vaccination, effective immunization in this age group remains a challenge. Many parameters of innate immune responses differ quantitatively and qualitatively from newborns to infants and adults, revealing a highly regulated developmental program.”

Vaccine • May 2013

Immune response to vaccine adjuvants during the first year of life

Ofer Levy, Stanislas Goriely, Tobias R. Kollmann

Abstract

Subunit vaccine formulations often include adjuvants that primarily stimulate innate immune cells. While young infants represent the major target population for vaccination, effective immunization in this age group remains a challenge. Many parameters of innate immune responses differ quantitatively and qualitatively from newborns to infants and adults, revealing a highly regulated developmental program. Herein, we discuss the potential implications of innate immune ontogeny for the activity of adjuvants contained in licensed infant vaccines, as well as future directions for rational design of adjuvanted vaccines for this age group.

- We comprehensively reviewed mechanisms of action of licensed adjuvants.
- We examined the changes of adjuvant responses with age in early life.
- We juxtaposed the current knowledge with safety considerations.
- We point to the need for targeted investigations of adjuvant activity early in life.

<http://www.sciencedirect.com/science/article/pii/S0264410X12014624>

Leukocyte transcript alterations in West-African girls following a booster vaccination with diphtheria-tetanus-pertussis vaccine

Author information

Orntoft NW1, Thorsen K, Benn CS, Lemvik G,
Nanque JR, Aaby P, Ostergaard L, Agergaard J.

Department of Medicine V (Hepatology and Gastroenterology)
Aarhus University Hospital, Aarhus, Denmark

Abstract

Background. Observational studies from low-income countries have shown that the vaccination against diphtheria, tetanus and pertussis (DTP) is associated with excess female mortality due to infectious diseases. **Methods.** To investigate possible changes in gene expression after DTP vaccination, we identified a group of nine comparable West African girls, from a biobank of 356 children, who were due to receive DTP booster vaccine at age 18 months. As a pilot experiment we extracted RNA from blood samples before, and 6 weeks after, vaccination to analyze the coding transcriptome in leukocytes using expression microarrays, and ended up with information from eight girls. The data was further analyzed using dedicated array pathway and network software. We aimed to study whether DTP vaccination introduced a systematic alteration in the immune system in girls. **Results.** We found very few transcripts to alter systematically. Those that did mainly belonged to the Interferon (IFN) signalling pathway. We scrutinized this pathway as well as the Interleukin (IL) pathways. Two out of eight showed a down-regulated IFN pathway and two showed an up-regulated IFN pathway. The two with down-regulated IFN pathway had also down-regulated IL-6 pathway. In the study of networks, two of the girls stood out as not having the inflammatory response as top altered network. **Conclusion.** The transcriptome changes following DTP booster vaccination were subtle, but although the material was small, it was possible to identify sub groups that deviate from each other, mainly in the IFN response.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23668887>

“Two out of eight showed a down-regulated IFN [Interferon] pathway and two showed an up-regulated IFN [Interferon] pathway.”

Video Q&A: what is ASIA? An interview with Yehuda Shoenfeld

Yehuda Shoenfeld
Zabludowicz Center for Autoimmune Diseases
Sheba Medical Center, Tel-Aviv University
Tel-Hashomer 52621, Israel

Introduction

Professor Yehuda Shoenfeld is the founder and head of the Zabludowicz Center for Autoimmune Diseases at the Sheba Medical Center, which is affiliated to the Sackler Faculty of Medicine at Tel-Aviv University, Israel. He is also the Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases at Tel-Aviv University. His clinical and scientific works focus on autoimmune and rheumatic diseases, and he has been the recipient of multiple awards, including a Life Contribution Prize in Internal Medicine in Israel, 2012.

In recent years, Professor Shoenfeld noted that four conditions: siliconosis, Gulf War syndrome (GWS), macrophagicmyofasciitis syndrome (MMF) and post-vaccination phenomena were linked with previous exposure to an adjuvant, and that the patients also presented with similar clinical symptoms. In 2011, this led Professor Shoenfeld to suggest these comparable conditions should be grouped under a common syndrome entitled 'ASIA', for 'Autoimmune (Autoinflammatory) Syndrome Induced by Adjuvants'.

In this Q&A we talk to Professor Shoenfeld about ASIA, and discuss his recommendations regarding further research in the field.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3662178/>

Video Interview

<https://www.youtube.com/watch?v=0n12pWMfHhs>

“In this Q&A we talk to Professor Shoenfeld about ASIA, and discuss his recommendations regarding further research in the field.”

Exercise challenge in Gulf War Illness reveals two subgroups with altered brain structure and function

Author information

Rayhan RU1, Stevens BW, Raksit MP, Ripple JA,
Timbol CR, Adewuyi O, VanMeter JW, Baraniuk JN.

Division of Rheumatology, Immunology and Allergy
Department of Medicine, Georgetown University Medical Center
Washington, District of Columbia, United States of America
rur@georgetown.edu

Abstract

Nearly 30% of the approximately 700,000 military personnel who served in Operation Desert Storm (1990-1991) have developed Gulf War Illness, a condition that presents with symptoms such as cognitive impairment, autonomic dysfunction, debilitating fatigue and chronic widespread pain that implicate the central nervous system. A hallmark complaint of subjects with Gulf War Illness is post-exertional malaise; defined as an exacerbation of symptoms following physical and/or mental effort. To study the causal relationship between exercise, the brain, and changes in symptoms, 28 Gulf War veterans and 10 controls completed an fMRI scan before and after two exercise stress tests to investigate serial changes in pain, autonomic function, and working memory. Exercise induced two clinical Gulf War Illness subgroups. One subgroup presented with orthostatic tachycardia (n=10). This phenotype correlated with brainstem atrophy, baseline working memory compensation in the cerebellar vermis, and subsequent loss of compensation after exercise. The other subgroup developed exercise induced hyperalgesia (n=18) that was associated with cortical atrophy and baseline working memory compensation in the basal ganglia. Alterations in cognition, brain structure, and symptoms were absent in controls. Our novel findings may provide an understanding of the relationship between the brain and post-exertional malaise in Gulf War Illness.

<http://www.ncbi.nlm.nih.gov/pubmed/23798990>

“Nearly 30% of the approximately 700,000 military personnel who served in Operation Desert Storm (1990-1991) have developed Gulf War Illness, a condition that presents with symptoms such as cognitive impairment, autonomic dysfunction, debilitating fatigue and chronic widespread pain that implicate the central nervous system.”

Databases and in silico tools for vaccine design

Author information

He Y1, Xiang Z.

Department of Microbiology and Immunology
Center for Computational Medicine and Bioinformatics
University of Michigan Medical School, Ann Arbor, MI, USA

Abstract

In vaccine design, databases and in silico tools play different but complementary roles. Databases collect experimentally verified vaccines and vaccine components, and in silico tools provide computational methods to predict and design new vaccines and vaccine components. Vaccine-related databases include databases of vaccines and vaccine components. In the USA, the Food and Drug Administration (FDA) maintains a database of licensed human vaccines, and the US Department of Agriculture keeps a database of licensed animal vaccines. Databases of vaccine clinical trials and vaccines in research also exist. The important vaccine components include vaccine antigens, vaccine adjuvants, vaccine vectors, and -vaccine preservatives. The vaccine antigens can be whole proteins or immune epitopes. Various in silico vaccine design tools are also available. The Vaccine Investigation and Online Information Network (VIOLIN; <http://www.violinet.org>) is a comprehensive vaccine database and analysis system. The VIOLIN database includes various types of vaccines and vaccine components. VIOLIN also includes Vaxign, a Web-based in silico vaccine design program based on the reverse vaccinology strategy. Vaccine information and resources can be integrated with Vaccine Ontology (VO). This chapter introduces databases and in silico tools that facilitate vaccine design, especially those in the VIOLIN system.

<http://www.ncbi.nlm.nih.gov/pubmed/23568467>

“Vaxign, a Web-based in silico vaccine design program based on the reverse vaccinology strategy.”

**ASIA or Shoenfeld's syndrome—
an autoimmune syndrome induced by adjuvants**

Cojocaru M, Chico□ B.

Abstract

Recently, reports have suggested grouping different autoimmune conditions that are triggered by external stimuli as a single syndrome called autoimmune syndrome induced by adjuvants (ASIA). This syndrome is characterized by the appearance of myalgia, myositis, muscle weakness, arthralgia, arthritis, chronic fatigue, sleep disturbances, cognitive impairment and memory loss, and the possible emergence of a demyelinating autoimmune disease caused by systemic exposure after vaccines and adjuvants. As there are no markers for ASIA, the authors intend to present ASIA, or Shoenfeld's syndrome, as an autoimmune syndrome induced by adjuvants.

<http://www.ncbi.nlm.nih.gov/pubmed/24620624>

“This syndrome is characterized by the appearance of myalgia, myositis, muscle weakness, arthralgia, arthritis, chronic fatigue, sleep disturbances, cognitive impairment and memory loss, and the possible emergence of a demyelinating autoimmune disease caused by systemic exposure after vaccines and adjuvants.”

Adverse events following immunization with vaccines containing adjuvants

Author information

Cerpa-Cruz S1, Paredes-Casillas P, Landeros Navarro E,
Bernard-Medina AG, Martínez-Bonilla G, Gutiérrez-Ureña S.

Rheumatology and Immunology Department
Hospital Civil de Guadalajara Fray Antonio Alcalde
Hospital 278, SH, Colonia El Retiro, 44280
Guadalajara, Jalisco, Mexico
sacer04@prodigy.net.mx

Abstract

A traditional infectious disease vaccine is a preparation of live attenuated, inactivated or killed pathogen that stimulates immunity. Vaccine immunologic adjuvants are compounds incorporated into vaccines to enhance immunogenicity. Adjuvants have recently been implicated in the new syndrome named ASIA autoimmune/inflammatory syndrome induced by adjuvants. The objective describes the frequencies of post-vaccination clinical syndrome induced by adjuvants. We performed a cross-sectional study; adverse event following immunization was defined as any untoward medical occurrence that follows immunization 54 days prior to the event. Data on vaccinations and other risk factors were obtained from daily epidemiologic surveillance. Descriptive statistics were done using means and standard deviation, and odds ratio adjusted for potential confounding variables was calculated with SPSS 17 software. Forty-three out of 120 patients with moderate or severe manifestations following immunization were hospitalized from 2008 to 2011. All patients fulfilled at least 2 major and 1 minor criteria suggested by Shoenfeld and Agmon-Levin for ASIA diagnosis. The most frequent clinical findings were pyrexia 68%, arthralgias 47%, cutaneous disorders 33%, muscle weakness 16% and myalgias 14%. Three patients had diagnosis of Guillain-Barre syndrome, one patient had Adult-Still's disease 3 days after vaccination. A total of 76% of the events occurred in the first 3 days post-vaccination. Two patients with previous autoimmune disease showed severe adverse reactions with the reactivation of their illness. Minor local reactions were present in 49% of patients. Vaccines containing adjuvants may be associated with an increased risk of autoimmune/inflammatory adverse events following immunization.

<http://www.ncbi.nlm.nih.gov/pubmed/23576057>

“Vaccines containing adjuvants
may be associated with an increased risk
of autoimmune/inflammatory adverse
events following immunization.”

“... a form of the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep, linked to the repetitive inoculation of aluminum-containing adjuvants through vaccination.

The syndrome shows an acute phase that affects less than 0.5% of animals in a given herd ...”

[a syndrome that affects 5,000 per each 1 million]

Immunology Research • July 2013

Autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep

Author information

Luján L1, Pérez M, Salazar E, Álvarez N, Gimeno M,
Pinczowski P, Irusta S, Santamaría J, Insausti N, Cortés Y,
Figueras L, Cuartielles I, Vila M, Fantova E, Chapullé JL.

Department of Animal Pathology
Veterinary Faculty, University of Zaragoza
177 Miguel Servet Street, 50013, Saragossa, Spain
Lluis.Lujan@unizar.es

Abstract

We describe a form of the autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep, linked to the repetitive inoculation of aluminum-containing adjuvants through vaccination. The syndrome shows an acute phase that affects less than 0.5% of animals in a given herd, it appears 2-6 days after an adjuvant-containing inoculation and it is characterized by an acute neurological episode with low response to external stimuli and acute meningoencephalitis, most animals apparently recovering afterward. The chronic phase is seen in a higher proportion of flocks, it can follow the acute phase, and it is triggered by external stimuli, mostly low temperatures. The chronic phase begins with an excitatory phase, followed by weakness, extreme cachexia, tetraplegia and death. Gross lesions are related to a cachectic process with muscular atrophy, and microscopic lesions are mostly linked to a neurodegenerative process in both dorsal and ventral column of the gray matter of the spinal cord. Experimental reproduction of ovine ASIA in a small group of repeatedly vaccinated animals was successful. Detection of Al(III) in tissues indicated the presence of aluminum in the nervous tissue of experimental animals. The present report is the first description of a new sheep syndrome (ovine ASIA syndrome) linked to multiple, repetitive vaccination and that can have devastating consequences as it happened after the compulsory vaccination against bluetongue in 2008. The ovine ASIA syndrome can be used as a model of other similar diseases affecting both human and animals. A major research effort is needed in order to understand its complex pathogenesis.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23579772>

Hidden in Plain Sight: Vaccines as a Major Risk Factor for Chronic Disease

Richard Moskowitz, MD

Abstract

The science and politics of vaccination in this country are examined, with a careful look at the rationale for mandatory vaccination, benefits, and harms, and illustrated by case examples showing injury, yet problematic medical-legal recognition.

Thirty-five years of medical practice have convinced me that all vaccines carry a significant risk of chronic disease that is inherent in the vaccination process and in fact central to how they work. Yet the growing concerns of parents and legislators and the media reports about them seldom elicit anything beyond automatic, scornful denials by medical and public health authorities alike. Reflecting on this discrepancy, the focal point of this essay, has also helped me appreciate how much the invisibility actually heightens the risk, and how intimately these phenomena are connected, like mirror-images of the same reality, so that it is wisest to study them together.

Since I am mainly a clinician, I will begin with a story. It concerns a twelve-year-old boy whom I know of solely from his mother's letter, but her words are so heartfelt and so congruent with the rest of my experience that I cannot doubt their veracity:

My son Adam was healthy until his first MMR shot at 15 months. Within 2 weeks he had flu and cold symptoms, which persisted for 6 weeks. Then his eyes became puffy, and he was hospitalized with nephrotic syndrome. A renal biopsy showed "focal sclerosing glomerulonephritis," but the illness didn't respond to steroids. I asked if it could be related to the vaccine, but they told me it couldn't, and we accepted that. Over the next 4 years he was hospitalized repeatedly, and missed many months of school, but finally went into remission, seeming normal and healthy and staying off all medications for about 5 years.

When he turned 10, his pediatrician recommended a booster, saying that a rise in measles cases made it dangerous for him not to be protected. I checked the PDR and other sources but found no

contraindication for kidney disease and no listing of nephrosis as a possible adverse reaction, so I agreed to it. In less than 2 weeks he relapsed, with 4+ protein in his urine, swelling, and weight gain, signs that we recognized immediately. He got worse even on Prednisone, and was admitted in hypertensive crisis, with blood in his urine, fluid in his lungs,*and massive weight gain. On Cytoxan, massive doses of Prednisone, and three other drugs, he slowly improved, but missed another 7 months of school.

It's been 2 years since that horrible episode, and he still needs Captopril daily for high blood pressure, and spills 4+ protein every day. The doctor says he sustained major kidney damage, will always need medication to control his blood pressure, and will worsen as he grows older, necessitating a transplant eventually. This time I was convinced that his condition was related to the vaccine, but still the doctors didn't take me seriously, and told me it was a coincidence.

I began searching for information, and even contacted the manufacturer of the vaccine. Finally they sent me two case reports of nephrotic syndrome following the MMR vaccine. It's very difficult for lay people to get information, or even ask questions, since we don't use the correct medical terms and are made to feel stupid. Please tell me if my ideas are reasonable.

I don't think my son could tolerate another episode, and I think he'd have normal blood pressure and kidney function today if not for that second vaccination. I also have a great concern for other children who develop nephritic syndrome some weeks after receiving MMR and whose doctors never make the connection. They could all be at great risk if revaccinated. I realize that this letter has taken up a great deal of your time, and I'd appreciate any help you can give me. If we were closer, I'd make an appointment to see you in person, so please feel free to charge me. Thank you.

Full Text

<http://www.whale.to/vaccine/moskowitz.html>

Advisory Commission on Childhood Vaccines • September 2013

**Updating the Vaccine Injury Table:
Guillain-Barré Syndrome (GBS) and
Seasonal Influenza Vaccines**

Ahmed Calvo, M.D., M.P.H.
Medical Officer
National Vaccine Injury Compensation Program (VICP)

Summary

The report leaves us understanding that the strength of evidence and association is high between (2009) H1N1 vaccines and Guillain Barre Syndrome.

Full Report

<http://www.hrsa.gov/vaccinecompensation/updatevaccineinjurytable2013.pdf>

Military risk factors for cognitive decline, dementia and Alzheimer's disease

Author information

Veitch DP1, Friedl KE, Weiner MW.

Center for Imaging of Neurodegenerative Diseases
Veterans Medical Center and Departments of
Radiology, Medicine, Psychiatry and Neurology
University of California, San Francisco
San Francisco, CA, USA
michael.weiner@ucsf.edu

Abstract

Delayed neurological health consequences of environmental exposures during military service have been generally underappreciated. The rapidly expanding understanding of Alzheimer's disease (AD) pathogenesis now makes it possible to quantitate some of the likely long-term health risks associated with military service. Military risk factors for AD include both factors elevated in military personnel such as tobacco use, traumatic brain injury (TBI), depression, and post-traumatic stress disorder (PTSD) and other nonspecific risk factors for AD including, vascular risk factors such as obesity and obesity-related diseases (e.g., metabolic syndrome), education and physical fitness. The degree of combat exposure, Vietnam era Agent Orange exposure and Gulf War Illness may also influence risk for AD. Using available data on the association of AD and specific exposures and risk factors, the authors have conservatively estimated 423,000 new cases of AD in veterans by 2020, including 140,000 excess cases associated with specific military exposures. The cost associated with these excess cases is approximately \$5.8 billion to \$7.8 billion. Mitigation of the potential impact of military exposures on the cognitive function of veterans and management of modifiable risk factors through specifically designed programs will be instrumental in minimizing the impact of AD in veterans in the future decades.

<http://www.ncbi.nlm.nih.gov/pubmed/23906002>

“... the authors have conservatively estimated 423,000 new cases of AD in veterans by 2020, including 140,000 excess cases associated with specific military exposures. The cost associated with these excess cases is approximately \$5.8 billion to \$7.8 billion.”

Distinctive clinical features
in arthro-myalgic patients with and without
aluminum hydroxyde-induced macrophagic myofasciitis:
an exploratory study

Author information

Ragunathan-Thangarajah N1, Le Beller C, Boutouyrie P,
Bassez G, Gherardi RK, Laurent S, Authier FJ.

INSERM U955-Equipe 10
Université Paris Est-Créteil, Créteil, France

Abstract

Macrophagic myofasciitis (MMF) is a specific histological lesion assessing the persistence of vaccine-derived aluminum oxyhydroxide in muscle tissue, at a site of previous immunization. Long-lasting MMF is usually detected in patients with arthromyalgias, chronic fatigue, and stereotyped cognitive dysfunction. MMF diagnosis requires muscle biopsy, an invasive procedure not suitable for the routine investigation of all patients with musculoskeletal pain. To help decision making in routine practice, we designed a retrospective analysis of 130 consecutive arthro-myalgic patients, previously immunized with aluminum-containing vaccines, in whom deltoid muscle biopsy was performed for diagnostic purposes. According to biopsy results, the patients were ascribed to either the MMF or the non-MMF group. MMF was diagnosed in 32.3% of the patients. MMF and non-MMF groups were similar according to both the injected vaccines and the delay between vaccination and biopsy. MMF patients had less frequent fibromyalgia than non-MMF patients (≥ 11 fibromyalgic tender points in 16.6 vs 55.5%, $p < 0.04$), and more often abnormal evoked potentials suggestive of CNS demyelination (38.5 vs 5.7%, $p < 0.01$). Predictive bioclinical scores based on simple variables such as the number of fibromyalgic tender points, arthralgias, and spinal pain, had sensitivity ranging from 50 to 88.1% and specificity from 36.4 to 76.1%.

In Conclusion

(i) most aluminum-containing vaccine receivers do not have long-lasting MMF in their muscle, but the prevalence of MMF among patients with arthromyalgia following immunization is substantial; (ii) patients with MMF have more CNS dysfunction and less fibromyalgic tender points than non-MMF patients; (iii) predictive scores may help to identify patients at high vs low risk of MMF.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23921285>

“most aluminum-containing vaccine receivers
do not have long-lasting MMF in their muscle,
but the prevalence of MMF among patients with
arthromyalgia following immunization is substantial
... patients with MMF have more CNS dysfunction ...”

Targeted vaccine selection in influenza vaccination

Author information

Wutzler P1, Hardt R, Knuf M, Wahle K.
Institute of Virology and Antiviral Therapy - University Hospital Jena

Catholic Clinic Mainz, St. Hildegardis Hospital
Department of Child and Adolescent Medicine
Dr. Horst Schmidt Clinic GmbH, Wiesbaden
German Association of General Practitioners, Münster

Abstract

BACKGROUND

The main target groups for influenza vaccination are the elderly, the chronically ill, infants, and toddlers. Influenza vaccines are needed that suit the immunological particularities of each of these age and risk groups. Recent years have seen the approval of influenza vaccines that are more immunogenic than before, but whose use in Germany is limited by the restriction of reimbursement to a small number of vaccines.

METHODS

The Medline database was selectively searched for pertinent literature.

RESULTS

The suboptimal immunogenicity of conventional influenza vaccines that contain inactivated viral cleavage products and subunits can be markedly improved by the use of squalene-based adjuvant systems, by the integration of viral antigens in virosomal particles, or by intradermal administration. The vaccination of elderly persons with a vaccine containing the adjuvant MF59 was found to lower the risk of hospitalization for influenza or pneumonia by 25% compared to vaccination with a trivalent inactivated vaccine (TIV). On the other hand, the adjuvant ASO3 was found to be associated with an up to 17-fold increase in the frequency of narcolepsy among 4- to 18-year-olds. In a prospective study, a virosomal vaccine lowered the frequency of laboratory-confirmed influenza in vaccinated children by 88% compared to unvaccinated children (2 versus 18 cases per 1000 individuals). A live, attenuated influenza vaccine lowered the rate of disease in children up to age 7 by 48% compared to a TIV (4.2% versus 8.1%).

CONCLUSION

The newer vaccines possess improved efficacy when used for primary and booster immunization in certain age and risk groups, and they are superior in this respect to conventional vaccines based on viral cleavage products and subunits. The risk/benefit profiles of all currently available vaccines vary depending on the age group or risk group in which they are used.

From the full report:

“... the adjuvant ASO3 [squalene] was found to be associated with an up to 17-fold increase in the frequency of narcolepsy among 4- to 18-year-olds.”

Case Of Vaccine-Associated Measles Five Weeks Post-Immunization, British Columbia, Canada, October 2013

Author Information

M Murti (1), M Krajden², M Petric²
J Hiebert³, F Hemming¹, B Hefford⁴
M Bigham¹, P Van Buynder¹

1. Fraser Health Authority
Surrey, British Columbia, Canada
2. Public Health Microbiology and
Reference Laboratory

British Columbia Centre for Disease Control
Vancouver, British Columbia, Canada

3. National Microbiology Laboratory
Public Health Agency of Canada
Winnipeg, Manitoba, Canada

4. 1-1400 George St., White Rock
British Columbia, Canada

We describe a case of vaccine-associated measles in a two-year-old patient from British Columbia, Canada, in October 2013, who received her first dose of measles-containing vaccine 37 days prior to onset of prodromal symptoms. Identification of this delayed vaccine-associated case occurred in the context of an outbreak investigation of a measles cluster.

Based on our review of the literature, this report documents the first case of MMR vaccine-associated measles, 37 days post-immunisation, well beyond 21 days and the

routine 30 days post-MMR immunisation period used by the Canadian adverse event following immunization (AEFI) surveillance system.

Measles-containing vaccines are used globally, have been part of the British Columbia immunisation schedule since 1969, and have an impressive record of safety validated by careful, ongoing AEFI surveillance. Rash and/or mild clinical illness following MMR vaccine are not uncommon [7]. Clinically significant vaccine-associated illness is rare, but when it occurs it is indistinguishable from wild-type measles, except by genotyping [8]. Detection of vaccine virus has been documented up to 14 days post-immunisation by RT-PCR, and up to 16 days by immunofluorescence microscopy of urine sediment [9-12]. Complications from vaccine-associated measles have been documented in both immune-competent and compromised individuals [13,14]. Of note, only one case report of transmission from vaccine-associated measles has been identified [15,16].

Possible explanations for this prolonged shedding of measles vaccine virus include interference with the immune response by host or vaccine factors. Immunoglobulin administration early in the incubation period has been reported to extend the time to onset of symptoms, but in this child there was no such history and no known immunosuppressive illness [5]. The two-fold rise between acute and convalescent measles-specific IgG suggests the vaccine-mediated immune response had been underway prior to the onset of symptoms. Investigations clarified that there were no shipping, handling or cold-chain deviations for the specific vaccine used, and that it was administered by a public health nurse trained in immunisations. The potential immunological impact of the older age of the child at the time of receiving the first dose of MMR vaccine, 33 months versus the typical 12-15 months of age, and the co-administration of meningococcal C and pneumococcal conjugate vaccines are areas for future investigation.

“We describe a case of vaccine-associated measles in a two-year-old patient from British Columbia, Canada, in October 2013, who received her first dose of measles-containing vaccine 37 days prior to onset of prodromal symptoms. Identification of this delayed vaccine-associated case occurred in the context of an outbreak investigation of a measles cluster. Possible explanations for this prolonged shedding of measles vaccine virus include interference with the immune response by host or vaccine factors.”

Full Report

The fetal inflammatory response syndrome is a risk factor for morbidity in preterm neonates

Author information

Hofer N1, Kothari R, Morris N, Müller W, Resch B.

Research Unit for Neonatal Infectious Diseases and Epidemiology
Medical University of Graz, Graz, Austria

Abstract

OBJECTIVE

The aim of this study was to show and discuss an association between fetal inflammatory response syndrome (FIRS) and an adverse neonatal outcome defined as combined severe neonatal morbidity and mortality in preterm neonates hospitalized in our neonatal intensive care unit.

STUDY DESIGN

This was an observational study including all preterm neonates hospitalized in our neonatal intensive care unit over a 21 month period. FIRS was defined as cord blood interleukin (IL)-6 greater than 11 pg/mL. Main outcome parameter was an adverse neonatal outcome defined as hospital mortality and/or the presence of any of 5 pre-specified morbidities (bronchopulmonary dysplasia, periventricular leukomalacia, intraventricular hemorrhage, and early- or late-onset sepsis).

RESULTS

Fifty-seven of 176 preterm infants hospitalized during the study period (32%) had an adverse neonatal outcome and 62 of these 176 infants (35%) had FIRS with median IL-6 values of 51.8 pg/mL (range, 11.2 to >1000 pg/mL). In a regression analysis, FIRS was significantly associated with adverse neonatal outcome ($P < .001$) and with the single outcome parameters, intraventricular hemorrhage and early-onset sepsis ($P = .006$ and $P = .018$, respectively). In the bivariate analysis, FIRS was associated with death and bronchopulmonary dysplasia ($P = .004$ and $P < .001$, respectively). IL-6 correlated with adverse neonatal outcome ($r = 0.411$, $P < .001$). When comparing the correlation in neonates less than 32 weeks' gestational age ($r = 0.481$, $P < .001$) with neonates 32 weeks or longer ($r = 0.233$, $P = .019$), the difference was nearly significant ($P = .065$).

CONCLUSION

FIRS is a risk factor for adverse neonatal outcome in preterm infants. In particular, the combination of IL-6 greater than 11 pg/mL and low gestational age increased the risk for severe neonatal morbidity or death.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23994220>

[hospitals do not routinely check interleukin (IL)-6 cord blood prior to vaccination, although they could]

**Autoimmune/inflammatory syndrome
induced by adjuvants (ASIA) 2013:
Unveiling the pathogenic, clinical and diagnostic aspects**

Author information

Perricone C1, Colafrancesco S, Mazor RD, Soriano A, Agmon-Levin N, Shoenfeld Y.

The Zabłudowicz Center for Autoimmune Diseases, Sheba Medical Center, Israel
Reumatologia, Dipartimento di Medicina Interna e Specialità Mediche
Sapienza Università di Roma, Rome, Italy

Abstract

In 2011 a new syndrome termed ‘ASIA Autoimmune/Inflammatory Syndrome Induced by Adjuvants’ was defined pointing to summarize for the first time the spectrum of immune-mediated diseases triggered by an adjuvant stimulus such as chronic exposure to silicone, tetramethylpentadecane, pristane, aluminum and other adjuvants, as well as infectious components, that also may have an adjuvant effect. All these environmental factors have been found to induce autoimmunity by themselves both in animal models and in humans: for instance, silicone was associated with siliconosis, aluminum hydroxide with post-vaccination phenomena and macrophagic myofasciitis syndrome. Several mechanisms have been hypothesized to be involved in the onset of adjuvant-induced autoimmunity; a genetic favorable background plays a key role in the appearance on such vaccine-related diseases and also justifies the rarity of these phenomena. This paper will focus on protean facets which are part of ASIA, focusing on the roles and mechanisms of action of different adjuvants which lead to the autoimmune/inflammatory response. The data herein illustrate the critical role of environmental factors in the induction of autoimmunity. Indeed, it is the interplay of genetic susceptibility and environment that is the major player for the initiation of breach of tolerance.

<http://www.ncbi.nlm.nih.gov/pubmed/24238833>

“In 2011 a new syndrome termed ‘ASIA Autoimmune/Inflammatory Syndrome Induced by Adjuvants’ was defined pointing to summarize for the first time the spectrum of immune-mediated diseases triggered by an adjuvant stimulus such as chronic exposure to silicone, tetramethylpentadecane, pristane, aluminum and other adjuvants, as well as infectious components, that also may have an adjuvant effect.”

Autoimmune (auto-inflammatory) syndrome induced by adjuvants (ASIA)— animal models as a proof of concept

Author information

Cruz-Tapias P1, Agmon-Levin N, Israeli E, Anaya JM, Shoenfeld Y.

Head of Zabłudowitz Center for Autoimmune Diseases
Sheba Medical Center, Tel Hashomer 52621, Israel
shoenfel@post.tau.ac.il

Abstract

ASIA syndrome, “Autoimmune (Auto-inflammatory) Syndromes Induced by Adjuvants” includes at least four conditions which share a similar complex of signs and symptoms and have been defined by hyperactive immune responses: silicosis, macrophagic myofasciitis syndrome, Gulf war syndrome and post-vaccination phenomena. Exposure to adjuvants has been documented in these four medical conditions, suggesting that the common denominator to these syndromes is a trigger entailing adjuvant activity. An important role of animal models in proving the ASIA concept has been established. Experimentally animal models of autoimmune diseases induced by adjuvants are currently widely used to understand the mechanisms and etiology and pathogenesis of these diseases and might thus promote the development of new diagnostic, predictive and therapeutic methods. In the current review we wish to unveil the variety of ASIA animal models associated with systemic and organ specific autoimmune diseases induced by adjuvants. We included in this review animal models for rheumatoid arthritis-like disease, for systemic lupus erythematosus-like disease, autoimmune thyroid disease-like disease, antiphospholipid syndrome, myocarditis and others. All these models support the concept of ASIA, as the Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants.

<http://www.ncbi.nlm.nih.gov/pubmed/23992328>

“We included in this review animal models for rheumatoid arthritis-like disease, for systemic lupus erythematosus-like disease, autoimmune thyroid disease-like disease, antiphospholipid syndrome, myocarditis and others. All these models support the concept of ASIA, as the Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants.”

“... vaccine-induced Febrile Seizures could be a problem, particularly in genetically predisposed children.”

Expert Review of Vaccines • 2013

Vaccines and febrile seizures

Abstract

Vaccine administration is the second leading cause of febrile seizures (FS). FS occurrence in children is a serious concern because it leads to public apprehension of vaccinations. This review discusses the clinical implications of FS, its potential link to vaccinations and its impact on official recommendations for vaccinations in children. Vaccines such as the pertussis antigen-containing vaccine, the measles-containing vaccine and the influenza vaccine have been linked to FS. However, FS events are very rare and are not usually associated with downstream complications or severe neurologic diseases. Considering their significant health benefits, vaccinations have not been restricted in the pediatric population. Nevertheless, vaccine-induced FS could be a problem, particularly in genetically predisposed children. Therefore, post-marketing surveillance studies are required to accurately assess the incidence of FS and identify individuals who are particularly susceptible to FS after vaccination.

<http://www.tandfonline.com/doi/abs/10.1586/14760584.2013.814781>

Mortality among recipients
of the Merck V710 Staphylococcus aureus vaccine
after postoperative S. aureus infections:
an analysis of possible contributing host factors

Author information

McNeely TB1, Shah NA, Fridman A, Joshi A,
Hartzel JS, Keshari RS, Lupu F, DiNubile MJ.

Merck Research Laboratories, West Point, PA USA

Abstract

In a blinded randomized trial, preoperative receipt of the Merck V710 Staphylococcus aureus vaccine was associated with a higher mortality rate than placebo in patients who later developed postoperative S. aureus infections. Of the tested patients, all 12 V710 recipients (but only 1 of 13 placebo recipients) with undetectable serum IL2 levels prior to vaccination and surgery died after postoperative S. aureus infection. The coincidence of 3 factors (low prevaccination IL-2 levels, receipt of V710, and postoperative S. aureus infection) appeared to substantially increase mortality in our study population after major cardiothoracic surgery. Furthermore, 9 of the 10 V710 recipients with undetectable preoperative IL17a levels and postoperative S. aureus infections died. Although the current study is hypothesis-generating and the exact pathophysiology remains speculative, these findings raise concern that immune predispositions may adversely impact the safety and efficacy of staphylococcal vaccines actively under development. The potential benefits of an effective vaccine against S. aureus justify continued but cautious pursuit of this elusive goal.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483690>

“In a blinded randomized trial, preoperative receipt of the Merck V710 Staphylococcus aureus vaccine was associated with a higher mortality rate than placebo in patients who later developed postoperative S. aureus infections. Of the tested patients, all 12 V710 recipients (but only 1 of 13 placebo recipients) with undetectable serum IL2 levels prior to vaccination and surgery died after postoperative S. aureus infection.”

Human Vaccines & Immunotherapeutics • 2014

Hepatitis B vaccine adverse events in China: risk control and regulation

Author information

Meina L1, Xiaodong L, Lulu Z.

1. The Second Military Medical University
Faculty of Health Service; Institute of Military Health Management
PLA; Shanghai, China

Abstract

The death of 17 children raised public fears over infant hepatitis B vaccination in China. Though the relation between hepatitis B and children's death was denied after prudent investigation, the negative impact remained. In order to prevent or minimize adverse events after vaccination, special strategy including regulation and reimbursement should be developed.

<http://www.ncbi.nlm.nih.gov/pubmed/25483642>

“The death of 17 children
raised public fears over infant
hepatitis B vaccination in China.”

Selective elevation of circulating CCL2/MCP1 levels in patients with longstanding post-vaccinal macrophagic myofasciitis and ASIA

Author information

Cadusseau J, Ragunathan-Thangarajah N, Surenaud M, Hue S, Authier FJ, Gherardi RK1.

Université Paris Est, Faculté de Sciences et Technologie
Créteil, 94000, France
romain.gherardi@hmn.aphp.fr

Abstract

Several medical conditions sharing similar signs and symptoms may be related to immune adjuvants. These conditions described as ASIA (Autoimmune/inflammatory Syndrome Induced by Adjuvants), include a condition characterized by macrophagic myofasciitis (MMF) assessing long-term persistence of vaccine derived-alum adjuvants into macrophages at sites of previous immunization. Despite increasing data describing clinical manifestations of ASIA have been reported, biological markers are particularly lacking for their characterization and follow up. We report an extensive cytokine screening performed in serum from 44 MMF patients compared both to sex and age matched healthy controls and to patients with various types of inflammatory neuromuscular diseases. Thirty cytokines were quantified using combination of Luminex® technology and ELISA. There was significant mean increase of serum levels of the monocyte chemoattractant protein 1 (CCL2/MCP-1) in MMF patients compared to healthy subjects. MMF patients showed no elevation of other cytokines. This contrasted with inflammatory patients in whom CCL2/MCP-1 serum levels were unchanged, whereas several other inflammatory cytokines were elevated (IL1 α , IL5 and CCL3/MIP1 α). These results suggest that CCL2 may represent a biological marker relevant to the pathophysiology of MMF rather than a non specific inflammatory marker and that it should be checked in the other syndromes constitutive of ASIA.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24083602>

“These conditions described as ASIA, include a condition characterized by macrophagic myofasciitis (MMF) assessing long-term persistence of vaccine derived-alum adjuvants into macrophages at sites of previous immunization.”

Immunological persistence in 5 year olds
previously vaccinated with
hexavalent DTPa-HBV-IPV/Hib
at 3, 5, and 11 months of age

Author information

Silfverdal SA1, Assudani D,
Kuriyakose S, Van Der Meeren O.

1. Department of Clinical Sciences
Pediatrics; Umeå University
Umeå, Sweden

Abstract

The combined diphtheria-tetanus-acellular pertussis-hepatitis B-polio-myelitis/Haemophilus influenza vaccine (DTPa-HBV-IPV/Hib: Infanrix™ hexa, GlaxoSmithKline Vaccines) is used for primary vaccination of infants in a range of schedules world-wide. Antibody persistence after 4 DTPa-HBV-IPV/Hib doses in the first 2 y of life has been documented, but long-term persistence data following the 3, 5, 11-12 months (3-5-11) infant vaccination schedule, employed for example in Nordic countries, are limited. We assessed antibody persistence in 57 5-year-old children who had received either DTPa-HBV-IPV/Hib or DTPa-IPV/Hib (Infanrix™-IPV/Hib, GlaxoSmith-Kline Vaccines) in the 3-5-11 schedule. Among DTPa-HBV-IPV/Hib recipients, 7/12 retained seroprotective antibody concentrations for diphtheria, 10/12 for tetanus, 5/12 for hepatitis and 10/12 for Hib. Detectable antibodies were observed for 0/12 children for pertussis toxin (PT), 12/12 for filamentous haemagglutinin (FHA) and 8/12 for pertactin (PRN). Among DTPa-IPV/Hib recipients, 28/45 retained seroprotective anti-diphtheria concentrations, 34/44 for tetanus and 40/45 for Hib. Detectable antibodies were observed for 9/45 children for PT, 41/45 for FHA and 34/45 for PRN. Antibody persistence in DTPa-HBV-IPV/Hib and DTPa-IPV/Hib-vaccinees appeared similar in 5 y olds to that previously observed in children of a similar age who had received 4 prior doses of DTPa-HBV-IPV/Hib (or DTPa-IPV/Hib). As in subjects primed with 4 prior doses, we observed that antibodies markedly declined by 5 y of age, calling for the administration of a pre-school booster dose in order to ensure continued protection against pertussis.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483640>

[regarding vaccine non-responders

and low-responders:

In this study 7 of 12 five year old children

retained seroprotective antibody concentrations

for diphtheria, 10 of 12 for tetanus, 5 of 12 for hepatitis

and 10 of 12 for Hib. The pro-vaccine lobby never

discusses non-responders and low responders and

the large variance in human response to vaccination.

Even vaccinated people can be fully non-responsive

or so low-responsive that they can communicate

diseases as easily as non-vaccinated people making

vaccination an entirely uncertain medical procedure

and adding substance and support to the position

that vaccination is not always effective]

Consumer reporting of adverse events following immunization

Author information

Clothier HJ1, Selvaraj G, Easton ML,
Lewis G, Crawford NW, Buttery JP.

1. SAEFVIC; Murdoch Childrens Research Institute
Melbourne; School of Population & Global Health
University of Melbourne; Melbourne, Victoria, Australia

Abstract

Surveillance of adverse events following immunisation (AEFI) is an essential component of vaccine safety monitoring. The most commonly utilized passive surveillance systems rely predominantly on reporting by health care providers (HCP). We reviewed adverse event reports received in Victoria, Australia since surveillance commencement in July 2007, to June 2013 (6 years) to ascertain the contribution of consumer (vaccinee or their parent/guardian) reporting to vaccine safety monitoring and to inform future surveillance system development directions. Categorical data included were: reporter type; serious and non-serious AEFI category; and, vaccinee age group. Chi-square test and 2-sample test of proportions were used to compare categories; trend changes were assessed using linear regression. Consumer reporting increased over the 6 years, reaching 21% of reports received in 2013 ($P < 0.001$), most commonly for children aged less than 7 years. Consumer reports were 5% more likely to describe serious AEFI than HCP ($P = 0.018$) and 10% more likely to result in specialist clinic attendance ($P < 0.001$). Although online reporting increased to 32% of all report since its introduction in 2010, 85% of consumers continued to report by phone. Consumer reporting of AEFI is a valuable component of vaccine safety surveillance in addition to HCP reporting. Changes are required to AEFI reporting systems to implement efficient consumer AEFI reporting, but may be justified for their potential impact on signal detection sensitivity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483686>

“Consumer reporting
increased over the 6 years,
reaching 21% of reports
received in 2013 ($P < 0.001$),
most commonly for children
aged less than 7 years.”

Human Vaccines And Immunotherapeutics • 2014

Immunocompetent mouse models to evaluate intrahepatic T cell responses to HCV vaccines

Author information

Yu W1, Grubor-Bauk B,
Mullick R, Das S, Gowans EJ.

1. Discipline of Surgery
University of Adelaide
Basil Hetzel Institute
Adelaide, SA, Australia

Abstract

Despite considerable progress in the development of immunocompetent mouse models using different high end technologies, most available small animal models for HCV study are unsuitable for challenge experiments, which are vital for vaccine development, as they fail to measure the T cell response in liver. A recently developed intra-hepatic challenge model results in HCV antigen expression in mouse hepatocytes and through the detection of the surrogate marker, SEAP, in serum, the effect of prior vaccination can be monitored longitudinally.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483684>

[vaccination is inherently experimental.

There are so many unknowns

that this is indisputable]

The persistence of anti-HBs antibody and anamnestic response 20 years after primary vaccination with recombinant hepatitis B vaccine at infancy

Author information

Bagheri-Jamebozorgi M1, Keshavarz J, Nemati M,
Mohammadi-Hossainabad S, Rezayati MT, Nejad-Ghaderi M,
Jamalizadeh A, Shokri F, Jafarzadeh A.
Molecular Medicine Research Center
Rafsanjan University of Medical Sciences
Rafsanjan, Iran

Abstract

Hepatitis B (HB) vaccine induces protective levels of antibody response (anti-HBs \geq 10 mIU/mL) in 90-99% of vaccinees. The levels of anti-HBs antibody decline after vaccination. The aim of this study was to evaluate the persistence of anti-HBs antibodies and immunologic memory in healthy adults at 20 years after primary vaccination with recombinant HB vaccine. Blood samples were collected from 300 adults at 20 years after primary HB vaccination and their sera were tested for anti-HBs antibody by ELISA technique. A single booster dose of HB vaccine was administered to a total of 138 subjects, whose anti-HBs antibody titer was <10 mIU/mL. The sera of subjects were re-tested for the anti-HBs antibody levels at 4 weeks after booster vaccination. At 20 years after primary vaccination 37.0% of participants had protective levels of antibody with geometric mean titer (GMT) of 55.44 \pm 77.01 mIU/mL. After booster vaccination, 97.1% of vaccinees developed protective levels of antibody and the GMT rose from 2.35 \pm 6.49 mIU/mL to 176.28 \pm 161.78 mIU/mL. 125/138 (90.6%) of re-vaccinated subjects also showed an anamnestic response to booster vaccination. At 20 years after primary vaccination with HB vaccine, low proportion of the subjects had protective levels of antibody. However, the majority of the re-vaccinated subjects developed protective levels of anti-HBs and showed an anamnestic response after booster vaccination. Additional follow-up studies are necessary to determine the duration of immunological memory.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483689>

“At 20 years after
primary vaccination
37.0% of participants
had protective levels of antibody ...”

Serum and mucosal antibody responses to inactivated polio vaccine after sublingual immunization using a thermoresponsive gel delivery system

Author information

White JA1, Blum JS, Hosken NA, Marshak JO,
Duncan L, Zhu C, Norton EB, Clements JD, Koelle DM,
Chen D, Weldon WC, Oberste MS, Lal M.

Abstract

Administering vaccines directly to mucosal surfaces can induce both serum and mucosal immune responses. Mucosal responses may prevent establishment of initial infection at the port of entry and subsequent dissemination to other sites. The sublingual route is attractive for mucosal vaccination, but both a safe, potent adjuvant and a novel formulation are needed to achieve an adequate immune response. We report the use of a thermoresponsive gel (TRG) combined with a double mutant of a bacterial heat-labile toxin (dmLT) for sublingual immunization with a trivalent inactivated poliovirus vaccine (IPV) in mice. This TRG delivery system, which changes from aqueous solution to viscous gel upon contact with the mucosa at body temperature, helps to retain the formulation at the site of delivery and has functional adjuvant activity from the inclusion of dmLT. IPV was administered to mice either sublingually in the TRG delivery system or intramuscularly in phosphate-buffered saline. We measured poliovirus type-specific serum neutralizing antibodies as well as polio-specific serum Ig and IgA antibodies in serum, saliva, and fecal samples using enzyme-linked immunosorbent assays. Mice receiving sublingual vaccination via the TRG delivery system produced both mucosal and serum antibodies, including IgA. Intramuscularly immunized animals produced only serum neutralizing and binding Ig but no detectable IgA. This study provides proof of concept for sublingual immunization using the TRG delivery system, comprising a thermoresponsive gel and dmLT adjuvant.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25483682>

“This study provides
proof of concept for
sublingual immunization ...”

Nanoparticle vaccines

Liang Zhaoa, 1, Arjun Setha, 1, Nani Wibowoa, Chun-Xia Zhaoa,
Neena Mitterb, Chengzhong Yua, Anton P.J. Middelberga

a. The University of Queensland
Australian Institute for Bioengineering and Nanotechnology
St. Lucia QLD 4072, Australia
b. The University of Queensland
Queensland Alliance for Agriculture and Food Innovation
St. Lucia QLD 4072, Australia

Abstract

Nanotechnology increasingly plays a significant role in vaccine development. As vaccine development orientates toward less immunogenic “minimalist” compositions, formulations that boost antigen effectiveness are increasingly needed. The use of nanoparticles in vaccine formulations allows not only improved antigen stability and immunogenicity, but also targeted delivery and slow release. A number of nanoparticle vaccines varying in composition, size, shape, and surface properties have been approved for human use and the number of candidates is increasing. However, challenges remain due to a lack of fundamental understanding regarding the in vivo behavior of nanoparticles, which can operate as either a delivery system to enhance antigen processing and/or as an immunostimulant adjuvant to activate or enhance immunity. This review provides a broad overview of recent advances in prophylactic nanovaccinology. Types of nanoparticles used are outlined and their interaction with immune cells and the biosystem are discussed. Increased knowledge and fundamental understanding of nanoparticle mechanism of action in both immunostimulatory and delivery modes, and better understanding of in vivo biodistribution and fate, are urgently required, and will accelerate the rational design of nanoparticle-containing vaccines.

<http://www.sciencedirect.com/science/article/pii/S0264410X13016319>

“As vaccine development orientates toward less immunogenic “minimalist” compositions, formulations that boost antigen effectiveness are increasingly needed. The use of nanoparticles in vaccine formulations allows not only improved antigen stability and immunogenicity, but also targeted delivery and slow release. A number of nanoparticle vaccines varying in composition, size, shape, and surface properties have been approved for human use and the number of candidates is increasing.”

Updates on the web-based VIOLIN vaccine database and analysis system

Author information

He Y1, Racz R, Sayers S, Lin Y, Todd T, Hur J, Li X, Patel M, Zhao B, Chung M, Ostrow J, Sylora A, Dungarani P, Ulysse G, Kochhar K, Vidri B, Strait K, Jourdian GW, Xiang Z.

Unit for Laboratory Animal Medicine, University of Michigan
Department of Microbiology and Immunology, University of Michigan
Center for Computational Medicine and Biology, University of Michigan
Comprehensive Cancer Center, University of Michigan
College of Pharmacy, University of Michigan
School of Public Health, University of Michigan
Division of Comparative Medicine, University of South Florida
Department of Neurology, University of Michigan
College of Literature, Science, and the Arts, University of Michigan
Department of Biomedical Engineering, University of Michigan
Department of Internal Medicine, University of Michigan Medical School
Department of Biological Chemistry, University of Michigan Medical School

Abstract

The integrative Vaccine Investigation and Online Information Network (VIOLIN) vaccine research database and analysis system (<http://www.violinet.org>) curates, stores, analyses and integrates various vaccine-associated research data. Since its first publication in NAR in 2008, significant updates have been made. Starting from 211 vaccines annotated at the end of 2007, VIOLIN now includes over 3240 vaccines for 192 infectious diseases and eight noninfectious diseases (e.g. cancers and allergies). Under the umbrella of VIOLIN, >10 relatively independent programs are developed. For example, Protegen stores over 800 protective antigens experimentally proven valid for vaccine development. VirmugenDB annotated over 200 ‘virmugens’, a term coined by us to represent those virulence factor genes that can be mutated to generate successful live attenuated vaccines. Specific patterns were identified from the genes collected in Protegen and VirmugenDB. VIOLIN also includes Vaxign, the first web-based vaccine candidate prediction program based on reverse vaccinology. VIOLIN collects and analyzes different vaccine components including vaccine adjuvants (Vaxjo) and DNA vaccine plasmids (DNAVaxDB). VIOLIN includes licensed human vaccines (Huvax) and veterinary vaccines (Vevax). The Vaccine Ontology is applied to standardize and integrate various data in VIOLIN. VIOLIN also hosts the Ontology of Vaccine Adverse Events (OVAE) that logically represents adverse events associated with licensed human vaccines.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3964998/>

“The integrative Vaccine Investigation and Online Information Network (VIOLIN) vaccine research database and analysis system curates, stores, analyses and integrates various vaccine-associated research data. Starting from 211 vaccines annotated at the end of 2007, VIOLIN now includes over 3,240 vaccines for 192 infectious diseases and eight noninfectious diseases ...”

Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only

An observational study from Guinea-Bissau

Author information

Fisker AB1, Ravn H2, Rodrigues A3, Østergaard MD4, Bale C5, Benn CS6, Aaby P7.

1. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau; Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark. Electronic address: a.fisker@bandim.org.
2. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau; Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark. Electronic address: hjn@ssi.dk.
3. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau. Electronic address: a.rodrigues@bandim.org.
4. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau. Electronic address: mariedrivsholm@gmail.com.
5. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau. Electronic address: c.bale@bandim.org.
6. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau; Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark. Electronic address: cb@ssi.dk.
7. Bandim Health Project, INDEPTH Network, Apartado 861, Bissau, Guinea-Bissau; Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark. Electronic address: p.aaby@bandim.org

Abstract

BACKGROUND

Studies from low-income countries indicate that co-administration of inactivated diphtheria-tetanus-pertussis (DTP) vaccine and live attenuated measles vaccine (MV) is associated with increased mortality compared with receiving MV only. Pentavalent (DTP-H. Influenza type B-Hepatitis B) vaccine is replacing DTP in many low-income countries and yellow fever vaccine (YF) has been introduced to be given together with MV. Pentavalent and YF vaccines were introduced in Guinea-Bissau in 2008. We investigated whether co-administration of pentavalent vaccine with MV and yellow fever vaccine has similar negative effects.

METHODS

In 2007-2011, we conducted a randomised placebo-controlled trial of vitamin A at routine vaccination contacts among children aged 6-23 months in urban and rural Guinea-Bissau. In the present study, we included 2331 children randomised to placebo who received live vaccines only (MV or MV+YF) or a combination of live and inactivated vaccines (MV+DTP or MV+YF+pentavalent). Mortality was compared in Cox proportional hazards models stratified for urban/rural enrolment adjusted for age and unevenly distributed baseline factors.

RESULTS

While DTP was still used 685 children received MV only and 358 MV+DTP; following the change in programme, 940 received MV+YF only and 348 MV+YF+pentavalent. During 6 months of follow-up, the adjusted mortality rate ratio (MRR) for co-administered live and inactivated vaccines compared with live vaccines only was 3.24 (1.20-8.73). For MV+YF+pentavalent compared with MV+YF only, the adjusted MRR was 7.73 (1.79-33.4).

CONCLUSION

In line with previous studies of DTP, the present results indicate that pentavalent vaccine co-administered with MV and YF is associated with increased mortality.

“In line with previous studies of DTP, the present results indicate that pentavalent vaccine co-administered with MV and YF is associated with increased mortality.”

A review on the association between inflammatory myopathies and vaccination

Author information

Stübgen JP.

Department of Neurology
Weill Cornell Medical College/New York Presbyterian Hospital
525 East 68th Street, New York, NY 10065-4885, USA
pstuebge@med.cornell.edu

Abstract

Several viruses and vaccines are among the environmental factors implicated as triggers of autoimmune inflammatory myopathies. Case histories report on the onset of dermatomyositis/polymyositis after immunization with various vaccines of patients with probable genetic predisposition. However, retrospective and epidemiological studies failed to ascertain an association between DM/PM and vaccines: no significant increase in the incidence of DM/PM was reported after large vaccination campaigns. The risk for vaccine-induced adverse events may be enhanced by adjuvants. Macrophagic myofasciitis is a novel inflammatory myopathy ascribed to an ongoing local immune reaction to a vaccine adjuvant. Isolated prospective studies showed that the administration of unadjuvanted, non-live vaccine to patients with DM/PM caused no short-term harmful effects to DM/PM immune processes. However, more research is warranted to clarify the incidence of vaccine-preventable infections, harmful effects of vaccination, and the influence of any immunomodulating agents on vaccination efficacy. Vaccination is an important disease prevention tool in modern medicine. This review does not address risk-benefit or cost-benefit analyses, and does not advocate the use of specific vaccines or vaccination programs. Despite a great deal of scientific uncertainty, the concept of a possible causal link between immunization and inflammatory myopathies should not be totally rejected.

<http://www.ncbi.nlm.nih.gov/pubmed/24001753>

“Macrophagic myofasciitis is a novel inflammatory myopathy ascribed to an ongoing local immune reaction to a vaccine adjuvant ... more research is warranted to clarify the incidence of vaccine-preventable infections, harmful effects of vaccination, and the influence of any immunomodulating agents on vaccination efficacy. Despite a great deal of scientific uncertainty, the concept of a possible causal link between immunization and inflammatory myopathies should not be totally rejected.”

Sjögren's syndrome:
another facet of the
autoimmune/inflammatory syndrome induced by adjuvants
(ASIA)

Author information

Colafrancesco S1, Perricone C1,
Priori R2, Valesini G2, Shoenfeld Y3.

1. Department of Internal Medicine and Medical Specialities, Rheumatology Unit, Sapienza University of Rome, Italy
The Zabłudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel
2. Department of Internal Medicine and Medical Specialities, Rheumatology Unit, Sapienza University of Rome, Italy
3. The Zabłudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer, Israel
Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases
Sackler Faculty of Medicine, Tel Aviv University, Israel
shoenfel@post.tau.ac.il

Abstract

Recently, a new syndrome, namely the “Autoimmune/inflammatory syndrome induced by adjuvants” (ASIA) has been defined. In this syndrome different conditions characterized by common signs and symptoms and induced by the presence of an adjuvant are included. The adjuvant is a substance capable of boosting the immune response and of acting as a trigger in the development of autoimmune diseases. Post-vaccination autoimmune phenomena represent a major issue of ASIA. Indeed, despite vaccines represent a mainstay in the improvement of human health, several of these have been implicated as a potential trigger for autoimmune diseases. Sjogren's Syndrome (SjS) is a systemic chronic autoimmune inflammatory disease characterized by the presence of an inflammatory involvement of exocrine glands accompanied by systemic manifestations. Own to the straight association between infectious agents exposure (mainly viruses) and sicca syndrome development, the possible link between vaccine and SjS is not surprising. Indeed, a few cases of SjS following vaccine delivery have been reported. At the same extent, the induction of SjS following silicone exposure has been described too. Thus, the aim of this review was to focus on SjS and its possible development following vaccine or silicone exposure in order to define another possible facet of the ASIA syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/24774584>

“despite vaccines represent a mainstay
in the improvement of human health, several of these have
been implicated as a potential trigger for autoimmune diseases.
Sjogren's Syndrome (SjS) is a systemic chronic autoimmune
inflammatory disease characterized by the presence of an
inflammatory involvement of exocrine glands accompanied
by systemic manifestations.”

Risk of intussusception after monovalent rotavirus vaccination

Author information

Weintraub ES1, Baggs J, Duffy J, Vellozzi C,
Belongia EA, Irving S, Klein NP, Glanz JM, Jacobsen SJ,
Naleway A, Jackson LA, DeStefano F.

From the Centers for Disease Control and Prevention
Immunization Safety Office, Atlanta (E.S.W., J.B., J.D., C.V., F.D.)
Marshfield Clinic Research Foundation, Marshfield, WI (E.A.B.)
Center for Health Research, Kaiser Permanente Northwest, Portland, OR (S.I., A.N.)
Vaccine Study Center, Kaiser Permanente Northern California, Oakland (N.P.K.)
Kaiser Permanente Colorado, Aurora (J.M.G.)
Kaiser Permanente Southern California, Pasadena (S.J.J.)
Group Health Research Institute, Seattle (L.A.J.)

Abstract

BACKGROUND

Although current rotavirus vaccines were not associated with an increased risk of intussusception in large trials before licensure, recent postlicensure data from international settings suggest the possibility of a small increase in risk of intussusception after monovalent rotavirus vaccination. We examined this risk in a population in the United States.

METHODS

Participants were infants between the ages of 4 and 34 weeks who were enrolled in six integrated health care organizations in the Vaccine Safety Datalink (VSD) project. We reviewed medical records and visits for intussusception within 7 days after monovalent rotavirus vaccination from April 2008 through March 2013. Using sequential analyses, we then compared the risk of intussusception among children receiving monovalent rotavirus vaccine with historical background rates. We further compared the risk after monovalent rotavirus vaccination with the risk in a concurrent cohort of infants who received the pentavalent rotavirus vaccine.

RESULTS

During the study period, 207,955 doses of monovalent rotavirus vaccine (including 115,908 first doses and 92,047 second doses) were administered in the VSD population. We identified 6 cases of intussusception within 7 days after the administration of either dose of vaccine. For the two doses combined, the expected number of intussusception cases was 0.72, resulting in a significant relative risk of 8.4. For the pentavalent rotavirus vaccine, 1,301,810 doses were administered during the study period, with 8 observed intussusception cases (7.11 expected), for a nonsignificant relative risk of 1.1. The relative risk of chart-confirmed intussusception within 7 days after monovalent rotavirus vaccination, as compared with the risk after pentavalent rotavirus vaccination, was 9.4 (95% confidence interval, 1.4 to 103.8). The attributable risk of intussusception after the administration of two doses of monovalent rotavirus vaccine was estimated to be 5.3 per 100,000 infants vaccinated.

CONCLUSIONS

In this prospective postlicensure study of more than 200,000 doses of monovalent rotavirus vaccine, we observed a significant increase in the rate of intussusception after vaccination, a risk that must be weighed against the benefits of preventing rotavirus-associated illness.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24422678>

“In this prospective postlicensure study of more than 200,000 doses of monovalent rotavirus vaccine, we observed a significant increase in the rate of intussusception after vaccination, a risk that must be weighed against the benefits of preventing rotavirus-associated illness.”

Trends In Microbiology • February 2014

Do we need a new vaccine to control the re-emergence of pertussis?

Author information

Mills KH, Ross PJ, Allen AC, Wilk MM.

School of Biochemistry and Immunology
Trinity Biomedical Sciences Institute
Trinity College Dublin, Dublin, Ireland

kingston.mills@tcd.ie

Abstract

Bordetella pertussis causes whooping cough and is re-emerging in developed countries despite widespread immunization with acellular pertussis vaccines (Pa), which are less effective than the whole cell vaccines that they replaced. Efficacy of Pa could be improved by switching from alum to alternative adjuvants that generate more potent cell mediated immunity.

<http://www.ncbi.nlm.nih.gov/pubmed/24485284>

“*Bordetella pertussis* causes whooping cough and is re-emerging in developed countries despite widespread immunization with acellular pertussis vaccines ...”

Evolution of multiple sclerosis in France since the beginning of hepatitis B vaccination

Author information

Le Houézec D

REVAHB (“Réseau Vaccin Hépatite B” in French)

32 rue du Clos Herbert, 14000, Caen, France

dominique.le.houezec@freesbee.fr

Abstract

Since the implementation of the mass vaccination campaign against hepatitis B in France, the appearance of multiple sclerosis, sometimes occurring in the aftermath of vaccinations, led to the publication of epidemiological international studies. This was also justified by the sharp increase in the annual incidence of multiple sclerosis reported to the French health insurance in the mid-1990s. Almost 20 years later, a retrospective reflection can be sketched from these official data and also from the national pharmacovigilance agency. Statistical data from these latter sources seem to show a significant correlation between the number of hepatitis B vaccinations performed and the declaration to the pharmacovigilance of multiple sclerosis occurring between 1 and 2 years later. The application of the Hill's criteria to these data indicates that the correlation between hepatitis B vaccine and multiple sclerosis may be causal.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25395338>

“The application of the Hill's criteria to these data indicates that the correlation between hepatitis B vaccine and multiple sclerosis may be causal.”

Toward a mechanism-based in vitro safety test for pertussis toxin

Stefan FC Vaessena, Martijn WP Bruystersb, Rob J Vandebrielb*,
Saertje Verkoeijena, Rogier Bosc, Cyrille AM Krula & Arnoud M Akkermansb

Research Centre Technology & innovation
innovative testing in Life sciences and Chemistry
University of Applied Sciences; Utrecht, the Netherlands
Center for Health Protection
National institute for Public Health and the environment
Bilthoven, the Netherlands
Central Committee on Research involving Human Subjects
Den Haag, the Netherlands

Abstract

Pertussis vaccines are routinely administered to infants to protect them from whooping cough. Still, an adequate safety test for pertussis toxin (PT), one of the main antigens in these vaccines, is not available. The histamine sensitization test is currently the only assay accepted by regulatory authorities to test for the absence of active PT in vaccines. This is however, a lethal animal test with poor reproducibility. In addition, it is not clear whether the assumed underlying mechanism, i.e., ADP-ribosylation of G proteins, is the only effect that should be considered in safety evaluation of PT. The in vitro safety test for PT that we developed is based on the clinical effects of PT in humans. For this, human cell lines were chosen based on the cell types involved in the clinical effects of PT. These cell lines were exposed to PT and analyzed by microarray. In this review, we discuss the clinical effects of PT and the mechanisms that underlie them. The approach taken may provide as an example for other situations in which an in vitro assay based on clinical effects in humans is required.

Full Report

<http://www.tandfonline.com/doi/pdf/10.4161/hv.28001>

From the full report:

“Taken together, the main clinical effects in humans where Pertussis Toxin is involved are increased insulin secretion with resulting hypoglycemia, leukocytosis, lung edema and inflammatory responses, together resulting in pulmonary hypertension and pneumonia.

Moreover, PT can induce systemic hypotension, and is possibly involved in inducing neurological problems.”

DNAVaxDB: the first web-based DNA vaccine database and its data analysis

Racz R, Li X, Patel M,
Xiang Z, He Y.

Abstract

Since the first DNA vaccine studies were done in the 1990s, thousands more studies have followed. Here we report the development and analysis of DNAVaxDB (<http://www.violinet.org/dnavaxdb>), the first publically available web-based DNA vaccine database that curates, stores, and analyzes experimentally verified DNA vaccines, DNA vaccine plasmid vectors, and protective antigens used in DNA vaccines. All data in DNAVaxDB are annotated from reliable resources, particularly peer-reviewed articles. Among over 140 DNA vaccine plasmids, some plasmids were more frequently used in one type of pathogen than others; for example, pCMVi-UB for G-bacterial DNA vaccines, and pCAGGS for viral DNA vaccines. Presently, over 400 DNA vaccines containing over 370 protective antigens from over 90 infectious and non-infectious diseases have been curated in DNAVaxDB. While extracellular and bacterial cell surface proteins and adhesin proteins were frequently used for DNA vaccine development, the majority of protective antigens used in Chlamydomonas DNA vaccines are localized to the inner portion of the cell. The DNA vaccine priming, other vaccine boosting vaccination regimen has been widely used to induce protection against infection of different pathogens such as HIV. Parasitic and cancer DNA vaccines were also systematically analyzed. User-friendly web query and visualization interfaces are available in DNAVaxDB for interactive data search. To support data exchange, the information of DNA vaccines, plasmids, and protective antigens is stored in the Vaccine Ontology (VO). DNAVaxDB is targeted to become a timely and vital source of DNA vaccines and related data and facilitate advanced DNA vaccine research and development.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4094999/>

“... the first publically available web-based DNA vaccine database that curates, stores, and analyzes experimentally verified DNA vaccines, DNA vaccine plasmid vectors, and protective antigens used in DNA vaccines. Presently, over 400 DNA vaccines containing over 370 protective antigens from over 90 infectious and non-infectious diseases have been curated in DNAVaxDB.”

Sudden infant death
following hexavalent vaccination:
a neuropathologic study

Author information

Matturri L, Del Corno G, Lavezzi AMI

“Lino Rossi” Research Center
Department of Biomedical
Surgical and Dental Sciences
University of Milan, Italy
Via della Commenda, 19 - 20122 Milan, Italy
anna.lavezzi@unimi.it

Abstract

We examined a large number of sudden infant death syndrome victims in order to point out a possible causal relationship between a previous hexavalent vaccination and the sudden infant death. We selected 110 cases submitted to in-depth histological examination of the autonomic nervous system and provided with detailed clinical and environmental information. In 13 cases (11.8%) the death occurred in temporal association with administration of the hexavalent vaccine (from 1 to 7 days). In none of these victims congenital developmental alterations of the main nervous structures regulating the vital functions were observed. Only the hypoplasia of the arcuate nucleus was present in 5 cases. In one case in particular an acquired hyperacute encephalitis of the tractus solitarius nucleus was diagnosed in the brainstem. This study does not prove a causal relationship between the hexavalent vaccination and SIDS. However, we hypothesize that vaccine components could have a direct role in sparking off a lethal outcome in vulnerable babies. In conclusion, we sustain the need that deaths occurring in a short space of time after hexavalent vaccination are appropriately investigated and submitted to a post-mortem examination particularly of the autonomic nervous system by an expert pathologist to objectively evaluate the possible causative role of the vaccine in SIDS.

<http://www.ncbi.nlm.nih.gov/pubmed/24083600>

“we hypothesize
that vaccine components
could have a direct role
in sparking off a lethal outcome
in vulnerable babies.”

Postural Orthostatic Tachycardia With Chronic Fatigue After HPV Vaccination as Part of the “Autoimmune/Auto-inflammatory Syndrome Induced by Adjuvants”: Case Report and Literature Review

Author information

Tomljenovic L1, Colafrancesco S2, Perricone C2, Shoenfeld Y3.

1. Sheba Medical Center, Tel-Hashomer, Israel
University of British Columbia, Vancouver, British Columbia, Canada
2. Sheba Medical Center, Tel-Hashomer, Israel
Sapienza University of Rome, Rome, Italy
3. Sheba Medical Center, Tel-Hashomer, Israel
Tel Aviv University, Tel Aviv, Israel

Abstract

We report the case of a 14-year-old girl who developed postural orthostatic tachycardia syndrome (POTS) with chronic fatigue 2 months following Gardasil vaccination. The patient suffered from persistent headaches, dizziness, recurrent syncope, poor motor coordination, weakness, fatigue, myalgias, numbness, tachycardia, dyspnea, visual disturbances, phonophobia, cognitive impairment, insomnia, gastrointestinal disturbances, and a weight loss of 20 pounds. The psychiatric evaluation ruled out the possibility that her symptoms were psychogenic or related to anxiety disorders. Furthermore, the patient tested positive for ANA (1:1280), lupus anticoagulant, and antiphospholipid. On clinical examination she presented livedo reticularis and was diagnosed with Raynaud’s syndrome. This case fulfills the criteria for the autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA). Because human papillomavirus vaccination is universally recommended to teenagers and because POTS frequently results in long-term disabilities (as was the case in our patient), a thorough follow-up of patients who present with relevant complaints after vaccination is strongly recommended.

<http://www.ncbi.nlm.nih.gov/pubmed/26425598>

“The patient suffered from persistent headaches, dizziness, recurrent syncope, poor motor coordination, weakness, fatigue, myalgias, numbness, tachycardia, dyspnea, visual disturbances, phonophobia, cognitive impairment, insomnia, gastrointestinal disturbances, and a weight loss of 20 pounds.”

Mitochondrial dysfunction in Gulf War illness revealed by 31Phosphorus Magnetic Resonance Spectroscopy: a case-control study

Author information

Koslik HJ1, Hamilton G2, Golomb BA3.

1. Department of Medicine, University of California San Diego, La Jolla, California, USA
2. Department of Radiology, University of California San Diego, La Jolla, California, USA
3. Department of Medicine, University of California San Diego, La Jolla, California, USA; Department of Family and Preventive Medicine, University of California San Diego, La Jolla, California, USA

Abstract

BACKGROUND

Approximately 1/3 of 1990-1 Gulf War veterans developed chronic multisymptom health problems. Implicated exposures bear mechanisms that adversely affect mitochondria. Symptoms emphasize fatigue, cognition and muscle (brain and muscle are aerobically demanding); with protean additional domains affected, compatible with mitochondrial impairment. Recent evidence supports treatments targeting cell bioenergetics (coenzyme10) to benefit Gulf War illness symptoms. However, no evidence has directly documented mitochondrial or bioenergetic impairment in Gulf War illness.

OBJECTIVE

We sought to objectively assess for mitochondrial dysfunction, examining post-exercise phosphocreatine-recovery time constant (PCr-R) using (31)Phosphorus Magnetic Resonance Spectroscopy ((31)P-MRS), in Gulf War veterans with Gulf War illness compared to matched healthy controls. PCr-R has been described as a “robust and practical” index of mitochondrial status.

DESIGN AND PARTICIPANTS

Case-control study from 2012-2013. Fourteen community-dwelling Gulf War veterans and matched controls from the San Diego area comprised 7 men meeting CDC and Kansas criteria for Gulf War illness, and 7 non-deployed healthy controls matched 1:1 to cases on age, sex, and ethnicity.

OUTCOME MEASURE

Calf muscle phosphocreatine was evaluated by (31)P-MRS at rest, through 5 minutes of foot pedal depression exercise, and in recovery, to assess PCr-R. Paired t-tests compared cases to matched controls.

RESULTS

PCr-R was significantly prolonged in Gulf War illness cases vs their matched controls: control values, mean \pm SD, 29.0 \pm 8.7 seconds; case values 46.1 \pm 18.0 seconds; difference 17.1 \pm 14.9 seconds; $p = 0.023$. PCr-R was longer for cases relative to their matched controls for all but one pair; moreover while values clustered under 31 seconds for all but one control, they exceeded 35 seconds (with a spread up to 70 seconds) for all but one case.

DISCUSSION

These data provide the first direct evidence supporting mitochondrial dysfunction in Gulf War illness. Findings merit replication in a larger study and/or corroboration with additional mitochondrial assessment tools.

“These data provide the first direct evidence supporting mitochondrial dysfunction in Gulf War illness.”

**Postural Orthostatic Tachycardia
With Chronic Fatigue After HPV Vaccination
as Part of the “Autoimmune/Auto-inflammatory Syndrome
Induced by Adjuvants”**

Lucija Tomljenovic, PhD^{1,2}, Serena Colafrancesco, MD^{1,3},
Carlo Perricone, MD^{1,3}, Yehuda Shoenfeld, MD, FRCP (Hon), MaACR^{1,4}

1. Sheba Medical Center, Tel-Hashomer, Israel
2. University of British Columbia, Vancouver, British Columbia, Canada
3. Sapienza University of Rome, Rome, Italy
4. Tel Aviv University, Tel Aviv, Israel
Shoenfel@post.tau.ac.il

Abstract

We report the case of a 14-year-old girl who developed postural orthostatic tachycardia syndrome (POTS) with chronic fatigue 2 months following Gardasil vaccination. The patient suffered from persistent headaches, dizziness, recurrent syncope, poor motor coordination, weakness, fatigue, myalgias, numbness, tachycardia, dyspnea, visual disturbances, phonophobia, cognitive impairment, insomnia, gastrointestinal disturbances, and a weight loss of 20 pounds. The psychiatric evaluation ruled out the possibility that her symptoms were psychogenic or related to anxiety disorders. Furthermore, the patient tested positive for ANA (1:1280), lupus anticoagulant, and antiphospholipid. On clinical examination she presented livedo reticularis and was diagnosed with Raynaud’s syndrome. This case fulfills the criteria for the autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA). Because human papillomavirus vaccination is universally recommended to teenagers and because POTS frequently results in long-term disabilities (as was the case in our patient), a thorough follow-up of patients who present with relevant complaints after vaccination is strongly recommended.

<http://hic.sagepub.com/content/2/1/2324709614527812.abstract>

“We report the case of a 14-year-old girl who developed postural orthostatic tachycardia syndrome (POTS) with chronic fatigue 2 months following Gardasil vaccination. The patient suffered from persistent headaches, dizziness, recurrent syncope, poor motor coordination, weakness, fatigue, myalgias, numbness, tachycardia, dyspnea, visual disturbances, phonophobia, cognitive impairment, insomnia, gastrointestinal disturbances, and a weight loss of 20 pounds. This case fulfills the criteria for the autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA).”

Alum, an aluminum-based adjuvant, induces Sjögren's syndrome-like disorder in mice

Author information

Bagavant H1, Nandula SR, Kaplonek P, Rybakowska PD, Deshmukh US.

Division of Nephrology, University of Virginia, Charlottesville
VA and Arthritis and Clinical Immunology Program
Oklahoma Medical Research Foundation, Oklahoma City, OK, USA
harini-bagavant@omrf.org

Abstract

OBJECTIVES

Adjuvant-induced innate immune responses have been suspected to play a role in the initiation of certain autoimmune disorders. This study investigates the role of alum, an aluminum-based adjuvant in the induction of Sjögren's syndrome-like disorder in mice.

METHODS

Inbred, female New Zealand Mixed (NZM) 2758 strain of mice were injected with alum. Control mice were treated similarly with PBS. The mice were monitored for salivary gland dysfunction by measuring pilocarpine-induced salivation. Presence of lymphocytic infiltrates within the submandibular glands was studied by histopathology. Autoantibodies to Ro and La proteins were analysed by ELISA and the presence of anti-nuclear antibodies (ANA) was analysed by indirect immunofluorescence.

RESULTS

By eight weeks after treatment, the saliva production in the alum-treated mice was significantly decreased in comparison to the PBS-treated mice. This functional loss persisted till the termination of experiments at 20 wks. The incidence and severity of sialoadenitis was significantly higher in the alum-treated mice. Although there were no differences in the levels of anti-Ro/La autoantibodies in sera of alum and PBS-treated groups, the alum group showed higher ANA reactivity.

CONCLUSIONS

In the NZM2758 mice, alum induces a Sjögren's syndrome-like disorder that is characterised by chronic salivary gland dysfunction and the presence of lymphocytic infiltrates within the salivary glands. Thus, the potential of aluminum-based adjuvants for induction of autoimmunity should be closely monitored in individuals genetically susceptible to developing autoimmune disorders.

“Adjuvant-induced innate immune responses have been suspected to play a role in the initiation of certain autoimmune disorders. This study investigates the role of alum, an aluminum-based adjuvant in the induction of Sjögren's syndrome-like disorder in mice.”

A key role for an impaired detoxification mechanism in the etiology and severity of autism spectrum disorders

Author information

Alabdali A, Al-Ayadhi L, El-Ansary A1.

Biochemistry Department, Science College
King Saud University, P,O box 22452, Zip code 11495
Riyadh, Saudi Arabia
elansary@ksu.edu.sa

Abstract

BACKGROUND

Autism Spectrum Disorders (ASD) is a syndrome with a number of etiologies and different mechanisms that lead to abnormal development. The identification of autism biomarkers in patients with different degrees of clinical presentation (i.e., mild, moderate and severe) will give greater insight into the pathogenesis of this disease and will enable effective early diagnostic strategies and treatments for this disorder.

METHODS

In this study, the concentration of two toxic heavy metals, lead (Pb) and mercury (Hg), were measured in red blood cells, while glutathione-s-transferase (GST) and vitamin E, as enzymatic and non-enzymatic antioxidants, respectively, were measured in the plasma of subgroups of autistic patients with different Social Responsiveness Scale (SRS) and Childhood Autism Rating Scale (CARS) scores. The results were compared to age- and gender-matched healthy controls.

RESULTS

The obtained data showed that the patients with autism spectrum disorder had significantly higher Pb and Hg levels and lower GST activity and vitamin E concentrations compared with the controls. The levels of heavy metals (Hg and Pb), GST and vitamin E were correlated with the severity of the social and cognitive impairment measures (SRS and CARS). Receiver Operating Characteristics (ROC) analysis and predictiveness curves indicated that the four parameters show satisfactory sensitivity, very high specificity and excellent predictiveness. Multiple regression analyses confirmed that higher levels of Hg and Pb, together with lower levels of GST and vitamin E, can be used to predict social and cognitive impairment in patients with autism spectrum disorders.

CONCLUSION

This study confirms earlier studies that implicate toxic metal accumulation as a consequence of impaired detoxification in autism and provides insight into the etiological mechanism of autism.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4017810/>

“This study confirms earlier studies that implicate toxic metal accumulation as a consequence of impaired detoxification in autism and provides insight into the etiological mechanism of autism.”

Pertussis resurgence:
waning immunity and pathogen adaptation—
two sides of the same coin

Author information

Mooi FR1, Van Der Maas NA2, De Melker HE2.

1. Laboratory for Infectious Disease
Centre for Infectious Disease Control
National Institute for Public Health and the Environment
Bilthoven, The Netherlands

2. Epidemiology and Surveillance
Centre for Infectious Disease Control
National Institute for Public Health and the Environment
Bilthoven, The Netherlands

Abstract

Pertussis or whooping cough has persisted and resurged in the face of vaccination and has become one of the most prevalent vaccine-preventable diseases in Western countries. The high circulation rate of *Bordetella pertussis* poses a threat to infants that have not been (completely) vaccinated and for whom pertussis is a severe, life-threatening, disease. The increase in pertussis is mainly found in age groups in which immunity has waned and this has resulted in the perception that waning immunity is the main or exclusive cause for the resurgence of pertussis. However, significant changes in *B. pertussis* populations have been observed after the introduction of vaccinations, suggesting a role for pathogen adaptation in the persistence and resurgence of pertussis. These changes include antigenic divergence with vaccine strains and increased production of pertussis toxin. Antigenic divergence will affect both memory recall and the efficacy of antibodies, while higher levels of pertussis toxin may increase suppression of the innate and acquired immune system. We propose these adaptations of *B. pertussis* have decreased the period in which pertussis vaccines are effective and thus enhanced the waning of immunity. We plead for a more integrated approach to the pertussis problem which includes the characteristics of the vaccines, the *B. pertussis* populations and the interaction between the two.

<http://www.ncbi.nlm.nih.gov/pubmed/23406868>

“We propose
these adaptations of *B. pertussis*
have decreased the period in which
pertussis vaccines are effective
and thus enhanced the
waning of immunity.”

Perinatal multiple exposure to neurotoxic
(lead, methylmercury, ethylmercury, and aluminum)
substances and neurodevelopment
at six and 24 months of age

Author information

Marques RC1, Bernardi JV2, Dórea JG3,
de Fatima R Moreira M4, Malm O5.

1. Federal University of Rio de Janeiro, Campus Macaé, CEP 27930-560 RJ, Brazil
2. University of Brasília, Brasília, 70919-970 DF, Brasil
3. University of Brasília, Brasília, 70919-970 DF, Brasil
4. Escola Nacional de Saúde Pública, Fundação Oswaldo Cruz, RJ, Brazil
5. Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, Brazil
jg.dorea@gmail.com

Abstract

We studied neurodevelopment in infants from two communities. Children living in the vicinity of tin-ore kilns and smelters - TOKS; n = 51) were compared to children from a fishing village (Itapuã; n = 45). Mean hair-Hg (HHg) concentrations were significantly higher in Itapuã children which received significantly ($p = 0.0000001$) less mean ethylmercury (88.6 μg) from Thimerosal-containing vaccines (TCV) than the TOKS children (120 μg). Breast-milk Pb concentrations were significantly higher in the TOKS mothers ($p = 0.000017$; 10.04 vs. 3.9 $\mu\text{g L}^{-1}$). Bayley mental development index (MDI) and psychomotor development index (PDI) were statistically significant (respectively $p < 0.0000001$, $p = 0.000007$) lower for the TOKS children only at 24 months of age. Multivariate regression analysis showed that MDI was negatively affected by breast-milk Pb and by HHg. PDI was positively affected by breastfeeding and negatively affected by ethylmercury. Milestone achievements were negatively affected by breast-milk Pb (age of walking) and by HHg (age of talking).

<http://www.ncbi.nlm.nih.gov/pubmed/24486466>

“Milestone achievements
were negatively affected by
breast-milk lead (age of walking)
and by Mean hair-mercury (age of talking).”

The non-specific effects of vaccines and other childhood interventions: the contribution of INDEPTH Health and Demographic Surveillance Systems

Author Information

Osman Sankoh,^{1,2,3,*} Paul Welaga,^{1,4} Cornelius Debpuur,^{1,4} Charles Zandoh,^{1,5} Stephney Gyaase,^{1,5} Mary Atta Poma,^{1,6} Martin Kavao Mutua,^{1,7} SM Manzoor Ahmed Hanifi,^{1,8} Cesario Martins,^{1,9} Eric Nebie,^{1,10} Moubassira Kagoné,^{1,10} Jacques BO Emina,¹ and Peter Aaby^{1,9}

1. INDEPTH Network, Accra, Ghana
2. School of Public Health, University of the Witwatersrand, Johannesburg, South Africa
3. Faculty of Public Health, Hanoi Medical University, Hanoi, Viet Nam
4. Navrongo Health Research Centre, Ghana Health Service, Navrongo, Ghana
5. Kintampo Health Research Centre, Ghana Health Service, Kintampo, Ghana
6. Dodowa Health Research Centre, Ghana Health Service, Dodowa, Ghana
7. African Population and Health Research Centre, Nairobi, Kenya
8. Chakaria Community Health Project Community Health Division, ICDDR, Dhaka, Bangladesh
9. Bandim Health Project, Bandim, Guiné-Bissau
10. Centre de Recherche en Santé de Nouna (CRSN), Nouna, Burkina Faso

Abstract

Most childhood interventions (vaccines, micronutrients) in low-income countries are justified by their assumed effect on child survival. However, usually the interventions have only been studied with respect to their disease/deficiency-specific effects and not for their overall effects on morbidity and mortality. In many situations, the population-based effects have been very different from the anticipated effects; for example, the measles-preventive high-titre measles vaccine was associated with 2-fold increased female mortality; BCG reduces neonatal mortality although children do not die of tuberculosis in the neonatal period; vitamin A may be associated with increased or reduced child mortality in different situations; effects of interventions may differ for boys and girls. The reasons for these and other contrasts between expectations and observations are likely to be that the immune system learns more than specific prevention from an intervention; such training may enhance or reduce susceptibility to unrelated infections. INDEPTH member centres have been in an ideal position to document such additional non-specific effects of interventions because they follow the total population long term. It is proposed that more INDEPTH member centres extend their routine data collection platform to better measure the use and effects of childhood interventions. In a longer perspective, INDEPTH may come to play a stronger role in defining health research issues of relevance to low-income countries.

Conclusion

Existing studies suggest a general pattern, namely that the live vaccines (BCG, measles vaccine, OPV and vaccinia) are associated with beneficial non-specific effects, leading to reduced all-cause mortality, whereas the inactivated, alum-adjuvated DTP vaccine is associated with increased susceptibility to other unrelated infections, particularly in females.

Full Report: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4052142/>

“... the inactivated,
alum-adjuvated DTP vaccine
is associated with increased
susceptibility to other unrelated
infections, particularly in females.”

Cytotoxic effect of organic solvents and surfactant agents on *Acanthamoeba castellanii* cysts

Author information

Ezz Eldin HM1, Sarhan RM.
Medical Parasitology Department, Faculty of Medicine
Ain Shams University, Cairo, Egypt
hayamezz@hotmail.com

Abstract

Acanthamoeba castellanii is a protozoan parasite that may cause sight-threatening keratitis in some individuals. Its eradication is difficult because the trophozoites encyst making organisms highly resistant to anti-amoebic drugs. To test new anti-*Acanthamoeba* agents, usually having low water solubility, organic solvents and surfactant agents should be used. Therefore, the lethal effect of different concentrations of the solvents acetone, methanol, ethanol, and DMSO and surfactant agents Tween 20, Tween 80, and Triton X-100 was tested. The minimal inhibitory concentrations (MIC) were determined against *Acanthamoeba* cysts. Results of the present study showed that the MIC for ethanol, methanol, acetone and DMSO was 25, 12.5, 12.5, and 10%, respectively and for Tween 20, Tween 80, and Triton X-100 was 0.25, 0.06, and 0.03%, respectively. There was no significant inhibitory effect on the multiplication of *Acanthamoeba* cysts as compared to parasite control when using the concentrations 3.12% for ethanol, 1.6% for methanol and acetone, 1.25% for DMSO, and 0.016% for Tween 20. On the other hand, both Tween 80 and Triton X-100 showed highly significant difference in comparison to parasite control almost among all the range of concentrations used in this study, and both showed lethal effect of 19 and 27.2%, respectively at their least concentration.

<http://www.ncbi.nlm.nih.gov/pubmed/24638907>

“... both Tween 80 and Triton X-100 showed ...
lethal effect of 19 and 27.2%, respectively
at their least concentration.”

“Adjuvants are necessary components to warrant the efficacy of vaccines, however the overstimulation of the immune system is also associated with adverse effects.”

International Immunopharmacology • May 2014

Systemic immunotoxicity reactions induced by adjuvanted vaccines

Author information

Batista-Duharte A1, Portuondo D2, Pérez O3, Carlos IZ2.

1. Immunotoxicology Laboratory, Toxicology and Biomedicine Center (TOXIMED), Medical Science University Autopista Nacional Km. 1 1/2, CP 90400 Santiago de Cuba, Cuba; Faculty of Pharmaceutical Sciences Universidade Estadual Paulista Julio Mesquita Filho (UNESP), Rua Expedicionarios do Brasil 1621 CEP 14801-902 Araraquara, SP, Brazil; CAPES-PVE/Brasil Grant, Foreigner Visiting Professor Program, Brazil
2. Faculty of Pharmaceutical Sciences, Universidade Estadual Paulista Julio Mesquita Filho (UNESP) Rua Expedicionarios do Brasil 1621, CEP 14801-902 Araraquara, SP, Brazil
3. Immunology Department, Institute of Preclinical and Basic Sciences (ICBP) “Victoria de Girón” University of Medical Sciences of Havana. 146 No. 2504. e/ 25 Ave and 31 Ave, Playa, Havana, Cuba

Abstract

Vaccine safety is a topic of concern for the treated individual, the family, the health care personnel, and the others involved in vaccination programs as recipients or providers. Adjuvants are necessary components to warrant the efficacy of vaccines, however the overstimulation of the immune system is also associated with adverse effects. Local reactions are the most frequent manifestation of toxicity induced by adjuvanted vaccines and, with the exception of the acute phase response (APR), much less is known about the systemic reactions that follow vaccination. Their low frequency or subclinical expression meant that this matter has been neglected. In this review, various systemic reactions associated with immune stimulation will be addressed, including: APR, hypersensitivity, induction or worsening of autoimmune diseases, modification of hepatic metabolism and vascular leak syndrome (VLS), with an emphasis on the mechanism involved. Finally, the authors analyze the current focus of discussion about vaccine safety and opportunities to improve the design of new adjuvanted vaccines in the future.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24607449>

Etiology of autism spectrum disorders: Genes, environment, or both?

C Shaw^{1*}, S Sheth¹, D Li¹, L Tomljenovic¹

(1) University of British Columbia
Vancouver, British Columbia, Canada
cashawlab@gmail.com

Abstract

Thus far, most of the research on both neurodevelopmental and neurodegenerative disorders has been focused on finding the presumed underlying genetic causes, while much less emphasis has been put on potential environmental factors. While some forms of autism are clearly genetic, the fact remains that heritability factors cannot adequately explain all reported cases nor their drastic increase over the last few decades. In particular, studies on twins have now shown that common environmental factors account for 55% of their risk for developing autism while genetic susceptibility explains only 37% of cases. Because the prenatal environment and early postnatal environment are shared between twins and because overt symptoms of autism emerge around the end of the first year of life, it is likely that at least some of the environmental factors contributing to the risk of autism exert their deleterious neurodevelopmental effect during this early period of life. Indeed, evidence has now emerged showing that autism may in part result from early-life immune insults induced by environmental xenobiotics. One of the most common xenobiotic with immuno-stimulating as well as neurotoxic properties to which infants under two years of age are routinely exposed worldwide is the aluminum (Al) vaccine adjuvant. In this review we discuss the mechanisms by which Al can induce adverse neurological and immunological effects and how these may provide important clues of Al's putative role in autism. Because of the tight connection between the development of the immune and the central nervous system, the possibility that immune-overstimulation in early infancy via vaccinations may play a role in neurobehavioural disorders needs to be carefully considered.

Conclusion

There is now sufficient evidence from both human and animal studies showing that cumulative exposure to aluminium adjuvants is not as benign as previously assumed. Given that vaccines are the only medical intervention that we attempt to deliver to every living human on earth and that by far the largest target population for vaccination are healthy children, a better appreciation and understanding of vaccine adjuvant risks appears warranted.

<http://www.oapublishinglondon.com/article/1368>

“Indeed, evidence has now emerged showing that autism may in part result from early-life immune insults induced by environmental xenobiotics. One of the most common xenobiotic with immuno-stimulating as well as neurotoxic properties to which infants under two years of age are routinely exposed worldwide is the aluminum (Al) vaccine adjuvant. In this review we discuss the mechanisms by which Al can induce adverse neurological and immunological effects and how these may provide important clues of Aluminum's putative role in autism.”

“... the United States Centers for Disease Control and Prevention states that Thimerosal is safe and there is no relationship between [T]himerosal[-]containing vaccines and autism rates in children.

This is puzzling because, in a study conducted directly by CDC epidemiologists, a 7.6-fold increased risk of autism from exposure to Thimerosal during infancy was found.”

Biomedical Research International • June 2014

Methodological issues and evidence of malfeasance in research purporting to show thimerosal in vaccines is safe

Author information

Hooker B1, Kern J2, Geier D3, Haley B4, Sykes L5, King P5, Geier M3.

1. Simpson University, 2211 College View Drive, Redding, CA 96001
2. Institute of Chronic Illness, Inc., 14 Redgate Court, Silver Spring, MD 20905
University of Texas Southwestern Medical Center at Dallas, Dallas, TX 75235
3. Institute of Chronic Illness, Inc., 14 Redgate Court, Silver Spring, MD 20905
4. University of Kentucky, Lexington, KY 40506
5. CoMeD, Inc., Silver Spring, MD, USA

Abstract

There are over 165 studies that have focused on Thimerosal, an organic-mercury (Hg) based compound, used as a preservative in many childhood vaccines, and found it to be harmful. Of these, 16 were conducted to specifically examine the effects of Thimerosal on human infants or children with reported outcomes of death; acrodynia; poisoning; allergic reaction; malformations; auto-immune reaction; Well's syndrome; developmental delay; and neurodevelopmental disorders, including tics, speech delay, language delay, attention deficit disorder, and autism. In contrast, the United States Centers for Disease Control and Prevention states that Thimerosal is safe and there is “no relationship between [T]himerosal[-]containing vaccines and autism rates in children.” This is puzzling because, in a study conducted directly by CDC epidemiologists, a 7.6-fold increased risk of autism from exposure to Thimerosal during infancy was found. The CDC’s current stance that Thimerosal is safe and that there is no relationship between Thimerosal and autism is based on six specific published epidemiological studies coauthored and sponsored by the CDC. The purpose of this review is to examine these six publications and analyze possible reasons why their published outcomes are so different from the results of investigations by multiple independent research groups over the past 75+ years.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4065774/>

The non-specific effects of vaccines
and other childhood interventions:
the contribution of INDEPTH
Health and Demographic Surveillance Systems

Author information

Sankoh O1, Welaga P2, Debpuur C2, Zandoh C2, Gyaase S2,
Poma MA2, Mutua MK2, Hanifi SM2, Martins C2, Nebie E2,
Kagoné M2, Emina JB3, Aaby P2.

INDEPTH Network, Accra, Ghana, School of Public Health
University of the Witwatersrand, Johannesburg, South Africa

Abstract

Most childhood interventions (vaccines, micronutrients) in low-income countries are justified by their assumed effect on child survival. However, usually the interventions have only been studied with respect to their disease/deficiency-specific effects and not for their overall effects on morbidity and mortality. In many situations, the population-based effects have been very different from the anticipated effects; for example, the measles-preventive high-titre measles vaccine was associated with 2-fold increased female mortality; BCG reduces neonatal mortality although children do not die of tuberculosis in the neonatal period; vitamin A may be associated with increased or reduced child mortality in different situations; effects of interventions may differ for boys and girls. The reasons for these and other contrasts between expectations and observations are likely to be that the immune system learns more than specific prevention from an intervention; such training may enhance or reduce susceptibility to unrelated infections. INDEPTH member centres have been in an ideal position to document such additional non-specific effects of interventions because they follow the total population long term. It is proposed that more INDEPTH member centres extend their routine data collection platform to better measure the use and effects of childhood interventions. In a longer perspective, INDEPTH may come to play a stronger role in defining health research issues of relevance to low-income countries.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4052142/>

“In many situations,
the population-based effects have been very different
from the anticipated effects; for example, the measles-preventive
high-titre measles vaccine was associated with
2-fold increased female mortality ...”

“Our results indicated that food emulsifier applied in relatively high concentrations in even the most frequently consumed foods can increase the absorption of DEHP, and its role may be related to the structure and function damages of mitochondria in enterocytes.”

Toxicology Science • June 2014

Food emulsifier polysorbate 80 increases intestinal absorption of di-(2-ethylhexyl) phthalate in rats

Author information

Lu Y1, Wang YY, Yang N, Zhang D, Zhang FY, Gao HT, Rong WT, Yu SQ, Xu Q.

Jiangsu Key Laboratory for Supramolecular Medicinal Materials and Applications
College of Life Sciences, Nanjing Normal University
Nanjing 210046, The People's Republic of China

Abstract

The aim of the present research was to explore whether food emulsifier polysorbate 80 can enhance the absorption of di-(2-ethylhexyl) phthalate (DEHP) and its possible mechanism. We established the high-performance liquid chromatography (HPLC) method for detecting DEHP and its major metabolite, mono-ethylhexyl phthalate (MEHP) in rat plasma, and then examined the toxicokinetic and bioavailability of DEHP with or without polysorbate 80 in rats. The study of its mechanism to increase the absorption of phthalates demonstrated that polysorbate 80 can induce mitochondrial dysfunction in time- and concentration-dependence manners in Caco-2 cells by reducing mitochondrial membrane potential, diminishing the production of the adenosine triphosphate, and decreasing the activity of electron transport chain. Our results indicated that food emulsifier applied in relatively high concentrations in even the most frequently consumed foods can increase the absorption of DEHP, and its role may be related to the structure and function damages of mitochondria in enterocytes.

Full Report

<http://toxsci.oxfordjournals.org/content/139/2/317.long>

Sex-based biology and the rational design of influenza vaccination strategies

Author information

Klein SL1, Pekosz A1.

W. Harry Feinstone Department of Molecular Microbiology and Immunology
Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland

Abstract

Biological (ie, sex) differences as well as cultural (ie, gender) norms influence the acceptance and efficacy of vaccines for males and females. These differences are often overlooked in the design and implementation of vaccination strategies. Using seasonal and pandemic influenza vaccines, we document profound differences between the sexes in the acceptance, correlates of protection, and adverse reactions following vaccination in both young and older adults. Females develop higher antibody responses, experience more adverse reactions to influenza vaccines, and show greater vaccine efficacy than males. Despite greater vaccine efficacy in females, both young and older females are often less likely to accept influenza vaccines than their male counterparts. Identification of the biological mechanisms, including the hormones and genes, that underlie differential responses to vaccination is necessary. We propose that vaccines should be matched to an individual's biological sex, which could involve systematically tailoring diverse types of FDA-approved influenza vaccines separately for males and females. One goal for vaccines designed to protect against influenza and even other infectious diseases should be to increase the correlates of protection in males and reduce adverse reactions in females in an effort to increase acceptance and vaccine-induced protection in both sexes.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4157517/>

“Biological (ie, sex) differences as well as cultural (ie, gender) norms influence the acceptance and efficacy of vaccines for males and females. These differences are often [always] overlooked in the design and implementation of vaccination strategies.”

“Seventy-nine infants received a total of 1,303 prescriptions comprising 77 formulations and 70 active drugs. Eighty-six excipients were identified, of which, 9 were harmful excipients (HE) and 48 were potentially harmful excipients (PHE).”

European Journal Of Pediatrics • July 2014

Toxic excipients in medications for neonates in Brazil

Author information

Souza A Jr1, Santos D, Fonseca S, Medeiros M, Batista L, Turner M, Coelho H.

Mother and Child Hospital of Brasilia, SGAS, Av. L2 Sul, Quadra 608
Módulo A Asa Sul, Brasília, Federal District, Brazil
alcidesiojr@gmail.com

Abstract

The aim was to describe the exposure to excipients among neonates hospitalised in the neonatal intensive care unit (NICU) of a public hospital in Brasilia, Brazil. This was a retrospective study based on medicines that were prescribed electronically to neonates (≤ 28 days) who were admitted to the NICU of a hospital in Brasilia between January 1 and March 31, 2012. Excipients were identified from the medicine package leaflets and were classified according to toxicity. Seventy-nine infants received a total of 1,303 prescriptions comprising 77 formulations and 70 active drugs. Eighty-six excipients were identified, of which, 9 were harmful excipients (HE) and 48 were potentially harmful excipients (PHE). Almost all the neonates (98.7 %) were exposed to at least one HE and PHE. Preterm neonates (n=64; 1,502 neonate days) presented high risk of exposure to polysorbate 80 (3.26/100 neonate days), sodium hydroxide (3.39), PG (3.19) and propylparaben (3.06). Full-term neonates (n=15; 289 neonate days) presented risks in relation to phenol (4.84), ethanol (3.8) and sodium citrate (3.46).

CONCLUSION

Neonates in NICUs in Brazil are exposed to a wide variety of HE and PHE with unpredictable results.

<http://www.ncbi.nlm.nih.gov/pubmed/24500397>

Measles-mumps-rubella vaccination timing and autism among young African American boys: a reanalysis of CDC data

Author information

Hooker BS.
Simpson University, Redding, CA, USA.

Abstract

BACKGROUND

A significant number of children diagnosed with autism spectrum disorder suffer a loss of previously-acquired skills, suggesting neurodegeneration or a type of progressive encephalopathy with an etiological basis occurring after birth. The purpose of this study is to investigate the effect of the age at which children got their first Measles-Mumps-Rubella (MMR) vaccine on autism incidence. This is a reanalysis of the data set, obtained from the U.S. Centers for Disease Control and Protection (CDC), used for the Destefano et al. 2004 publication on the timing of the first MMR vaccine and autism diagnoses.

METHODS

The author embarked on the present study to evaluate whether a relationship exists between child age when the first MMR vaccine was administered among cases diagnosed with autism and controls born between 1986 through 1993 among school children in metropolitan Atlanta. The Pearson's chi-squared method was used to assess relative risks of receiving an autism diagnosis within the total cohort as well as among different race and gender categories.

RESULTS

When comparing cases and controls receiving their first MMR vaccine before and after 36 months of age, there was a statistically significant increase in autism cases specifically among African American males who received the first MMR prior to 36 months of age. Relative risks for males in general and African American males were 1.69 ($p=0.0138$) and 3.36 ($p=0.0019$), respectively. Additionally, African American males showed an odds ratio of 1.73 ($p=0.0200$) for autism cases in children receiving their first MMR vaccine prior to 24 months of age versus 24 months of age and thereafter.

CONCLUSIONS

The present study provides new epidemiologic evidence showing that African American males receiving the MMR vaccine prior to 24 months of age or 36 months of age are more likely to receive an autism diagnosis.

<http://www.ncbi.nlm.nih.gov/pubmed/25114790>

“The present study provides new epidemiologic evidence showing that African American males receiving the MMR vaccine prior to 24 months of age or 36 months of age are more likely to receive an autism diagnosis.”

Interaction between neonatal vitamin A supplementation and timing of measles vaccination: a retrospective analysis of three randomized trials from Guinea-Bissau

Author information

Benn CS1, Martins CL2, Fisker AB3, Diness BR3, Garly ML3, Balde I2, Rodrigues A2, Whittle H4, Aaby P5.

1. Research Center for Vitamins and Vaccines (CVIVA)
Bandim Health Project, Artillerivej 5, 2300 Copenhagen S, Denmark
Institute of Clinical Research
University of Southern Denmark/Odense University Hospital, Denmark
cb@ssi.dk.
2. Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau
3. Research Center for Vitamins and Vaccines (CVIVA)
Bandim Health Project, Artillerivej 5, 2300 Copenhagen S, Denmark
4. The London School of Hygiene and Tropical Medicine, Keppel Street, London, UK
5. Research Center for Vitamins and Vaccines (CVIVA)
Bandim Health Project, Artillerivej 5, 2300 Copenhagen S, Denmark
Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau

Abstract

BACKGROUND

In Guinea-Bissau we conducted three trials of neonatal vitamin A supplementation (NVAS) from 2002 to 2008. None of the trials found a beneficial effect on mortality. From 2003 to 2007, an early measles vaccine (MV) trial was ongoing, randomizing children 1:2 to early MV at 4.5 months or no early MV, in addition to the usual MV at 9 months. We have previously found interactions between vitamin A and vaccines.

OBJECTIVE

We investigated whether there were interactions between NVAS and early MV.

DESIGN

We compared the mortality of NVAS and placebo recipients: first, from 4.5 to 8 months for children randomized to early MV or no early MV; and second, from 9 to 17 months in children who had received two MV or one MV. Mortality rates (MR) were compared in Cox models producing mortality rate ratios (MRR).

RESULTS

A total of 5141 children were randomized to NVAS (N=3015) or placebo (N=2126) and were later randomized to early MV (N=1700) or no early MV (N=3441). Between 4.5 and 8 months, NVAS compared with placebo was associated with higher mortality in early MV recipients (MR=30 versus MR=0, $p=0.01$), but not in children who did not receive early MV (p for interaction between NVAS and early MV=0.03). From 9 to 17 months NVAS was not associated with mortality. Overall, from 4.5 to 17 months NVAS was associated with increased mortality in early MV recipients (Mortality rate ratio=5.39 (95% confidence interval: 1.62, 17.99)).

CONCLUSIONS

These observations indicate that NVAS may interact with vaccines given several months later. This may have implications for the planning of future child intervention programs.

<http://www.ncbi.nlm.nih.gov/pubmed/25131735>

“These observations indicate that neonatal vitamin A supplementation may interact with vaccines given several months later.”

Neonatal vitamin A supplementation associated with a cluster of deaths and poor early growth in a randomised trial among low-birth-weight boys of vitamin A versus oral polio vaccine at birth

Najaaraq Lund,1,2,3 Sofie Biering-Sørensen,1 Andreas Andersen,1 Ivan Monteiro,3 Luis Camala,4 Mathias Jul Jørgensen,3 Peter Aaby,1,3 and Christine Stabell Benn1,5

1Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project Statens Serum Institut, Copenhagen, Denmark

2Department of Infectious Diseases, Aarhus University Hospital, Aarhus, Denmark

3Bandim Health Project, InDEPTH Network, Bissau, Guinea-Bissau

4Maternidade, Hospital Nacional Simão Mendes, Bissau, Guinea-Bissau

5OPEN, Institute of Clinical Research, University of Southern Denmark/Odense University Hospital Odense, Denmark

Abstract

Background

The effect of oral polio vaccine administered already at birth (OPV0) on child survival was not examined before being recommended in 1985. Observational data suggested that OPV0 was harmful for boys, and trials have shown that neonatal vitamin A supplementation (NVAS) at birth may be beneficial for boys. We set out to test this research question in a randomised trial.

Methods

The trial was carried out at the Bandim Health Project, Guinea-Bissau. We planned to enrol 900 low-birth weight (LBW) boys in a randomised trial to investigate whether NVAS instead of OPV0 could lower infant mortality for LBW boys. At birth, the children were randomised to OPV (usual treatment) or VAS (intervention treatment) and followed for 6 months for growth and 12 months for survival. Hazard Ratios (HR) for mortality were calculated using Cox regression. We compared the individual anthropometry measurements to the 2006 WHO growth reference. We compared differences in z-scores by linear regression. Relative risks (RR) of being stunted or underweight were calculated in Poisson regression models with robust standard errors.

Results

In the rainy season we detected a cluster of deaths in the VAS group and the trial was halted immediately with 232 boys enrolled. The VAS group had significantly higher mortality than the OPV group in the rainy season (HR: 9.91 (1.23 – 80)). All deaths had had contact with the neonatal nursery; of seven VAS boys enrolled during one week in September, six died within two months of age, whereas only one died among the six boys receiving OPV ($p = 0.05$). Growth (weight and arm-circumference) in the VAS group was significantly worse until age 3 months.

Conclusion

VAS at birth instead of OPV was not beneficial for the LBW boys in this study. With the premature closure of the trial it was not possible to answer the research question. However, the results of this study call for extra caution when testing the effect of NVAS in the future.

[example of the experimental nature of vaccination.

This test using Vitamin A Supplementation versus

Oral Polio Vaccine resulted in the deaths of 6 African boys]

Vaccination to prevent varicella: Goldman and King's response to Myers' interpretation of Varicella Active Surveillance Project data

Author information

Goldman GS1, King PG2.

1. Independent Computer Scientist, Pearblossom, CA, USA
gsgoldman@roadrunner.com
2. Facility Automation Management Engineering (FAME) Systems, Lake Hiawatha, NJ,
USA

Abstract

BACKGROUND

There is increasing evidence that herpes zoster (HZ) incidence rates among children and adults (aged <60 years) with a history of natural varicella are influenced primarily by the frequency of exogenous exposures, while asymptomatic endogenous reactivations help to cap the rate at approximately 550 cases/100,000 person-years when exogenous boosting becomes rare. The Antelope Valley Varicella Active Surveillance Project was funded by the Centers for Disease Control and Prevention in 1995 to monitor the effects of varicella vaccination in one of the three representative regions of the United States. The stability in the data collection and number of reporting sites under varicella surveillance from 1995-2002 and HZ surveillance during 2000-2001 and 2006-2007 contributed to the robustness of the discerned trends.

DISCUSSION

Varicella vaccination may be useful for leukemic children; however, the target population in the United States is all children. Since the varicella vaccine inoculates its recipients with live, attenuated varicella-zoster virus (VZV), clinical varicella cases have dramatically declined. Declining exogenous exposures (boosts) from children shedding natural VZV have caused waning cell-mediated immunity. Thus, the protection provided by varicella vaccination is neither lifelong nor complete. Moreover, dramatic increases in the incidence of adult shingles cases have been observed since HZ was added to the surveillance in 2000. In 2013, this topic is still debated and remains controversial in the United States.

SUMMARY

When the costs of the booster dose for varicella and the increased shingles recurrences are included, the universal varicella vaccination program is neither effective nor cost-effective.

<http://www.ncbi.nlm.nih.gov/pubmed/24275643>

“When the costs of the booster dose for varicella and the increased shingles recurrences are included, the universal varicella vaccination program is neither effective nor cost-effective.”

Interaction between neonatal vitamin A supplementation and timing of measles vaccination: a retrospective analysis of three randomized trials from Guinea-Bissau

Author information

Benn CS1, Martins CL2, Fisker AB3, Diness BR3, Garly ML3, Balde I2, Rodrigues A2, Whittle H4, Aaby P5.

1. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project 2300 Copenhagen S, Denmark; OPEN, Institute of Clinical Research, University of Southern Denmark/Odense University Hospital, Denmark
2. Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau.
3. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Artillerivej 5, 2300 Copenhagen S, Denmark.
4. The London School of Hygiene and Tropical Medicine, Keppel Street, London, UK.
5. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Artillerivej 5 2300 Copenhagen S, Denmark; Bandim Health Project, Indepth Network, Bissau, Guinea-Bissau

Abstract

BACKGROUND

In Guinea-Bissau we conducted three trials of neonatal vitamin A supplementation (NVA) from 2002 to 2008. None of the trials found a beneficial effect on mortality. From 2003 to 2007, an early measles vaccine (MV) trial was ongoing, randomizing children 1:2 to early MV at 4.5 months or no early MV, in addition to the usual MV at 9 months. We have previously found interactions between vitamin A and vaccines.

OBJECTIVE

We investigated whether there were interactions between NVA and early MV.

DESIGN

We compared the mortality of NVA and placebo recipients: first, from 4.5 to 8 months for children randomized to early MV or no early MV; and second, from 9 to 17 months in children who had received two MV or one MV. Mortality rates (MR) were compared in Cox models producing mortality rate ratios (MRR).

RESULTS

A total of 5141 children were randomized to NVA (N=3015) or placebo (N=2126) and were later randomized to early MV (N=1700) or no early MV (N=3441). Between 4.5 and 8 months, NVA compared with placebo was associated with higher mortality in early MV recipients (MR=30 versus MR=0, $p=0.01$), but not in children who did not receive early MV (p for interaction between NVA and early MV=0.03). From 9 to 17 months NVA was not associated with mortality. Overall, from 4.5 to 17 months NVA was associated with increased mortality in early MV recipients (Mortality rate ratio=5.39 (95% confidence interval: 1.62, 17.99)).

CONCLUSIONS

These observations indicate that NVA may interact with vaccines given several months later. This may have implications for the planning of future child intervention programs.

“These observations indicate that neonatal vitamin A supplementation may interact with vaccines given several months later.”

“This is the first report of measles transmission from a twice vaccinated individual.”

Oxford Journals Clinical Infectious Diseases • October 2014

Outbreak of Measles Among Persons With Prior Evidence of Immunity New York City, 2011

Author Information

Jennifer B. Rosen¹, Jennifer S. Rota², Carole J. Hickman², Sun Sowers², Sara Mercader², Paul A. Rota², William J. Bellini², Ada J. Huang³, Margaret K. Doll¹, Jane R. Zucker^{1,2}, and Christopher M. Zimmerman¹

1. Bureau of Immunization New York City Department of Health and Mental Hygiene
New York City, New York

2. National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC)
Atlanta, GA

3. Westchester County Department of Health, New Rochelle, New York

Abstract

Background

Measles was eliminated in the United States through high vaccination coverage and a public health system able to rapidly respond to measles. Measles may occur among vaccinated individuals, but secondary transmission from such individuals has not been documented.

Methods

Suspected cases and contacts exposed during a measles outbreak in New York City in 2011 were investigated. Medical histories and immunization records were obtained. Cases were confirmed by detection of measles-specific IgM and/or RNA. Tests for measles IgG, IgG avidity, measurement of measles neutralizing antibody titers, and genotyping were performed to characterize the cases.

Results

The index case had two doses of measles-containing vaccine. Of 88 contacts, four secondary cases were confirmed that had either two doses of measles-containing

vaccine or a past positive measles IgG antibody. All cases had laboratory confirmation of measles infection, clinical symptoms consistent with measles, and high avidity IgG antibody characteristic of a secondary immune response. Neutralizing antibody titers of secondary cases reached >80,000 mIU/mL 3-4 days post-rash onset while that of the index was <500 mIU/mL 9 days post-rash onset. No additional cases occurred among 231 contacts of secondary cases.

Conclusions

This is the first report of measles transmission from a twice vaccinated individual. The clinical presentation and laboratory data of the index were typical of measles in a naïve individual. Secondary cases had robust anamnestic antibody responses. No tertiary cases occurred despite numerous contacts. This outbreak underscores the need for thorough epidemiologic and laboratory investigation of suspected measles cases regardless of vaccination status.

Thimerosal as discrimination: vaccine disparity in the UN Minamata Convention on mercury

Sykes LK1, Geier DA2, King PG1, Kern JK3,
Haley BE1, Chaigneau CG1, Megson MN4, Love JM5, Reeves RE1, Geier MR2.

Author information

1. CoMeD, Inc, Silver Spring, MD United States
2. CoMeD, Inc, Silver Spring, MD; Institute of Chronic Illnesses, Inc, Silver Spring, MD
3. Institute of Chronic Illnesses, Inc, Silver Spring, MD United States
4. Pediatric and Adolescent Ability Center, Richmond, VA United States
5. CoMeD, Inc, Silver Spring, MD

Abstract

When addressing toxins, one unmistakable parallel exists between biology and politics: developing children and developing nations are those most vulnerable to toxic exposures. This disturbing parallel is the subject of this critical review, which examines the use and distribution of the mercury (Hg)-based compound, thimerosal, in vaccines. Developed in 1927, thimerosal is 49.55% Hg by weight and breaks down in the body into ethyl-Hg chloride, ethyl-Hg hydroxide and sodium thiosalicylate. Since the early 1930s, there has been evidence indicating that thimerosal poses a hazard to the health of human beings and is ineffective as an antimicrobial agent. While children in the developed and predominantly western nations receive doses of mostly no-thimerosal and reduced-thimerosal vaccines, children in the developing nations receive many doses of several unreduced thimerosal-containing vaccines (TCVs). Thus, thimerosal has continued to be a part of the global vaccine supply and its acceptability as a component of vaccine formulations remained unchallenged until 2010, when the United Nations (UN), through the UN Environment Programme, began negotiations to write the global, legally binding Minamata Convention on Hg. During the negotiations, TCVs were dropped from the list of Hg-containing products to be regulated. Consequently, a double standard in vaccine safety, which previously existed due to ignorance and economic reasons, has now been institutionalised as global policy. Ultimately, the Minamata Convention on Hg has sanctioned the inequitable distribution of thimerosal by specifically exempting TCVs from regulation, condoning a two-tier standard of vaccine safety: a predominantly no-thimerosal and reduced-thimerosal standard for developed nations and a predominantly thimerosal-containing one for developing nations. This disparity must now be evaluated urgently as a potential form of institutionalised discrimination.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25101548>

“the Minamata Convention on Mercury has sanctioned the inequitable distribution of thimerosal by specifically exempting TCVs from regulation, condoning a two-tier standard of vaccine safety; a predominantly no-thimerosal and reduced-thimerosal standard for developed nations and a predominantly thimerosal-containing one for developing nations. This disparity must now be evaluated urgently as a potential form of institutionalized discrimination.”

**Hepatitis B vaccination
and associated oral manifestations:
a non-systematic review of literature and case reports**

Author information

Tarakji B1, Ashok N1, Alakeel R2, Azzeghaibi S1,
Umair A1, Darwish S1, Mahmoud R3, Elkhatat E3.

Abstract

Hepatitis B vaccine has been administered in children and adults routinely to reduce the incidence of the disease. Even though, hepatitis B vaccine is considered as highly safe, some adverse reactions have been reported. A literature search was carried out in PubMed, accessed via the National Library of Medicine PubMed interface, searching used the following keywords: Hepatitis B vaccine and complications from 1980 to 2014. A total of 1147 articles were obtained out of which articles, which discuss the complications occurring orally or occurring elsewhere in the body, which have the potential to manifest orally after hepatitis B vaccination were selected. A total of 82 articles were identified which included 58 case series or case reports, 15 review articles, 4 cross sectional studies, 3 prospective cohort studies, one retrospective cohort study and a case control study. After reviewing the literature, we observed that complications seen after Hepatitis B vaccination are sudden infant death syndrome, multiple sclerosis, chronic fatigue syndrome, idiopathic thrombocytopenic purpura, vasculitis optic neuritis, anaphylaxis, systemic lupus erythematosus, lichen planus and neuro-muscular disorder. Of these complications, some are manifested orally or have the potential to manifest orally. Although, most of the complications are self-limiting, some are very serious conditions, which require hospitalization with immediate medical attention.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4250977/>

“A total of 82 articles were identified which included 58 case series or case reports, 15 review articles, 4 cross sectional studies, 3 prospective cohort studies, one retrospective cohort study and a case control study. After reviewing the literature, we observed that complications seen after Hepatitis B vaccination are sudden infant death syndrome, multiple sclerosis, chronic fatigue syndrome, idiopathic thrombocytopenic purpura, vasculitis optic neuritis, anaphylaxis, systemic lupus erythematosus, lichen planus and neuro-muscular disorder. Of these complications, some are manifested orally or have the potential to manifest orally.”

Longitudinal analysis of the association between removal of dental amalgam, urine mercury and 14 self-reported health symptoms

Author information

Zwicker JD1, Dutton DJ, Emery JC.

Abstract

BACKGROUND

Mercury vapor poses a known health risk with no clearly established safe level of exposure. Consequently there is debate over whether the level of prolonged exposure to mercury vapor from dental amalgam fillings, combining approximately 50% mercury with other metals, is sufficiently high to represent a risk to health. The objective of our study is to determine if mercury exposure from amalgam fillings is associated with risk of adverse health effects.

METHODS

In a large longitudinal non-blind sample of participants from a preventative health program in Calgary, Canada we compared number of amalgam fillings, urine mercury measures and changes in 14 self-reported health symptoms, proposed to be mercury dependent sub-clinical measures of mental and physical health. The likelihood of change over one year in a sample of persons who had their fillings removed was compared to a sample of persons who had not had their fillings removed. We use non-parametric statistical tests to determine if differences in urine mercury were statistically significant between sample groups. Logistic regression models were used to estimate the likelihood of observing symptom improvement or worsening in the sample groups.

RESULTS

At baseline, individuals with dental amalgam fillings have double the measured urine mercury compared to a control group of persons who have never had amalgam fillings. Removal of amalgam fillings decreases measured urine mercury to levels in persons without amalgam fillings. Although urine mercury levels in our sample are considered by Health Canada to be too low to pose health risks, removal of amalgam fillings reduced the likelihood of self-reported symptom deterioration and increased the likelihood of symptom improvement in comparison to people who retained their amalgam fillings.

CONCLUSIONS

Our findings suggest that mercury exposure from amalgam fillings adversely impact health and therefore are a health risk. The use of safer alternative materials for dental fillings should be encouraged to avoid the increased risk of health deterioration associated with unnecessary exposure to mercury.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4273453/>

“Our findings suggest that mercury exposure from amalgam fillings adversely impact health and therefore are a health risk.”

Immunization with hepatitis B vaccine accelerates SLE-like disease in a murine model

Author information

Agmon-Levin N1, Arango MT2, Kivity S3,
Katzav A4, Gilburd B5, Blank M5, Tomer N5,
Volkov A6, Barshack I6, Chapman J4, Shoenfeld Y7

1. Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer 52621 Israel; Sackler Medical School, Tel Aviv University, Israel
2. Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer 52621 Israel; Doctoral Program in Biomedical Sciences Universidad del Rosario, Bogota 111221, Colombia Center for Autoimmune Diseases Research - CREA, Universidad del Rosario, Bogota 111221, Colombia
3. Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer 52621 Israel; Sackler Medical School, Tel Aviv University, Israel
The Dr. Pinchas Borenstein Talpiot Medical Leadership Program 2013, Sheba Medical Center, Tel-Hashomer 52621, Israel
4. Department of Neurology and Sagol Neuroscience Center, Sheba Medical Center, Tel-Hashomer 52621, Israel
5. Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer 52621, Israel
6. Institute of Pathology, Sheba Medical Center, Tel Hashomer 52621, Israel
7. Zabudowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel-Hashomer 52621, Israel
Incumbent of the Laura Schwarz-Kip Chair for Autoimmunity, Tel-Aviv University, Israel
shoenfel@post.tau.ac.il

Abstract

Hepatitis-B vaccine (HBVv) can prevent HBV-infection and associated liver diseases. However, concerns regarding its safety, particularly among patients with autoimmune diseases (i.e. SLE) were raised. Moreover, the aluminum adjuvant in HBVv was related to immune mediated adverse events. Therefore, we examined the effects of immunization with HBVv or alum on SLE-like disease in a murine model. NZBWF1 mice were immunized with HBVv (Engerix), or aluminum hydroxide (alum) or phosphate buffered saline (PBS) at 8 and 12 weeks of age. Mice were followed for weight, autoantibodies titers, blood counts, proteinuria, kidney histology, neurocognitive functions (novel object recognition, staircase, Y-maze and the forced swimming tests) and brain histology. Immunization with HBVv induced acceleration of kidney disease manifested by high anti-dsDNA antibodies ($p < 0.01$), early onset of proteinuria ($p < 0.05$), histological damage and deposition of HBs antigen in the kidney. Mice immunized with HBVv and/or alum had decreased cells counts mainly of the red cell lineage ($p < 0.001$), memory deficits ($p < 0.01$), and increased activated microglia in different areas of the brain compare with mice immunized with PBS. Anxiety-like behavior was more pronounced among mice immunized with alum. In conclusion, herein we report that immunization with the HBVv aggravated kidney disease in an animal model of SLE. Immunization with either HBVv or alum affected blood counts, neurocognitive functions and brain gliosis. Our data support the concept that different component of vaccines may be linked with immune and autoimmune mediated adverse events.

<http://www.ncbi.nlm.nih.gov/pubmed/25042822>

“... concerns regarding its safety, [hepatitis B vaccine] particularly among patients with autoimmune diseases (i.e. SLE) were raised. Moreover, the aluminum adjuvant in HBVv was related to immune mediated adverse events. Our data support the concept that different component of vaccines may be linked with immune and autoimmune mediated adverse events.”

Clinical features in patients with long-lasting macrophagic myofasciitis

Author information

Rigolet M1, Aouizerate J2, Couette M3, Ragunathan-Thangarajah N2,
Aoun-Sebaiti M3, Gherardi RK4, Cadusseau J5, Authier FJ4.

1. Faculty of Medicine, INSERM U955-Team 10, Créteil, France

2. Faculty of Medicine, INSERM U955-Team 10, Créteil, France

Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye

3. Neurology Department, Henri Mondor University Hospital, Créteil, France

4. Faculty of Medicine, INSERM U955-Team 10, Créteil, France

Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye

Créteil, France; Paris Est-Créteil University, Créteil, France

5. Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye

Créteil, France; Paris Est-Créteil University, Créteil, France

Abstract

Macrophagic myofasciitis (MMF) is an emerging condition characterized by specific muscle lesions assessing abnormal long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients usually are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and marked cognitive deficits, not related to pain, fatigue, or depression. Clinical features usually correspond to that observed in chronic fatigue syndrome/myalgic encephalomyelitis. Representative features of MMF-associated cognitive dysfunction include dysexecutive syndrome, visual memory impairment, and left ear extinction at dichotic listening test. Most patients fulfill criteria for non-amnesic/dysexecutive mild cognitive impairment, even if some cognitive deficits appear unusually severe. Cognitive dysfunction seems stable over time despite marked fluctuations. Evoked potentials may show abnormalities in keeping with central nervous system involvement, with a neurophysiological pattern suggestive of demyelination. Brain perfusion SPECT shows a pattern of diffuse cortical and subcortical abnormalities, with hypoperfusions correlating with cognitive deficiencies. The combination of musculoskeletal pain, chronic fatigue, and cognitive disturbance generates chronic disability with possible social exclusion. Classical therapeutic approaches are usually unsatisfactory making patient care difficult.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4246686/>

“The combination of musculoskeletal pain, chronic fatigue, and cognitive disturbance generates chronic disability with possible social exclusion. Classical therapeutic approaches are usually unsatisfactory making patient care difficult.”

Longitudinal analysis of the association between removal of dental amalgam, urine mercury and 14 self-reported health symptoms

Author information

Zwicker JD1, Dutton DJ, Emery JC.
School of Public Policy, University of Calgary
Calgary, AB T2P 1H9, Canada
zwicker1@ucalgary.ca

Abstract

BACKGROUND

Mercury vapor poses a known health risk with no clearly established safe level of exposure. Consequently there is debate over whether the level of prolonged exposure to mercury vapor from dental amalgam fillings, combining approximately 50% mercury with other metals, is sufficiently high to represent a risk to health. The objective of our study is to determine if mercury exposure from amalgam fillings is associated with risk of adverse health effects.

METHODS

In a large longitudinal non-blind sample of participants from a preventative health program in Calgary, Canada we compared number of amalgam fillings, urine mercury measures and changes in 14 self-reported health symptoms, proposed to be mercury dependent sub-clinical measures of mental and physical health. The likelihood of change over one year in a sample of persons who had their fillings removed was compared to a sample of persons who had not had their fillings removed. We use non-parametric statistical tests to determine if differences in urine mercury were statistically significant between sample groups. Logistic regression models were used to estimate the likelihood of observing symptom improvement or worsening in the sample groups.

RESULTS

At baseline, individuals with dental amalgam fillings have double the measured urine mercury compared to a control group of persons who have never had amalgam fillings. Removal of amalgam fillings decreases measured urine mercury to levels in persons without amalgam fillings. Although urine mercury levels in our sample are considered by Health Canada to be too low to pose health risks, removal of amalgam fillings reduced the likelihood of self-reported symptom deterioration and increased the likelihood of symptom improvement in comparison to people who retained their amalgam fillings.

CONCLUSIONS

Our findings suggest that mercury exposure from amalgam fillings adversely impact health and therefore are a health risk. The use of safer alternative materials for dental fillings should be encouraged to avoid the increased risk of health deterioration associated with unnecessary exposure to mercury.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4273453/>

“Our findings suggest that mercury exposure from amalgam fillings adversely impact health and therefore are a health risk.”

Vaccine-associated varicella and rubella infections in severe combined immunodeficiency with isolated CD4 lymphocytopenia and mutations in IL7R detected by tandem whole exome sequencing and chromosomal microarray

Author information

Bayer DK1, Martinez CA, Sorte HS, Forbes LR, Demmler-Harrison GJ, Hanson IC, Pearson NM, Noroski LM, Zaki SR, Bellini WJ, Leduc MS, Yang Y, Eng CM, Patel A, Rodningen OK, Muzny DM, Gibbs RA, Campbell IM, Shaw CA, Baker MW, Zhang V, Lupski JR, Orange JS, Seeborg FO, Stray-Pedersen A.

Department of Pediatrics
Section of Immunology, Allergy, and Rheumatology
Baylor College of Medicine and Texas Children's Hospital
Houston, TX, USA

Abstract

In areas without newborn screening for severe combined immunodeficiency (SCID), disease-defining infections may lead to diagnosis, and in some cases, may not be identified prior to the first year of life. We describe a female infant who presented with disseminated vaccine-acquired varicella (VZV) and vaccine-acquired rubella infections at 13 months of age. Immunological evaluations demonstrated neutropenia, isolated CD4 lymphocytopenia, the presence of CD8(+) T cells, poor lymphocyte proliferation, hypergammaglobulinaemia and poor specific antibody production to VZV infection and routine immunizations. A combination of whole exome sequencing and custom-designed chromosomal microarray with exon coverage of primary immunodeficiency genes detected compound heterozygous mutations (one single nucleotide variant and one intragenic copy number variant involving one exon) within the IL7R gene. Mosaicism for wild-type allele (20-30%) was detected in pretransplant blood and buccal DNA and maternal engraftment (5-10%) demonstrated in pretransplant blood DNA. This may be responsible for the patient's unusual immunological phenotype compared to classical interleukin (IL)-7R α deficiency. Disseminated VZV was controlled with anti-viral and immune-based therapy, and umbilical cord blood stem cell transplantation was successful. Retrospectively performed T cell receptor excision circle (TREC) analyses completed on neonatal Guthrie cards identified absent TREC. This case emphasizes the danger of live viral vaccination in severe combined immunodeficiency (SCID) patients and the importance of newborn screening to identify patients prior to high-risk exposures. It also illustrates the value of aggressive pathogen identification and treatment, the influence newborn screening can have on morbidity and mortality and the significant impact of newer genomic diagnostic tools in identifying the underlying genetic aetiology for SCID patients.

<http://www.ncbi.nlm.nih.gov/pubmed/25046553>

“This case emphasizes the danger of live viral vaccination in severe combined immunodeficiency (SCID) patients and the importance of newborn screening to identify patients prior to high-risk exposures.”

‘Poisonous, Filthy, Loathsome, Damnable Stuff’: The Rhetorical Ecology of Vaccination Concern

Author Information

Bernice L. Hausman, PhD, Mecal Ghebremichael, BS, Philip Hayek, MA, and Erin Mack, BS

Department Of English, Virginia Tech, Blacksburg, VA
Mailman School of Public Health, Columbia University, New York, NY

Abstract

In this article, we analyze newspaper articles and advertisements mentioning vaccination from 1915 to 1922 and refer to historical studies of vaccination practices and attitudes in the early 20th century in order to assess historical continuities and discontinuities in vaccination concern. In the Progressive Era period, there were a number of themes or features that resonated with contemporary issues and circumstances: 1) fears of vaccine contamination; 2) distrust of medical professionals; 3) resistance to compulsory vaccination; and 4) the local nature of vaccination concern. Such observations help scholars and practitioners understand vaccine skepticism as longstanding, locally situated, and linked to the sociocultural contexts in which vaccination occurs and is mandated for particular segments of the population. A rhetorical approach offers a way to understand how discourses are engaged and mobilized for particular purposes in historical contexts. Historically situating vaccine hesitancy and addressing its articulation with a particular rhetorical ecology offers scholars and practitioners a robust understanding of vaccination concerns that can, and should, influence current approaches to vaccination skepticism.

Introduction

On June 26, 2014, Eric Kodish, MD, a medical ethicist at the Cleveland Clinic, wrote in the *Washington Post* that “The anti-vaccination movement is a relatively new one that has taken hold over the past decade. Started by a small community of parents, it is based on myths that have been perpetuated by the power of the Internet and endorsements from celebrities such as actress Jenny McCarthy, who has suggested that vaccinations may have caused her son’s autism” [1]. This statement encapsulates mainstream public health attitudes toward vaccine skepticism in the early 21st century — that it constitutes a unified national movement, that the movement is relatively new, and that it has gained authority due to the power of the Internet and celebrity endorsements.

Indeed, it does seem as if the medical and public health consensus concerning the value of vaccination is unraveling culturally in the United States. Medical researchers routinely study health messaging about vaccination, finding most recently that popular public health promotion programs do not convince committed non-vaccinators to change their minds [2]. A discourse of crisis pervades media reporting on outbreaks of infectious disease, and every flu season brings with it a series of escalating media exhortations to be vaccinated. Physicians report increasing frustrations with parents who refuse to vaccinate their children or who seek a different vaccination schedule [3,4]. The American Academy of Pediatrics (AAP) has had to state unequivocally that it is against firing patients as a result of their vaccination status [5]; and, as with Erik Kodish, medical ethicists accuse parents who do not vaccinate their children of negligence [1,6].

Yet national vaccination rates for most routine infectious diseases of childhood in the United States remain high, suggesting that ongoing concerns about vaccination occur in tandem with the general success of public health efforts to vaccinate children against what were once routine childhood diseases. National immunization rates suggest that there is no widespread refusal to vaccinate (see Table 1). Kodish repeats a common statistic indicating “1 in 10 parents in the United States now forgo or delay vaccinations for their kids,” yet without more information about what those parents eventually do, it is difficult to accept that statement as a threat to national public health [1]. After all, in those families are children whose parents simply delay vaccinations due to child illness at the time of the doctors’ visit or due to a specific decision to slow the pace of vaccination during infancy. In either case, Table 1 suggests that by 36 months, most children are caught up with individual vaccines and many of the national rates for those vaccines are at herd immunity levels.

Evolution of multiple sclerosis in France since the beginning of hepatitis B vaccination

Author information

Le Houézec D1.

REVAHB (“Réseau Vaccin Hépatite B” in French)
32 rue du Clos Herbert, 14000
Caen, France
dominique.le.houezec@freesbee.fr

Abstract

Since the implementation of the mass vaccination campaign against hepatitis B in France, the appearance of multiple sclerosis, sometimes occurring in the aftermath of vaccinations, led to the publication of epidemiological international studies. This was also justified by the sharp increase in the annual incidence of multiple sclerosis reported to the French health insurance in the mid-1990s. Almost 20 years later, a retrospective reflection can be sketched from these official data and also from the national pharmacovigilance agency. Statistical data from these latter sources seem to show a significant correlation between the number of hepatitis B vaccinations performed and the declaration to the pharmacovigilance of multiple sclerosis occurring between 1 and 2 years later. The application of the Hill’s criteria to these data indicates that the correlation between hepatitis B vaccine and multiple sclerosis may be causal.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25395338>

“The application of the Hill’s criteria to these data indicates that the correlation between hepatitis B vaccine and multiple sclerosis may be causal.”

Chronic fatigue syndrome and fibromyalgia
following immunization with the hepatitis B vaccine:
another angle of the
'autoimmune (auto-inflammatory) syndrome induced by adjuvants'
(ASIA)

Author information

Agmon-Levin N1, Zafirir Y, Kivity S,
Balofsky A, Amital H, Shoenfeld Y.
The Zabłudowicz Center for Autoimmune Diseases
Chaim Sheba Medical Center, 52621, Tel-Hashomer, Israel

Abstract

The objectives of this study were to gather information regarding demographic and clinical characteristics of patients diagnosed with either fibromyalgia (FM) or chronic fatigue (CFS) following hepatitis B vaccination (HBVv) and furthermore to apply the recently suggested criteria of autoimmune (auto-inflammatory) syndromes induced by adjuvants (ASIA), in the aim of identifying common characteristics that may suggest an association between fibromyalgia, chronic fatigue and HBV vaccination. Medical records of 19 patients with CFS and/or fibromyalgia following HBVv immunization were analyzed. All of which were immunized during 1990-2008 in different centers in the USA. All medical records were evaluated for demographics, medical history, the number of vaccine doses, as well as immediate and long term post-immunization adverse events and clinical manifestations. In addition, available blood tests, imaging results, treatments and outcomes were analyzed. ASIA criteria were applied to all patients. The mean age of patients was 28.6 ± 11 years, of which 68.4 % were females. 21.05 % had either personal or familial background of autoimmune disease. The mean latency period from the last dose of HBVv to onset of symptoms was 38.6 ± 79.4 days, ranging from days to a year. Eight (42.1 %) patients continued with the immunization program despite experiencing adverse events. Manifestations that were commonly reported included neurological manifestations (84.2 %), musculoskeletal (78.9 %), psychiatric (63.1 %), fatigue (63.1 %), gastrointestinal complains (58 %) and mucocutaneous manifestations (36.8 %). Autoantibodies were detected in 71 % of patients tested. All patients fulfilled the ASIA criteria. This study suggests that in some cases CFS and FM can be temporally related to immunization, as part of ASIA syndrome. The appearance of adverse event during immunization, the presence of autoimmune susceptibility and higher titers of autoantibodies all can be suggested as risk factors. ASIA criteria were fulfilled in all patients eluding the plausible link between ASIA and CFS/FM.

<http://www.ncbi.nlm.nih.gov/pubmed/25427994>

“This study suggests that
in some cases Chronic Fatigue Syndrome (CFS)
and fibromyalgia (FM) can be temporally related to
immunization, as part of ASIA syndrome.”

“... a causal link with vaccine cannot be excluded in some individuals.”

Immunology Research • December 2014

A sudden onset of a pseudo-neurological syndrome
after HPV-16/18 AS04-adjuvated vaccine: might it be an
autoimmune/inflammatory syndrome induced by adjuvants (ASIA)
presenting as a somatoform disorder?

Author information

Poddighe D1, Castelli L, Marseglia GL, Bruni P.

Department of Pediatrics, Azienda Ospedaliera di Melegnano, Milan, Italy
dimimedpv@yahoo.it

Abstract

In last centuries, vaccines reduced the incidence of several infectious diseases. In last decades, some vaccines aimed at preventing also some cancers, where viruses play a causative role. However, several adverse events have been described after vaccines, but a causal relationship has been established only in a minority of cases. Here, we describe a pseudo-neurological syndrome occurred shortly after the administration of the bivalent HPV vaccine. Some autoimmune disorders, including neurological demyelinating diseases, have been reported after HPV vaccines, but the patient showed no organic lesions. The patient was diagnosed as having a functional somatoform syndrome, which was supposed to be autoimmune/inflammatory syndrome induced by adjuvants (ASIA), seen the temporal link with vaccination and the presence of anti-phospholipid autoantibodies. Immunological mechanisms of vaccines-and of adjuvants-have not been completely elucidated yet, and although there is no evidence of statistical association with many post-vaccination events, a causal link with vaccine cannot be excluded in some individuals.

<http://www.ncbi.nlm.nih.gov/pubmed/25388965>

Altered inflammatory activity associated with reduced hippocampal volume and more severe posttraumatic stress symptoms in Gulf War veterans

Author information

O'Donovan A1, Chao LL2, Paulson J3,
Samuelson KW4, Shigenaga JK2, Grunfeld C2,
Weiner MW2, Neylan TC2.

Abstract

BACKGROUND

Inflammation may reduce hippocampal volume by blocking neurogenesis and promoting neurodegeneration. Posttraumatic stress disorder (PTSD) has been linked with both elevated inflammation and reduced hippocampal volume. However, few studies have examined associations between inflammatory markers and hippocampal volume, and none have examined these associations in the context of PTSD.

METHODS

We measured levels of the inflammatory markers interleukin-6 (IL-6) and soluble receptor II for tumor necrosis factor (sTNF-RII) as well as hippocampal volume in 246 Gulf War veterans with and without current and past PTSD as assessed with the Clinician Administered PTSD Scale (CAPS). Enzyme-linked immunosorbent assays were used to measure inflammatory markers, and 1.5Tesla magnetic resonance imaging (MRI) and Freesurfer version 4.5 were used to quantify hippocampal volume. Hierarchical linear regression and analysis of covariance models were used to examine if hippocampal volume and PTSD status would be associated with elevated levels of IL-6 and sTNF-RII.

RESULTS

Increased sTNF-RII, but not IL-6, was significantly associated with reduced hippocampal volume ($\beta=-0.14$, $p=0.01$). The relationship between sTNF-RII and hippocampal volume was independent of potential confounds and covariates, including PTSD status. Although we observed no PTSD diagnosis-related differences in either IL-6 or sTNF-RII, higher PTSD severity was associated with significantly increased sTNF-RII ($\beta=0.24$, $p=0.04$) and reduced IL-6 levels ($\beta=-0.24$, $p=0.04$).

CONCLUSIONS

Our results indicate that specific inflammatory proteins may be associated with brain structure and function as indexed by hippocampal volume and PTSD symptoms.

“Our results indicate that specific inflammatory proteins may be associated with brain structure and function as indexed by hippocampal volume and PTSD symptoms.”

“Macrophagic myofasciitis (MMF) characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization has been reported with increasing frequency in the past 10 years.

The vaccines containing this adjuvant may trigger MMF in some patients.”

Rheumatology International • January 2015

Macrophagic myofasciitis and vaccination: consequence or coincidence?

Author information

Santiago T1, Rebelo O, Negrão L, Matos A.

Rheumatology Unit
Centro Hospitalar e Universitário de Coimbra
Praceta Prof. Mota Pinto, 3000-075
Coimbra, Portugal
tlousasantiago@hotmail.com

Abstract

Macrophagic myofasciitis (MMF) characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization has been reported with increasing frequency in the past 10 years. We describe clinical and laboratory findings in patients with MMF. We did a retrospective analysis of 16 cases observed in our Neuropathology Laboratory, between January 2000 and July 2013. The mean age of the 16 patients was 48.8 ± 18.0 years; 80.0 % were female. Chronic fatigue syndrome was found in 8 of 16 patients. Half of the patients had elevated creatinine kinase levels, and 25.0 % had a myopathic electromyogram. Thirteen patients received intramuscular administration of aluminum-containing vaccine prior to the onset of symptoms. MMF may mirror a distinctive pattern of an inflammatory myopathy. The vaccines containing this adjuvant may trigger MMF in some patients.

<http://www.ncbi.nlm.nih.gov/pubmed/24923906>

Harefuah • February 2015

The sick building syndrome as a part of 'ASIA'

(autoimmune/auto-inflammatory syndrome induced by adjuvants)

by Maoz-Segal R, Agmon-Levin N, Israeli E, Shoenfeld Y.

Abstract

The entity 'sick building syndrome' is poorly defined and comprises of a set of symptoms resulting from environmental exposure to a work or a living environment. The symptoms are mainly "allergic"-like and include nasal, eye, and mucous membrane irritation, dry skin as well as respiratory symptoms and general symptoms such as fatigue, lethargy, headaches and fever. The Autoimmune [Auto-inflammatory] Syndrome Induced by Adjuvants (ASIA) is a wider term which describes the role of various environmental factors in the pathogenesis of immune mediated diseases. Factors entailing an immune adjuvant activity such as infectious agents, silicone, aluminium salts and others were found in association with defined and non-defined immune mediated diseases. The sick building syndrome and ASIA share a similar complex of signs and symptoms and probably the same immunological mechanisms which further support a common denominator.

<http://www.ncbi.nlm.nih.gov/pubmed/25856869>

“Factors entailing an immune adjuvant activity such as infectious agents, silicone, aluminium salts and others were found in association with defined and non-defined immune mediated diseases.”

“... 2,207 cases were considered probably or possibly related to vaccination.

These represent the largest ASIA cohort ever reported ...”

Immunology Research • February 2015

The epidemiological profile of ASIA syndrome after HPV vaccination: an evaluation based on the Vaccine Adverse Event Reporting Systems

Author information

Pellegrino P1, Perrone V, Pozzi M,
Carnovale C, Perrotta C, Clementi E, Radice S.

Unit of Clinical Pharmacology
Department of Biomedical and Clinical Sciences
University Hospital “Luigi Sacco”, University of Milan
Via GB Grassi 74, 20157, Milan, Italy

Abstract

The term “ASIA-Autoimmune/inflammatory Syndrome Induced by Adjuvants” describes an umbrella of clinical conditions sharing similar signs or symptoms, including post-vaccination phenomena. No information is available on the epidemiology of the ASIA syndrome, especially following HPV vaccination. We carried out an analysis of the VAERS database to retrieve all cases of suspected ASIA syndrome according to the Shoenfeld and Agmon-Levin’s guideline for the diagnosis. After causality assessment and case validation, 2,207 cases were considered probably or possibly related to vaccination. These represent the largest ASIA cohort ever reported and allowed us to estimate epidemiological and clinical characteristic of this syndrome. The commonest clinical manifestation observed were pyrexia (58%), myalgia (27%) and arthralgia or arthritis (19%), and the estimated reporting rate was of 3.6 cases per 100,000 doses of HPV vaccine distributed (95% CI 3.4-3.7). This study presents the first systematic estimation of ASIA incidence and expands the knowledge on this pathology. Further analyses are needed to identify genetic and non-genetic risk factors for ASIA syndrome.

<http://www.ncbi.nlm.nih.gov/pubmed/25381482>

Pertussis outbreak in university students and evaluation of acellular pertussis vaccine effectiveness in Japan

Author information

Hara M1, Fukuoka M2, Tashiro K3, Ozaki I4,
Ohfuji S5, Okada K6, Nakano T7, Fukushima W8, Hirota Y9,10.

Abstract

BACKGROUND

Recent studies worldwide have reported increasing numbers of adults diagnosed with *Bordetella pertussis* despite receiving childhood vaccinations. This study describes a pertussis outbreak at a university medical faculty campus and examines the effectiveness of diphtheria, tetanus, and pertussis (DTaP) vaccination completed during infancy in Japan.

METHODS

After the outbreak, self-administered questionnaires and serum samples were collected from students on campus to determine the incidence of pertussis and underlying diseases. Pertussis was diagnosed on the basis of clinical criteria and serum anti-pertussis toxin antibody levels. Using data collected from 248 first and second grade students who had submitted copies of their vaccination records, we evaluated the effectiveness of DTaP vaccination in infancy against adult pertussis.

RESULTS

Questionnaire responses were obtained from 636 students (of 671 registered students; 95% response rate). Of 245 students who reported a continuous cough during the outbreak period, 84 (attack rate: 13.2%) were considered “probable” pertussis cases that met clinical criteria. The outbreak occurred mainly in first and second grade students in the Faculty of Medicine. Of 248 students who provided vaccination records, 225 had received 4 DTaP doses (coverage: 90.7%); the relative risk of the complete vaccination series compared to those with fewer than 4 doses or no doses for probable cases was 0.48 (95% confidence interval: 0.24-0.97).

CONCLUSIONS

Waning protection was suspected due to over time. Booster vaccination for teenagers and development of highly efficacious pertussis vaccines are needed.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25656486>

“Waning protection was suspected ...”

“The emerging epidemic of Hodgkin and non-Hodgkin lymphomas worldwide
continues to defy our understanding ...”

Immunology Research • February 2015

Adjuvants and lymphoma risk as part of the ASIA spectrum

Author information

Butnaru D1, Shoenfeld Y.

The Zabłudowicz Center for Autoimmune Diseases
Sheba Medical Center, Tel Hashomer, Israel
dana_medis@iberserv.es

Abstract

The emerging epidemic of Hodgkin and non-Hodgkin lymphomas worldwide continues to defy our understanding and forces the search for the causative factors. Adjuvants are known to act as triggers of immune and inflammatory responses. Animal experiments have demonstrated that long-term inflammation is related to aggravation of the immune network resulting in cellular and humoral responses leading to autoimmunity and lymphoma development. Chronic stimulation of the immune system is thought to be the key mechanism through which infectious diseases as well as autoimmune diseases can lead to lymphomagenesis. Many adjuvants can act similarly perturbing immune system's function, inducing a state of prolonged immune activation related to chronic lymphatic drainage. Several mechanisms were proposed by which adjuvants induce inflammation, and they are discussed herein. Some of them are triggering inflammasome; others bind DNA, lipid moieties in cells, induce uric acid production or act as lipophilic and/or hydrophobic substances. The sustained inflammation increases the risk of genetic aberrations, where the initial polyclonal activation ends in monoclonality. The latter is the hallmark of malignant lymphoma. Thus, chronic adjuvant stimulation may lead to lymphoma.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25582758>

Ethylmercury and Hg²⁺ induce the formation of neutrophil extracellular traps (NETs) by human neutrophil granulocytes

Author information

Haase H1,2, Hebel S3, Engelhardt G3, Rink L4.

Department of Food Chemistry and Toxicology
Berlin Institute of Technology
Gustav-Meyer-Allee 25
13355, Berlin, Germany

Medical Faculty, Institute of Immunology
RWTH Aachen University Hospital, Pauwelsstrasse 30
52074, Aachen, Germany
haase@tu-berlin.de.

Abstract

Humans are exposed to different mercurial compounds from various sources, most frequently from dental fillings, preservatives in vaccines, or consumption of fish. Among other toxic effects, these substances interact with the immune system. In high doses, mercurials are immunosuppressive. However, lower doses of some mercurials stimulate the immune system, inducing different forms of autoimmunity, autoantibodies, and glomerulonephritis in rodents. Furthermore, some studies suggest a connection between mercury exposure and the occurrence of autoantibodies against nuclear components and granulocyte cytoplasmic proteins in humans. Still, the underlying mechanisms need to be clarified. The present study investigates the formation of neutrophil extracellular traps (NETs) in response to thimerosal and its metabolites ethyl mercury (EtHg), thiosalicylic acid, and mercuric ions (Hg²⁺). Only EtHg and Hg²⁺ triggered NETosis. It was independent of PKC, ERK1/2, p38, and zinc signals and not affected by the NADPH oxidase inhibitor DPI. Instead, EtHg and Hg²⁺ triggered NADPH oxidase-independent production of ROS, which are likely to be involved in mercurial-induced NET formation. This finding might help understanding the autoimmune potential of mercurial compounds. Some diseases, to which a connection with mercurials has been shown, such as Wegener's granulomatosis and systemic lupus erythematosus, are characterized by high prevalence of autoantibodies against neutrophil-specific auto-antigens. Externalization in the form of NETs may be a source for exposure to these self-antigens. In genetically susceptible individuals, this could be one step in the series of events leading to autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25701957>

“lower doses of some mercurials stimulate the immune system, inducing different forms of autoimmunity, autoantibodies, and glomerulonephritis in rodents. Furthermore, some studies suggest a connection between mercury exposure and the occurrence of autoantibodies ... This finding might help understanding the autoimmune potential of mercurial compounds.”

Tween-80 and impurity induce anaphylactoid reaction in zebrafish

Author information

Yang R1, Lao QC, Yu HP, Zhang Y,
Liu HC, Luan L, Sun HM, Li CQ.
National Institutes for Food and Drug Control
China Food and Drug Administration (CFDA)
No. 2 Tiantan Xili, Dongcheng District
Beijing, 100050, China

Abstract

A number of recent reports suspected that Tween-80 in injectable medicines, including traditional Chinese medicine injections could cause life-threatening anaphylactoid reaction, but no sound conclusion was drawn. A drug-induced anaphylactoid reaction is hard to be assayed in vitro and in conventional animal models. In this study, we developed a microplate-based quantitative in vivo zebrafish assay for assessing anaphylactoid reaction and live whole zebrafish mast cell tryptase activity was quantitatively measured at a wavelength of 405 nm using N-benzoyl-dl-arginine p-nitroanilide as a substrate. We assessed 10 batches of Tween-80 solutions from various national and international suppliers and three Tween-80 impurities (ethylene glycol, 2-chloroethanol and hydrogen peroxide) in this model and found that three batches of Tween-80 (nos 2, 20080709 and 20080616) and one Tween-80 impurity, hydrogen peroxide (H₂O₂), induced anaphylactoid reactions in zebrafish. Furthermore, we found that H₂O₂ residue and peroxide value were much higher in Tween-80 samples 2, 20080709 and 20080616. These findings suggest that H₂O₂ residue in combination with oxidized fatty acid residues (measured as peroxide value) or more likely the oxidized fatty acid residues in Tween-80 samples, but not Tween-80 itself, may induce anaphylactoid reaction. High-throughput zebrafish tryptase assay developed in this report could be used for assessing safety of Tween-80-containing injectable medicines and potentially for screening novel mast cell-modulating drugs.

<http://www.ncbi.nlm.nih.gov/pubmed/25345596>

“A number of recent reports suspected that Tween-80 in injectable medicines, including traditional Chinese medicine injections could cause life-threatening anaphylactoid reaction, but no sound conclusion was drawn. These findings suggest that H₂O₂ residue in combination with oxidized fatty acid residues (measured as peroxide value) or more likely the oxidized fatty acid residues in Tween-80 samples, but not Tween-80 itself, may induce anaphylactoid reaction.”

Adverse events following Haemophilus influenzae type b vaccines in the Vaccine Adverse Event Reporting System 1990-2013

Author information

Moro PL1, Jankosky C2, Menschik D2,
Lewis P3, Duffy J3, Stewart B3, Shimabukuro TT3.

1. Immunization Safety Office
Centers for Disease Control and Prevention, Atlanta, GA
pmoro@cdc.gov
2. Center for Biologics Evaluation and Research
US Food and Drug Administration, Silver Spring, MD
3. Immunization Safety Office
Centers for Disease Control and Prevention, Atlanta, GA

Abstract

Objective

To characterize adverse events (AEs) after Haemophilus influenzae type b (Hib) vaccines reported to the US Vaccine Adverse Event Reporting System (VAERS), a spontaneous reporting surveillance system.

Study Design

We searched VAERS for US reports after Hib vaccines among reports received from January 1, 1990, to December 1, 2013. We reviewed a random sample of reports and accompanying medical records for reports classified as serious. All reports of death were reviewed. Physicians assigned a primary clinical category to each reviewed report. We used empirical Bayesian data mining to identify AEs that were disproportionately reported after Hib vaccines.

Results

VAERS received 29,747 reports after Hib vaccines; 5179 (17%) were serious, including 896 reports of deaths. Median age was 6 months (range 0-1022 months). Sudden infant death syndrome was the stated cause of death in 384 (51%) of 749 death reports with autopsy/death certificate records. The most common nondeath serious AE categories were neurologic (80; 37%), other noninfectious (46; 22%) (comprising mainly constitutional signs and symptoms); and gastrointestinal (39; 18%) conditions. No new safety concerns were identified after clinical review of reports of AEs that exceeded the data mining statistical threshold.

Conclusion

Review of VAERS reports did not identify any new or unexpected safety concerns for Hib vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/25598306>

“VAERS received 29,747 reports after Hib vaccines; 5179 (17%) were serious, including 896 reports of deaths.

Median age was 6 months (range 0-1022 months). Sudden infant death syndrome was the stated cause of death in 384 (51%) of 749 death reports with autopsy/death certificate records.

The most common nondeath serious AE categories were neurologic (80; 37%), other noninfectious (46; 22%) (comprising mainly constitutional signs and symptoms); and gastrointestinal (39; 18%) conditions.”

Seroprevalence of pertussis in the Gambia: evidence for continued circulation of bordetella pertussis despite high vaccination rates

Author information

Scott S1, van der Sande M, Faye-Joof T, Mendy M, Sanneh B,
Barry Jallow F, de Melker H, van der Klis F, van Gageldonk P, Mooi F, Kampmann B.

From the *Medical Research Council (MRC) Unit, The Gambia, Fajara, The Gambia, West Africa; †Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, United Kingdom; ‡National Institute of Public Health and the Environment (RIVM), Centre for Infectious Diseases Control (CIb), Bilthoven, The Netherlands; §Julius Centre for Health Sciences and Primary Care, Utrecht University, Utrecht, The Netherlands; ¶International Agency for Research on Cancer, Lyon, France; and Department of Paediatrics, Imperial College, London, United Kingdom

Abstract

BACKGROUND

Bordetella pertussis can cause severe respiratory disease and death in children. In recent years, large outbreaks have occurred in high-income countries; however, little is known about pertussis incidence in sub-Saharan Africa.

METHODS

We evaluated antibody responses to pertussis toxin (Ptx) from individuals aged between 2 and 90 years in rural Gambia. IgG-Ptx was measured using luminex xMAP technology. IgG-Ptx geometric mean concentrations (GMC) and their 95% confidence intervals were calculated. The proportion seropositive (>20 EU/mL or ≥ 62.5 EU/mL) and GMCs were compared by age, sex, ethnic group, vaccination status, birth order and number of siblings per household using logistic and linear regression.

RESULTS

76.3% had anti-Ptx levels <20 EU/mL, 17.5% had concentrations between 20 and 62.5 EU/mL, 4.4% had concentrations between 62.5 and 125 EU/mL and 1.8% had concentrations ≥ 125 EU/mL. The overall Ptx antibody GMC was 6.4 EU/mL (95% confidence interval: 5.8-6.9). Higher antibody concentrations were observed in older populations with evidence for an increase in infection risk with increasing age (1.9% yearly increase, 95% confidence interval: 1.3-2.5). No child under 6 years of age had GMC above 62.5 EU/mL but 29.5% had concentrations between 20 and 62.5 EU/mL.

CONCLUSIONS

These data provide evidence that *B. pertussis* is being transmitted within this population despite high vaccination coverage. Re-infection may occur implying that immunity from childhood vaccination may not be lifelong. In the absence of data on actual clinical cases of pertussis, seroprevalence studies remain valuable tools to assess the transmission dynamics of *B. pertussis*.

“These data provide evidence that *B. pertussis* is being transmitted within this population despite high vaccination coverage. Re-infection may occur implying that immunity from childhood vaccination may not be lifelong.”

The mechanisms of action of vaccines containing aluminum adjuvants: an in vitro vs in vivo paradigm

Tirth Raj Ghimire

Division of Veterinary and Primate Health
Global Primate Network, Kathmandu, Nepal
Department of Zoology, Birendra Multiple Campus
Tribhuvan University, Chitwan, Nepal

The theory of ‘inflammation’

The use of adjuvants in vaccination is usually associated with some degree of injection site inflammation, and this process is considered an essential part of adjuvant function (Qin et al. 2009). This is consistent with the ‘Danger Theory’ of immune activation as proposed by Polly Matzinger in 1994 (Matzinger 1994). According to this theory, initiation of the immune response is not dependent on microbial recognition, but rather on the ability of pathogens or other agents such as adjuvants to cause tissue damage. The danger signals released from damaged tissues then have the capacity to drive inflammation and initiate an adaptive immune response (Matzinger 1994). This provides an important mechanistic theory for alum adjuvants with many reports of inflammatory effects at the injection site and the induction of danger signals from cells following alum interaction. For example, nodule or granuloma formation in humans and animals following alum injection has been reported from the 1930s to present day (Glenny 1931; Harrison 1935; Farago 1940; Holt 1950; White et al. 1955; Munks et al. 2010; Lu and Hogenesch 2013; Vogelbruch et al. 2000; Bordet et al. 2001; Chong et al. 2006; Rock et al. 2010; Marsee et al. 2008). The development of alum granuloma is independent of the route of immunization and occurs from a few days to several years (e.g., up to >12 years) following immunization, supporting the hypothesis that vaccines containing alum lead to a short-term inflammatory effect in a normal environment as well as long-term inflammatory effects in a pathological environment, at the site of injection (Gherardi et al. 2001; Kool et al. 2008a). It has been shown that alum induces uric acid or monosodium urate (MSU) crystal as a danger signal (Kool et al. 2008a). Subsequently, other signals such as heat shock protein 70 (HSP70) (Wang et al. 2012), and deoxyribonucleic acid (DNA) (Marichal et al. 2011; McKee et al. 2013) have been illustrated as inducers of alum-mediated immune responses, indicating that the mechanisms by which alum particles induce inflammation is central to understanding its adjuvant properties.

A clear causal association of alum in triggering immune responses via cellular death and or enhancing the quality, duration, and magnitude of T- and B- cell responses will make a significant contribution to the rational design of effective and safe vaccines and development of new adjuvants for future use.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4406982/>

“The use of adjuvants in vaccination is usually associated with some degree of injection site inflammation, and this process is considered an essential part of adjuvant function. This is consistent with the ‘Danger Theory’ of immune activation as proposed by Polly Matzinger in 1994. According to this theory, initiation of the immune response is not dependent on microbial recognition, but rather on the ability of pathogens or other agents such as adjuvants to cause tissue damage.”

Ugeskrift For Laeger • April 2015

Aluminium allergy and granulomas induced by vaccinations for children

Author information

Andersen RM1, Zachariae C, Johansen JD.

Videncenter for Allergi
Hud- og Allergiafdelingen
Gentofte Hospital
Niels Andersens vej 65
2900 Hellerup
jeanne.Duus.Johansen@regionh.dk

Abstract

Vaccination with aluminium-adsorbed vaccines can induce aluminium allergy with persistent itching subcutaneous nodules at the injection site - vaccination granulomas. In this article we give an overview of childhood aluminium-adsorbed vaccines available in Denmark. Through literature studies we examine the incidence, the symptoms and the prognosis for the vaccination granulomas and the allergy. Finally we discuss the status in Denmark.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25350883>

“Vaccination with aluminium-adsorbed vaccines can induce aluminium allergy with persistent itching subcutaneous nodules at the injection site - vaccination granulomas.”

Prescrire International • May 2015

Efficacy of the HPV vaccine in late 2014

[No authors listed]

Abstract

Initial evaluation of the HPV 6, 11, 16, 18 vaccine showed about a 40% reduction in high-grade cervical dysplasia due to all virus genotypes among young women aged 16 to 23 years who were not yet sexually active. These results were obtained after 4 years of follow-up and were confirmed after an additional 3 years. Clinical assessment of the HPV 16, 18 vaccine yielded similar results. The interval between initial HPV infection and diagnosis of cervical cancer seems to be at least 20 years. Comparisons of vaccinated and unvaccinated cohorts are consistent with the results of clinical trials, but follow-up is still too short because most of the women studied have not reached the age at which the incidence of high-grade dysplasia peaks. The available evidence shows no replacement of HPV vaccine genotypes by other highly oncogenic genotypes but, once again, follow-up is relatively short. In late 2014, follow-up is still too short to show whether HPV vaccination prevents cervical cancer in young women before they become sexually active. Earlier clinical trials showing efficacy in preventing high-grade dysplasia have not been challenged by epidemiological data. Overall, it will be several more years before conclusive evidence is obtained. In 2015, screening remains the cornerstone for reducing the incidence of invasive cervical cancer.

<http://www.ncbi.nlm.nih.gov/pubmed/26034805>

“ In late 2014, follow-up is still too short to show whether HPV vaccination prevents cervical cancer in young women before they become sexually active. Earlier clinical trials showing efficacy in preventing high-grade dysplasia have not been challenged by epidemiological data. Overall, it will be several more years before conclusive evidence is obtained. In 2015, screening remains the cornerstone for reducing the incidence of invasive cervical cancer.”

Cutaneous reactions to vaccinations

Author information

Rosenblatt AE1, Stein SL2.

1. Department of Medicine, Section of Dermatology
University of Chicago, Pritzker School of Medicine
5841 S. Maryland Ave MC 5067, Chicago, IL 60637

2. Department of Medicine, Section of Dermatology
University of Chicago, Pritzker School of Medicine
5841 S. Maryland Ave MC 5067, Chicago, IL 60637

Department of Pediatrics
University of Chicago Pritzker School of Medicine
5841 S. Maryland Ave MC, 5067 Chicago, IL 60637

Abstract

Vaccinations are important for infectious disease prevention; however, there are adverse effects of vaccines, many of which are cutaneous. Some of these reactions are due to nonspecific inflammation and irritation at the injection site, whereas other reactions are directly related to the live attenuated virus. Rarely, vaccinations have been associated with generalized hypersensitivity reactions, such as erythema multiforme, Stevens-Johnson syndrome, urticaria, acute generalized exanthematous pustulosis, and drug hypersensitivity syndrome. The onset of certain inflammatory dermatologic conditions, such as lichen planus, granuloma annulare, and pemphigoid, were reported to occur shortly after vaccine administration. Allergic contact dermatitis can develop at the injection site, typically due to adjuvant ingredients in the vaccine, such as thimerosal and aluminum. Vaccinations are important to promote development of both individual and herd immunity. Although most vaccinations are considered relatively safe, there may be adverse effects associated with any vaccine. Cutaneous manifestations make up a large portion of the types of reactions associated with vaccines. There are many different reasons for the development of a cutaneous reaction to a vaccination. Some are directly related to the injection of a live attenuated virus, such as varicella or vaccinia (for immunity to smallpox), whereas others cause more nonspecific erythema and swelling at the injection site, as a result of local inflammation or irritation. Vaccinations have also been associated in rare reports with generalized hypersensitivity reactions, such as erythema multiforme, Stevens-Johnson syndrome, urticaria, acute generalized exanthematous pustulosis, and drug hypersensitivity syndrome. There have been case reports associating the administration of a vaccine with the new onset of a dermatologic condition, such as lichen planus, granuloma annulare, and Sweet syndrome. Finally, allergic contact dermatitis can develop at the injection site, typically due to adjuvant ingredients in the vaccine, such as thimerosal and aluminum.

“there are adverse effects of vaccines, many of which are cutaneous ... vaccinations have been associated with generalized hypersensitivity reactions, such as erythema multiforme, Stevens-Johnson syndrome, urticaria, acute generalized exanthematous pustulosis, and drug hypersensitivity syndrome.

The onset of certain inflammatory dermatologic conditions, such as lichen planus, granuloma annulare, and pemphigoid, were reported to occur shortly after vaccine administration.”

The avian influenza vaccine Emerflu Why did it fail?

Author information

Young BE1, Sadarangani SP, Leo YS.
Communicable Diseases Centre
Institute of Infectious Diseases and Epidemiology
Communicable Diseases Centre,
144 Moulmein Road, Singapore

Abstract

Emerflu is an inactivated, split-virion pandemic preparedness vaccine, containing 30 µg of hemagglutinin (HA) and 600 µg of aluminum hydroxide adjuvant. It is administered in two doses, 3 weeks apart. Only moderate immunogenicity was evident from clinical studies with the vaccine in adults, and HA antibody responses were below the criteria established by the EMA and US FDA for licensure. With the exception of Australia, the vaccine remains unlicensed. Further clinical development appears to have been suspended, and newer adjuvants such as MF59 and AS03 have since demonstrated safety and superior immunogenicity with lower HA doses. Emerflu is symbolic of the failure of aluminum salts as an adjuvant for influenza vaccines. Reasons for this failure are unclear, and may reflect problems with the adjuvant-antigen complex or interference in the immune response by heterosubtypic immunity.

<http://www.ncbi.nlm.nih.gov/pubmed/26098721>

“Emerflu is symbolic
of the failure of aluminum salts
as an adjuvant for
influenza vaccines.”

“These results provide a neurobiological substrate for brain dysfunction in aluminum hydroxide adjuvant-induced MMF patients.”

PLoS One • June 2015

Neuropsychological Correlates of Brain Perfusion SPECT in Patients with Macrophagic Myofasciitis

Author information

Van Der Gucht A1, Aoun Sebaiti M2, Itti E1, Aouizerate J3, Evangelista E1, Chalaye J1, Gherardi RK3, Rangunathan-Thangarajah N4, Bachoud-Levi AC5, Authier FJ3.

1. Department of Nuclear Medicine, H. Mondor Hospital Assistance Publique-Hôpitaux de Paris/Paris-Est University, Créteil, F-94010, France
2. Department of Neurology, H. Mondor Hospital Assistance Publique-Hôpitaux de Paris/Paris-Est University, Créteil, F-94010, France
3. Department of Pathology, H. Mondor Hospital Assistance Publique-Hôpitaux de Paris/Paris-Est University Créteil, F-94010, France; Reference Center for Neuromuscular Disorders H. Mondor Hospital, Assistance Publique-Hôpitaux de Paris, Créteil, F-94010, France INSERM U955-Team 10, Créteil, F-94010, France
4. Reference Center for Neuromuscular Disorders, H. Mondor Hospital Assistance Publique-Hôpitaux de Paris, Créteil, F-94010, France INSERM U955-Team 10, Créteil, F-94010, France
5. Department of Neurology, H. Mondor Hospital, Assistance Publique-Hôpitaux de Paris/Paris-Est University Créteil, F-94010, France; INSERM U955-Team 1, Créteil, F-94010, France

Abstract

BACKGROUND

Patients with aluminum hydroxide adjuvant-induced macrophagic myofasciitis (MMF) complain of arthromyalgias, chronic fatigue and cognitive deficits. This study aimed to characterize brain perfusion in these patients.

METHODS

Brain perfusion SPECT was performed in 76 consecutive patients (aged 49±10 y) followed in the Garches-Necker-Mondor-Hendaye reference center for rare neuromuscular diseases. Images were acquired 30 min after intravenous injection of 925 MBq 99mTc-ethylcysteinate dimer (ECD) at rest. All patients also underwent a comprehensive battery of neuropsychological tests, within 1.3±5.5 mo from SPECT. Statistical parametric maps (SPM12) were obtained for each test using linear regressions between each performance score and brain perfusion, with adjustment for age, sex, socio-cultural level and time delay between brain SPECT and neuropsychological testing.

RESULTS

SPM analysis revealed positive correlation between neuropsychological scores (mostly exploring executive functions) and brain perfusion in the posterior associative cortex, including cuneus/precuneus/occipital lingual areas, the periventricular white matter/corpus callosum, and the cerebellum, while negative correlation was found with amygdalo-hippocampal/entorhinal complexes. A positive correlation was also observed between brain perfusion and the posterior associative cortex when the time elapsed since last vaccine injection was investigated.

CONCLUSIONS

Brain perfusion SPECT showed a pattern of cortical and subcortical changes in accordance with the MMF-associated cognitive disorder previously described. These results provide a neurobiological substrate for brain dysfunction in aluminum hydroxide adjuvant-induced MMF patients.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4451975/>

“The fluorescent nanodiamond technology is able to overcome the limitations of previously used organic fluorophores, thus appearing as a choice methodology for studying distribution, persistence and long-term neurotoxicity of alum adjuvants and beyond ...”

BMC Medicine • June 2015

Fluorescent nanodiamonds as a relevant tag for the assessment of alum adjuvant particle biodisposition

Author information

Eidi H1,2, David MO3, Crépeaux G4, Henry L5, Joshi V6,
Berger MH7, Sennour M8, Cadusseau J9,10, Gherardi RK11, Curmi PA12.

1. Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204 Université Evry-Val d'Essonne, Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France
2. Inserm - U955, Université Paris Est, Faculté de Médecine, Créteil, France - housam.eidi@gmail.com
3. Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204, Université Evry-Val d'Essonne Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France - MO.David@iut.univ-evry.fr
4. Inserm - U955, Université Paris Est, Faculté de Médecine, Créteil, France - guillemette.crepeaux@gmail.com
5. Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204, Université Evry-Val d'Essonne Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France. laetitia.henry@wanadoo.fr
6. Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204, Université Evry-Val d'Essonne Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France. vandana.joshi@univ-evry.fr
7. Laboratoire Pierre-Marie Fourt, Centre des Matériaux de l'Ecole des Mines de Paris and CNRS UMR 7633 Evry, France. marie-helene.berger@mines-paristech.fr
8. Laboratoire Pierre-Marie Fourt, Centre des Matériaux de l'Ecole des Mines de Paris and CNRS UMR 7633 Evry, France. mohamed.sennour@ensmp.fr
9. Inserm - U955, Université Paris Est, Faculté de Médecine, Créteil, France. josette.cadusseau@inserm.fr
10. Faculté des Sciences et Technologie UPEC, Créteil, France. josette.cadusseau@inserm.fr
11. Inserm - U955, Université Paris Est, Faculté de Médecine, Créteil, France. romain.gherardi@hmn.aphp.fr
12. Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204, Université Evry-Val d'Essonne, Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France. pcurmi@univ-evry.fr

Abstract

BACKGROUND

Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunologic adjuvant of vaccines. Concerns linked to alum particles have emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion in patients

with myalgic encephalomyelitis, revealing an unexpectedly long-lasting biopersistence of alum within immune cells and a fundamental misconception of its biodisposition. Evidence that aluminum-coated particles phagocytosed in the injected muscle and its draining lymph nodes can disseminate within phagocytes throughout the body and slowly accumulate in the brain further suggested that alum safety should be evaluated in the long term. However, lack of specific staining makes difficult the assessment of low quantities of bona fide alum adjuvant particles in tissues.

METHODS

We explored the feasibility of using fluorescent functionalized nanodiamonds (mfNDs) as a permanent label of alum (Alhydrogel(®)). mfNDs have a specific and perfectly photostable fluorescence based on the presence within the diamond lattice of nitrogen-vacancy centers (NV centers). As the NV center does not bleach, it allows the microspectrometric detection of mfNDs at very low levels and in the long-term. We thus developed fluorescent nanodiamonds functionalized by hyperbranched polyglycerol (mfNDs) allowing good coupling and stability of alum:mfNDs (AluDia) complexes. Specificities of AluDia complexes were comparable to the whole reference vaccine (anti-hepatitis B vaccine) in terms of particle size and zeta potential.

RESULTS

In vivo, AluDia injection was followed by prompt phagocytosis and AluDia particles remained easily detectable by the specific signal of the fND particles in the injected muscle, draining lymph nodes, spleen, liver and brain. In vitro, mfNDs had low toxicity on THP-1 cells and AluDia showed cell toxicity similar to alum alone. Expectedly, AluDia elicited autophagy, and allowed highly specific detection of small amounts of alum in autophagosomes.

CONCLUSIONS

The fluorescent nanodiamond technology is able to overcome the limitations of previously used organic fluorophores, thus appearing as a choice methodology for studying distribution, persistence and long-term neurotoxicity of alum adjuvants and beyond of other types of nanoparticles.

<http://www.ncbi.nlm.nih.gov/pubmed/26082187>

An enigma: why vitamin A supplementation does not always reduce mortality even though vitamin A deficiency is associated with increased mortality

Author information

Benn CS1, Aaby P2, Arts RJ3, Jensen KJ4, Netea MG3, Fisker AB2.

1. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project, Statens Serum Institut Copenhagen, Denmark, OPEN, Institute of Clinical Research, University of Southern Denmark Odense University Hospital, Odense, Denmark
2. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project Statens Serum Institut Copenhagen, Denmark, Bandim Health Project, INDEPTH Network, Bissau, Guinea-Bissau
3. Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands
4. Research Center for Vitamins and Vaccines (CVIVA), Bandim Health Project Statens Serum Institut, Copenhagen, Denmark

Abstract

BACKGROUND

Vitamin A deficiency (VAD) is associated with increased mortality. To prevent VAD, WHO recommends high-dose vitamin A supplementation (VAS) every 4-6 months for children aged between 6 months and 5 years of age in countries at risk of VAD. The policy is based on randomized clinical trials (RCTs) conducted in the late 1980s and early 1990s. Recent RCTs indicate that the policy may have ceased to be beneficial. In addition, RCTs attempting to extend the benefits to younger children have yielded conflicting results. Stratified analyses suggest that whereas some subgroups benefit more than expected from VAS, other subgroups may experience negative effects.

METHODS AND RESULTS

We reviewed the potential modifiers of the effect of VAS. The variable effect of VAS was not explained by underlying differences in VAD. Rather, the effect may depend on the sex of the child, the vaccine status and previous supplementation with vitamin A. Vitamin A is known to affect the Th1/Th2 balance and, in addition, recent evidence suggests that vitamin A may also induce epigenetic changes leading to down-regulation of the innate immune response. Thus VAS protects against VAD but has also important and long-lasting immunological effects, and the effect of providing VAS may vary depending on the state of the immune system.

CONCLUSIONS

To design optimal VAS programmes which target those who benefit and avoid those harmed, more studies are needed. Work is ongoing to define whether neonatal VAS should be considered in subgroups. In the most recent RCT in older children, VAS doubled the mortality for males but halved mortality for females. Hence, we urgently need to re-assess the effect of VAS on older children in large-scale RCTs powered to study effect modification by sex and other potential effect modifiers, and with nested immunological studies.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4521135/>

“To prevent Vitamin A deficiency, WHO recommends high-dose vitamin A supplementation every 4-6 months for children aged between 6 months and 5 years of age in countries at risk of Vitamin A deficiency. The policy is based on randomized clinical trials conducted in the late 1980s and early 1990s. Recent RCTs indicate that the policy may have ceased to be beneficial.”

**Hypothesis:
Human papillomavirus vaccination syndrome-
small fiber neuropathy and dysautonomia
could be its underlying pathogenesis**

Author information

Martínez-Lavín M.
Rheumatology Department
Instituto Nacional de Cardiología Ignacio Chávez
Juan Badiano 1, 14080, Mexico City, Mexico
drmartinezlavin@gmail.com

Abstract

Vaccination has been one of the most effective public health measures in the history of medicine. However, seemingly inexplicit adverse reactions have been described after the injection of the newer vaccines vs. human papillomavirus (HPV). The symptoms more often reported are chronic pain with paresthesias, headaches, fatigue, and orthostatic intolerance. Adverse reactions appear to be more frequent after HPV vaccination when compared to other type of immunizations. Different isolated cases and small series have described the development of complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), and fibromyalgia after HPV vaccination. These are illnesses often difficult to diagnose that have overlapping clinical features. Sympathetic nervous system dysfunction seems to play a major role in the pathogenesis of these syndromes. Also, small fiber neuropathy has been recently recognized in CRPS, POTS, and fibromyalgia. This article forwards the hypothesis that small fiber neuropathy and dysautonomia could be the common underlying pathogenesis to the group of rare, but severe reactions that follow HPV vaccination. Clinicians should be aware of the possible association between HPV vaccination and the development of these difficult to diagnose painful dysautonomic syndromes.

<http://www.ncbi.nlm.nih.gov/pubmed/25990003>

“Different isolated cases and small series have described the development of complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), and fibromyalgia after HPV vaccination. These are illnesses often difficult to diagnose that have overlapping clinical features. Sympathetic nervous system dysfunction seems to play a major role in the pathogenesis of these syndromes. Also, small fiber neuropathy has been recently recognized in CRPS, POTS, and fibromyalgia.”

Potentially harmful excipients in neonatal medicines: a pan-European observational study

Nellis G1, Metsvaht T2, Varendi H3, Toompere K4,
Lass J5, Mesek I6, Nunn AJ7, Turner MA8, Lutsar I6;
ESNEE consortium with Collaborators (31)

Author information

1. Institute of Microbiology, Tartu University, Tartu, Tartumaa, Estonia Neonatal Unit, Tartu University Hospital, Childrens Clinic, Tartu, Tartumaa, Estonia
2. Institute of Microbiology, Tartu University, Tartu, Tartumaa, Estonia Paediatric Intensive Care Unit, Tartu University Hospital, Clinic of Anaesthesiology and Intensive Care, Tartu, Tartumaa, Estonia
3. Neonatal Unit, Tartu University Hospital, Childrens Clinic, Tartu, Tartumaa, Estonia
4. Department of Public Health, Tartu University, Tartu, Tartumaa, Estonia
5. Institute of Microbiology, Tartu University, Tartu, Tartumaa, Estonia Pharmacy Department, Tartu University Hospital, Estonia
6. Institute of Microbiology, Tartu University, Tartu, Tartumaa, Estonia
7. Alder Hey Children's NHS Foundation Trust, Liverpool, UK
8. Neonatal Unit, Liverpool Women's Hospital, Liverpool, UK Institute of Translational Medicine, University of Liverpool, UK

Abstract

OBJECTIVES

We aimed to describe administration of eight potentially harmful excipients of interest (EOI)-parabens, polysorbate 80, propylene glycol, benzoates, saccharin sodium, sorbitol, ethanol and benzalkonium chloride-to hospitalised neonates in Europe and to identify risk factors for exposure.

METHODS

All medicines administered to neonates during 1 day with individual prescription and demographic data were registered in a web-based point prevalence study. Excipients were identified from the Summaries of Product Characteristics. Determinants of EOI administration (geographical region, gestational age (GA), active pharmaceutical ingredient, unit level and hospital teaching status) were identified using multivariable logistical regression analysis.

RESULTS

Overall 89 neonatal units from 21 countries participated. Altogether 2095 prescriptions for 530 products administered to 726 neonates were recorded. EOI were found in 638 (31%) prescriptions and were administered to 456 (63%) neonates through a relatively small number of products (n=142; 27%). Parabens, found in 71 (13%) products administered to 313 (43%) neonates, were used most frequently. EOI administration varied by geographical region, GA and route of administration. Geographical region remained a significant determinant of the use of parabens, polysorbate 80, propylene glycol and saccharin sodium after adjustment for the potential covariates including anatomical therapeutic chemical class of the active ingredient.

CONCLUSIONS

European neonates receive a number of potentially harmful pharmaceutical excipients. Regional differences in EOI administration suggest that EOI-free products are available and provide the potential for substitution to avoid side effects of some excipients.

“We aimed to describe administration of eight potentially harmful excipients of interest— (EOI)- parabens, polysorbate 80, propylene glycol, benzoates, saccharin sodium, sorbitol, ethanol and benzalkonium chloride—to hospitalised neonates in Europe and to identify risk factors for exposure.”

Expert Review Of Vaccines • July 2015

Are we entering a new age for human vaccine adjuvants?

Author information

O'Hagan DT1, Fox CB.

Novartis Vaccines, Cambridge, MA, USA

Abstract

Major advances in adjuvant development for human vaccines have been reported recently for a range of indications, including malaria, influenza and varicella zoster virus. Furthermore, there is an increased understanding of adjuvant mechanisms of action and a greater emphasis on the importance of formulation and characterization.

This progress may signify a new golden age of vaccine adjuvant discovery and development.

<http://www.ncbi.nlm.nih.gov/pubmed/25947042>

Word-finding impairment in veterans of the 1991 Persian Gulf War

Author information

Moffett K1, Crosson B2, Spence JS3, Case K4, Levy I5,
Gopinath K6, Shah P7, Goyal A8, Fang Y9, Briggs RW10,
Hart J Jr11, Moore A12, Haley RW13.

1. Department of Clinical and Health Psychology, University of Florida, 1225 Center Drive, Room 3151, Gainesville, FL 32611, USA. Electronic address: kmoffett@phhp.ufl.edu.
2. Department of Veterans Affairs Rehabilitation Research and Development, Brain Rehabilitation Research Center of Excellence, Malcolm Randall VA Medical Center, 1601 S.W. Archer Road, Gainesville, FL 32608-1197, USA; Department of Veterans Affairs Rehabilitation Research and Development, Center of Excellence for Visual and Neurocognitive Rehabilitation, 1670 Clairmont Rd., Decatur, GA 30033, USA; Departments of Neurology and Radiology, Emory University, 101 Woodruff Circle, Suite 6000, Atlanta, GA 30322, USA; Department of Psychology, Georgia State University, PO Box 5010, Atlanta, GA 303025010, USA. Electronic address: bruce.crosson@emory.edu.
3. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: jss130230@utdallas.edu.
4. Department of Clinical and Health Psychology, University of Florida, 1225 Center Drive, Room 3151, Gainesville, FL 32611, USA. Electronic address: kim.case@ufl.edu.
5. Department of Clinical and Health Psychology, University of Florida, 1225 Center Drive, Room 3151, Gainesville, FL 32611, USA. Electronic address: ilana.f.levy@gmail.com.
6. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: Kaundinya.s.gopinath@emory.edu.
7. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: parina.shah30@yahoo.com.
8. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: goyala@yorku.ca.
9. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: fangyan331@gmail.com.
10. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA; Department of Physics & Astronomy, Georgia State University, Atlanta, GA 30302-5060, USA. Electronic address: rbriggs1@gsu.edu.

11. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: jhart@utdallas.edu.
12. Center for Rehabilitation Medicine, Emory University, 101 Woodruff Circle, Suite 6000, Atlanta, GA 30322, USA. Electronic address: annabmoore@gmail.com.
13. Departments of Internal Medicine (Epidemiology Division) and Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., Dallas, TX 75390-8874, USA. Electronic address: Robert.Haley@UTSouthwestern.edu.

Abstract

Approximately one quarter of 1991 Persian Gulf War Veterans experience cognitive and physiological sequelae that continue to be unexplained by known medical or psychological conditions. Difficulty coming up with words and names, familiar before the war, is a hallmark of the illness. Three Gulf War Syndrome subtypes have been identified and linked to specific war-time chemical exposures. The most functionally impaired veterans belong to the Gulf War Syndrome 2 (Syndrome 2) group, for which subcortical damage due to toxic nerve gas exposure is the suspected cause. Subcortical damage is often associated with specific complex language impairments, and Syndrome 2 veterans have demonstrated poorer vocabulary relative to controls. 11 Syndrome 1, 16 Syndrome 2, 9 Syndrome 3, and 14 age-matched veteran controls from the Seabees Naval Construction Battalion were compared across three measures of complex language. Additionally, functional magnetic resonance imaging (fMRI) was collected during a covert category generation task, and whole-brain functional activity was compared between groups. Results demonstrated that Syndrome 2 veterans performed significantly worse on letter and category fluency relative to Syndrome 1 veterans and controls. They also exhibited reduced activity in the thalamus, putamen, and amygdala, and increased activity in the right hippocampus relative to controls. Syndrome 1 and Syndrome 3 groups tended to show similar, although smaller, differences than the Syndrome 2 group. Hence, these results further demonstrate specific impairments in complex language as well as subcortical and hippocampal involvement in Syndrome 2 veterans. Further research is required to determine the extent of language impairments in this population and the significance of altered neurologic activity in the aforementioned brain regions with the purpose of better characterizing the Gulf War Syndromes.

<http://www.ncbi.nlm.nih.gov/pubmed/26114921>

“Results demonstrated that Syndrome 2 veterans performed significantly worse on letter and category fluency relative to Syndrome 1 veterans and controls. They also exhibited reduced activity in the thalamus, putamen, and amygdala, and increased activity in the right hippocampus relative to controls. Hence, these results further demonstrate specific impairments in complex language as well as subcortical and hippocampal involvement in Syndrome 2 veterans.”

Shared Brain Connectivity Issues, Symptoms, and Comorbidities in Autism Spectrum Disorder, Attention Deficit/Hyperactivity Disorder, and Tourette Syndrome

Author information

Kern JK1, Geier DA1, King PG2,
Sykes LK2, Mehta JA3, Geier MR1.

1. Institute of Chronic Illnesses, Inc., Silver Spring, Maryland
2. CoMeD, Inc. , Silver Spring, Maryland
3. Communication Sciences & Disorders
Texas Woman's University, Denton, Texas

Abstract

The prevalence of neurodevelopmental disorders, including autism spectrum disorder (ASD), attention deficit/hyperactivity disorder (ADHD), and Tourette syndrome (TS), has increased over the past two decades. Currently, about one in six children in the United States is diagnosed as having a neurodevelopmental disorder. Evidence suggests that ASD, ADHD, and TS have similar neuropathology, which includes long-range underconnectivity and short-range overconnectivity. They also share similar symptomatology with considerable overlap in their core and associated symptoms and a frequent overlap in their comorbid conditions. Consequently, it is apparent that ASD, ADHD, and TS diagnoses belong to a broader spectrum of neurodevelopmental illness. Biologically, long-range underconnectivity and short-range overconnectivity are plausibly related to neuronal insult (e.g., neurotoxicity, neuroinflammation, excitotoxicity, sustained microglial activation, proinflammatory cytokines, toxic exposure, and oxidative stress). Therefore, these disorders may share a similar etiology. The main purpose of this review is to critically examine the evidence that ASD, ADHD, and TS belong to a broader spectrum of neurodevelopmental illness, an abnormal connectivity spectrum disorder, which results from neural long-range underconnectivity and short-range overconnectivity. The review also discusses the possible reasons for these neuropathological connectivity findings. In addition, this review examines the role and issue of axonal injury and regeneration in order to better understand the neuropathophysiological interplay between short- and long-range axons in connectivity issues.

<http://www.ncbi.nlm.nih.gov/pubmed/25602622>

“The prevalence of neurodevelopmental disorders, including autism spectrum disorder (ASD), attention deficit/hyperactivity disorder (ADHD), and Tourette syndrome (TS), has increased over the past two decades. Currently, about one in six children in the United States is diagnosed as having a neurodevelopmental disorder.”

[this defines a pandemic of neurological disorders]

Autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA) after quadrivalent human papillomavirus vaccination in Colombians: a call for personalised medicine

Author information

Anaya JM1, Reyes B1, Perdomo-Arciniegas AM2, Camacho-Rodríguez B2, Rojas-Villarraga A1.

1. Centre for Autoimmune Diseases Research (CREA) Universidad del Rosario; and Mederi Hospital Universitario Mayor Bogota, Colombia
2. Banco de Sangre, Tejidos y Células Hemocentro Distrital, Secretaría de Salud de Bogota Bogota, Colombia

Abstract

This was a case study in which 3 patients with autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA) after quadrivalent human papillomavirus vaccination (HPV) were evaluated and described. All the patients were women. Diagnosis consisted of HLA-B27 enthesitis related arthritis, rheumatoid arthritis and systemic lupus erythematosus, respectively. Our results highlight the risk of developing ASIA after HPV vaccination and may serve to increase the awareness of such a complication. Factors that are predictive of developing autoimmune diseases should be examined at the population level in order to establish preventive measures in at-risk individuals for whom healthcare should be personalized and participatory.

<http://www.ncbi.nlm.nih.gov/pubmed/25962455>

“This was a case study in which 3 patients with autoimmune/auto-inflammatory syndrome induced by adjuvants (ASIA) after quadrivalent human papillomavirus vaccination (HPV) were evaluated and described. All the patients were women.”

Spontaneous reports of vasculitis as an adverse event following immunization: A descriptive analysis across three international databases

Felicetti P1, Trotta F2, Bonetto C2, Santuccio C2, Brauchli Pernus Y3, Burgner D4, Chandler R5, Girolomoni G6, Hadden RD7, Kochar S8, Kucuku M9, Monaco G10, Ozen S11, Pahud B12, Phuong L13, Bachtiar NS14, Teeba A15, Top K16, Varricchio F17, Wise RP18, Zaroni G19, Ivkovic S20, Bonhoeffer J21; Brighton Collaboration Vasculitis Working Group

Author information

1. Italian Medicines Agency, Rome, Italy. Electronic address: contact@brightoncollaboration.org
2. Italian Medicines Agency, Rome, Italy
3. Brighton Collaboration Foundation, Basel, Switzerland
4. Monash Children's Hospital-Clayton, Melbourne, Australia; Murdoch Children's Research Institute (MCRI) Department of Paediatrics, Melbourne University, Australia
5. Uppsala Monitoring Centre, Uppsala, Sweden
6. University of Verona, Department of Medicine, Section of Dermatology and Venereology, Verona, Italy
7. King's College Hospital, London, UK
8. USAID, Deliver Project, JSIPL, New Delhi, India
9. Department of Vaccines Control, National Agency for Medicine & Medical Devices, Tirana, Albania
10. Centre for Pharmacovigilance, The Lombardy Region, Milan, Italy
11. Hacettepe University, Department of Pediatric Rheumatology, Ankara, Turkey
12. Children's Mercy Hospital, Kansas City, MO, USA
13. Monash Children's and Royal Children's Hospitals, Melbourne, Australia
14. Bio Farma Vaccine Institute, Bandung, West Java, Indonesia
15. Centre National Anti Poison et de Pharmacovigilance, Rabat, Morocco
16. Department of Pediatrics, Dalhousie University, Halifax, NS, Canada
17. Independent Consultant Vaccinologist, Wakefield, RI, USA
18. MedImmune/AstraZeneca, Gaithersburg, MD, USA
19. Immunology Unit, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy
20. University of Pittsburgh Medical Center and Neurology service, MSL, VA Pittsburgh Healthcare System, Pittsburgh, PA, USA
21. University of Basel Children's Hospital, Basel, Switzerland; Brighton Collaboration Foundation, Basel, Switzerland

Abstract

BACKGROUND

Vasculitides have been reported as adverse events following immunization (AEFI) following various vaccines. We describe reports of vasculitis to three international spontaneous reporting systems.

RESULTS

We retrieved 1797 reports of vasculitis in EV, 1171 in VAERS, and 2606 in VigiBase®. Vasculitis was predominantly reported in children aged 1-17 years, and less frequently in the elderly (>65 years). The generic term "vasculitis" was the most frequently reported AEFI in this category across the three databases (range 21.9% to 27.5% of all reported vasculitis for vaccines). For the more specific terms, Henoch-Schoenlein Purpura (HSP) was most frequently reported, (19.1% on average), followed by Kawasaki disease (KD) (16.1% on average) and polymyalgia rheumatica (PMR) (9.2% on average). Less frequently reported subtypes were cutaneous vasculitis (CuV), vasculitis of the central nervous system (CNS-V), and Behcet's syndrome (BS). HSP, PMR and CuV were more frequently reported with influenza vaccines: on average in 29.3% for HSP reports, 61.5% for PMR reports and in 39.2% for CuV reports. KD was reported with pneumococcal vaccines in 32.0% of KD reports and with rotavirus vaccines in more than 20% of KD reports. BS was most frequently reported after hepatitis and HPV vaccines and CNS-V after HPV vaccines.

CONCLUSION

Similar reporting patterns of vasculitides were observed in different databases. Implementation of standardized case definitions for specific vasculitides could improve overall data quality and comparability of reports.

<http://www.ncbi.nlm.nih.gov/pubmed/26392009>

"We retrieved 1797 reports of vasculitis in EV, 1171 in VAERS, and 2606 in VigiBase®. Vasculitis was predominantly reported in children aged 1-17 years, and less frequently in the elderly (>65 years). The generic term "vasculitis" was the most frequently reported AEFI in this category across the three databases (range 21.9% to 27.5% of all reported vasculitis for vaccines). For the more specific terms, Henoch-Schoenlein Purpura (HSP) was most frequently reported, (19.1% on average), followed by Kawasaki disease (KD) (16.1% on average) and polymyalgia rheumatica (PMR) (9.2% on average). Less frequently reported subtypes were cutaneous vasculitis (CuV), vasculitis of the central nervous system (CNS-V), and Behcet's syndrome (BS). HSP, PMR and CuV were more frequently reported with influenza vaccines: on average in 29.3% for HSP reports, 61.5% for PMR reports and in 39.2% for CuV reports. KD was reported with pneumococcal vaccines in 32.0% of KD reports and with rotavirus vaccines in more than 20% of KD reports. BS was most frequently reported after hepatitis and HPV vaccines and CNS-V after HPV vaccines."

Antigenic variability of *Bordetella pertussis* strains isolated in 1967-2010 in the Czech Republic—possible explanation for the rise in cases of pertussis?

by Zavadilová J, Lzicarová D, Musílek M, Krízová P, Fabiánová K.

Abstract

OBJECTIVE

Comparison of antigenic structures of *Bordetella pertussis* (*B. pertussis*) strains isolated from 1967 to 2010 in the Czech Republic.

MATERIAL AND METHODS

Seventy strains of *B. pertussis* were referred to the National Reference Laboratory (NRL) for Pertussis and Diphtheria within the surveillance of pertussis from all over the Czech Republic (CR) between 1967 and 2010. To study the strains, the analysis was performed of the genome sequences encoding the surface immunogenic structures--the pertussis toxin S1 subunit gene (*ptxA*), pertactin gene region 1 (*prnA*), type 3 fimbriae gene (*fim3*)-and pertussis toxin promoter (*ptxP*) responsible for the regulation of the production of pertussis toxin.

RESULTS

For the study set of *B. pertussis* strains, the sequencing analysis revealed changes in all genomic regions studied. The isolates from three periods differ in the allelic profile. In period I (1967-1978) with the use of whole cell pertussis vaccine (wP), the following two profiles were the most common: *ptxP*(1), *ptxA*(2), *prnA*(1), *fim3*(1) and *ptxP*(1), *ptxA*(1), *prnA*(3), *fim3*(1). In period 2 (1990-2007) with the switch to acellular pertussis vaccine (aP), the most common profile was: *ptxP*(3), *ptxA*(1), *prnA*(2), *fim3*(2). Period 3 (2008-2010) with the use of aP was characterized by the predominance of the following two profiles which had never been found in period 1: *ptxP*(3), *ptxA*(1), *prnA*(2), *fim3*(2) and *ptxP*(3) *ptxA*(1), *prnA*(2), *fim3*(1).

CONCLUSIONS

Sequencing of the genomic regions *ptxP*, *ptxA*, *prnA*, and *fim3* of *B. pertussis* strains isolated in the CR between 1967 and 2010 confirmed changes in the allelic variants of these regions. The incidence of strains carrying the new allelic variants was increasing after 1995 at the expense of those carrying the original variants. The study results can be interpreted as a partial genetic escape of pathogenic strains of *B. pertussis* beyond the reach of the pertussis vaccines.

“The study results can be interpreted as a partial genetic escape of pathogenic strains of *B. pertussis* beyond the reach of the pertussis vaccines.”

“Since then [1964], the literature has been **flooded** with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines ...”

Lupus • September 2015

Human adjuvant-related syndrome or
autoimmune/inflammatory syndrome induced by adjuvants.
Where have we come from? Where are we going?
A proposal for new diagnostic criteria

Author information

Alijotas J.-Reig J.

Systemic Autoimmune Disease Unit, Department of Internal Medicine I
Vall d'Hebron University Hospital, Barcelona, Spain

Faculty of Medicine, Universitat Autònoma, Barcelona, Spain
16297jar@comb.es
jalijotas@vhebron.net

Abstract

In 1964, Miyoshi reported a series of patients with diverse symptoms after receiving treatment with silicone or paraffin fillers. Miyoshi named this condition ‘human adjuvant disease’. Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines, infection or other adjuvants such as silicone and other biomaterials. A new term -autoimmune/inflammatory syndrome induced by adjuvants--has recently been coined for a process that includes several clinical features previously described by Miyoshi plus other clinical and laboratory parameters related to exposure to diverse external stimuli. Disorders such as siliconosis, Gulf War syndrome, macrophagic myofasciitis syndrome, sick building syndrome and post-vaccination syndrome have been included in autoimmune/inflammatory syndrome induced by adjuvants. Disorders such as Spanish toxic oil syndrome and Ardystil syndrome could also be included. Furthermore, biomaterials other than silicone should also be considered as triggering factors for these adjuvant-related syndromes. New diagnostic criteria in this field have been proposed. Nevertheless, many of these criteria are too subjective, leading to some patients being diagnosed with chronic fatigue syndrome or other ‘central sensitization syndromes’. Diagnostic criteria based only on objective clinical and laboratory data to be further discussed and validated are proposed herein.

<http://www.ncbi.nlm.nih.gov/pubmed/25813870>

Vaccines and Drug-induced Lung Injury

Yamamoto Y*

Respiratory Center
Asahikawa Medical University
Asahikawa, Hokkaido, Japan

Abstract

The corresponding author has no conflict of interest to declare. The author is invited to submit this manuscript in the Short Communication section. Drug-induced lung injuries (DLIs) are adverse drug reactions that specifically occur in the pulmonary system. The main causative agents include cytotoxic drugs, antibiotics, interferon, and anti-rheumatic drugs. More recently, biological reaction modifiers and molecular targeted drugs have emerged as causes of DLIs. Interstitial lung diseases are the most common form of DLIs [1].

Vaccines have rarely been associated with DLIs. One possible reason is that the causal relationship is difficult to prove. This problem is true for vaccines against human papilloma virus (HPV). The author has recently reported a case of interstitial pneumonia that occurred after the vaccination with HPV-16/18 adjuvant system 04 (AS04) vaccines (Cervarix) [2]. Detailed information of this case is available on the respiratory medicine case reports website (<http://www.dx.doi.org/10.1016/j.rmcr.2015.06.003>).

A middle-aged woman, who had no pre-existing pulmonary diseases, completed three doses of Cervarix. Non-specific interstitial pneumonia developed three months after the last vaccination. A lung biopsy specimen showed lymphocytic alveolitis, providing evidence that cell-mediated immunity likely contributed to the occurrence. The patient had increased levels of serum biomarkers specific to interstitial pneumonias such as Krebs von der Lungen (KL)-6 and surfactant protein (SP)-D. Other causes except

the vaccination were eliminated. Of note was that the interstitial pneumonia spontaneously resolved with complete remission of chest radiographic findings and serum biomarkers. The self-limiting course suggested that the interstitial pneumonia occurred with a temporal association with the vaccination. A re-challenge test to Cervarix was not conducted for safety reasons. The interstitial pneumonia was finally diagnosed as a DLI according to the clinical course, chest images, pathological findings, and specific use of Cervarix. Assuming that all drugs are capable of causing a lung injury is the first step for diagnosing DLIs [1]. Vaccines are not exceptions in that DLIs can develop even after the treatment has been completed [1]. Most cases of vaccine-associated DLIs have been diagnosed by clinical judgments [3-5]. Gold standard tests have not been established for the diagnosis of DLIs; however the likelihood of an adverse reaction can be semi-quantified using the Naranjo algorithm. Such algorithms can reduce inter- and intra-individual variations with regard to the assessment [6]. Chest imaging findings are non-specific but useful for early diagnosis. [1] Measurements of KL-6 and SP-D may play a supplementary role in the diagnosis of DLIs [1,7]. An *ex vivo* drug stimulation test using peripheral lymphocytes has a quite limited diagnostic value [7]. Further studies are required to develop diagnostic procedures, which are more sensitive and specific to a drug adverse reaction.

Influenza vaccines can cause several types of DLIs, including acute respiratory distress syndrome [3-5]. Watanabe et al. reviewed 7 cases (4 males and 3 females) of DLIs secondary to the influenza vaccination [5]. The median age of onset was relatively high (59 years). Previous pulmonary diseases

were present in four cases. All patients had acute symptoms. The time to onset was 1 to 10 days. They all had severe clinical manifestations, but recovered after receiving corticosteroid therapy. Of note, 6 of the 7 cases were Asians [5]. Genetic and environmental factors may affect difference in the susceptibility to DLIs [7].

Unlike influenza vaccines, Cervarix caused a mild and subclinical form of DLI. How did Cervarix affect the pulmonary system? In the disease process of DLIs, drugs can act as a hapten, interact with immune receptors, and trigger danger signals [7]. These actions probably underlie the onset of immune-mediated DLIs [1,7]. These processes were probably attributed to the Cervarix-associated DLI. As a reason, the pathologically proven lymphocytic alveolitis was suggestive of cell-mediated immune responses [2]. Of the constituents of Cervarix, the AS04 adjuvant appeared to be most responsible owing to its strong immunogenicity [8].

Large-scale analyses have not shown that AS04-adjuvanted vaccines increase risks for developing autoimmune disorders [9,10]. This trend still remains significant when the subjects are stratified by age [10]. However, the immune-mediated diseases assessed are confined to gastrointestinal, metabolic, musculoskeletal, neuroinflammatory, and skin disorders [10]. Any lung disorders including interstitial pneumonia are not listed. Further studies are needed to clarify the prevalence, outcomes, and risk factors for the Cervarix-associated DLI.

Full Report With References

<http://www.omicsonline.org/open-access/vaccines-and-druginduced-lung-injury-2157-7560-1000291.pdf>

Formaldehyde Crosslinking: A Tool for the Study of Chromatin Complexes

Author information

Hoffman EA1, Frey BL2, Smith LM2, Auble DT3.

1. The Department of Biochemistry and Molecular Genetics
University of Virginia Health System, Charlottesville, Virginia 22908 and
2. The Department of Chemistry and Genome Center of Wisconsin
University of Wisconsin, Madison, Wisconsin 53706 and
3. The Department of Biochemistry and Molecular Genetics
University of Virginia Health System, Charlottesville, Virginia 22908
auble@virginia.edu

Abstract

Formaldehyde has been used for decades to probe macromolecular structure and function and to trap complexes, cells, and tissues for further analysis. Formaldehyde crosslinking is routinely employed for detection and quantification of protein-DNA interactions, interactions between chromatin proteins, and interactions between distal segments of the chromatin fiber. Despite widespread use and a rich biochemical literature, important aspects of formaldehyde behavior in cells have not been well described. Here, we highlight features of formaldehyde chemistry relevant to its use in analyses of chromatin complexes, focusing on how its properties may influence studies of chromatin structure and function.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26354429>

“ Formaldehyde [a vaccine ingredient] has been used for decades to probe macromolecular structure and function and to trap complexes, cells, and tissues for further analysis. Despite widespread use and a rich biochemical literature, important aspects of formaldehyde behavior in cells have not been well described.”

A case of polymyalgia rheumatica following influenza B infection

Kentaro Iwata¹ and Yasushi Mizuno²

¹Division of Infectious Diseases
Kobe University Hospital, Kobe, Japan

²Department of General Medicine
Kobe City Medical Center General Hospital
Kobe, Japan

Abstract

Polymyalgia rheumatica (PMR) is relatively common among the elderly, and is characterized by multiple body aches with an elevated erythrocyte sedimentation rate. Even though the etiology of PMR remains unknown, a number of infectious agents have been suggested to cause PMR. Also, there are reports of PMR after influenza vaccination. The exact role of influenza vaccination on the development of PMR remains unknown, but may be associated with specific human leukocyte antigens (HLAs), such as HLA-DRB1 and HLA-DQB1. Whether postvaccination PMR is caused by influenza virus antigen or adjuvants in the vaccine is another unanswered question. We herein report a case of an 85-year-old woman who developed PMR shortly after contracting influenza virus B. Even though infections are hypothesized to be one of the causes of PMR, this is the first-ever case of PMR following influenza virus infection. Further studies may elucidate the exact role of influenza virus infection on the etiology and pathogenesis of PMR.

<http://www.ncbi.nlm.nih.gov/pubmed/26527896>

“this is the first-ever case of Polymyalgia rheumatica following influenza virus infection. Further studies may elucidate the exact role of influenza virus infection on the etiology and pathogenesis of Polymyalgia rheumatica.”

A Prospective Longitudinal Assessment of Medical Records for Diagnostic Substitution among Subjects Diagnosed with a Pervasive Developmental Disorder in the United States

Author information

Geier DA1, Kern JK1, Hooker BS2, Sykes LK3, Geier MR1.

1. The Institute of Chronic Illnesses, Inc , Silver Spring, MD , USA.
2. Simpson University , Redding, CA , USA.
3. CoMeD, Inc , Silver Spring, MD , USA.

Abstract

BACKGROUND

Previously, investigators suggested that diagnostic substitution from other diagnoses, e.g., mental retardation (MR) and/or cerebral palsy (CP) to pervasive developmental disorder (PDD) is a driving factor behind increases in autism. This study evaluated potential diagnostic substitution among subjects diagnosed with PDD vs. MR or CP by examining birth characteristic overlap.

METHODS

SAS(®) and StatsDirect software examined medical records for subjects within the Vaccine Safety Datalink database who were Health Maintenance Organization-enrolled from birth until diagnosed with an International Classification of Disease, 9th revision (ICD-9) outcome of PDD (299.xx, n=84), CP (343.xx, n=300), or MR (317.xx, 318.xx, or 319.xx, n=51).

RESULTS

Subjects with PDD had significantly ($p < 0.01$) increased: male/female ratio (PDD=5.5 vs. CP=1.5 or MR=1.3), mean age of initial diagnosis in years (PDD=3.13 vs. CP=1.09 or MR=1.62), mean gestational age in weeks at birth (PDD=38.73 vs. CP=36.20 or MR=34.84), mean birth weight in grams (PDD=3,368 vs. CP=2,767 or MR=2,406), and mean Appearance-Pulse-Grimace-Activity-Respiration scores at 1 min (PDD=7.82 vs. CP=6.37 or MR=6.76) and 5 min (PDD=8.77 vs. CP=7.92 or MR=8.04), as compared to subjects diagnosed with CP or MR.

CONCLUSION

This study suggests diagnostic substitution cannot fully explain increased PDD prevalence during the 1990s within the United States.

<http://www.ncbi.nlm.nih.gov/pubmed/26528457>

“This study suggests diagnostic substitution cannot fully explain increased pervasive developmental disorder (PDD) prevalence during the 1990s within the United States.”

On vaccine's adjuvants and autoimmunity: Current evidence and future perspectives

Author information

Pellegrino P1, Clementi E2, Radice S1.

1. Unit of Clinical Pharmacology

Department of Biomedical and Clinical Sciences
University Hospital "Luigi Sacco", Università di Milano
20157 Milan, Italy

2. Scientific Institute IRCCS E. Medea

23842 Bosisio Parini, Lecco, Italy

Unit of Clinical Pharmacology

Department of Biomedical and Clinical Sciences
Consiglio Nazionale delle Ricerche Institute of Neuroscience
University Hospital "Luigi Sacco", Università di Milano
20157 Milan, Italy
emilio.clementi@unimi.it

Abstract

Adjuvants are compounds incorporated into vaccines to enhance immunogenicity and the development of these molecules has become an expanding field of research in the last decades. Adding an adjuvant to a vaccine antigen leads to several advantages, including dose sparing and the induction of a more rapid, broader and strong immune response. Several of these molecules have been approved, including aluminium salts, oil-in-water emulsions (MF59, AS03 and AF03), virosomes and AS04. Adjuvants have recently been implicated in the new syndrome named "ASIA-Autoimmune/inflammatory Syndrome Induced by Adjuvants", which describes an umbrella of clinical conditions including post-vaccination adverse reactions. Recent studies implicate a web of mechanisms in the development of vaccine adjuvant-induced autoimmune diseases, in particular, in those associated with aluminium-based compounds. Fewer and unsystematised data are instead available about other adjuvants, despite recent evidence indicating that vaccines with different adjuvants may also cause specific autoimmune adverse reactions possible towards different pathogenic mechanisms. This topic is of importance as the specific mechanism of action of each single adjuvant may have different effects on the course of different diseases. Herein, we review the current evidence about the mechanism of action of currently employed adjuvants and discuss the mechanisms by which such components may trigger autoimmunity.

<http://www.ncbi.nlm.nih.gov/pubmed/26031899>

"Adding an adjuvant to a vaccine antigen leads to several advantages, including dose sparing and the induction of a more rapid, broader and strong immune response. Adjuvants have recently been implicated in the new syndrome named "ASIA-Auto-immune/inflammatory Syndrome Induced by Adjuvants", which describes an umbrella of clinical conditions including post-vaccination adverse reactions. Recent studies implicate a web of mechanisms in the development of vaccine adjuvant-induced autoimmune diseases, in particular, in those associated with aluminium-based compounds."

Future Microbiology • October 2015

Investigating pertussis toxin and its impact on vaccination

Author information

Coutte L1, Loch C.

Center for Infection & Immunity of Lille
Institut Pasteur de Lille
1 rue du Prof. Calmette, F-59019
Lille Cedex, France

Abstract

Whooping cough, caused by *Bordetella pertussis*, remains a major global health problem. Each year around 40 million of pertussis cases resulting in 200,000-400,000 annual deaths occur worldwide. Pertussis toxin is a major virulence factor of *B. pertussis*. Murine studies have shown its importance in bacterial colonization and in immunomodulation to evade innate or adaptive immunity. The toxin is composed of an A protomer expressing ADP-ribosyltransferase activity and a B oligomer, responsible for toxin binding to target cells. The toxin is also a major protective antigen in all currently available vaccines. However, vaccine escape mutants with altered toxin expression have recently been isolated in countries with high vaccination coverage illustrating the need for improved pertussis vaccines.

<http://www.ncbi.nlm.nih.gov/pubmed/25689536>

“[pertussis toxin] is also a major protective antigen in all currently available vaccines. However, vaccine escape mutants with altered toxin expression have recently been isolated in countries with high vaccination coverage illustrating the need for improved pertussis vaccines.”

Pertussis Toxin Exploits Specific Host Cell Signaling Pathways for Promoting Invasion and Translocation of Escherichia coli K1 RS218 in Human Brain-derived Microvascular Endothelial Cells

Author information

Karassek S1, Starost L1, Solbach J1, Greune L1,
Sano Y2, Kanda T2, Kim K3, Schmidt MA4.

1. From the Institute of Infectiology, Center for Molecular Biology of Inflammation, Westfälische Wilhelms-Universität Münster
2. the Department of Neurology and Clinical Neuroscience, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan
3. the Pediatric Infectious Diseases Division, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287
4. From the Institute of Infectiology, Center for Molecular Biology of Inflammation, Westfälische Wilhelms-Universität Münster
infekt@uni-muenster.de

Abstract

Pertussis toxin (PTx), an AB₅ toxin and major virulence factor of the whooping cough-causing pathogen *Bordetella pertussis*, has been shown to affect the blood-brain barrier. Dysfunction of the blood-brain barrier may facilitate penetration of bacterial pathogens into the brain, such as *Escherichia coli* K1 (RS218). In this study, we investigated the influence of PTx on blood-brain barrier permissiveness to *E. coli* infection using human brain-derived endothelial HBMEC and TY10 cells as in vitro models. Our results indicate that PTx acts at several key points of host cell intracellular signaling pathways, which are also affected by *E. coli* K1 RS218 infection. Application of PTx increased the expression of the pathogen binding receptor gp96. Further, we found an activation of STAT3 and of the small GTPase Rac1, which have been described as being essential for bacterial invasion involving host cell actin cytoskeleton rearrangements at the bacterial entry site. In addition, we showed that PTx induces a remarkable relocation of VE-cadherin and β -catenin from intercellular junctions. The observed changes in host cell signaling molecules were accompanied by differences in intracellular calcium levels, which might act as a second messenger system for PTx. In summary, PTx not only facilitates invasion of *E. coli* K1 RS218 by activating essential signaling cascades; it also affects intercellular barriers to increase paracellular translocation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26324705>

“Pertussis toxin (PTx), [an ingredient in several vaccines] an AB₅ toxin and major virulence factor of the whooping cough-causing pathogen *Bordetella pertussis*, has been shown to affect the blood-brain barrier. Dysfunction of the blood-brain barrier may facilitate penetration of bacterial pathogens into the brain, such as *Escherichia coli* K1 (RS218).”

Genetic diversity and population dynamics of *Bordetella pertussis* in China between 1950-2007

Author information

Xu Y1, Zhang L1, Tan Y1, Wang L1, Zhang S1, Wang J2.

1. Key Laboratory of the Ministry of Health for Research on Quality and Standardization of Biotech Products, National Institutes for Food and Drug Control, No. 2, Tiantan Xili, Beijing 100050, PR China
2. Key Laboratory of the Ministry of Health for Research on Quality and Standardization of Biotech Products, National Institutes for Food and Drug Control, No. 2, Tiantan Xili, Beijing 100050, PR China
wangjz@nifdc.org.cn

Abstract

Pertussis is an acute respiratory infectious disease caused by the bacterium *Bordetella pertussis*. Although pertussis vaccination was introduced in the 1960s, pertussis is still an endemic disease in China. To better understand the genetic diversity of the Chinese *B. pertussis* population, we characterized 115 clinical isolates obtained in China during 1950-2007 using multilocus variable-number tandem repeat analysis (MLVA). Forty-six different *B. pertussis* MLVA profiles (MTs) were identified, of which 13 were new MTs. Analysis using a minimum-spanning tree showed that distinct MTs were prevalent during different periods, suggesting that a dynamic change in *B. pertussis* MTs occurred over time in China. The predominant MTs in recent isolates from China were different from those of many developed countries. A decreasing trend in genetic diversity of the *B. pertussis* population was observed following the introduction of pertussis vaccines. Similar to the pertactin 2 (prn2) allele, the novel pertussis toxin promoter (ptxP3) allele first emerged in 2000, but unlike trends elsewhere, ptxP1 remained predominant among the isolates, further reflecting the unique temporal trends in the *B. pertussis* population in China. Our results suggest that temporal changes in the *B. pertussis* population may be closely associated with vaccination coverage and the vaccine types used. These data may lead to an improved understanding of the virulence mechanism of *B. pertussis* and facilitate new strategies for controlling this infectious disease.

<http://www.ncbi.nlm.nih.gov/pubmed/26409140>

“Although pertussis vaccination was introduced in the 1960s, pertussis is still an endemic disease in China.

Our results suggest that temporal changes in the *B. pertussis* population may be closely associated with vaccination coverage ...”

[viral mutation or ‘drift’]

Comparative Safety of Vaccine Adjuvants: A Summary of Current Evidence and Future Needs

Author information

Petrovsky N.

Department of Endocrinology and Diabetes
Flinders University, Adelaide, SA, 5042, Australia
nikolai.petrovsky@flinders.edu.au
Vaxine Pty Ltd, Adelaide, SA, Australia
nikolai.petrovsky@flinders.edu.au

Abstract

Use of highly pure antigens to improve vaccine safety has led to reduced vaccine immunogenicity and efficacy. This has led to the need to use adjuvants to improve vaccine immunogenicity. The ideal adjuvant should maximize vaccine immunogenicity without compromising tolerability or safety. Unfortunately, adjuvant research has lagged behind other vaccine areas such as antigen discovery, with the consequence that only a very limited number of adjuvants based on aluminium salts, monophosphoryl lipid A and oil emulsions are currently approved for human use. Recent strategic initiatives to support adjuvant development by the National Institutes of Health should translate into greater adjuvant choices in the future. Mechanistic studies have been valuable for better understanding of adjuvant action, but mechanisms of adjuvant toxicity are less well understood. The inflammatory or danger-signal model of adjuvant action implies that increased vaccine reactogenicity is the inevitable price for improved immunogenicity. Hence, adjuvant reactogenicity may be avoidable only if it is possible to separate inflammation from adjuvant action. The biggest remaining challenge in the adjuvant field is to decipher the potential relationship between adjuvants and rare vaccine adverse reactions, such as narcolepsy, macrophagic myofasciitis or Alzheimer's disease. While existing adjuvants based on aluminium salts have a strong safety record, there are ongoing needs for new adjuvants and more intensive research into adjuvants and their effects.

<http://www.ncbi.nlm.nih.gov/pubmed/26446142>

“Use of highly pure antigens to improve vaccine safety has led to reduced vaccine immunogenicity and efficacy. The biggest remaining challenge in the adjuvant field is to decipher the potential relationship between adjuvants and rare vaccine adverse reactions, such as narcolepsy, macrophagic myofasciitis or Alzheimer's disease.”

A measles outbreak in a middle school with high vaccination coverage and evidence of prior immunity among cases, Beijing, P.R. China

Author information

Ma R1, Lu L2, Zhangzhu J1, Chen M1, Yu X1, Wang F3, Peng X3, Wu J1.

1. EPI Department, Beijing Center for Disease Control and Prevention, Beijing 100013, PR China
2. EPI Department, Beijing Center for Disease Control and Prevention, Beijing 100013, PR China
3. EPI Department, Shunyi District Center for Disease Control and Prevention, Beijing 101300, PR China

Abstract

BACKGROUND

Age-appropriate receipt of ≥ 2 measles-containing vaccine (MCV) doses has been considered evidence of immunity against measles. Transmission of measles is rarely reported among such persons.

METHODS

We report a measles outbreak in a middle school in Beijing that has high coverage with ≥ 2 documented MCV doses. History of previous measles and documentation of MCV receipt were collected for all individuals. Cases were identified by active surveillance and confirmed by laboratory tests. Measles immunoglobulin G (IgG) titers and clinical presentations were obtained for each case.

RESULTS

Of 1331 individuals without a prior history of measles, 1172 (88.1% [95%CI:86.4-91.5%]) and 1078 (81.0% [95%CI:78.9-83.1%]) had age-appropriate receipt of ≥ 2 MCV doses by domestic and U.S. CDC/ACIP criteria, respectively. Thirteen measles cases occurred in the outbreak. The index case and 3 secondary cases were students. The 9 tertiary cases included 2 teachers and 7 students. All 11 student cases received ≥ 2 age-appropriate MCV doses by Chinese domestic criteria; 8 were age-appropriately vaccinated by U.S. CDC/ACIP criteria. Measles IgG was detected during the acute phase of measles for all but 2 cases -the first case and 1 tertiary case. Among students with age-appropriate receipt of ≥ 2 MCV doses, the length of time since the last MCV was significantly associated with risk of measles: for the 1172 students, the risk was 4.6 [OR5.6;95%CI:1.4-22.9] and 5.5 [OR6.5;95%CI:1.4-29.8] times higher when the last MCV dose was 5-9 years and ≥ 10 years prior, respectively, compared with < 5 years prior; for the 1078 students, the risk was 4.1 [OR5.1;95%CI:1.3-20.7] times higher when the last MCV dose was 5-9 years prior compared with < 5 years prior.

CONCLUSIONS

This is the first report from China showing measles transmission among persons with prior evidence of immunity. Secondary vaccine failure may have played an important role in measles transmission. Further laboratory surveillance is needed to assess the persistence of vaccine-induced immunity of domestically-produced MCV in China.

<http://www.ncbi.nlm.nih.gov/pubmed/26589518>

“This is the first report from China showing measles transmission among persons with prior evidence of immunity. Secondary vaccine failure may have played an important role in measles transmission.”

Risk of spontaneous abortion and other pregnancy outcomes in 15-25 year old women exposed to human papillomavirus-16/18 AS04-adjuvanted vaccine in the United Kingdom

Author information

Baril L1, Rosillon D2, Willame C2, Angelo MG2, Zima J2, van den Bosch JH3, Van Staa T4, Boggon R4, Bunge EM3, Hernandez-Diaz S5, Chambers CD6
1. GSK Vaccines, 20, Avenue Fleming, B-1300 Wavre, Belgium
laurence.x.baril@gsk.com
2. GSK Vaccines, 20, Avenue Fleming, B-1300 Wavre, Belgium
3. Pallas, Health Research and Consultancy, Rotterdam, The Netherlands
4. CPRD Research Group, London, United Kingdom
5. Harvard School of Public Health, Cambridge, USA
6. University of California San Diego School of Medicine, USA

Abstract

BACKGROUND

We assessed the risk of spontaneous abortion (SA) after inadvertent exposure to HPV-16/18-vaccine during pregnancy using an observational cohort design.

METHODS

The study population included women aged 15-25 years registered with the Clinical Practice Research Datalink General Practice OnLine Database in the United Kingdom (UK), who received at least one HPV-16/18-vaccine dose between 1st September 2008 and 30th June 2011. Exposed women had the first day of gestation between 30 days before and 45 days (90 days for the extended exposure period) after any HPV-16/18-vaccine dose. Non-exposed women had the first day of gestation 120 days-18 months after the last dose. SA defined as foetal loss between weeks 1 and 23 of gestation (UK definition).

RESULTS

The frequency of SA was 11.6% (among 207 exposed) and 9.0% (632 non-exposed), women: hazard ratio (HR) adjusted for age at first day of gestation 1.30 (95% confidence interval: 0.79-2.12). Sensitivity analysis per number of doses administered (-30 to +45-day risk period) showed a HR for SA of 1.11 (0.64-1.91) for 18/178 women with one dose during the risk period versus 2.55 (1.09-5.93) in 6/29 women with two doses within a 4-5 weeks period. The proportion of pre-term/full-term/postterm deliveries, small/large for gestational age infants, and birth defects was not significantly different between exposed and non-exposed women. Results were consistent using a (United States) SA definition of foetal loss between weeks 1-19 and/or the extended risk period.

CONCLUSION

There was no evidence of an increased risk of SA and other adverse pregnancy outcomes in young women inadvertently HPV-16/18-vaccinated around gestation. Nevertheless, women who are pregnant or trying to become pregnant are advised to postpone vaccination until completion of pregnancy.

<http://www.ncbi.nlm.nih.gov/pubmed/26206268>

Full Report: <http://www.sciencedirect.com/science/article/pii/S0264410X15009688>

“The frequency of SA was 11.6% (among 207 exposed) and 9.0% (632 non-exposed) ... Results were consistent using a (United States) SA definition of foetal loss between weeks 1-19 and/or the extended risk period ... women who are pregnant or trying to become pregnant are advised to postpone vaccination until completion of pregnancy.”

The prevalence and pattern of pharmaceutical and excipient exposure in a neonatal unit in Slovenia

Author information

Fister P1, Urh S2, Karner A1, Krzan M3, Paro-Panjan D1.

1. Department of Neonatology, Division of Pediatrics
University Medical Centre Ljubljana, Ljubljana, Slovenia

2. Department of Pharmacy, University Medical Centre Ljubljana
Ljubljana, Slovenia

3. Faculty of Medicine, Institute of Pharmacology and Experimental Toxicology
University of Ljubljana, Ljubljana, Slovenia.

Abstract

OBJECTIVE

Because of the restraints on conducting studies on pharmaceutical use in sick newborns, many drugs are used off-label in this population. Moreover, industrially manufactured pharmaceuticals may contain different excipients, which may be either untested or not licensed for use in neonates. The aim of our study was to determine the prevalence and pattern of pharmaceutical and excipient exposure in newborns hospitalized at the Department of Neonatology, Ljubljana, Slovenia.

METHODS

A longitudinal prospective cross-sectional study was performed during a one-month period and included all hospitalized neonates. Route of administration, site of action, type of manufacture, licensing status, type and concentrations of excipients for all pharmaceuticals given to the neonates were determined.

RESULTS

Twenty seven different pharmaceutical preparations were prescribed to a total of 48 hospitalized newborns. In most cases, newborns were prescribed various pharmaceuticals that were not approved for use in this population. Newborns were exposed to 60 different excipients in industrially manufactured pharmaceutical preparations. More than half of the received pharmaceuticals contained potentially harmful and harmful excipients.

CONCLUSIONS

Two-thirds of pharmaceutical preparations for neonates were used off-label. Newborns receive more auxiliary substances, which may be unsuitable for this age group and may even be toxic to them, via industrially manufactured pharmaceuticals.

“Newborns receive more auxiliary substances, which may be unsuitable for this age group and may even be toxic to them, via industrially manufactured pharmaceuticals.”

A sera-epidemiological study on pertussis immunity levels among community populations and an analysis of the underlying factors in Tianjin China

Author information

Zhang Y1, Huang H2, Gao Z2, Liu Y2, Liu P2, Ding Y2, Wang L3, Chen D4, Wu S5.

1. Tianjin Centers for Disease Control and Prevention, Tianjin, 300011, China
2. Tianjin Centers for Disease Control and Prevention, Tianjin, 300011, China
3. Hangu Centers for Disease Control and Prevention, Tianjin, 300480, China
4. Hongqiao Centers for Disease Control and Prevention, Tianjin, 300132, China
5. Beichen Centers for Disease Control and Prevention, Tianjin, 300400, China
cdc Zhangying@sina.com

Abstract

BACKGROUND

The aim of this study is to characterize the sera-epidemiology of pertussis immunity levels among community populations and to identify the underlying factors. Moreover, our study will help resolve new issues encountered during the control and prevention of pertussis reemergence.

METHODS

The anti-pertussis antibody levels among community populations were examined using enzyme linked immunosorbent assays (ELISA) over three years. Comparative studies were carried out to assess the efficacy of different types of vaccines. Meanwhile, the duration of protection provided by DTaP within the under-7 age group was subjected to further analysis.

RESULTS

The average positive rate for anti-pertussis antibody was 49.15% across all community populations, among which the 4-12 age group showed a rate substantially lower than those of other groups ($P < 0.001$). There was no statistically significant difference in anti-pertussis antibody levels ($P = 0.977$) between people receiving three and four doses of the vaccine. The surveillance results showed that the positive antibody response rate elicited by component pertussis combo (DTcP) vaccines (84.44%) was strikingly higher than that elicited by acellular pertussis combo (DTaP) vaccines (37.22%, $P < 0.001$). More specifically, when given 4 doses of DTcP vaccines, 66.67% of the people showed positive anti-pertussis toxin (PT) antibody levels, which was higher than the ratio of 9.87% ($P < 0.001$) in the case of DTaP vaccines. The positive anti-pertussis antibody levels peaked at 73% within the first five months following vaccination and then gradually decreased to below 20% in four years. The positive rate was inversely correlated with the length of time after vaccination ($r = -0.929$, $P = 0.003$).

CONCLUSIONS

The anti-pertussis antibody levels were not only relatively low among community populations, but also dropped excessively rapidly among vaccinated populations. Natural infection is an important contributor to the high pertussis immunity levels seen in adolescents and adults. The efficacy of DTaP remains to be improved.

“The anti-pertussis antibody levels were not only relatively low among community populations, but also dropped excessively rapidly among vaccinated populations. Natural infection is an important contributor to the high pertussis immunity levels seen in adolescents and adults. The efficacy of DTaP remains to be improved.”

The Decline of Pertussis-Specific Antibodies After Tetanus, Diphtheria, and Acellular Pertussis Immunization in Late Pregnancy

Author information

Abu Raya B1, Srugo I2, Kessel A3,
Peterman M4, Vaknin A5, Bamberger E6.

1. Department of Pediatrics The Ruth and Bruce Rappaport Faculty of Medicine Technion-Israel Institute of Technology, Haifa
2. Department of Pediatrics Clinical Microbiology Laboratory The Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa
3. Division of Allergy and Clinical Immunology, Bnai Zion Medical Center The Ruth and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa
4. Clinical Microbiology Laboratory
5. The Ruth and Bruce Rappaport Faculty of Medicine Technion-Israel Institute of Technology, Haifa
6. Clinical Microbiology Laboratory The Ruth and Bruce Rappaport Faculty of Medicine Technion-Israel Institute of Technology, Haifa

Abstract

We prospectively measured pertussis-specific antibodies 9-15 months after delivery in women immunized with tetanus, diphtheria, and acellular pertussis (Tdap) after the 20th week of their recent pregnancy. The Tdap-immunized women (n = 38) exhibited a decline in geometric mean concentrations between their peripartum and follow-up levels for immunoglobulin G to pertussis toxin (21.48 [95% confidence interval, 12.51-36.89] vs 11.72 [7.09-19.37] IU/mL); filamentous hemagglutinin (185.95 [157.93-218.94] vs 140.33 IU/mL [113.46-173.57] IU/mL); and pertactin (171.52 [120.73-243.67] vs 83.74 [60.58-115.75] IU/mL) (all P < .001). For women immunized with Tdap during late pregnancy, pertussis-specific immunoglobulin G levels decreased significantly 9-15 months after delivery.

<http://www.ncbi.nlm.nih.gov/pubmed/26160743>

“For women immunized with Tdap during late pregnancy, pertussis-specific immunoglobulin G levels decreased significantly 9-15 months after delivery.”

Why are Excipients Important to Neonates?

Author information

Turner MA1, Shah U.
Department of Women's and Children's Health
Institute of Translational Medicine, University of Liverpool
Liverpool Women's Hospital, Crown Street, Liverpool, L8 7SS, UK
mark.turner@liverpool.ac.uk

Abstract

Neonates are given many medicines. A significant proportion of these medicines contain excipients. Excipients are used to facilitate the manufacture and use of medicines. Without excipients, it would not be feasible to formulate some drugs into appropriate medicinal products. For others the removal of excipients would reduce the shelf life and make them uneconomic to produce or too expensive for users to purchase. Excipients are also important because some of them can cause harm. Accordingly, it is important to minimize excipient exposure when possible and to only use them when there is a clear pharmaceutical requirement. On balance it is generally safe to use medicines containing excipients. This review introduces physicians and nurses to the functions of excipients in medicines and describes some potential adverse effects of excipients in neonates. The review also provides pharmaceutical scientists with an insight to issues that arise when excipients are administered to neonates. The review answers some key questions about excipients, addresses some case studies of excipient use, proposes approaches for clinicians who prescribe and administer medicines containing excipients and identifies areas for research that seeks to establish the safety profiles of excipients in neonates.”

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26323411>

“Accordingly, it is important to minimize excipient exposure when possible and to only use them when there is a clear pharmaceutical requirement.”

Current Pharmaceutical Design • 2015

Neonatal Formulations: The Need for a Tailored, Knowledge Driven Approach

Author information

Allegaert K1, Cosaert K, van den Anker JN.

Neonatal Intensive Care Unit, University Hospital
Herestraat 49, 3000 Leuven, Belgium
karel.allegaert@uzleuven.be

Abstract

To attain effective and safe pharmacotherapy in neonates, caregivers have to consider both the clinical characteristics of the newborn and the pharmacokinetic estimates of a given compound during prescription and administration. Overall, clearance in neonates is low when compared to other pediatric subpopulations. Despite this overall low clearance, there is already extensive between individual variability in clearance in early life. As a consequence, neonates are in urgent need of tailored drug product development that considers the need for both low and flexible dosing to maintain dose accuracy. During the development of such formulations tailored for neonates, there is also a need for guidance on excipient exposure. The available knowledge on the safety or toxicity of excipients is limited and difficult to retrieve, but there are initiatives (e.g. Safety and Toxicity of Excipients for Pediatrics [STEP] database initiative) to improve the present situation. In addition, population focussed studies on aspects of clinical pharmacology of excipients in neonates should be conducted. The propylene glycol research project and the European Study for Neonatal Excipient Exposure (ESNEE) initiative illustrate its feasibility. Finally, until tailored formulations make it to the market, compounding practices for drug formulations in neonates should be evaluated to guarantee correct dosing, product stability, safety and to support pharmacists in their daily practice.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26323412>

“Overall,
clearance in neonates
is low when compared to
other pediatric subpopulations.”

Development of a Physiologically-Based Pharmacokinetic Model for Preterm Neonates: Evaluation with In Vivo Data

Author information

Claassen K, Thelen K, Coboeken K,
Gaub T, Lippert J, Allegaert K, Willmann S1.

Bayer Pharma AG, Clinical Pharmacometrics
42113 Wuppertal, Germany
stefan.willmann@bayer.com

Abstract

Among pediatric patients, preterm neonates and newborns are the most vulnerable subpopulation. Rapid developmental changes of physiological factors affecting the pharmacokinetics of drug substances in newborns require extreme care in dose and dose regimen decisions. These decisions could be supported by in silico methods such as physiologically-based pharmacokinetic (PBPK) modeling. In a comprehensive literature search, the physiological information of preterm neonates that is required to establish a PBPK model has been summarized and implemented into the database of a generic PBPK software. Physiological parameters include the organ weights and blood flow rates, tissue composition, as well as ontogeny information about metabolic and elimination processes in the liver and kidney. The aim of this work is to evaluate the model's accuracy in predicting the pharmacokinetics following intravenous administration of two model drugs with distinct physicochemical properties and elimination pathways based on earlier reported in vivo data. To this end, PBPK models of amikacin and paracetamol have been set up to predict their plasma levels in preterm neonates. Predicted plasma concentration-time profiles were compared to experimentally obtained in vivo data. For both drugs, plasma concentration-time profiles following single and multiple dosing were appropriately predicted for a large range gestational and postnatal ages. In summary, PBPK simulations in preterm neonates appear feasible and might become a useful tool in the future to support dosing decisions in this special patient population.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26323410>

“Among pediatric patients,
preterm neonates and newborns
are the most vulnerable subpopulation. Rapid
developmental changes of physiological factors
affecting the pharmacokinetics of drug
substances in newborns require extreme
care in dose and dose regimen decisions.”

Needle-free and adjuvant-free epicutaneous boosting of pertussis immunity: Preclinical proof of concept

Author information

Gavillet BM1, Mondoulet L2, Dhelft V2, Eberhardt CS3,
Auderset F3, Pham HT4, Petre J4, Lambert PH3, Benhamou PH2, Siegrist CA3.

1. World Health Organization Collaborating Center for Vaccine Immunology
Departments of Pathology-Immunology, University of Geneva, 1211 Geneva,
Switzerland
2. DBV Technologies, Green Square, 80/84 rue des Meuniers, 92220 Bagneux,
France
3. World Health Organization Collaborating Center for Vaccine Immunology
Departments of Pathology-Immunology, University of Geneva, 1211 Geneva,
Switzerland
4. BioNet-Asia Co., Ltd., 19 Udomsuk 37, Sukhumvit 103
Bangjak, Prakanong, Bangkok 10260, Thailand

Abstract

The limited durability of pertussis vaccine-induced protection requires novel approaches to reactivate immunity and limit pertussis resurgence in older children and adults. We propose that periodic boosters could be delivered using a novel epicutaneous delivery system (Viaskin) to deliver optimized pertussis antigens such as genetically-detoxified pertussis toxin (rPT). To best mimic the human situation in which vaccine-induced memory cells persist, whereas antibodies wane, we developed a novel adoptive transfer murine model of pertussis immunity. This allowed demonstrating that a single application of Viaskin delivering rPT and/or pertactin and filamentous hemagglutinin effectively reactivates vaccine-induced pertussis immunity and protects against *Bordetella pertussis* challenge. Recalling pertussis immunity without needles nor adjuvant may considerably facilitate the acceptance and application of periodic boosters.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26067183>

“Recalling pertussis immunity
without needles nor adjuvant may
considerably facilitate the acceptance
and application of periodic boosters.”

NIHJ Research Portfolio Online Reporting Tools
RePORT

Project Number:

1R15ES012209-01

Contact PI / Project Leader:

Kinningham, Kinsley K.

Title:

Mechanism Of Thimerosal Induced Neurotoxicity

Awardee Organization:

Marshall University

Abstract Text:

DESCRIPTION (provided by applicant):

Mercurials are potent neurotoxins, which localize to both neurons and glia within the central nervous system and elicit a range of deleterious actions. Sodium ethylmercurithiosalicylate (thimerosal) is a widely used ethyl mercury containing preservative used in over-the-counter medications, cleaners and cosmetics. Recent concern has been raised on the use of thimerosal in over 30 vaccines licensed in the United States. With the addition of several important vaccines over the last few years, exposure to mercury has increased among infants, leading some investigators to suggest an association between thimerosal exposure and autism. There is limited toxicological information regarding ethyl mercury; therefore, estimates of health risks from thimerosal exposure have been based on mechanistic studies of methyl mercury, a close chemical relative about which much is known. These estimates may actually underestimate the toxicity of ethyl mercury containing agents. The wide use of thimerosal makes understanding the mechanism(s) of its toxicity a significant human health issue. The overall goal of this project is to investigate the mechanism by which thimerosal causes neuronal cell death. The hypothesis to be tested is that thimerosal results in dose-dependent activation of specific signaling molecules and redox-sensitive transcription factors known to activate pro-death genes in neurons. If this hypothesis is correct then pharmacological intervention should attenuate toxicity as a result of thimerosal exposure. Using a human neuroblastoma cell line, SK-N-SH, this project will test the hypothesis in four specific aims. Aim 1 will identify in a dose-dependent manner the predominant cell death pathway (apoptotic versus necrotic) associated with thimerosal exposure and to determine if it is associated with an increase in reactive oxygen species and caspase-3 dependent. Aim 2 will determine if cell death is mediated through an AP-1-dependent pathway. In addition, this specific aim will establish the role of c-Jun-N-terminal kinase; an enzyme, which phosphorylates and activates AP-1, in thimerosal-mediated neuronal death. Aim 3 will determine if the cell death pathway is mediated through an NFkappaB-dependent mechanism. Aim 4 will determine if thimerosal toxicity can be attenuated by the administration of S-adenosylmethionine, an enzyme which increases endogenous levels of glutathione. This project will generate mechanistic data on thimerosal neurotoxicity and potentially identify specific targets for pharmacological intervention.

“This project will generate mechanistic data on thimerosal neurotoxicity and potentially identify specific targets for pharmacological intervention.”

Chapter Six

Autism

1987 - 2015

In 1976, children received 10 vaccines before attending school. Today they will receive over 36 injections. The American Academy of Pediatrics and the Center for Disease Control assured parents that it was safe to not only give these vaccines, but that they could be given at one time with complete safety. Is this true? Or are we being lied to on a grand scale?

The medical establishment has created a set of terms, which they use constantly to boost their egos and firm up their authority as the unique holders of medical wisdom—the mantra is “evidence-based medicine”, as if everything outside their anointing touch is bogus and suspect. A careful examination of many of the accepted treatments reveals that most have little or no scientific “evidence-based” data to support it. One often repeated study found that almost 80% of medical practice had no scientific backing.

Most men of medicine recognize that some things are obvious without a placebo controlled, double-blind, randomized study. For example, there has never been such a study to see if smashing your finger with a hammer will be painful, but we accept it without such pristine evidence. The same is true with removing brain tumors or sewing up severe lacerations.

I find it interesting that there exist an incredible double standard when it comes to our evidence versus theirs. The proponents of vaccination safety can just say they are safe, without any supporting evidence what-so-ever, and it is to be accepted without question. They can announce that mercury is not only safe, but that it seems to actually increase the IQ, and we are to accept it. They can proclaim thimerosal safe to use in vaccines without their having ever been a single study on its safety in over 60 years of use, and we are to accept it.

Yet, let me, or anyone else, suggest that excessive vaccination can increase the risk of not only autism, but also schizophrenia and neurodegenerative diseases, and they will scream like banshees –Where is the evidence? Where is the evidence? When we produce study after study, they always proclaim them to be insufficient evidence or unacceptable studies. More often than not, they just completely ignore the evidence. This is despite the fact that we produce dozens or even hundreds of studies that not only demonstrate the link clinically and scientifically, but also clearly show the mechanism by which the damage is being done—even on a molecular level. These include cell culture studies, mixed cell cultures, organotypic tissue studies, in vivo animal studies using multiple species and even human studies. To the defenders of vaccine safety—our evidence is never sufficient and, if we face reality—never will be.

~ Dr. Russell Blaylock

The Vaccine Court

The United States federal court has presided over landmark cases for the autism community, filing official court decisions that have linked vaccinations as an environmental trigger of autism. The court in which all of these decisions are rendered is the Office of Special Masters of the United States Courts of Federal Claims, otherwise known as “Vaccine Court.”

The U.S. government created this specific court in 1986 to protect pharmaceutical companies from the direct lawsuits that were arising due to the preponderance of illnesses and injuries that were stemming from the company’s vaccination products. By establishing the Vaccine Court, the government now protects the pharmaceutical industry by trying the cases and awarding damages from a federal excise tax added to the cost of each dosage of a vaccine.

In the “Vaccine Court,” the burden of proof lays squarely on the claimant. In other words, a family must show a clear causal connection between a vaccination and its adverse effects. For the autism community, this standard is made more challenging because the “Vaccine Court” does not accept “autism” as a legal determination. This is because autism is a clinical diagnosis, labeled on the basis of a collection of clinical features and created by causes that are still unknown. But the autism community has still persevered, and compelled the court to acknowledge the link between their children’s autism diagnoses and vaccinations’ environmental triggers.

Vaccine Injury Court

The Bailey Banks Case

The judge rules that the Banks family successfully demonstrates that “the MMR vaccine at issue actually caused the conditions from which Bailey suffered and continues to suffer.” This includes Bailey’s diagnosis of Pervasive Developmental Disorder-Not Otherwise Specified, which has long been recognized as an autism spectrum disorder by the CDC and other federal health agencies.

BOX LINK

Vaccine Injury Court

The Eric Lassiter Case

The Lassiter family presents Eric’s diphtheria-pertusis-tetanus vaccination as the cause of his injuries, a diagnosis described as “static encephalopathy with autistic tendencies in addition to delayed development.” The judge rules that the Department of Health & Human Services’ “respondent’s evidence and proffered explanations are weak, unconvincing and insufficient” and that the Lassiter family “has presented a better case in support of . . . injury. The Court concludes that a preponderance of the evidence requires a finding for the petitioner.”

BOX LINK

Vaccine Injury Court

The Richelle Oxley Case

The Oxley family presents their case that Richelle’s disabilities, including encephalopathy and autistic behaviors, are a result of the pertussis vaccine. The judge rules in their favor, stating that their “claim is strongly supported” by the presented evidence, and that there is “not a preponderance of the evidence that Richelle’s condition is due to factors unrelated to the administration of the vaccine.”

BOX LINK

Vaccine Injury Court

The Hannah Poling Case

The Division of Vaccine Injury Compensation, Department of Health and Human Services concedes that Hannah’s vaccinations aggravated her mitochondrial disorder, resulting in “features of autism spectrum disorder.”

BOX LINK

Reduced natural killer cell activity in autism

Warren RP, Foster A, Margaretten NC.

Dr. Warren is Associate Professor of Biology
and the Developmental Center for Handicapped Persons
Utah State University, Logan, Utah.

Ms. Foster is Nursing Supervisor, Inpatient Psychiatric Unit,
Primary Children's Medical Center
Salt Lake City, Utah.

Dr. Margaretten is currently a Postdoctoral Fellow
Oakridge National Laboratory, Oakridge, Tennessee.

Abstract

Natural killer (NK) cells are believed to afford protection against malignancy and viral infections. In addition, these cells may be involved in regulating the immune response because altered NK activity is often associated with autoimmune disorders. An investigation of the natural cytotoxic potential of peripheral blood mononuclear cells from 31 patients with autism has been carried out using K562 tumor cells as target cells. Cells of 12 of the patients induced significantly reduced levels of cytotoxicity; this was not correlated with a quantitative alteration in patient NK cells as determined by use of the Leu-11 monoclonal antibody. This observation of altered NK cell activity, and previously reported findings of other immune abnormalities in autism, suggest that immune changes may be directly related to underlying biological processes of autism or that these changes may be an indirect reflection of the actual pathological mechanism.

[http://www.jaacap.com/article/S0890-8567\(09\)65685-9/abstract](http://www.jaacap.com/article/S0890-8567(09)65685-9/abstract)

“This observation of altered NK cell activity, and previously reported findings of other immune abnormalities in autism, suggest that immune changes may be directly related to underlying biological processes of autism or that these changes may be an indirect reflection of the actual pathological mechanism.”

Trace element analysis in hair: factors determining accuracy, precision, and reliability

Author information

Bass DA1, Hickock D, Quig D, Urek K.

Doctors Data Inc., St. Charles, IL 60174, USA
dbass@doctorsdata.com

Abstract

Trace element analysis in biological samples has improved significantly over the last 40 years. Improvements in instrumentation such as inductively coupled plasma-mass spectrometry and microwave digestion have resulted in improved precision, accuracy, reliability, and detection limits. The analysis of human scalp hair has benefited significantly from these improvements. A recent article in the Journal of the American Medical Association found significant inter-laboratory variation amongst several laboratories performing trace metal hair testing. It concluded that standardization was necessary to improve inter-laboratory comparability, and an accompanying commentary described the characteristics of a laboratory that should be used in performing hair analysis. The objective of this study is to demonstrate that good laboratory practices will generate precise, accurate, and reliable results. A method for establishing reference ranges and specific data on an analytical method will also be presented. The use of prescribed clinical quality control, including method validation, proficiency testing, split sampling, and good laboratory practices clearly demonstrates that measuring trace elements in hair can be analytically valid.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=11703167>

“The use of prescribed clinical quality control, including method validation, proficiency testing, split sampling, and good laboratory practices clearly demonstrates that measuring trace elements in hair can be analytically valid.”

Vaccines and Autism

Author Information

Bernard Rimland, PhD, Woody McGinnis, MD
Autism Research Institute, San Diego, CA

Abstract

Autism research is characterized by diverse findings.

There is no consensus about the biological determinants of autism.

This paper examines the autistic immune profile
and the possible role of vaccines in autism.

Vaccinations may be one of the triggers for autism. Substantial data demonstrate immune abnormality in many autistic children consistent with impaired resistance to infection, activation of inflammatory response, and autoimmunity. Impaired resistance may predispose to vaccine injury in autism.

A mercurial preservative in childhood vaccines, thimerosal, may cause direct neurotoxic, immunodepressive, and autoimmune injury and contribute to early-onset and regressed autism. Live viruses in measles, mumps, and rubella (MMR) may result in chronic infection of the gut and trigger regressed autism. Thimerosal injection may potentiate MMR injury.

Consideration of vaccine etiology must include recognition of compromised gut and nutrition in most autistic children. An integrated view of the underlying biological problems in autistic children serves our understanding of the possible role of vaccines. Development of screening methods for deferral of vaccines in at-risk children is a worthy goal.

<http://labmed.oxfordjournals.org/content/labmed/33/9/708.full.pdf>

“Vaccinations may be one of the triggers for autism.

Development of screening methods for deferral

of vaccines in at-risk children is a worthy goal.”

“In this study, we postulated that infectious agent antigens such as streptokinase, dietary peptides (gliadin and casein) and ethyl mercury (xenobiotic) bind to different lymphocyte receptors and tissue enzyme ...”

International Journal Of Immunopathology And Pharmacology • September 2003

Infections, toxic chemicals and dietary peptides binding to lymphocyte receptors and tissue enzymes are major instigators of autoimmunity in autism

Author information

Vojdani A1, Pangborn JB, Vojdani E, Cooper EL.

Laboratory Of Comparative Immunology, Department Of Neurobiology
UCLA Medical Center, Los Angeles, CA, USA
DrAri@msn.com

Abstract

Similar to many complex autoimmune diseases, genetic and environmental factors including diet, infection and xenobiotics play a critical role in the development of autism. In this study, we postulated that infectious agent antigens such as streptokinase, dietary peptides (gliadin and casein) and ethyl mercury (xenobiotic) bind to different lymphocyte receptors and tissue enzyme (DPP IV or CD26). We assessed this hypothesis first by measuring IgG, IgM and IgA antibodies against CD26, CD69, streptokinase (SK), gliadin and casein peptides and against ethyl mercury bound to human serum albumin in patients with autism. A significant percentage of children with autism developed anti-SK, anti-gliadin and casein peptides and anti-ethyl mercury antibodies, concomitant with the appearance of anti-CD26 and anti-CD69 autoantibodies. These antibodies are synthesized as a result of SK, gliadin, casein and ethyl mercury binding to CD26 and CD69, indicating that they are specific. Immune absorption demonstrated that only specific antigens, like CD26, were capable of significantly reducing serum anti-CD26 levels. However, for direct demonstration of SK, gliadin, casein and ethyl mercury to CD26 or CD69, microtiter wells were coated with CD26 or CD69 alone or in combination with SK, gliadin, casein or ethyl mercury and then reacted with enzyme labeled rabbit anti-CD26 or anti-CD69. Adding these molecules to CD26 or CD69 resulted in 28-86% inhibition of CD26 or CD69 binding to anti-CD26 or anti-CD69 antibodies. The highest % binding of these antigens or peptides to CD26 or CD69 was attributed to SK and the lowest to casein peptides. We, therefore, propose that bacterial antigens (SK), dietary peptides (gliadin, casein) and Thimerosal (ethyl mercury) in individuals with pre-disposing HLA molecules, bind to CD26 or CD69 and induce antibodies against these molecules. In conclusion, this study is apparently the first to demonstrate that dietary peptides, bacterial toxins and xenobiotics bind to lymphocyte receptors and/or tissue enzymes, resulting in autoimmune reaction in children with autism.

Neuroglial activation and neuroinflammation in the brain of patients with autism

Author information

Vargas DL1, Nascimbene C, Krishnan C, Zimmerman AW, Pardo CA.

Department of Neurology
Johns Hopkins University School of Medicine
600 North Wolfe Street, Baltimore, MD 21287, USA

Abstract

Autism is a neurodevelopmental disorder characterized by impaired communication and social interaction and may be accompanied by mental retardation and epilepsy. Its cause remains unknown, despite evidence that genetic, environmental, and immunological factors may play a role in its pathogenesis. To investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism, we used immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays to study brain tissues and cerebrospinal fluid (CSF) from autistic patients and determined the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles. Brain tissues from cerebellum, midfrontal, and cingulate gyrus obtained at autopsy from 11 patients with autism were used for morphological studies. Fresh-frozen tissues available from seven patients and CSF from six living autistic patients were used for cytokine protein profiling. We demonstrate an active neuroinflammatory process in the cerebral cortex, white matter, and notably in cerebellum of autistic patients. Immunocytochemical studies showed marked activation of microglia and astroglia, and cytokine profiling indicated that macrophage chemoattractant protein (MCP)-1 and tumor growth factor-beta1, derived from neuroglia, were the most prevalent cytokines in brain tissues. CSF showed a unique proinflammatory profile of cytokines, including a marked increase in MCP-1. Our findings indicate that innate neuroimmune reactions play a pathogenic role in an undefined proportion of autistic patients, suggesting that future therapies might involve modifying neuroglial responses in the brain.

<http://www.ncbi.nlm.nih.gov/pubmed/15546155>

Immunological findings in autism

Author information

Cohly HH1, Panja A.

Department of Biology, Jackson State University, Mississippi 39217, USA

Abstract

The immunopathogenesis of autism is presented schematically in Fig. 1. Two main immune dysfunctions in autism are immune regulation involving pro-inflammatory cytokines and autoimmunity. Mercury and an infectious agent like the measles virus are currently two main candidate environmental triggers for immune dysfunction in autism. Genetically immune dysfunction in autism involves the MHC region, as this is an immunologic gene cluster whose gene products are Class I, II, and III molecules. Class I and II molecules are associated with antigen presentation. The antigen in virus infection initiated by the virus particle itself while the cytokine production and inflammatory mediators are due to the response to the putative antigen in question. The cell-mediated immunity is impaired as evidenced by low numbers of CD4 cells and a concomitant T-cell polarity with an imbalance of Th1/Th2 subsets toward Th2. Impaired humoral immunity on the other hand is evidenced by decreased IgA causing poor gut protection. Studies showing elevated brain specific antibodies in autism support an autoimmune mechanism. Viruses may initiate the process but the subsequent activation of cytokines is the damaging factor associated with autism. Virus specific antibodies associated with measles virus have been demonstrated in autistic subjects. Environmental exposure to mercury is believed to harm human health possibly through modulation of immune homeostasis. A mercury link with the immune system has been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines. The occupational hazard exposure to mercury causes edema in astrocytes and, at the molecular level, the CD95/Fas apoptotic signaling pathway is disrupted by Hg²⁺. Inflammatory mediators in autism usually involve activation of astrocytes and microglial cells. Proinflammatory chemokines (MCP-1 and TARC), and an anti-inflammatory and modulatory cytokine, TGF-beta1, are consistently elevated in autistic brains. In measles virus infection, it has been postulated that there is immune suppression by inhibiting T-cell proliferation and maturation and downregulation MHC class II expression. Cytokine alteration of TNF-alpha is increased in autistic populations. Toll-like-receptors are also involved in autistic development. High NO levels are associated with autism. Maternal antibodies may trigger autism as a mechanism of autoimmunity. MMR vaccination may increase risk for autism via an autoimmune mechanism in autism. MMR antibodies are significantly higher in autistic children as compared to normal children, supporting a role of MMR in autism. Autoantibodies (IgG isotype) to neuron-axon filament protein (NAFP) and glial fibrillary acidic protein (GFAP) are significantly increased in autistic patients (Singh et al., 1997). Increase in Th2 may explain the increased autoimmunity, such as the findings of antibodies to MBP and neuronal axonal filaments in the brain. There is further evidence that there are other participants in the autoimmune phenomenon. (Kozlovskaia et al., 2000). The possibility of its involvement in autism cannot be ruled out. Further investigations at immunological, cellular, molecular, and genetic levels will allow researchers to continue to unravel the immunopathogenic mechanisms' associated with autistic processes in the developing brain. This may open up new avenues for prevention and/or cure of this devastating neurodevelopmental disorder.

“Mercury and an infectious agent like the measles virus are currently two main candidate environmental triggers for immune dysfunction in autism. Studies showing elevated brain specific antibodies in autism support an autoimmune mechanism. Viruses may initiate the process but the subsequent activation of cytokines is the damaging factor associated with autism. Virus specific antibodies associated with measles virus have been demonstrated in autistic subjects.”

Large brains in autism: the challenge of pervasive abnormality

Author information

Herbert MR1.

Pediatric Neurology
Center for Morphometric Analysis
Massachusetts General Hospital
Charleston, MA 02129, USA
mherbert1@partners.org

Abstract

The most replicated finding in autism neuroanatomy—a tendency to unusually large brains—has seemed paradoxical in relation to the specificity of the abnormalities in three behavioral domains that define autism. We now know a range of things about this phenomenon, including that brains in autism have a growth spurt shortly after birth and then slow in growth a few short years afterward, that only younger but not older brains are larger in autism than in controls, that white matter contributes disproportionately to this volume increase and in a nonuniform pattern suggesting postnatal pathology, that functional connectivity among regions of autistic brains is diminished, and that neuroinflammation (including microgliosis and astrogliosis) appears to be present in autistic brain tissue from childhood through adulthood. Alongside these pervasive brain tissue and functional abnormalities, there have arisen theories of pervasive or widespread neural information processing or signal coordination abnormalities (such as weak central coherence, impaired complex processing, and underconnectivity), which are argued to underlie the specific observable behavioral features of autism. This convergence of findings and models suggests that a systems- and chronic disease-based reformulation of function and pathophysiology in autism needs to be considered, and it opens the possibility for new treatment targets.

<http://www.ncbi.nlm.nih.gov/pubmed/16151044>

“This convergence of findings and models suggests that a systems- and chronic disease-based reformulation of function and pathophysiology in autism needs to be considered ...”

“Although the etiology of autism is unknown,
data suggest that autism results from multiple etiologies with both genetic and environmental contributions,
which may explain the spectrum of behaviors seen in this disorder.”

Journal of NeuroVirology • November 2005

Autistic disorder and viral infections

Jane E Libbey,¹ Thayne L Sweeten,¹ William M McMahon,² and Robert S Fujinami¹

Departments of ¹Neurology and ²Psychiatry
University of Utah, Salt Lake City, Utah, USA

Autistic disorder (autism) is a behaviorally defined developmental disorder with a wide range of behaviors. Although the etiology of autism is unknown, data suggest that autism results from multiple etiologies with both genetic and environmental contributions, which may explain the spectrum of behaviors seen in this disorder. One proposed etiology for autism is viral infection very early in development. The mechanism, by which viral infection may lead to autism, be it through direct infection of the central nervous system (CNS), through infection elsewhere in the body acting as a trigger for disease in the CNS, through alteration of the immune response of the mother or offspring, or through a combination of these, is not yet known. Animal models in which early viral infection results in behavioral changes later in life include the influenza virus model in pregnant mice and the Borna disease virus model in newborn Lewis rats. Many studies over the years have presented evidence both for and against the association of autism with various viral infections. The best association to date has been made between congenital rubella and autism; however, members of the herpes virus family may also have a role in autism. Recently, controversy has arisen as to the involvement of measles virus and/or the measles, mumps, rubella (MMR) vaccine in the development of autism. Biological assays lend support to the association between measles virus or MMR and autism whereas epidemiologic studies show no association between MMR and autism. Further research is needed to clarify both the mechanisms whereby viral infection early in development may lead to autism and the possible involvement of the MMR vaccine in the development of autism.

[http://www.jneurovirol.com/o_pdf/11\(1\)/001-010.pdf](http://www.jneurovirol.com/o_pdf/11(1)/001-010.pdf)

Developmental Regression and Mitochondrial Dysfunction in a Child With Autism

Author Information

Jon S. Poling, MD, PhD, Richard E. Frye, MD, PhD, John Shoffner, MD, and Andrew W. Zimmerman, MD

Department of Neurology and Neurosurgery, Johns Hopkins Hospital, Baltimore, MD

Case Report

A 19-month-old girl was born after a normal full-term pregnancy. There was no family history of autism or affective, neuromuscular, or hearing disorders. Her development was progressing well, with normal receptive and expressive language and use of prelinguistic gestures, such as pointing for joint attention. Imaginary play and social reciprocity were typical for age. She used at least 20 words and could point to five body parts on command. Several immunizations were delayed owing to frequent bouts of otitis media with fever.

Within 48 hours after immunizations to diphtheria, tetanus, and pertussis; Haemophilus influenzae B; measles, mumps, and rubella; polio; and varicella (Varivax), the patient developed a fever to 38.9°C, inconsolable crying, irritability, and lethargy and refused to walk. Four days later, the patient was waking up multiple times in the night, having episodes of opistho-tonus, and could no longer normally climb stairs. Instead, she crawled up and down the stairs. Low-grade intermittent fever was noted for the next 12 days. Ten days following immunization, the patient developed a generalized erythematous macular rash beginning in the abdomen. The patient's pediatrician diagnosed this as due to varicella vaccination. For 3 months, the patient was irritable and increasingly less responsive verbally, after which the patient's family noted clear autistic behaviors, such as spinning, gaze avoidance, disrupted sleep/wake cycle, and perseveration on specific television programs. All expressive language was lost by 22 months. The patient continued to have chronic yellow watery diarrhea intermittently for 6 months, which was evaluated with negative testing for Clostridium difficile, ova/parasites, and culture. Four months later, an evaluation with the Infant and Toddlers Early Intervention program for possible autism was initiated. Along with the regression, her appetite remained poor for 6 months and her body weight did not increase. This resulted in a decline on a standard growth chart for weight from the 97th to the 75th percentile.

Evaluation at 23 months showed atopic dermatitis, slow hair growth, generalized mild hypotonia, toe walking, and normal tendon reflexes. The Childhood Autism Rating Scale (CARS) score was 33 (mild autism range), and she also met Diagnostic and Statistical Manual for Mental Disorders-IV criteria for autism. Laboratory findings included repeated measurements of aspartate aminotransferase 40 IU/L (normal < 31 IU/L), serum bicarbonate 20 mmol/L (normal 21–31 mmol/L), serum creatine kinase level 203 IU/L (normal < 170 IU/L), and fasting lactic acid 3.3 mmol/L (normal 0.5–2.2 mmol/L). Quantitative urinary organic acid analyses showed trace amounts of dicarboxylic acids (adipic, suberic, octenedioic acids) and small amounts of ethylmalonic and methylsuccinic acids, consistent

with a fatty acid oxidation dysfunction. Quantitative plasma amino acids were all within the normal range; however, the alanine to lysine ratio (a surrogate marker for pyruvate; Dr Richard Kelley, personal communication, 2001) was elevated at 3.2 (normal 1.5–2.5). Cranial magnetic resonance imaging, otoacoustic emission testing, overnight electroencephalography with slow-wave sleep, serum lead, chromosomes, and fragile X by DNA testing were all normal.

The patient was referred for muscle biopsy (J.S.) because of persistent mild lactic acidosis, elevated serum creatine kinase level, and increased aspartate aminotransferase. A fresh vastus lateralis biopsy was performed and examined as described previously.^{7,8} The biopsy showed abnormal histology with type I myofiber atrophy, increased myofiber lipid content, and reduced cytochrome c oxidase activity. Oxidative phosphorylation enzymology showed markedly reduced complex I, I + III, and III activity. Complex IV activity was near the 5% confidence limit of the control group (Table 1). Mitochondrial DNA sequencing of the skeletal muscle was normal.

Now 6 years old, our patient has been treated with vitamin supplements since 2½ years of age. Even before starting supplementation, the patient began speaking again at 23 months old and had a four-word vocabulary of “bubbles,” “ball,” “drink,” and “cracker.” Levocarnitine 250 mg and thiamine 50 mg three times per day were initiated when the patient was 29 months old. Coenzyme Q10 was added at age 33 months. Although she still exhibits mild autistic behaviors, our patient has continued to improve in language functions and sociability such that she now attends a regular kindergarten with an aide. There have been slow yet steady improvements in muscle tone, motor coordination, and gastrointestinal symptoms with occupational therapy, applied behavioral analysis interventions, and mitochondrial enzyme cofactor supplements. After the age of 2 years, growth trajectory has continued along the 75th percentile for both height and weight. Laboratory tests were repeated at ages 2 years and 10 months (aspartate aminotransferase 47 IU/L, normal < 38 IU/L; alanine transferase 20 IU/L, normal < 40 IU/L; serum creatine kinase level 105 IU/L, normal < 194 IU/L), 4 years old (aspartate aminotransferase 36 IU/L; alanine transferase 19 IU/L; serum creatine kinase level 169 IU/L), and 6 years old (aspartate aminotransferase 36 IU/L; alanine transferase 21 IU/L; alanine to lysine ratio 1.58, normal < 1.5 to 2.5). During an acute illness owing to C difficile, the aspartate aminotransferase was on one occasion elevated to 50 IU/L; however, the serum creatine kinase level remained normal at 169 IU/L. Urine organic acids and serum amino acids have been normal at ages 3 and 6 years. Childhood Autism Rating Scale scores since beginning kindergarten have been under 30.

Full Report

Porphyrinuria in childhood autistic disorder: implications for environmental toxicity

Author information

Nataf R1, Skorupka C, Amet L, Lam A, Springbett A, Lathe R.
Laboratoire Philippe Auguste, Paris, France

Abstract

To address a possible environmental contribution to autism, we carried out a retrospective study on urinary porphyrin levels, a biomarker of environmental toxicity, in 269 children with neurodevelopmental and related disorders referred to a Paris clinic (2002-2004), including 106 with autistic disorder. Urinary porphyrin levels determined by high-performance liquid chromatography were compared between diagnostic groups including internal and external control groups. Coproporphyrin levels were elevated in children with autistic disorder relative to control groups. Elevation was maintained on normalization for age or to a control heme pathway metabolite (uroporphyrin) in the same samples. The elevation was significant ($P < 0.001$). Porphyrin levels were unchanged in Asperger's disorder, distinguishing it from autistic disorder. The atypical molecule precoproporphyrin, a specific indicator of heavy metal toxicity, was also elevated in autistic disorder ($P < 0.001$) but not significantly in Asperger's. A subgroup with autistic disorder was treated with oral dimercaptosuccinic acid (DMSA) with a view to heavy metal removal. Following DMSA there was a significant ($P = 0.002$) drop in urinary porphyrin excretion. These data implicate environmental toxicity in childhood autistic disorder.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=16782144>

“These data implicate environmental toxicity in childhood autistic disorder.”

[note: in the medical literature vaccination is considered an environmental toxicant]

Prevalence of disorders of the autism spectrum in a population cohort of children in South Thames: the Special Needs and Autism Project (SNAP)

Author information

Baird G1, Simonoff E, Pickles A, Chandler S,
Loucas T, Meldrum D, Charman T.

Newcomen Centre
Guy's and St Thomas' NHS Foundation Trust
London, UK
gillian.baird@gstt.nhs.uk

Abstract

BACKGROUND

Recent reports have suggested that the prevalence of autism and related spectrum disorders (ASDs) is substantially higher than previously recognised. We sought to quantify prevalence of ASDs in children in South Thames, UK.

METHODS

Within a total population cohort of 56 946 children aged 9-10 years, we screened all those with a current clinical diagnosis of ASD (n=255) or those judged to be at risk for being an undetected case (n=1515). A stratified subsample (n=255) received a comprehensive diagnostic assessment, including standardised clinical observation, and parent interview assessments of autistic symptoms, language, and intelligence quotient (IQ). Clinical consensus diagnoses of childhood autism and other ASDs were derived. We used a sample weighting procedure to estimate prevalence.

FINDINGS

The prevalence of childhood autism was 38.9 per 10,000 (95% CI 29.9-47.8) and that of other ASDs was 77.2 per 10,000 (52.1-102.3), making the total prevalence of all ASDs 116.1 per 10,000 (90.4-141.8). A narrower definition of childhood autism, which combined clinical consensus with instrument criteria for past and current presentation, provided a prevalence of 24.8 per 10,000 (17.6-32.0). The rate of previous local identification was lowest for children of less educated parents.

INTERPRETATION

Prevalence of autism and related ASDs is substantially greater than previously recognised. Whether the increase is due to better ascertainment, broadening diagnostic criteria, or increased incidence is unclear. Services in health, education, and social care will need to recognise the needs of children with some form of ASD, who constitute 1% of the child population.

“Prevalence of autism
and related ASDs is substantially greater
than previously recognised.”

The immune response in autism: a new frontier for autism research

Author information

Ashwood P1, Wills S, Van de Water J.
Medical Microbiology and Immunology and the M.I.N.D
Institute, University of California Davis
Sacramento, CA 95817, USA
pashwood@ucdavis.edu

Abstract

Autism spectrum disorders (ASD) are part of a broad spectrum of neurodevelopmental disorders known as pervasive developmental disorders, which occur in childhood. They are characterized by impairments in social interaction, verbal and nonverbal communication and the presence of restricted and repetitive stereotyped behaviors. At the present time, the etiology of ASD is largely unknown, but genetic, environmental, immunological, and neurological factors are thought to play a role in the development of ASD. Recently, increasing research has focused on the connections between the immune system and the nervous system, including its possible role in the development of ASD. These neuroimmune interactions begin early during embryogenesis and persist throughout an individual's lifetime, with successful neurodevelopment contingent upon a normal balanced immune response. Immune aberrations consistent with a dysregulated immune response, which so far, have been reported in autistic children, include abnormal or skewed T helper cell type 1 (T(H)1)/T(H)2 cytokine profiles, decreased lymphocyte numbers, decreased T cell mitogen response, and the imbalance of serum immunoglobulin levels. In addition, autism has been linked with autoimmunity and an association with immune-based genes including human leukocyte antigen (HLA)-DRB1 and complement C4 alleles described. There is potential that such aberrant immune activity during vulnerable and critical periods of neurodevelopment could participate in the generation of neurological dysfunction characteristic of ASD. This review will examine the status of the research linking the immune response with ASD.

Abstract: <http://www.ncbi.nlm.nih.gov/pubmed/?term=16698940>

Full Report: <http://www.jleukbio.org/content/80/1/1.long>

“There is potential that such aberrant immune activity during vulnerable and critical periods of neurodevelopment could participate in the generation of neurological dysfunction characteristic of ASD. This review will examine the status of the research linking the immune response with ASD.”

Pathophysiology • August 2006

Oxidative stress in autism

Author information

Chauhan A1, Chauhan V.

NYS Institute for Basic Research in Developmental Disabilities
1050 Forest Hill Road, Staten Island, NY 10314, USA

Abstract

Autism is a severe developmental disorder with poorly understood etiology. Oxidative stress in autism has been studied at the membrane level and also by measuring products of lipid peroxidation, detoxifying agents (such as glutathione), and antioxidants involved in the defense system against reactive oxygen species (ROS). Lipid peroxidation markers are elevated in autism, indicating that oxidative stress is increased in this disease. Levels of major antioxidant serum proteins, namely transferrin (iron-binding protein) and ceruloplasmin (copper-binding protein), are decreased in children with autism. There is a positive correlation between reduced levels of these proteins and loss of previously acquired language skills in children with autism. The alterations in ceruloplasmin and transferrin levels may lead to abnormal iron and copper metabolism in autism. The membrane phospholipids, the prime target of ROS, are also altered in autism. The levels of phosphatidylethanolamine (PE) are decreased, and phosphatidylserine (PS) levels are increased in the erythrocyte membrane of children with autism as compared to their unaffected siblings. Several studies have suggested alterations in the activities of antioxidant enzymes such as superoxide dismutase, glutathione peroxidase, and catalase in autism. Additionally, altered glutathione levels and homocysteine/methionine metabolism, increased inflammation, excitotoxicity, as well as mitochondrial and immune dysfunction have been suggested in autism. Furthermore, environmental and genetic factors may increase vulnerability to oxidative stress in autism. Taken together, these studies suggest increased oxidative stress in autism that may contribute to the development of this disease. A mechanism linking oxidative stress with membrane lipid abnormalities, inflammation, aberrant immune response, impaired energy metabolism and excitotoxicity, leading to clinical symptoms and pathogenesis of autism is proposed.

<http://www.ncbi.nlm.nih.gov/pubmed/16766163>

“According to the Autism Society of America, autism is now considered to be an epidemic.”

Journal Of Toxicology And Environmental Health Part B, Critical Review • November 2006

Evidence of toxicity, oxidative stress, and neuronal insult in autism

Author information

Kern JK1, Jones AM.

Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas
Dallas, Texas 75390-9119, USA
janet.kern@UTSouthwestern.edu

Abstract

According to the Autism Society of America, autism is now considered to be an epidemic. The increase in the rate of autism revealed by epidemiological studies and government reports implicates the importance of external or environmental factors that may be changing. This article discusses the evidence for the case that some children with autism may become autistic from neuronal cell death or brain damage sometime after birth as result of insult; and addresses the hypotheses that toxicity and oxidative stress may be a cause of neuronal insult in autism. The article first describes the Purkinje cell loss found in autism, Purkinje cell physiology and vulnerability, and the evidence for postnatal cell loss. Second, the article describes the increased brain volume in autism and how it may be related to the Purkinje cell loss. Third, the evidence for toxicity and oxidative stress is covered and the possible involvement of glutathione is discussed. Finally, the article discusses what may be happening over the course of development and the multiple factors that may interplay and make these children more vulnerable to toxicity, oxidative stress, and neuronal insult.

<http://www.ncbi.nlm.nih.gov/pubmed/17090484>

Neurotoxicology • May 2008

Immunologic and neurodevelopmental susceptibilities of autism

Author information

Pessah IN1, Seegal RF, Lein PJ, LaSalle J, Yee BK, Van De Water J, Berman RF.
School of Veterinary Medicine, University of California, Davis, CA 95616, USA
inpessah@ucdavis.edu

Abstract

Symposium 5 focused on research approaches that are aimed at understanding common patterns of immunological and neurological dysfunction contributing to neurodevelopmental disorders such as autism and ADHD. The session focused on genetic, epigenetic, and environmental factors that might act in concert to influence autism risk, severity and co-morbidities, and immunological and neurobiological targets as etiologic contributors. The immune system of children at risk of autism may be therefore especially susceptible to psychological stressors, exposure to chemical triggers, and infectious agents. Identifying early biomarkers of risk provides tangible approaches toward designing studies in animals and humans that yield a better understanding of environmental risk factors, and can help identify rational intervention strategies to mitigate these risks.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2475601/>

The history of vaccinations in the light of the autism epidemic

Author information

Cave SF.

Cypress Integrative Medicine
Baton Rouge, Louisiana, USA

Abstract

Autism has been characterized as a behavioral disorder since it was first described by Leo Kanner in 1943. The number of autistic children has increased over the last decade. The incidence of autism was 1 in 10000 before the 1970s and has steadily increased to 1 in 150 in 2008 with a male:female predominance of 4:1. The cause of this epidemic has remained unknown, but several hypotheses have been studied. Many of these suggest an environmental trigger, such as the ethyl mercury contained in the preservative thimerosal, which has been used in vaccines since 1931. Other possible triggers associated with vaccinations are chemical toxins and live viruses. James has published studies suggesting a genetic predisposition in the families of autistic children, exposing them to a deficiency in glutathione and an inability to detoxify heavy metals. Vargas has shown autism to encompass ongoing inflammation in the brains of autistic children. The Hannah Poling vaccine decision was a landmark case. Poling's family was awarded funds for ongoing medical care of an autistic child who was found to have mitochondrial dysfunction exacerbated by vaccines that left her with autistic behavior and seizures. Several studies have emerged supporting the fact that a significant number of autistic children do have mitochondrial dysfunction. The impact that the Poling case will have on the ability of parents of autistic children to gain access to funds to enable them to properly care for their children remains to be seen.

<http://www.ncbi.nlm.nih.gov/pubmed/19043939>

“The Hannah Poling vaccine decision was a landmark case. Poling's family was awarded funds for ongoing medical care of an autistic child who was found to have mitochondrial dysfunction exacerbated by vaccines that left her with autistic behavior and seizures. Several studies have emerged supporting the fact that a significant number of autistic children do have mitochondrial dysfunction. The impact that the Poling case will have on the ability of parents of autistic children to gain access to funds to enable them to properly care for their children remains to be seen.”

A possible central mechanism in autism spectrum disorders Part 1

Author information

Blaylock RL.

Belhaven College
Jackson, Mississippi, USA

Abstract

The autism spectrum disorders (ASD) are a group of related neurodevelopmental disorders that have been increasing in incidence since the 1980s. Despite a considerable amount of data being collected from cases, a central mechanism has not been offered. A careful review of ASD cases discloses a number of events that adhere to an immunotoxic mechanism. This mechanism explains the link between excessive vaccination, use of aluminum and ethylmercury as vaccine adjuvants, food allergies, gut dysbiosis, and abnormal formation of the developing brain. It has now been shown that chronic microglial activation is present in autistic brains from age 5 years to age 44 years. A considerable amount of evidence, both experimental and clinical, indicates that repeated microglial activation can initiate priming of the microglia and that subsequent stimulation can produce an exaggerated microglial response that can be prolonged. It is also known that one phenotypic form of microglia activation can result in an outpouring of neurotoxic levels of the excitotoxins, glutamate and quinolinic acid. Studies have shown that careful control of brain glutamate levels is essential to brain pathway development and that excesses can result in arrest of neural migration, as well as dendritic and synaptic loss. It has also been shown that certain cytokines, such as TNF-alpha, can, via its receptor, interact with glutamate receptors to enhance the neurotoxic reaction. To describe this interaction I have coined the term immunotoxicity, which is described in this article.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19043938>

“This mechanism explains the link between excessive vaccination, use of aluminum and ethylmercury as vaccine adjuvants, food allergies, gut dysbiosis, and abnormal formation of the developing brain.”

A possible central mechanism
in autism spectrum disorders,
Part 2
immunoexcitotoxicity

Author information

Blaylock RL.

Belhaven College
Jackson, Mississippi, USA

Abstract

In this section, I explore the effects of mercury and inflammation on transsulfuration reactions, which can lead to elevations in androgens, and how this might relate to the male preponderance of autism spectrum disorders (ASD). It is known that mercury interferes with these biochemical reactions and that chronically elevated androgen levels also enhance the neurodevelopmental effects of excitotoxins. Both androgens and glutamate alter neuronal and glial calcium oscillations, which are known to regulate cell migration, maturation, and final brain cytoarchitectural structure. Studies have also shown high levels of DHEA and low levels of DHEA-S in ASD, which can result from both mercury toxicity and chronic inflammation. Chronic microglial activation appears to be a hallmark of ASD. Peripheral immune stimulation, mercury, and elevated levels of androgens can all stimulate microglial activation. Linked to both transsulfuration problems and chronic mercury toxicity are elevations in homocysteine levels in ASD patients. Homocysteine and especially its metabolic products are powerful excitotoxins. Intimately linked to elevations in DHEA, excitotoxicity and mercury toxicity are abnormalities in mitochondrial function. A number of studies have shown that reduced energy production by mitochondria greatly enhances excitotoxicity. Finally, I discuss the effects of chronic inflammation and elevated mercury levels on glutathione and metallothionein.

<http://www.ncbi.nlm.nih.gov/pubmed/19161050>

“In this section, I explore
the effects of mercury and inflammation
on transsulfuration reactions, which can
lead to elevations in androgens, and how this
might relate to the male preponderance of
autism spectrum disorders (ASD).”

A possible central mechanism
in autism spectrum disorders
Part 3
the role of excitotoxin food additives and the
synergistic effects of other environmental toxins

Author information

Blaylock RL.

Belhaven College, Jackson, Mississippi, USA.

Abstract

There is compelling evidence from a multitude of studies of various design indicating that foodborne excitotoxin additives can elevate blood and brain glutamate to levels known to cause neurodegeneration and in the developing brain, abnormal connectivity. Excitotoxins are also secreted by microglial activation when they are in an activated state. Recent studies, discussed in part 1 of this article, indicate that chronic microglial activation is common in the autistic brain. The interaction between excitotoxins, free radicals, lipid peroxidation products, inflammatory cytokines, and disruption of neuronal calcium homeostasis can result in brain changes suggestive of the pathological findings in cases of autism spectrum disorders. In addition, a number of environmental neurotoxins, such as fluoride, lead, cadmium, and aluminum, can result in these pathological and biochemical changes.

<http://www.ncbi.nlm.nih.gov/pubmed/19284184>

“There is compelling evidence from a multitude of studies of various design indicating that foodborne excitotoxin additives can elevate blood and brain glutamate to levels known to cause neurodegeneration and in the developing brain, abnormal connectivity.”

Dr. Paul Offit and Dr. Jon Poling: New England Journal of Medicine

By Anne Dachel

On August 7, the New England Journal of Medicine published the opposing opinions of Dr. Jon Poling, father of Hannah Poling, and Dr. Paul Offit, Infectious Disease Specialist from Children's Hospital of Philadelphia, on the Vaccine Court case in which the federal government conceded that vaccines were a factor in the development of autism in Hannah. Titled, Vaccines and Autism Revisited, the letters run in the "Correspondance" section of NEJM.

In the May 15 NEJM Perspective section, Offit split every hair he could to try and lessen the impact of the Poling case. He tried to convince the public that there was no scientific basis for the concession. Offit's remarks led to the August 7 response by Dr. Poling.

In his August 7 piece, Poling went after Offit's opinion about his daughter's case using phrases like "*Offit misrepresents my position,*" "*Offit confuses issues,*" and "*His opinion is unsupported by clinical trials.*"

Poling also said that he agreed with the remarks made by former head of the National Institutes of Health, Dr. Bernadine Healy, on CBS News, who said, "*I don't think you should ever turn your back on any scientific hypothesis because you're afraid of what it might show. . . . If you know that susceptible group, you can save those children. If you turn your back on the notion there is a susceptible group . . . what can I say?*"

The fair and balanced NEJM then allowed Offit to respond to Poling at the bottom of the article. Offit defended his remarks by claiming that the science is on his side and the facts support his view. He made one stunning comment. He brought up Healy's remarks about the need for further study of a subgroup of children who might be damaged by vaccines. Offit wrote, "*Now, Poling and Healy are standard-bearers for the poorly conceived hypothesis that children receive too many vaccines too early. As a consequence, some parents are choosing to delay, withhold, or separate vaccines.*"

That was really a low blow. To claim that one of the top doctors in the U.S. was promoting a "*poorly conceived hypothesis*" and that "*the public airing of that hypothesis caused thousands of parents to avoid the MMR; many children were hospitalized and several died from measles as a result,*" was really pitting doctor against doctor in the vaccine war. (Amanda Peet just told us on Good Morning America, "*Please don't listen to me. . . . Go to the experts.*" Well, here they are and they don't agree!)

I had to go back to the remarks made by Healy on CBS Evening News (Click [HERE](#)) on May 12 to figure out what exactly she said that could be described as a "*poorly conceived hypothesis.*" Soft-spoken and reasonable in her conversation with CBS reporter Sharyl Attkisson, Healy called for more studies on vaccines and autism. She said that we need to do the studies to find out if there is a subgroup of children who are susceptible to a particular vaccine, to vaccines plural, or to components in vaccines. She urged scientists "*to take another look at that hypothesis, not deny it.*"

Healy said nothing to undermine that vaccine program. She told the public, "*A susceptible group does not mean that vaccines aren't good.*" She firmly stated that she didn't believe "*the public would lose faith in vaccines.*"

We have the most heated controversy in medicine today over vaccines and Healy addressed it by saying, "*It is the job of the public health community and of physicians to be out there and to say yes, we can make it safer because we are able to say, this is a subset. We're going to deliver it in a way we think is safer.*"

Sharyl Attkisson then brought up the fact that health officials will deny there is a link between vaccines and autism. They say there's no evidence.

Healy, shaking her head, firmly stated twice, "*You can't say that.*"

Why? Because they haven't studied "*the population that got sick.*"

Healy said that she hasn't seen "*major studies that focus on 300 kids who got autistic symptoms within a period of a few weeks of getting a vaccine.*"

Healy noted the primate and mouse studies that have been too quickly dismissed. She challenged the conclusions of the IOM Report of 2004 where we were told not to "*pursue susceptibility groups.*" Healy said, "*I really take issue with that conclusion. The reason they didn't want to look for those susceptibility groups was because if they found them, . . . that would scare the public away.*"

Offit might think that the endless epidemiological studies have settled the question, but Healy made it clear, "*Populations do not test causality, they test associations. You have to go into the laboratory.*"

Healy chided the medical community by saying, "*The fact that there is concern that you don't want to know that susceptible group is a real disappointment to me.*"

She ended a chilling comment about vaccines and the link to autism: "*The question has not been answered.*"

From his remarks, it's pretty obvious that Offit is opposed to any open scientific inquiry. Healy didn't say that all children were receiving too many too soon, as Offit claimed. She said we need to find that subgroup of children.

The CDC studies that are always being promoted in the press haven't settled a thing. The public is growing increasingly skeptical of health officials and their claims. They don't want to risk the health of their children by giving them vaccines with possibly damaging side effects. Healy's was the refreshing voice of reason in this debate. Too bad Offit refused to listen.

Perhaps the ending of the Poling/Offit pieces said it all. After Poling's remarks, he listed his conflicts from the lecturing and consulting fees he had received from different pharmaceutical companies. At the end of Offit's, all we see is "Children's Hospital of Philadelphia." Here's the body copy from NEJM:

Vaccines and Autism Revisited
Related Article
by Offit, P. A.

To the Editor: In his Perspective article on a possible connection between vaccines and autism, Offit (May 15 issue)1 speculates about my daughter, Hannah, and repeats inaccuracies from a March New York Times opinion piece that was officially corrected by the Times and our April 5 letter.

By omitting critical information from my March 6, 2008, statement, Offit misrepresents my position. I said, "*Many in the autism community and their champions believe that the result in this case may well signify a land-*

mark decision as it pertains to children developing autism following vaccinations. This still remains to be seen, but currently there are almost 5,000 other cases pending.”

Offit’s remarks about Hannah’s case are not evidence-based. He has no access to my daughter’s personal medical records, legal documents, or affidavits. In contrast, physicians from the Department of Health and Human Services (DHHS) who studied this information recommended that the government concede Hannah’s case. The clinical history Offit presents contains significant inaccuracies, and the resulting conclusions are consequently flawed.

Offit confuses issues by comparing Hannah’s case with unrelated decisions in “vaccine court.” The Office of the Secretary of DHHS, through the Department of Justice, conceded Hannah’s case. There was no courtroom hearing and no decision from the “unusual vaccine court.”

Offit is frequently cited regarding the “biologically plausible” theory that simultaneous administration of multiple vaccines is safe. His opinion is unsupported by clinical trials, much less investigations in potentially susceptible subpopulations.

Despite the high frequency of mitochondrial dysfunction in autistic children,² studies have not established primary or secondary roles. To explore this question, we need an immunization database for children with metabolic disorders to establish safety guidelines³ and improve vaccine safety for minority subgroups of children.

I agree with the statement of Bernadine Healy, former director of the National Institutes of Health, who said, “*I don’t think you should ever turn your back on any scientific hypothesis because you’re afraid of what it might*

*show. . . . If you know that susceptible group, you can save those children. If you turn your back on the notion there is a susceptible group . . . what can I say?”*⁴ Also commendable is the new 5-year research plan of the National Vaccine Advisory Committee, which will entail the study of minority subpopulations, including patients with mitochondrial disorders.⁵

A strong, safe vaccination program is a cornerstone of public health. Misrepresenting Hannah Poling v. HHS to the medical profession does not improve confidence in the immunization program or advance science toward an understanding of how and why regressive encephalopathy with autistic features follows vaccination in susceptible children.

Jon S. Poling, M.D., Ph.D.
Athens Neurological Associates
Athens, GA 30606

Dr. Poling is the father of Hannah Poling and reports receiving consulting or lecture fees from Pfizer, Eisai, Ortho-McNeil, Biogen, Teva, Immunex, and Allergan. No other potential conflict of interest relevant to this letter was reported.

References

1. Offit PA. Vaccines and autism revisited -- the Hannah Poling case. *N Engl J Med* 2008;358:2089-2091. [Free Full Text]
2. Oliveira G, Ataíde A, Marques C, et al. Epidemiology of autism spectrum disorder in Portugal: prevalence, clinical characterization, and medical conditions. *Dev Med Child Neurol* 2007;49:726-733. [ISI][Medline]
3. Brady MT. Immunization recommendations for children with metabolic disorders: more data would help. *Pediatrics* 2006;118:810-813. [Free Full Text]
4. CBS News. The “open question” on vaccines and autism. May 2008. (Accessed July 18, 2008, at <http://www.cbsnews.com/blogs/2008/05/12/couricandco/entry4090144.shtml>.)
5. Draft ISO Scientific Agenda for NVAC Vaccine Safety Working Group. Centers for Disease Control and Prevention’s Immunization Safety Office scientific agenda: draft recommendations. April 4, 2008. In: Scientific review. Washington, DC: National Vaccine Advisory Committee Vaccine Safety Working Group, April 11, 2008:30. (Accessed July 18, 2008, at http://www.cdc.gov/vaccinesafety/00_pdf/draft_agenda_recommendations_080404.pdf.)

The author replies: Poling implies that by omitting his phrase “*many in the autism community and their champions,*” I unfairly attributed the notion that vaccines might cause autism to him alone. However, Dr. Poling’s public announcement of the DHHS concession to the press and his subsequent appearances on national television and at autism conferences suggest that he is, at the very least, a vocal centerpiece of that community.

Poling claims that I didn’t have access to his daughter’s medical records. My information was based on a verbatim transcript of the DHHS concession, which stated that his daughter had had frequent ear infections and a series of viral infections early in life. These infections, which are a far greater immunologic challenge than attenuated or inactivated vaccines, are not in dispute.

Poling states that my assertion that the administration of multiple vaccines is safe is an “*opinion . . . unsupported by clinical trials.*” But studies of concomitant use, which are required by the Food and Drug Administration before licensure to show that new vaccines do not affect the safety or immunogenicity of existing vaccines or vice versa, have clearly shown that multiple vaccines can be administered safely.

Poling agrees with Healy that “*you should [n]ever turn your back on any scientific hypothesis because you’re afraid of what it might show.*” However, scientists have not been afraid to test the hypothesis that vaccines might cause autism. Far from it: the ill-founded notion that the measles–mumps–rubella (MMR) vaccine caused autism was tested in 10 epidemiologic studies. Unfortunately, the public airing of that hypothesis caused thousands of parents to avoid the MMR; many children were hospitalized and several died from measles as a result.^{1,2,3,4} Now, Poling and Healy are standard-bearers for the poorly conceived hypothesis that children receive too many vaccines too early. As a consequence, some parents are choosing to delay, withhold, or separate vaccines. The problem here is not a failure of scientists to consider hypotheses; rather, it is a failure of the media and the public to distinguish hypotheses from scientific evidence.

Paul A. Offit, M.D.
Children’s Hospital of Philadelphia
Philadelphia, PA 19104

“Younger ages at diagnosis, differential migration, changes in diagnostic criteria, and inclusion of milder cases do not fully explain the observed increases.”

Epidemiology • January 2009

The Rise in Autism and the Role of Age at Diagnosis

Hertz-Picciotto, Irva^{a,b}; Delwiche, Loraa

Abstract

Background

Autism prevalence in California, based on individuals eligible for state-funded services, rose throughout the 1990s. The extent to which this trend is explained by changes in age at diagnosis or inclusion of milder cases has not been previously evaluated.

Methods

Autism cases were identified from 1990 through 2006 in databases of the California Department of Developmental Services, which coordinates services for individuals with specific developmental disorders. The main outcomes were population incident cases younger than age 10 years for each quarter, cumulative incidence by age and birth year, age-specific incidence rates stratified by birth year, and proportions of diagnoses by age across birth years.

Results

Autism incidence in children rose throughout the period. Cumulative incidence to 5 years of age per 10,000 births rose consistently from 6.2 for 1990 births to 42.5 for 2001 births. Age-specific incidence rates increased most steeply for 2- and 3-year olds. The proportion diagnosed by age 5 years increased only slightly, from 54% for 1990 births to 61% for 1996 births. Changing age at diagnosis can explain a 12% increase, and inclusion of milder cases, a 56% increase.

Conclusions

Autism incidence in California shows no sign yet of plateauing. Younger ages at diagnosis, differential migration, changes in diagnostic criteria, and inclusion of milder cases do not fully explain the observed increases. Other artifacts have yet to be quantified, and as a result, the extent to which the continued rise represents a true increase in the occurrence of autism remains unclear.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4113600/>

Elevated immune response in the brain of autistic patients

Author information

Li X1, Chauhan A, Sheikh AM, Patil S,
Chauhan V, Li XM, Ji L, Brown T, Malik M.

Department of Neurochemistry
NY State Institute for Basic Research in Developmental Disabilities
NY 10314, New York, USA
xiaohong.li@mssm.edu

Abstract

This study determined immune activities in the brain of ASD patients and matched normal subjects by examining cytokines in the brain tissue. Our results showed that proinflammatory cytokines (TNF-alpha, IL-6 and GM-CSF), Th1 cytokine (IFN-gamma) and chemokine (IL-8) were significantly increased in the brains of ASD patients compared with the controls. However the Th2 cytokines (IL-4, IL-5 and IL-10) showed no significant difference. The Th1/Th2 ratio was also significantly increased in ASD patients.

CONCLUSION

ASD patients displayed an increased innate and adaptive immune response through the Th1 pathway, suggesting that localized brain inflammation and auto-immune disorder may be involved in the pathogenesis of ASD.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2770268/>

“ASD patients displayed an increased innate and adaptive immune response through the Th1 pathway, suggesting that localized brain inflammation and autoimmune disorder may be involved in the pathogenesis of ASD.”

Immune-glutamatergic dysfunction as a central mechanism of the autism spectrum disorders

Author information

Blaylock RL1, Strunecka A.
Belhaven College
Jackson, Mississippi, USA

Abstract

Despite the great number of observations being made concerning cellular and the molecular dysfunctions associated with autism spectrum disorders (ASD), the basic central mechanism of these disorders has not been proposed in the major scientific literature. Our review brings evidence that most heterogeneous symptoms of ASD have a common set of events closely connected with dysregulation of glutamatergic neurotransmission in the brain with enhancement of excitatory receptor function by pro-inflammatory immune cytokines as the underlying mechanism. We suggest that environmental and dietary excitotoxins, mercury, fluoride, and aluminum can exacerbate the pathological and clinical problems by worsening excitotoxicity and by microglial priming. In addition, each has effects on cell signaling that can affect neurodevelopment and neuronal function. Our hypothesis opens the door to a number of new treatment modes, including the nutritional factors that naturally reduce excitotoxicity and brain inflammation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19149568>

“... environmental and dietary excitotoxins, mercury, fluoride, and aluminum can exacerbate the pathological and clinical problems by worsening excitotoxicity and by microglial priming. In addition, each has effects on cell signaling that can affect neurodevelopment and neuronal function.”

Journal Of Toxicology • August 2009

The severity of autism is associated with toxic metal body burden and red blood cell glutathione levels

Author information

Adams JB1, Baral M, Geis E, Mitchell J, Ingram J, Hensley A, Zappia I, Newmark S, Gehn E, Rubin RA, Mitchell K, Bradstreet J, El-Dahr JM.

Division of Basic Medical Sciences
Southwest College of Naturopathic Medicine
Tempe, AZ 85282, USA

Abstract

This study investigated the relationship of children's autism symptoms with their toxic metal body burden and red blood cell (RBC) glutathione levels. In children ages 3-8 years, the severity of autism was assessed using four tools: ADOS, PDD-BI, ATEC, and SAS. Toxic metal body burden was assessed by measuring urinary excretion of toxic metals, both before and after oral dimercaptosuccinic acid (DMSA). Multiple positive correlations were found between the severity of autism and the urinary excretion of toxic metals. Variations in the severity of autism measurements could be explained, in part, by regression analyses of urinary excretion of toxic metals before and after DMSA and the level of RBC glutathione (adjusted R(2) of 0.22-0.45, P < .005 in all cases). This study demonstrates a significant positive association between the severity of autism and the relative body burden of toxic metals.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20107587>

“Multiple positive correlations were found between the severity of autism and the urinary excretion of toxic metals.”

One carbon metabolism disturbances and the C677T MTHFR gene polymorphism in children with autism spectrum disorders

Author information

Paca SP1, Dronca E, Kaucsár T, Craciun EC,
Endreffy E, Ferencz BK, Iftene F, Benga I, Cornean R, Banerjee R, Dronca M.

Department of Medical Biochemistry
Faculty of Medicine, Iuliu HaTieganu University of Medicine and Pharmacy
Cluj-Napoca, Romania

Abstract

Autism spectrum disorders (ASDs), which include the prototypic autistic disorder (AD), Asperger's syndrome (AS) and pervasive developmental disorders not otherwise specified (PDD-NOS), are complex neurodevelopmental conditions of unknown aetiology. The current study investigated the metabolites in the methionine cycle, the transsulphuration pathway, folate, vitamin B(12) and the C677T polymorphism of the MTHFR gene in three groups of children diagnosed with AD (n= 15), AS (n= 5) and PDD-NOS (n= 19) and their age- and sex-matched controls (n= 25). No metabolic disturbances were seen in the AS patients, while in the AD and PDD-NOS groups, lower plasma levels of methionine (P= 0.01 and P= 0.03, respectively) and alpha-aminobutyrate were observed (P= 0.01 and P= 0.001, respectively). Only in the AD group, plasma cysteine (P= 0.02) and total blood glutathione (P= 0.02) were found to be reduced. Although there was a trend towards lower levels of serine, glycine, N, N-dimethylglycine in AD patients, the plasma levels of these metabolites as well as the levels of homocysteine and cystathionine were not statistically different in any of the ASDs groups. The serum levels of vitamin B(12) and folate were in the normal range. The results of the MTHFR gene analysis showed a normal distribution of the C677T polymorphism in children with ASDs, but the frequency of the 677T allele was slightly more prevalent in AD patients. Our study indicates a possible role for the alterations in one carbon metabolism in the pathophysiology of ASDs and provides, for the first time, preliminary evidence for metabolic and genetic differences between clinical subtypes of ASDs.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4496129/>

“Our study indicates
a possible role for the alterations
in one carbon metabolism in the
pathophysiology of ASDs and provides,
for the first time, preliminary evidence
for metabolic and genetic differences
between clinical subtypes of ASDs.”

Immune-glutamatergic dysfunction as a central mechanism of the autism spectrum disorders

Author information

Blaylock RL1, Strunecka A.

Belhaven College
Jackson, Mississippi, USA

Abstract

Despite the great number of observations being made concerning cellular and the molecular dysfunctions associated with autism spectrum disorders (ASD), the basic central mechanism of these disorders has not been proposed in the major scientific literature. Our review brings evidence that most heterogeneous symptoms of ASD have a common set of events closely connected with dysregulation of glutamatergic neurotransmission in the brain with enhancement of excitatory receptor function by pro-inflammatory immune cytokines as the underlying mechanism. We suggest that environmental and dietary excitotoxins, mercury, fluoride, and aluminum can exacerbate the pathological and clinical problems by worsening excitotoxicity and by microglial priming. In addition, each has effects on cell signaling that can affect neurodevelopment and neuronal function. Our hypothesis opens the door to a number of new treatment modes, including the nutritional factors that naturally reduce excitotoxicity and brain inflammation.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=19149568>

“We suggest that environmental and dietary excitotoxins, mercury, fluoride, and aluminum can exacerbate the pathological and clinical problems by worsening excitotoxicity and by microglial priming. In addition, each has effects on cell signaling that can affect neurodevelopment and neuronal function.”

The review of most frequently
occurring medical disorders related to
aetiology of autism and the methods of treatment

Author information

Cubala-Kucharska M.

Foundation for the Development of Integrative Medicine
Piaseczno, Poland
info@drcubala.com

Abstract

The medical understanding of autism has changed since it was first defined by Kanner. Nowadays medicine identifies many medical abnormalities and diseases, which may underline or aggravate the cognitive aspect, behavioural issues and general health in autists. This includes chronic inflammation of gastrointestinal tract, dysbiosis, maldigestion, malabsorption, malnutrition, food intolerance, allergies, chronic viral, fungal and bacterial infections, impaired kidney function, impaired detoxification of endo- and exotoxins, disorders of metal ion transportation. Treatment of the above mentioned conditions combined with improving detoxification mechanisms, followed by a special diet and individually customized supplementation of nutritional deficiencies may lead to the improvement of the functioning of these patients, changing their level of functioning and self-dependence. The aim of this paper is to present medical problems of children with autism which may be identified and treated by general practitioners as a review of current medical papers related to Autism Spectrum Disorder, in the context of author's professional experience, based on the medical cases from author's practice.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20628438>

“This includes
chronic inflammation
of gastrointestinal tract,
dysbiosis, maldigestion,
malabsorption, malnutrition,
food intolerance, allergies,
chronic viral, fungal and bacterial infections,
impaired kidney function,
impaired detoxification of endo- and exotoxins,
disorders of metal ion transportation.”

Age-dependent lower or higher levels of hair mercury in autistic children than in healthy controls

Maria Dorota Majewska^{1*}, Ewa Urbanowicz³,
Paulina Rok-Bujko³, Irena Namyslowska³, Pawel Mierzejewski²

1. Marie Curie Chair, Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology, Warsaw, Poland
majewska@ipin.edu.pl

2. Department of Pharmacology and Physiology of the Nervous System
Institute of Psychiatry and Neurology, Warsaw, Poland

3. Department of Child and Adolescent Psychiatry
Institute of Psychiatry and Neurology, Warsaw, Poland

Abstract

An association between autism and early life exposure to mercury is a hotly debated issue. In this study, 91 autistic Polish children, male and female, 3-4 and 7-9 years old, were compared to 75 age- and sex-matched healthy children with respect to: demographic, perinatal, clinical and developmental measures, parental age, birth order, morphometric measures, vaccination history, and hair mercury content. In demographic and perinatal measures there were no consistent differences between the autistic and control groups. Autistic children had a significantly greater prevalence of adverse reactions after vaccinations and abnormal development than controls. Between 45 and 80% of autistic children experienced developmental regress. Autistic children significantly differed from healthy peers in the concentrations of mercury in hair: younger autistics had lower levels, while older - higher levels than their respective controls. The results suggest that autistic children differ from healthy children in metabolism of mercury, which seems to change with age.

<https://app.box.com/s/938bs6e55098v78c4tnuyca38p2xnnqu>

“The results suggest that
autistic children differ from healthy children
in metabolism of mercury ...”

Sorting out the spinning of autism: heavy metals and the question of incidence

Mary Catherine DeSoto* and Robert T. Hitlan

Department of Psychology, University of Northern Iowa
Cedar Falls, Iowa USA
cathy.desoto@uni.edu

Abstract

The reasons for the rise in autism prevalence are a subject of heated professional debate. Featuring a critical appraisal of some research used to question whether rising levels of autism are related to environmental exposure to toxins (Soden et al. 2007, Barbaresi et al. 2009, Thompson et al. 2007) we aim to evaluate the actual state of scientific knowledge. In addition, we surveyed the empirical research on the topic of autism and heavy metal toxins. In our opinion empirical investigations are finding support for a link with heavy metal toxins. The various causes that have led to the increase in autism diagnosis are likely multi-faceted, and understanding the causes is one of the most important health topics today. We argue that scientific research does not support rejecting the link between the neurodevelopmental disorder of autism and toxic exposures.

<https://app.box.com/s/rs4j52jgdbvj0a7qroo8sgxv7t06ly9>

“We argue that scientific research does not support rejecting the link between the neurodevelopmental disorder of autism and toxic exposures.”

Association of autism with polyomavirus infection in postmortem brains

Author information

Lintas C1, Altieri L, Lombardi F, Sacco R, Persico AM.

Laboratory of Molecular Psychiatry and Neurogenetics
University Campus Bio-Medico, Rome, Italy

Abstract

Autism is a highly heritable behavioral disorder. Yet, two decades of genetic investigation have unveiled extremely few cases that can be solely explained on the basis of de novo mutations or cytogenetic abnormalities. Vertical viral transmission represents a nongenetic mechanism of disease compatible with high parent-to-offspring transmission and with low rates of disease-specific genetic abnormalities. Vertically transmitted viruses should be found more frequently in the affected tissues of autistic individuals compared to controls. Our initial step was thus to assess by nested polymerase chain reaction (PCR) and DNA sequence analysis the presence of cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus type 1 (HSV1), herpes simplex virus type 2 (HSV2), human herpes virus 6 (HHV6), BK virus (BKV), JC virus (JCV), and simian virus 40 (SV40) in genomic DNA extracted from post-mortem temporocortical tissue (Brodmann areas 41/42) belonging to 15 autistic patients and 13 controls. BKV, JCV, and SV40 combined are significantly more frequent among autistic patients compared to controls (67% versus 23%, respectively; $P < .05$). The majority of positives yielded archetypal sequences, whereas six patients and two controls unveiled single-base pair changes in two or more sequenced clones. No association is present with the remaining viruses, which are found in relatively few individuals ($N \leq 3$). Also polyviral infections tend to occur more frequently in the brains of autistic patients compared to controls (40% versus 7.7%, respectively; $P = .08$). Follow-up studies exploring vertical viral transmission as a possible pathogenic mechanism in autistic disorder should focus on, but not be limited to, the role of polyomaviruses.

<http://www.ncbi.nlm.nih.gov/pubmed/20345322>

“BKV, JCV, and SV40 [viruses] combined are significantly more frequent among autistic patients compared to controls (67% versus 23%, respectively; $P < .05$).”

Autism spectrum disorders in extremely preterm children

Author information

Johnson S1, Hollis C, Kochhar P,
Hennessy E, Wolke D, Marlow N.

Institute for Women's Health
University College, London
United Kingdom

Abstract

OBJECTIVES

To investigate the prevalence, correlates, and antecedents of autism spectrum disorders (ASD) in extremely preterm children.

STUDY DESIGN

We conducted a prospective study of all births <26 weeks gestation in the United Kingdom and Ireland in 1995. Of 307 survivors at 11 years, 219 (71%) were assessed and compared with 153 term-born classmates. Parents completed the Social Communication Questionnaire (SCQ) to assess autism spectrum symptoms, and ASD were diagnosed by using a psychiatric evaluation. An IQ test and clinical evaluation were also administered. Longitudinal outcome data were available for extremely preterm children.

RESULTS

Extremely preterm children had significantly higher SCQ scores than classmates (mean difference, 4.6 points; 95% CI, 3.4-5.8). Sixteen extremely preterm children (8%) were assigned an ASD diagnosis, compared with none of the classmates. By hospital discharge, male sex, lower gestation, vaginal breech delivery, abnormal cerebral ultrasound scanning results, and not having had breast milk were independently associated with autism spectrum symptoms. By 6 years, independent associates were cognitive impairment, inattention and peer problems, withdrawn behavior at 2.5 years, and not having had breast milk.

CONCLUSIONS

Extremely preterm children are at increased risk for autism spectrum symptoms and ASD in middle childhood. These symptoms and disorders were associated with neurocognitive outcomes, suggesting that ASD may result from abnormal brain development in this population.

“Extremely preterm children
are at increased risk for autism
spectrum symptoms and ASD
in middle childhood.”

Autism spectrum disorders in extremely preterm children

Author information

Johnson S1, Hollis C, Kochhar P,
Hennessy E, Wolke D, Marlow N.

Institute for Women's Health
University College, London
United Kingdom
s.j.johnson@ucl.ac.uk

Abstract

OBJECTIVES

To investigate the prevalence, correlates, and antecedents of autism spectrum disorders (ASD) in extremely preterm children.

STUDY DESIGN

We conducted a prospective study of all births <26 weeks gestation in the United Kingdom and Ireland in 1995. Of 307 survivors at 11 years, 219 (71%) were assessed and compared with 153 term-born classmates. Parents completed the Social Communication Questionnaire (SCQ) to assess autism spectrum symptoms, and ASD were diagnosed by using a psychiatric evaluation. An IQ test and clinical evaluation were also administered. Longitudinal outcome data were available for extremely preterm children.

RESULTS

Extremely preterm children had significantly higher SCQ scores than classmates (mean difference, 4.6 points; 95% CI, 3.4-5.8). Sixteen extremely preterm children (8%) were assigned an ASD diagnosis, compared with none of the classmates. By hospital discharge, male sex, lower gestation, vaginal breech delivery, abnormal cerebral ultrasound scanning results, and not having had breast milk were independently associated with autism spectrum symptoms. By 6 years, independent associates were cognitive impairment, inattention and peer problems, withdrawn behavior at 2.5 years, and not having had breast milk.

CONCLUSIONS

Extremely preterm children are at increased risk for autism spectrum symptoms and ASD in middle childhood. These symptoms and disorders were associated with neurocognitive outcomes, suggesting that ASD may result from abnormal brain development in this population.

Porphyrinuria in Korean children with autism: correlation with oxidative stress

Author information

Youn SI1, Jin SH, Kim SH, Lim S.

Department of Basic Eastern Medical Science
Graduate School, KyungHee University
Seoul, Republic of Korea

Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder believed to be associated with heavy metal exposure, especially mercury (Hg), and is characterized by disturbances in metal elimination. Various studies correlated elevated heavy metal body burden with ASD diagnoses as evidenced by increased urinary porphyrin levels in patients. Urinary porphyrins were also determined in Korean patients diagnosed with ASD (n = 65) who visited AK Eastern Medicinal Clinic in Kangnam-gu, Seoul, from June 2007 to September 2008, compared to controls (n = 9) residing in the same area, by means of Metamatrix (CLIA-approved) laboratory testing. Further, urinary organic acids as indicators of hepatic detoxification/oxidative stress were also analyzed among patients diagnosed with ASD. Significant increases were found in patients diagnosed with ASD for proporphyrins, pentacarboxyporphyrin, precoproporphyrin, coproporphyrins, and total porphyrins. Significant correlations were observed between hepatic detoxification/oxidative stress markers and urinary porphyrins. In agreement with published data, the present results demonstrated that measurement of porphyrins serves as a reliable tool for diagnosis of heavy metal involvement in ASD.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=20391113>

“Autism spectrum disorder (ASD) is a neurodevelopmental disorder believed to be associated with heavy metal exposure, especially mercury (Hg), and is characterized by disturbances in metal elimination. Significant correlations were observed between hepatic detoxification/oxidative stress markers and urinary porphyrins. In agreement with published data, the present results demonstrated that measurement of porphyrins serves as a reliable tool for diagnosis of heavy metal involvement in Autistic Spectrum Disorder.”

The biological basis of autism spectrum disorders: Understanding causation and treatment by clinical geneticists

Geier DA1, Kern JK, Geier MR.

Author information

The Institute of Chronic Illnesses, Inc.
Silver Spring, Maryland, USA

Abstract

Autism spectrum disorders (ASDs) also known as pervasive developmental disorders (PDD) are a behaviorally defined group of neurodevelopmental disorders that are usually diagnosed in early childhood. ASDs disproportionately affect male children. Mercury (Hg) a heavy metal, is widespread and persistent in the environment. Mercury is a ubiquitous source of danger in fish, drugs, fungicides/herbicides, dental fillings, thermometers, and many other products. Elevated Hg concentrations may remain in the brain from several years to decades following exposure. This is important because investigators have long recognized that Hg is a neurodevelopmental poison; it can cause problems in neuronal cell migration and division, and can ultimately cause cell degeneration and death. Case-reports of patients have described developmental regressions with ASD symptoms following fetal and/or early childhood Hg exposure, and epidemiological studies have linked exposure to Hg with an elevated risk of a patient being diagnosed with an ASD. Immune, sensory, neurological, motor, and behavioral dysfunctions similar to traits defining or associated with ASDs were reported following Hg intoxication with similarities extending to neuroanatomy, neurotransmitters, and biochemistry. The sexual dimorphism of ASDs may result from synergistic neurotoxicity caused by the interaction of testosterone and Hg; in contrast, estrogen is protective, mitigating the toxicity of Hg. Mercury exposure may significantly increase androgen levels, and as a result, patients diagnosed with an ASD may significantly benefit from anti-androgen therapy. Finally, the clinical geneticist has a wealth of biomarkers to evaluate and treat patients diagnosed with an ASD.

<http://www.ncbi.nlm.nih.gov/pubmed/20628444>

Theoretical aspects of autism: causes—a review

Author information

Ratajczak HV1.
hratajcz@comcast.net

Abstract

Autism, a member of the pervasive developmental disorders (PDDs), has been increasing dramatically since its description by Leo Kanner in 1943. First estimated to occur in 4 to 5 per 10,000 children, the incidence of autism is now 1 per 110 in the United States, and 1 per 64 in the United Kingdom, with similar incidences throughout the world. Searching information from 1943 to the present in PubMed and Ovid Medline databases, this review summarizes results that correlate the timing of changes in incidence with environmental changes. Autism could result from more than one cause, with different manifestations in different individuals that share common symptoms. Documented causes of autism include genetic mutations and/or deletions, viral infections, and encephalitis following vaccination. Therefore, autism is the result of genetic defects and/or inflammation of the brain. The inflammation could be caused by a defective placenta, immature blood-brain barrier, the immune response of the mother to infection while pregnant, a premature birth, encephalitis in the child after birth, or a toxic environment.

<http://www.ncbi.nlm.nih.gov/pubmed/21299355>

Trends in the prevalence of developmental disabilities in US children, 1997-2008

Author information

Boyle CA1, Boulet S, Schieve LA, Cohen RA,
Blumberg SJ, Yeargin-Allsopp M, Visser S, Kogan MD.

National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention, Atlanta, GA 30333, USA
cboyle@cdc.gov

Abstract

OBJECTIVE

To fill gaps in crucial data needed for health and educational planning, we determined the prevalence of developmental disabilities in US children and in selected populations for a recent 12-year period.

PARTICIPANTS AND METHODS

We used data on children aged 3 to 17 years from the 1997-2008 National Health Interview Surveys, which are ongoing nationally representative samples of US households. Parent-reported diagnoses of the following were included: attention deficit hyperactivity disorder; intellectual disability; cerebral palsy; autism; seizures; stuttering or stammering; moderate to profound hearing loss; blindness; learning disorders; and/or other developmental delays.

RESULTS

Boys had a higher prevalence overall and for a number of select disabilities compared with girls. Hispanic children had the lowest prevalence for a number of disabilities compared with non-Hispanic white and black children. Low income and public health insurance were associated with a higher prevalence of many disabilities. Prevalence of any developmental disability increased from 12.84% to 15.04% over 12 years. Autism, attention deficit hyperactivity disorder, and other developmental delays increased, whereas hearing loss showed a significant decline. These trends were found in all of the sociodemographic subgroups, except for autism in non-Hispanic black children.

CONCLUSIONS

Developmental disabilities are common and were reported in ~1 in 6 children in the United States in 2006-2008. The number of children with select developmental disabilities (autism, attention deficit hyperactivity disorder, and other developmental delays) has increased, requiring more health and education services. Additional study of the influence of risk-factor shifts, changes in acceptance, and benefits of early services is needed.

“Developmental disabilities are common and were reported in 1 in 6 children in the United States in 2006-2008. The number of children with select developmental disabilities (autism, attention deficit hyperactivity disorder, and other developmental delays) has increased, requiring more health and education services.”

Prevalence of Autism Spectrum Disorders

Autism and Developmental Disabilities Monitoring Network • 14 Sites USA
Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008

Corresponding author: Jon Baio, EdS, National Center on Birth Defects and Developmental Disabilities
CDC, 1600 Clifton Road, MS E-86, Atlanta, GA 30333
Telephone: 404-498-3873; Fax: 404-498-3550
jbaio@cdc.gov.

Abstract

Problem/Condition

Autism spectrum disorders (ASDs) are a group of developmental disabilities characterized by impairments in social interaction and communication and by restricted, repetitive, and stereotyped patterns of behavior. Symptoms typically are apparent before age 3 years. The complex nature of these disorders, coupled with a lack of biologic markers for diagnosis and changes in clinical definitions over time, creates challenges in monitoring the prevalence of ASDs. Accurate reporting of data is essential to understand the prevalence of ASDs in the population and can help direct research.

Period Covered

2008

Description of System

The Autism and Developmental Disabilities Monitoring (ADDM) Network is an active surveillance system that estimates the prevalence of ASDs and describes other characteristics among children aged 8 years whose parents or guardians reside within 14 ADDM sites in the United States. ADDM does not rely on professional or family reporting of an existing ASD diagnosis or classification to ascertain case status. Instead, information is obtained from children's evaluation records to determine the presence of ASD symptoms at any time from birth through the end of the year when the child reaches age 8 years. ADDM focuses on children aged 8 years because a baseline study conducted by CDC demonstrated that this is the age of identified peak prevalence. A child is included as meeting the surveillance case definition for an ASD if he or she displays behaviors (as described on a comprehensive evaluation completed by a qualified professional) consistent with the American Psychiatric Association's Diagnostic and Statistical Manual-IV, Text Revision (DSM-IV-TR) diagnostic criteria for any of the following conditions: Autistic Disorder; Pervasive Developmental Disorder–Not Otherwise Specified (PDD-NOS, including Atypical Autism); or Asperger Disorder. The first phase of the ADDM methodology involves screening and abstraction of

comprehensive evaluations completed by professional providers at multiple data sources in the community. Multiple data sources are included, ranging from general pediatric health clinics to specialized programs for children with developmental disabilities. In addition, many ADDM sites also review and abstract records of children receiving special education services in public schools. In the second phase of the study, all abstracted evaluations are reviewed by trained clinicians to determine ASD case status. Because the case definition and surveillance methods have remained consistent across all ADDM surveillance years to date, comparisons to results for earlier surveillance years can be made. This report provides updated ASD prevalence estimates from the 2008 surveillance year, representing 14 ADDM areas in the United States. In addition to prevalence estimates, characteristics of the population of children with ASDs are described, as well as detailed comparisons of the 2008 surveillance year findings with those for the 2002 and 2006 surveillance years.

Results

For 2008, the overall estimated prevalence of ASDs among the 14 ADDM sites was 11.3 per 1,000 (one in 88) children aged 8 years who were living in these communities during 2008. Overall ASD prevalence estimates varied widely across all sites (range: 4.8–21.2 per 1,000 children aged 8 years). ASD prevalence estimates also varied widely by sex and by racial/ethnic group. Approximately one in 54 boys and one in 252 girls living in the ADDM Network communities were identified as having ASDs. Comparison of 2008 findings with those for earlier surveillance years indicated an increase in estimated ASD prevalence of 23% when the 2008 data were compared with the data for 2006 (from 9.0 per 1,000 children aged 8 years in 2006 to 11.0 in 2008 for the 11 sites that provided data for both surveillance years) and an estimated increase of 78% when the 2008 data were compared with the data for 2002 (from 6.4 per 1,000 children aged 8 years in 2002 to 11.4 in 2008 for the 13 sites that provided data for both surveillance years). Because the ADDM Network sites do not make up a nationally representative sample, these combined prevalence estimates should not be generalized to the United States as a whole.

“For 2008, the overall estimated prevalence of Autistic Spectrum Disorder among the 14 ADDM sites was 11.3 per 1,000 (one in 88) ...”

A review of research trends in physiological abnormalities
in autism spectrum disorders: immune dysregulation, inflammation,
oxidative stress, mitochondrial dysfunction and
environmental toxicant exposures

Author information

Rossignol DA1, Frye RE.

International Child Development Resource Center
Melbourne, FL 32934, USA
rossignolmd@gmail.com

Abstract

Recent studies have implicated physiological and metabolic abnormalities in autism spectrum disorders (ASD) and other psychiatric disorders, particularly immune dysregulation or inflammation, oxidative stress, mitochondrial dysfunction and environmental toxicant exposures ('four major areas'). The aim of this study was to determine trends in the literature on these topics with respect to ASD. A comprehensive literature search from 1971 to 2010 was performed in these four major areas in ASD with three objectives. First, publications were divided by several criteria, including whether or not they implicated an association between the physiological abnormality and ASD. A large percentage of publications implicated an association between ASD and immune dysregulation/inflammation (416 out of 437 publications, 95%), oxidative stress (all 115), mitochondrial dysfunction (145 of 153, 95%) and toxicant exposures (170 of 190, 89%). Second, the strength of evidence for publications in each area was computed using a validated scale. The strongest evidence was for immune dysregulation/inflammation and oxidative stress, followed by toxicant exposures and mitochondrial dysfunction. In all areas, at least 45% of the publications were rated as providing strong evidence for an association between the physiological abnormalities and ASD. Third, the time trends in the four major areas were compared with trends in neuroimaging, neuropathology, theory of mind and genetics ('four comparison areas'). The number of publications per 5-year block in all eight areas was calculated in order to identify significant changes in trends. Prior to 1986, only 12 publications were identified in the four major areas and 51 in the four comparison areas (42 for genetics). For each 5-year period, the total number of publications in the eight combined areas increased progressively. Most publications (552 of 895, 62%) in the four major areas were published in the last 5 years (2006-2010). Evaluation of trends between the four major areas and the four comparison areas demonstrated that the largest relative growth was in immune dysregulation/inflammation, oxidative stress, toxicant exposures, genetics and neuroimaging. Research on mitochondrial dysfunction started growing in the last 5 years. Theory of mind and neuropathology research has declined in recent years. Although most publications implicated an association between the four major areas and ASD, publication bias may have led to an overestimation of this association. Further research into these physiological areas may provide insight into general or subset-specific processes that could contribute to the development of ASD and other psychiatric disorders.

[the state of autism research]

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3317062/>

The co-morbidity burden of children and young adults with autism spectrum disorders

Author information

Kohane IS¹, McMurry A, Weber G, MacFadden D, Rappaport L, Kunkel L, Bickel J, Wattanasin N, Spence S, Murphy S, Churchill S.

¹Center for Biomedical Informatics
Harvard Medical School, Boston, Massachusetts, USA
Isaac_kohane@harvard.edu

Abstract

OBJECTIVES

Use electronic health records Autism Spectrum Disorder (ASD) to assess the comorbidity burden of ASD in children and young adults.

STUDY DESIGN

A retrospective prevalence study was performed using a distributed query system across three general hospitals and one pediatric hospital. Over 14,000 individuals under age 35 with ASD were characterized by their co-morbidities and conversely, the prevalence of ASD within these comorbidities was measured. The comorbidity prevalence of the younger (Age<18 years) and older (Age 18-34 years) individuals with ASD was compared.

RESULTS

19.44% of ASD patients had epilepsy as compared to 2.19% in the overall hospital population (95% confidence interval for difference in percentages 13.58-14.69%), 2.43% of ASD with schizophrenia vs. 0.24% in the hospital population (95% CI 1.89-2.39%), inflammatory bowel disease (IBD) 0.83% vs. 0.54% (95% CI 0.13-0.43%), bowel disorders (without IBD) 11.74% vs. 4.5% (95% CI 5.72-6.68%), CNS/cranial anomalies 12.45% vs. 1.19% (95% CI 9.41-10.38%), diabetes mellitus type I (DM1) 0.79% vs. 0.34% (95% CI 0.3-0.6%), muscular dystrophy 0.47% vs 0.05% (95% CI 0.26-0.49%), sleep disorders 1.12% vs. 0.14% (95% CI 0.79-1.14%). Autoimmune disorders (excluding DM1 and IBD) were not significantly different at 0.67% vs. 0.68% (95% CI -0.14-0.13%). Three of the studied comorbidities increased significantly when comparing ages 0-17 vs 18-34 with p<0.001: Schizophrenia (1.43% vs. 8.76%), diabetes mellitus type I (0.67% vs. 2.08%), IBD (0.68% vs. 1.99%) whereas sleeping disorders, bowel disorders (without IBD) and epilepsy did not change significantly.

CONCLUSIONS

The comorbidities of ASD encompass disease states that are significantly overrepresented in ASD with respect to even the patient populations of tertiary health centers. This burden of comorbidities goes well beyond those routinely managed in developmental medicine centers and requires broad multidisciplinary management that payors and providers will have to plan for.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3325235/>

[autism encompasses far more than just neurological disorders. Autism includes epilepsy, schizophrenia, inflammatory bowel disease, bowel disorders, cranial anomalies, diabetes mellitus type 1, muscular dystrophy, sleep disorders, autoimmune disorders and more...]

Observed prevalence of autism spectrum disorders in two Norwegian counties

Author information

Isaksen JI, Diseth TH, Schjølberg S, Skjeldal OH.

Department of Habilitation
Innlandet Hospital Trust, Maihaugveien 4
2609 Lillehammer, Norway
jorn.isaksen@sykehuset-innlandet.no

Abstract

BACKGROUND

The prevalence of autism spectrum disorders (ASD) has previously been reported to be increasing dramatically in European and non-European countries. No similar increase in prevalence rates has been documented in Norway to date. The current study reports on ASD prevalence rates in two Norwegian counties.

METHODS

The population comprised 31,015 children, ages six to 12. Information about special needs services was provided by the school authorities and the public health service. Multiple search strategies were applied to identify children at risk of ASD or diagnosed with ASD. Hospital registers were searched and a mapping tool was used in all local schools.

RESULTS

The total number of patients with ASD found in the population was 158. This gives a prevalence of 51 per 10,000 (95% CI, 0.43-0.59).

CONCLUSION

Compared with the previously reported prevalence of ASD in Norway, there has been almost a fourfold increase in the occurrence of childhood autism and a tenfold increase in the occurrence of all ASD groups. These findings have significant implications for designing and dimensioning appropriate intervention programmes for children with ASD and their families.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=22342070>

“there has been
almost a fourfold increase
in the occurrence of
childhood autism and a
tenfold increase in the
occurrence of all ASD groups.”

Hair toxic metal concentrations and autism spectrum disorder severity in young children

Author information

Geier DA1, Kern JK, King PG, Sykes LK, Geier MR.

Institute of Chronic Illnesses, Silver Spring, MD 20905, USA
davidallengeier@comcast.net.net

Abstract

Previous studies have found a higher body-burden of toxic metals, particularly mercury (Hg), among subjects diagnosed with an autism spectrum disorder (ASD) in comparison to neurotypical controls. Moreover, Hg body-burden was associated with ASD severity. This cross-sectional study examined the potential correlation between hair toxic metal concentrations and ASD severity in a prospective cohort of participants diagnosed with moderate to severe ASD. The Institutional Review Board at the University of Texas Southwestern Medical Center at Dallas (Dallas, TX) approved the present study. Qualifying study participants (n = 18) were evaluated for ASD severity using the Childhood Autism Rating Scale (CARS) and quantitatively for arsenic, Hg, cadmium, lead, chromium, cobalt, nickel, aluminum, tin, uranium, and manganese using hair toxic element testing by Doctor's Data (a CLIA-approved laboratory). CARS scoring and hair toxic element testing were blinded to one another. Increasing hair Hg concentrations significantly correlated with increased ASD severity. In contrast, no significant correlations were observed between any other of the hair toxic metals examined and ASD severity. This study helps to provide additional mechanistic support for Hg in the etiology of ASD severity, and is supported by an increasing number of recent critical reviews that provide biological plausibility for the role of Hg exposure in the pathogenesis of ASDs.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546773/>

“This study helps to provide additional mechanistic support for Hg [ethyl mercury or thimerosal] in the etiology of Autistic Spectrum Disorder [ASD] severity, and is supported by an increasing number of recent critical reviews that provide biological plausibility for the role of ethyl mercury [Hg] exposure in the pathogenesis of Autistic Spectrum Disorder”

Evidence of parallels between mercury intoxication and the brain pathology in autism

Author information

Kern JK1, Geier DA, Audhya T, King PG, Sykes LK, Geier MR.

Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA
jkern@dfwair.net

Abstract

The purpose of this review is to examine the parallels between the effects mercury intoxication on the brain and the brain pathology found in autism spectrum disorder (ASD). This review finds evidence of many parallels between the two, including: (1) microtubule degeneration, specifically large, long-range axon degeneration with subsequent abortive axonal sprouting (short, thin axons); (2) dendritic overgrowth; (3) neuroinflammation; (4) microglial/astrocytic activation; (5) brain immune response activation; (6) elevated glial fibrillary acidic protein; (7) oxidative stress and lipid peroxidation; (8) decreased reduced glutathione levels and elevated oxidized glutathione; (9) mitochondrial dysfunction; (10) disruption in calcium homeostasis and signaling; (11) inhibition of glutamic acid decarboxylase (GAD) activity; (12) disruption of GABAergic and glutamatergic homeostasis; (13) inhibition of IGF-1 and methionine synthase activity; (14) impairment in methylation; (15) vascular endothelial cell dysfunction and pathological changes of the blood vessels; (16) decreased cerebral/cerebellar blood flow; (17) increased amyloid precursor protein; (18) loss of granule and Purkinje neurons in the cerebellum; (19) increased pro-inflammatory cytokine levels in the brain (TNF- α , IFN- γ , IL-1 α , IL-8); and (20) aberrant nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kappaB). This review also discusses the ability of mercury to potentiate and work synergistically with other toxins and pathogens in a way that may contribute to the brain pathology in ASD. The evidence suggests that mercury may be either causal or contributory in the brain pathology in ASD, possibly working synergistically with other toxic compounds or pathogens to produce the brain pathology observed in those diagnosed with an ASD.

Full Report

<http://www.ncbi.nlm.nih.gov/pubmed/22810216>

“The evidence suggests that mercury may be either causal or contributory in the brain pathology in Autistic Spectrum Disorder, possibly working synergistically with other toxic compounds or pathogens to produce the brain pathology observed in those diagnosed with an Autistic Spectrum Disorder”

Translational Neurodegeneration • August 2013

Evidence of neurodegeneration in autism spectrum disorder

Author information

Kern JK1, Geier DA, Sykes LK, Geier MR.

Institute of Chronic Illnesses, Incorporation, Silver Spring, MD, USA
jkern@dfwair.net

Abstract

Autism spectrum disorder (ASD) is a neurological disorder in which a significant number of children experience a developmental regression characterized by a loss of previously-acquired skills and abilities. Loss of neurological function in ASD, as observed in affected children who have regressed, can be explained as neurodegeneration. Although there is research evidence of neurodegeneration or progressive encephalopathy in ASD, the issue of neurodegeneration in ASD is still under debate. Evidence of neurodegeneration in the brain in ASD includes: (1) neuronal cell loss, (2) activated microglia and astrocytes, (3) proinflammatory cytokines, (4) oxidative stress, and (5) elevated 8-oxo-guanosine levels. The evidence from this review suggests that neurodegeneration underlies the loss of neurological function in children with ASD who have experienced regression and loss of previously acquired skills and abilities, and that research into treatments to address the issue of neurodegeneration in ASD are warranted.

<http://www.ncbi.nlm.nih.gov/pubmed/23925007>

“Evidence of neurodegeneration in the brain in ASD [autistic spectrum disorder] includes:

- (1) neuronal cell loss,
- (2) activated microglia and astrocytes,
- (3) proinflammatory cytokines,
- (4) oxidative stress, and
- (5) elevated 8-oxo-guanosine levels.”

Autism

Author Information

Tomljenovic, Lucija; Dórea, José G.; Shaw, Christopher A.

Abstract

Autism is a multisystem developmental disorder characterized by dysfunctional immunity and impaired brain function. Although autism is partly determined by genetic susceptibility factors, reported dramatic increases in the prevalence of autism in developed countries have intensified scientific focus on environmental exposures. Pre- and perinatal immunotoxic insults are now strongly suspected as contributors to this increase. Mercury (Hg) is both a neuro- and an immunotoxin and continues to be used in some pediatric vaccines in the form of the preservative thimerosal. Although currently there are no direct human studies on the risks of Hg exposure from thimerosal-containing vaccines (TCVs), animal studies show that doses relevant to human TCV exposure can result in adverse neurodevelopmental outcomes. To date, TCVs continue to be administered on a regular basis to potentially the most vulnerable populations: pregnant women and children. In light of existing experimental evidence, the rationale for using this known immunotoxic and neurotoxic substance in human vaccines should be reconsidered.

Early brain enlargement and elevated extra-axial fluid in infants who develop autism spectrum disorder

Shen MD1, Nordahl CW, Young GS, Wootton-Gorges SL,
Lee A, Liston SE, Harrington KR, Ozonoff S, Amaral DG.

Abstract

Prospective studies of infants at risk for autism spectrum disorder have provided important clues about the early behavioural symptoms of autism spectrum disorder. Diagnosis of autism spectrum disorder, however, is not currently made until at least 18 months of age. There is substantially less research on potential brain-based differences in the period between 6 and 12 months of age. Our objective in the current study was to use magnetic resonance imaging to identify any consistently observable brain anomalies in 6-9 month old infants who would later develop autism spectrum disorder. We conducted a prospective infant sibling study with longitudinal magnetic resonance imaging scans at three time points (6-9, 12-15, and 18-24 months of age), in conjunction with intensive behavioural assessments. Fifty-five infants (33 'high-risk' infants having an older sibling with autism spectrum disorder and 22 'low-risk' infants having no relatives with autism spectrum disorder) were imaged at 6-9 months; 43 of these (27 high-risk and 16 low-risk) were imaged at 12-15 months; and 42 (26 high-risk and 16 low-risk) were imaged again at 18-24 months. Infants were classified as meeting criteria for autism spectrum disorder, other developmental delays, or typical development at 24 months or later (mean age at outcome: 32.5 months). Compared with the other two groups, infants who developed autism spectrum disorder ($n = 10$) had significantly greater extra-axial fluid at 6-9 months, which persisted and remained elevated at 12-15 and 18-24 months. Extra-axial fluid is characterized by excessive cerebrospinal fluid in the subarachnoid space, particularly over the frontal lobes. The amount of extra-axial fluid detected as early as 6 months was predictive of more severe autism spectrum disorder symptoms at the time of outcome. Infants who developed autism spectrum disorder also had significantly larger total cerebral volumes at both 12-15 and 18-24 months of age. This is the first magnetic resonance imaging study to prospectively evaluate brain growth trajectories from infancy in children who develop autism spectrum disorder. The presence of excessive extra-axial fluid detected as early as 6 months and the lack of resolution by 24 months is a hitherto unreported brain anomaly in infants who later develop autism spectrum disorder. This is also the first magnetic resonance imaging evidence of brain enlargement in autism before age 2. These findings raise the potential for the use of structural magnetic resonance imaging to aid in the early detection of children at risk for autism spectrum disorder or other neurodevelopmental disorders.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3754460/>

A Comparison of the Autism Treatment Evaluation Checklist (ATEC) and the Childhood Autism Rating Scale (CARS) for the Quantitative Evaluation of Autism

Author information

Geier DA1, Kern JK, Geier MR.

Institute of Chronic Illnesses, Inc.
Silver Spring, Maryland

Abstract

The purpose of this study was to evaluate scores generated from the Autism Treatment Evaluation Checklist (ATEC), a parent-rated measure, and those derived from professionally completed Childhood Autism Rating Scale (CARS) evaluations. A cohort of 56 participants diagnosed with an autism spectrum disorder was used for the study, and each child was evaluated independently by the parent using the ATEC and a health care professional using the CARS. The Spearman's rank correlation statistic ρ was used to evaluate the correlation between ATEC and CARS scores. It was observed that there was a significant correlation between total ATEC and CARS scores ($\rho = .71$). Specific domains in the ATEC evaluation significantly correlated with CARS scores. Sensitivity, specificity, and receiver operating characteristic confirmed the association between CARS and ATEC domains. The results help to validate the utility of the parentally completed ATEC in comparison with an established, professional-related measure of autism.

<http://www.ncbi.nlm.nih.gov/pubmed/23914277>

“The results help to validate the utility of the parentally completed ATEC in comparison with an established, professional-related measure of autism.”

Redox Regulation and the Autistic Spectrum: Role of Tryptophan Catabolites, Immuno-inflammation, Autoimmunity and the Amygdala

George Anderson^{1,*} and Michael Maes^{2,3}

1. CRC, Rm:30, 57 Laurel Street, Glasgow, Scotland
2. Department of Psychiatry, Chulalongkorn University, Bangkok, Thailand
3. Department of Psychiatry, Deakin University, Geelong, Australia

Abstract

The autistic spectrum disorders (ASD) form a set of multi-faceted disorders with significant genetic, epigenetic and environmental determinants. Oxidative and nitrosative stress (O&NS), immuno-inflammatory pathways, mitochondrial dysfunction and dysregulation of the tryptophan catabolite (TRYCATs) pathway play significant interactive roles in driving the early developmental etiology and course of ASD. O&NS interactions with immuno-inflammatory pathways mediate their effects centrally via the regulation of astrocyte and microglia responses, including regional variations in TRYCATs produced. Here we review the nature of these interactions and propose an early developmental model whereby different ASD genetic susceptibilities interact with environmental and epigenetic processes, resulting in glia biasing the patterning of central interarea interactions. A role for decreased local melatonin and N-acetylserotonin production by immune and glia cells may be a significant treatment target.

Full Report

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3964746/>

Parental obesity and risk of autism spectrum disorder

Author information

Surén P1, Gunnes N2, Roth C2, Bresnahan M3, Hornig M4, Hirtz D5, Lie KK6, Lipkin WI4, Magnus P6, Reichborn-Kjennerud T7, Schjølberg S6, Susser E3, Oyen AS8, Smith GD9, Stoltenberg C10.

1. Norwegian Institute of Public Health, Oslo, Norway; Centre for Paediatric Epidemiology and Biostatistics UCL Institute of Child Health, London, United Kingdom
2. Norwegian Institute of Public Health, Oslo, Norway; Mailman School of Public Health, Columbia University, New York, New York
3. Mailman School of Public Health, Columbia University, New York, New York; New York State Psychiatric Institute, New York, New York
4. Mailman School of Public Health, Columbia University, New York, New York
5. National Institute of Neurologic Disorders and Stroke, Bethesda, Maryland
6. Norwegian Institute of Public Health, Oslo, Norway
7. Norwegian Institute of Public Health, Oslo, Norway; Institute of Psychiatry, University of Oslo, Oslo, Norway
8. Norwegian Institute of Public Health, Oslo, Norway; Nic Waals Institute, Lovisenberg Hospital, Oslo, Norway
9. MRC Centre for Causal Analysis in Translational Epidemiology, University of Bristol, Bristol, United Kingdom and
10. Norwegian Institute of Public Health, Oslo, Norway; Department of Public Health and Primary Health Care University of Bergen, Bergen, Norway

Abstract

OBJECTIVES

The objective of the study was to investigate the associations among maternal prepregnancy BMI, paternal BMI, and the risk of autism spectrum disorders (ASDs) in children.

METHODS

The study sample of 92 909 children was derived from the population-based, prospective Norwegian Mother and Child Cohort Study. The age range was 4.0 through 13.1 (mean 7.4) years. Relative risks of ASDs were estimated by odds ratios (ORs) and 95% confidence intervals (CIs) from logistic regression models.

RESULTS

At the end of follow-up on December 31, 2012, 419 children in the study sample had been diagnosed with ASDs: 162 with autistic disorder, 103 with Asperger disorder, and 154 with pervasive developmental disorder not otherwise specified. Maternal obesity (BMI ≥ 30) was only weakly associated with ASD risk, whereas paternal obesity was associated with an increased risk of autistic disorder and Asperger disorder. The risk of autistic disorder was 0.27% (25 of 9267) in children of obese fathers and 0.14% (59 of 41 603) in children of fathers with normal weight (BMI < 25), generating an adjusted OR of 1.73 (95% CI: 1.07-2.82). For Asperger disorder, analyses were limited to children aged ≥ 7 years (n = 50 116). The risk was 0.38% (18 of 4761) in children of obese fathers and 0.18% (42 of 22 736) in children of normal-weight fathers, and the adjusted OR was 2.01 (95% CI: 1.13-3.57). No associations were found for pervasive developmental disorder not otherwise specified.

CONCLUSIONS

Paternal obesity is an independent risk factor for ASDs in children. The associations should be investigated further in genetic and epigenetic studies.

“Several of these influences, including polybrominated diphenyl ethers, aluminum adjuvants, the herbicide glyphosate, and obesity among U.S. women, have increasing trends that are positively correlated to the rise in autism. However, most of the toxins surveyed, including lead, PCBs, organochlorine pesticides, vehicular emissions and air pollution, have flat or declining trends, making it less likely that they can be driving the increase in diagnosed autism seen over the 35-year period of the composite data set.”

Environmental Health • September 2014

A comparison of temporal trends in United States autism prevalence to trends in suspected environmental factors

Cynthia D Nevison

Abstract

Background

The prevalence of diagnosed autism has increased rapidly over the last several decades among U.S. children. Environmental factors are thought to be driving this increase and a list of the top ten suspected environmental toxins was published recently.

Methods

Temporal trends in autism for birth years 1970–2005 were derived from a combination of data from the California Department of Developmental Services (CDDS) and the United States Individuals with Disabilities Education Act (IDEA). Temporal trends in suspected toxins were derived from data compiled during an extensive literature survey. Toxin and autism trends were compared by visual inspection and computed correlation coefficients. Using IDEA data, autism prevalence vs. birth year trends were calculated independently from snapshots of data from the most recent annual report, and by tracking prevalence at a constant age over many years of reports. The ratio of the snapshot:tracking trend slopes was used to estimate the “real” fraction of the increase in autism.

Results

The CDDS and IDEA data sets are qualitatively consistent in suggesting a strong increase in autism prevalence over recent decades. The quantitative comparison of IDEA snapshot and constant-age tracking trend slopes suggests that ~75-80% of the tracked increase in autism since 1988 is due to an actual increase in the disorder rather than to changing diagnostic criteria. Most of the suspected environmental toxins examined have flat or decreasing

temporal trends that correlate poorly to the rise in autism. Some, including lead, organochlorine pesticides and vehicular emissions, have strongly decreasing trends. Among the suspected toxins surveyed, polybrominated diphenyl ethers, aluminum adjuvants, and the herbicide glyphosate have increasing trends that correlate positively to the rise in autism.

Conclusions

Diagnosed autism prevalence has risen dramatically in the U.S over the last several decades and continued to trend upward as of birth year 2005. The increase is mainly real and has occurred mostly since the late 1980s. In contrast, children’s exposure to most of the top ten toxic compounds has remained flat or decreased over this same time frame. Environmental factors with increasing temporal trends can help suggest hypotheses for drivers of autism that merit further investigation.

Summary

Temporal trends in autism were constructed both by tracking prevalence at a constant age in a series of historical IDEA reports and by computing prevalence from age-resolved snapshots in individual, recent IDEA reports. Both the snapshot and tracking approaches suggest a strong increase in autism that took off in the late 1980s and was ongoing as of birth year 2005. The ratio of the snapshot:tracking slopes suggests that among states with the most reliable data, about 75 to 80% of the tracked increase in IDEA autism since 1988 is due to a real increase in the disorder rather than just to better or expanded diagnosis. The trend in California IDEA autism prevalence was shown to be broadly representative of the mean United States trend and was extended to span birth years 1970–2005 using a composite CDDS plus IDEA dataset. The composite dataset, which shows that a more gradual increase in autism had begun already by 1980, was compared to the corresponding trends in a list of suspected toxins and environmental influences. Several of these influences, including polybrominated diphenyl ethers, aluminum adjuvants, the herbicide glyphosate, and obesity among U.S. women, have increasing trends that are positively correlated to the rise in autism. However, most of the toxins surveyed, including lead, PCBs, organochlorine pesticides, vehicular emissions and air pollution, have flat or declining trends, making it less likely that they can be driving the increase in diagnosed autism seen over the 35-year period of the composite data set.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4177682/>

Dysregulation of estrogen receptor beta (ER β), aromatase (CYP19A1), and ER co-activators in the middle frontal gyrus of autism spectrum disorder subjects

Author information

Crider A1, Thakkar R2, Ahmed AO1, Pillai A1.

1. Department of Psychiatry and Health Behavior, Medical College of Georgia, Georgia Regents University, 997 St. Sebastian Way, Augusta, GA 30912 USA
2. Department of Neuroscience and Regenerative Medicine, Medical College of Georgia, Georgia Regents University, 997 St. Sebastian Way, Augusta, GA 30912 USA

Abstract

BACKGROUND

Autism spectrum disorders (ASD) are much more common in males than in females. Molecular alterations within the estrogen receptor (ER) signaling pathway may contribute to the sex difference in ASD, but the extent of such abnormalities in the brain is not known.

METHODS

Postmortem middle frontal gyrus tissues (13 ASD and 13 control subjects) were used. The protein levels were examined by western blotting. The gene expression was determined by qRT-PCR.

RESULTS

Gene expression analysis identified a 35% decrease in ER α mRNA expression in the middle frontal gyrus of ASD subjects. In addition, a 38% reduction in aromatase (CYP19A1) mRNA expression was observed in ASD subjects. We also found significant decreases in ER co-activators that included a 34% decrease in SRC-1, a 77% decrease in CBP, and a 52% decrease in P/CAF mRNA levels in ASD subjects relative to controls. There were no differences in the mRNA levels of TIF-2, AIB-1 (ER co-activators), ER co-repressors (SMRT and nCoR) and ER β in the middle frontal gyrus of ASD subjects as compared to controls. We observed significant correlations between ER β , CYP19A1, and co-activators in the study subjects. Immunoblot analysis further confirmed the changes in ER β and aromatase at the protein level in the control and ASD subjects.

<http://www.ncbi.nlm.nih.gov/pubmed/25221668>

Impact of environmental factors on the prevalence of autistic disorder after 1979

Author Information

Theresa A. Deisher*, Ngoc V. Doan, Angelica Omaiye,
Kumiko Koyama and Sarah Bwabye

Sound Choice Pharmaceutical Institute
1749 Dexter Ave N, Seattle, WA 98109, USA

Abstract

The aim of this study was to investigate a previously overlooked, universally introduced environmental factor, fetal and retroviral contaminants in childhood vaccines, absent prior to change points (CPs) in autistic disorder (AD) prevalence with subsequent dose-effect evidence and known pathologic mechanisms of action. Worldwide population based cohort study was used for the design of this study. The United States, Western Australia, United Kingdom and Denmark settings were used. All live born infants who later developed autistic disorder delivered after 1 January 1970, whose redacted vaccination and autistic disorder diagnosis information is publicly available in databases maintained by the US Federal Government, Western Australia, UK, and Denmark. The live births, grouped by father's age, were from the US and Australia. The children vaccinated with MMRII, Varicella and Hepatitis A vaccines varied from 19 to 35 months of age at the time of vaccination. Autistic disorder birth year change points were identified as 1980.9, 1988.4 and 1996 for the US, 1987 for UK, 1990.4 for Western Australia, and 1987.5 for Denmark. Change points in these countries corresponded to introduction of or increased doses of human fetal cell line-manufactured vaccines, while no relationship was found between paternal age or Diagnostic and Statistical Manual (DSM) revisions and autistic disorder diagnosis. Further, linear regression revealed that Varicella and Hepatitis A immunization coverage was significantly correlated to autistic disorder cases. R software was used to calculate change points. Autistic disorder change points years are coincident with introduction of vaccines manufactured using human fetal cell lines, containing fetal and retroviral contaminants, into childhood vaccine regimens. This pattern was repeated in the US, UK, Western Australia and Denmark. Thus, rising autistic disorder prevalence is directly related to vaccines manufactured utilizing human fetal cells. Increased paternal age and DSM revisions were not related to rising autistic disorder prevalence.

<http://soundchoice.org/scpiJournalPubHealthEpidem092014.pdf>

“R software was used to calculate change points.

Autistic disorder change points years are coincident with introduction of vaccines manufactured using human fetal cell lines, containing fetal and retroviral contaminants, into childhood vaccine regimens ... rising autistic disorder prevalence is directly related to vaccines manufactured utilizing human fetal cells.”

Autism: a form of lead and mercury toxicity

Author information

Yassa HA

Forensic Medicine and Clinical Toxicology Department
Faculty of Medicine, Assiut University, Egypt
heba612@hotmail.com

Abstract

AIM

Autism is a developmental disability characterized by severe deficits in social interaction and communication. The definite cause of autism is still unknown. The aim of this study is to find out the relation between exposure to Lead and/or mercury as heavy metals and autistic symptoms, dealing with the heavy metals with chelating agents can improve the autistic symptoms.

METHOD

Blood and hair samples were obtained from 45 children from Upper Egypt with autism between the ages of 2 and 10 years and 45 children served as controls in the same age range, after taken an informed consent and fill a questionnaire to assess the risk factors. The samples were analyzed blindly for lead and mercury by using atomic absorption and ICP-MS. Data from the two groups were compared, then follow up of the autistic children after treatment with chelating agents were done.

RESULTS

The results obtained showed significant difference among the two groups, there was high level of mercury and lead among those kids with autism. Significant decline in the blood level of lead and mercury with the use of DMSA as a chelating agent. In addition, there was decline in the autistic symptoms with the decrease in the lead and mercury level in blood.

CONCLUSION

Lead and mercury considered as one of the main causes of autism. Environmental exposure as well as defect in heavy metal metabolism is responsible for the high level of heavy metals. Detoxification by chelating agents had great role in improvement of those kids.

<http://www.ncbi.nlm.nih.gov/pubmed/25461563>

“Lead and mercury considered as one of the main causes of autism. Environmental exposure as well as defect in heavy metal metabolism is responsible for the high level of heavy metals.”

Environmental chemical exposures and autism spectrum disorders: a review of the epidemiological evidence

Author information

Kalkbrenner AE1, Schmidt RJ2, Penlesky AC1.

1. Zilber School of Public Health, University of Wisconsin-Milwaukee, Milwaukee, WI
2. Department of Public Health Sciences, University of California Davis School of Medicine, Davis, CA
Medical Investigation of Neurodevelopmental Disorders (MIND) Institute
University of California Davis, Sacramento, CA

Abstract

In the past decade, the number of epidemiological publications addressing environmental chemical exposures and autism has grown tremendously. These studies are important because it is now understood that environmental factors play a larger role in causing autism than previously thought and because they address modifiable risk factors that may open up avenues for the primary prevention of the disability associated with autism. In this review, we covered studies of autism and estimates of exposure to tobacco, air pollutants, volatile organic compounds and solvents, metals (from air, occupation, diet, dental amalgams, and thimerosal-containing vaccines), pesticides, and organic endocrine-disrupting compounds such as flame retardants, non-stick chemicals, phthalates, and bisphenol A. We included studies that had individual-level data on autism, exposure measures pertaining to pregnancy or the 1st year of life, valid comparison groups, control for confounders, and adequate sample sizes. Despite the inherent error in the measurement of many of these environmental exposures, which is likely to attenuate observed associations, some environmental exposures showed associations with autism, especially traffic-related air pollutants, some metals, and several pesticides, with suggestive trends for some volatile organic compounds (e.g., methylene chloride, trichloroethylene, and styrene) and phthalates. Whether any of these play a causal role requires further study. Given the limited scope of these publications, other environmental chemicals cannot be ruled out, but have not yet been adequately studied. Future research that addresses these and additional environmental chemicals, including their most common routes of exposures, with accurate exposure measurement pertaining to several developmental windows, is essential to guide efforts for the prevention of the neurodevelopmental damage that manifests in autism symptoms.

<http://www.ncbi.nlm.nih.gov/pubmed/25199954>

A Review of the Differences in Developmental, Psychiatric, and Medical Endophenotypes Between Males and Females with Autism Spectrum Disorder

Eric Rubenstein, Lisa D. Wiggins, and Li-Ching Lee

Department of Epidemiology
Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe Street, Room E6032
Baltimore, MD 21205, USA

Abstract

Autism spectrum disorder (ASD) is over four times more prevalent in males compared to females. Increased understanding of sex differences in ASD endophenotypes could add insight into possible etiologies and the assessment and management of the disorder. Consequently, the purpose of this review is to describe current literature regarding sex differences in the developmental, psychiatric, and medical endophenotypes of ASD in order to illustrate current knowledge and areas in need of further research. Our review found that repetitive behaviors and restricted interests are more common in males than females with ASD. Intellectual disability is more common in females than males with ASD. Attention to detail may be more common in males than females with ASD and epilepsy may be more common in females than males with ASD, although limited research in these areas prevent definitive conclusions from being drawn. There does not appear to be a sex difference in other developmental, psychiatric, and medical symptoms associated with ASD, or the research was contradictory or too sparse to establish a sex difference. Our review is unique in that it offers detailed discussion of sex differences in three major endophenotypes of ASD. Further research is needed to better understand why sex differences exist in certain ASD traits and to evaluate whether phenotypic sex differences are related to different pathways of development, assessment, and treatment of the disorder.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4490156/>

“Further research is needed to better understand why sex differences exist in certain ASD traits and to evaluate whether phenotypic sex differences are related to different pathways of development, assessment, and treatment of the disorder.”

Are ASD and ADHD a Continuum? A Comparison of Pathophysiological Similarities Between the Disorders

Author information

Kern JK1, Geier DA2, Sykes LK3, Geier MR4, Deth RC5.

1. Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA
University of Texas Southwestern Medical Center at Dallas, TX. USA
2. Institute of Chronic Illnesses, Inc., Silver Spring, MD, USA
3. CoMeD, Inc., Silver Spring, MD, USA
4. ASD Centers, LLC, Silver Spring, MD, USA
5. Northeastern University, Boston, MA, USA
jkern@dfwair.net

Abstract

OBJECTIVE

The objective of this study was to review and compare the similarities between autism spectrum disorder (ASD) and ADHD with regard to symptomatology, neurological deficits, metabolic and endocrine-related conditions, and brain pathology.

METHOD

A comprehensive review of the relevant research literature was carried out.

RESULTS

A number of important similarities between ASD and ADHD were identified, including recent increases in prevalence, male-biased incidence, shared involvement of sensory processing, motor and impulse control, abnormal patterns of neural connectivity, and sleep disturbances. Studies suggest involvement of androgen metabolism, impaired methylation, and heavy metal toxicity as possible contributing factors for both disorders.

CONCLUSION

ASD and ADHD share a number of features and pathophysiological conditions, which suggests that the two disorders may be a continuum and have a common origin.

“ASD and ADHD share a number of features and pathophysiological conditions, which suggests that the two disorders may be a continuum and have a common origin.”

Autism Spectrum Disorder in the Emergency Department: Looking Beyond Behavior

Richard E Frye

Autism Research Program, Arkansas Children's Hospital Research Institute, Little Rock, AR, USA
Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Corresponding Author :
E-mail: REFrye@uams.edu

Abstract

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition that is behaviorally defined by its well-recognized impairments in verbal and non-verbal communication and social interactions in addition to distinctive restrictive and repetitive behaviors (APA, 1994). Over the past decades the incidence of this disorder has dramatically increased. Although the reason or reasons for this increase is still up for debate, the fact remains that ASD is now estimated to affect 1 in 68 children in the United States (Developmental Disabilities Monitoring Network Surveillance Year Principal, Centers for Disease, & Prevention, 2014). ASD is defined by behavioral manifestations, yet children with ASD have a high prevalence of many medical conditions including recurrent infections (Doshi-Velez, Ge, & Kohane, 2014), gastrointestinal (GI) disturbances (Chaidez, Hansen, & Hertz-Picciotto, 2013), seizures and epilepsy (Frye et al., 2013), anxiety (Sukhodolsky, Bloch, Panza, & Reichow, 2013), allergies (Angelidou et al., 2011) and metabolic disorders (Frye & James, 2014; Frye & Rossignol, 2012) including mitochondrial disease (Frye & Rossignol, 2011; Rossignol & Frye, 2012). With the increase in prevalence and the significant co-morbidity of medical problems, it is likely that medical professionals in the emergency and urgent care facilities will have increasing exposure to individuals with ASD for urgent medical management, particularly acute behavioral dysregulation. When this occurs it will be important to consider their special needs and understand the unique manner in which common medical problem may present in individuals with ASD. Indeed, children without typical communication skills, aberrant behaviors may be the manner in which the child is communicating the need for medical attention (Buie et al., 2010).

ASD is associated with a wide spectrum of behavioral manifestations. Some of the most disruptive behaviors, referred to as aberrant behaviors, can cause significant disability and distress to the patient and caregiver (Baghdadli, Pry, Michelon, & Rattaz, 2014). Aberrant behavior is divided into subcategories by the Aberrant Behavior Checklist (Slosson Educational Publications Inc, East Aurora, NY). These categories include Irritability, Social Withdrawal, Stereotypy, Hyperactivity and Inappropriate Speech. Irritability, which includes severe tantrums, aggression, and self-injury, is one of the major and most disruptive aberrant behaviors (Stigler, 2014). Irritability is commonly treated with antipsychotic medication with or without behavior therapy (Aman et al., 2009). Treating with a medication to suppression symptoms rather than understanding if there is an underlying medical cause for such behaviors can be problematic for several reasons. First, treating symptoms instead of identifying a cause can lead to increased morbidity and mortality from an undiagnosed disorder. Second, antipsychotic medications can detrimentally affect glucose, cholesterol and lipids and weight, even in the short-term (Correll et al., 2009; Wink et al., 2014) and long-term anti-psychotic use increases the risk for type II diabetes (Bobo et al., 2013) and can result in tardive dyskinesia, a potentially permanent movement disorder (Correll & Kane, 2007). Thus, it may be best to look beyond the obvious of controlling behavior and understanding what the behavior means in order to solve potentially important medical conditions to improve the long-term health of a child with ASD. Several examples are given below of the medical condition that can present as behavioral dysregulation in children with ASD.

GI disturbances have been reported to occur in 9% to 70% of children with ASD, with high quality studies suggesting that GI symptoms are very prevalent. GI symptoms commonly manifest as behavioral manifestations in children with ASD (Buie et al., 2010). For example, abdominal pain, gastroesophageal reflux disease and/ or constipation can manifest as vocal symptoms such as frequent repetitive throat clearing or swallowing and/or screaming, crying, whining or sobbing for no reason; motor behaviors such as facial grimacing, teeth grinding, chewing on clothes or other objects, applying pressure to the abdomen or aggressive or self-injurious behavior; and/or general behaviors such sleep disturbance or irritability (Buie et al., 2010). Thus, it is important to obtain a GI history, including symptoms of gastroesophageal reflux, stool frequency and consistency, and perform a careful GI examination to look for abdominal distention and/or impaction. Many of the GI symptoms may drive aberrant behavior through causing pain. When a child cannot communicate verbally, aberrant and unusual behaviors may be the only manner in which the child can communicate that pain exists. Thus, the clinician needs to have a high index of suspicion for obvious and non-obvious sources of pain. For example, head banging is sometimes associated with headache. Other sources of pain not uncommon in childhood such as pharyngitis, sinusitis, otitis media and dental caries, just to name a few, must also be considered. A trial of analgesics might be appropriate if pain is believed to be driving the behavior. Interestingly celecoxib has been shown to be an effective adjunctive treatment to risperidone for irritability in a double-blind placebo-controlled trial. (Asadabadi et al., 2013).

Full Report With References

Sleep disruption is estimated to affect from 44% to 83% of individuals with ASD, with delayed sleep onset and nighttime waking being the most predominant symptoms (Krakowiak et al., 2008). Several studies have demonstrated that disruption in sleep patterns is associated with problem behaviors during the day, particularly in low-functioning ASD individuals (Cohen et al., 2014), and lower overall functioning in several measures of development including greater problems with language and communication (Taylor, Schreck, & Mulick, 2012). Melatonin is a safe and effective treatment sleep duration and sleep onset latency but is less effective for night time waking (Rossignol & Frye, 2011) and has been shown to improve daytime behavior and parenting stress (Malow et al., 2012). In addition, a case series reported that the selective melatonin receptor agonist ramelteon can also be effective for improving sleep and daytime behavior (Kawabe, Horiuchi, Oka, & Ueno, 2014). Thus, a careful focused sleep history may provide important information which can lead to appropriate evaluation and treatment.

Anxiety is very common in ASD (Vasa & Mazurek, 2015), particularly in high-functioning ASD children (Chandler et al., 2015). Anxiety is related to aggressive behavior (Pugliese, White, White, & Ollendick, 2013), more severe repetitive behaviors and lower overall development (Magiati et al., 2015) and sleep disruption (Mazurek & Petroski, 2015). A wide variety of treatments for anxiety have been studied in individuals with ASD. The best studied treatments for anxiety in ASD include intranasal oxytocin (Hofmann, Fang, & Brager, 2015) and cognitive-behavioral therapy (Ung, Sells, Small, & Storch, 2015). Although selective serotonin reuptake inhibitors were previously considered useful in the ASD population, such medications may increase the risk of behavioral activation (Vasa & Mazurek, 2015) and may be best suited for treating repetitive behavior (Hollander et al., 2012). Thus, it is important to screen for symptoms of anxiety as such a significant psychiatric comorbidity could be driving disruptive behavior.

There appears to be a wide range of behavioral manifestations that are related to immune dysregulation, although the treatments for these disorders are not well studied. Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections (PANDAS), a disorder which can result in sudden onset obsessive compulsive behavior, tics and Tourette like behavior (Martino, Defazio, & Giovannoni, 2009), is associated with ASD (Libbey & Fujinami, 2010). Recently PANDAS has been brought in under the umbrella of Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

and recommendation for diagnostic workup have been outlined in a consensus conference (Chang et al., 2015). The recent recognition of the association of PANDAS/PANS with specific antibodies titers to basal ganglia has provided a medical test to help with diagnosis of these patients (Cox et al., 2015). Other immune abnormalities, which are less well-studied, have been reported. These include the association between depressed plasma immunoglobulin concentrations with aberrant behavior (Heuer et al., 2008) and the recognition of a subset of children with ASD with behavioral dysregulation following episodes of immune activation (Jyonouchi, Geng, Streck, & Toruner, 2012). Although treatments for immune abnormalities are not well studied, identifying immune abnormalities can result in appropriate referral and treatment.

A disorder related to depressed folate concentration in the brain appears to be rather common is ASD and may be related to behavioral dysregulation. The folate receptor alpha autoantibody is prevalent in ASD with up to 75% of ASD patients being positive for the blocking or binding autoantibody (Frye et al., 2013). Autoantibody titers are directly correlated with increased aggressive behavior (Ramaekers et al., 2007). Titers are increased by the ingestion of milk and behavior can be improved with the treatment of a milk free diet (Ramaekers, Sequeira, Blau, & Quadros, 2008). Since this autoantibody blocks the ability of folate from crossing the blood-brain barrier, an alternative form of folate, high-dose folic acid, can improve behavior in ASD patient with folate receptor alpha autoantibodies (Frye et al., 2013; Moretti et al., 2005).

These medical conditions which are associated with behavioral dysregulation are under recognized across many medical settings, but it is of the utmost importance for medical professional in the emergency and urgent care departments to recognize these potential medical conditions since many children with ASD will arrive in the emergency department when behavior suddenly escalates. Unfortunately, the evaluation of children with ASD and behavioral dysregulation has not been standardized and many of the medical abnormalities associated with behavioral dysregulation have not been well studied, especially in regards to treatment. Recognition of these conditions can lead to appropriate management and referrals. With the rising number of children with ASD it is important for front line medical professional to be comfortable with evaluating children with ASD and to consider the medical complexities associated with ASD.

Assessment of Hair Aluminum, Lead, and Mercury in a Sample of Autistic Egyptian Children: Environmental Risk Factors of Heavy Metals in Autism

Author information

Mohamed Fel B1, Zaky EA1, El-Sayed AB2, Elhossieny RM1,
Zahra SS1, Salah Eldin W3, Youssef WY1, Khaled RA1, Youssef AM1

1. Pediatrics Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
2. National Institute of Standards, Giza, Egypt
3. Community Medicine Department, Ain Shams University, Cairo, Egypt

Abstract

Background and Aims. The etiological factors involved in the etiology of autism remain elusive and controversial, but both genetic and environmental factors have been implicated. The aim of this study was to assess the levels and possible environmental risk factors and sources of exposure to mercury, lead, and aluminum in children with autism spectrum disorder (ASD) as compared to their matched controls.

Methods. One hundred ASD children were studied in comparison to 100 controls. All participants were subjected to clinical evaluation and measurement of mercury, lead, and aluminum through hair analysis which reflects past exposure.

Results. The mean Levels of mercury, lead, and aluminum in hair of the autistic patients were significantly higher than controls. Mercury, lead, and aluminum levels were positively correlated with maternal fish consumptions, living nearby gasoline stations, and the usage of aluminum pans, respectively.

Conclusion. Levels of mercury, lead, and aluminum in the hair of autistic children are higher than controls. Environmental exposure to these toxic heavy metals, at key times in development, may play a causal role in autism.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=26508811>

“Levels of mercury, lead, and aluminum in the hair of autistic children are higher than controls. Environmental exposure to these toxic heavy metals, at key times in development, may play a causal role in autism.”

Chapter Seven
Short Essays On Vaccination

Herd Immunity: Can Infectious Diseases be Prevented by High Vaccination Coverage?

By Lucija Tomljenovic, PhD

The frequent statement that high levels of vaccination prevent disease outbreaks is not accurate as infectious diseases do in fact occur even in fully vaccinated populations [1] as well as individuals. [2] (See Table 1 for more examples)

The likely reason for this is that vaccines primarily stimulate humoral immunity (antibody-based or Th2 responses) while they have little or no effect on cellular immunity (cytotoxic T-cells, Th1 responses), which is absolutely crucial for protection against viral as well as some bacterial pathogens. [3]

This may be the reason why vaccine-induced immunities are transient, requiring booster shots; while naturally acquired immunity conferred by the cellular immune system tends to be permanent in the absence of vaccination.

Taken together, these observations may explain why outbreaks of allegedly vaccine-preventable diseases do occur in fully vaccinated populations and why, immunity (or its absence) cannot be reliably determined by measuring antibody levels, [4] which is the most common measure of vaccine efficacy in clinical trials. [5-7]

It should be noted that there is an instance where vaccinations can induce T-cell (Th1) responses. This is possible in the case of repetitive immunizations with the same antigen (i.e., closely spaced “booster shots”).

However, the induction of such immune responses is deleterious as demonstrated by Tsumiyama et al. [8] who showed that CD4+ T cells from repeatedly-immunized mice acquire the ability to induce autoantibodies which result in autoimmune tissue injury akin to that seen in human autoimmune diseases.

From these experiments Tsumiyama et al. [8] concluded that systemic autoimmunity appears to be the inevitable consequence of over-stimulating the host's immune ‘system’ by repeated immunization with antigen.

Full Report

<http://sanevax.org/wp-content/uploads/2015/05/Herd-Immunity-.pdf>

Forced Vaccinations: For the Greater Good?

by Lucija Tomljenovic, PhD

Full Report

<http://vaccinechoicecanada.com/wp-content/uploads/Forced-Vaccinations-For-the-Greater-Good-Tomljenovic.pdf>

Dr. Lucija Tomljenovic was awarded a PhD in 2009 in Biochemistry from the Comparative Genomics Centre at James Cook University in Townsville, Australia. In 2010, she joined the Neural Dynamics Research Group at the University of British Columbia (Chris Shaw's lab) and is currently researching the neurotoxic effects of aluminium vaccine adjuvants.

Lawsuits claiming Merck lied about mumps vaccine efficacy headed to trial

September 9, 2014 by Carly Helfand

Two lawsuits claiming Merck (\$MRK) lied about the efficacy of its mumps vaccine won't be going away anytime soon. A federal judge in Pennsylvania refused to dismiss the suits, filed by a pair of whistleblowers and a group of doctors and payers, and now, they're on their way to trial.

On Thursday, U.S. District Judge C. Darnell Jones II ruled that the whistleblowers--two former Merck virologists--had sufficiently showed that the company may have misstated the vaccine's efficacy to the government, Law360 reports. And the direct purchasers produced enough evidence to establish that those false statements could have helped give Merck a monopoly, the judge said. Now, the plaintiffs will have to prove their cases at trial.

Merck has been the sole manufacturer with an FDA license to produce mumps vaccine since 1967, the news service points out, and the company has long touted a 95% efficacy rate for the shot. The drugmaker brought in \$621 million on mumps vaccine sales last year, between its M-M-R II vaccine and ProQuad, a pediatric combo jab.

But rather than using the "gold standard" approach and testing the vaccine against a wild-type mumps virus, Merck tested it against the attenuated virus strain that had created the vaccine in the 1960s--likely overstating the vaccine's effectiveness, the whistleblowers claim, according to the judge's memorandum. And if Merck "fraudulently misled the government and omitted, concealed, and adulterated material information regarding the efficacy of its mumps vaccine" in violation of the False Claims Act, as they allege, it may have discouraged competition.

"As with the market for any product, a potential competitor's decision to enter a market hinges on whether its product can compete with those products already being sold in the market," the complaint reads, as quoted by Law360. "If an existing vaccine is represented as safe and at least 95% effective, as Merck has falsely represented its vaccine to be, it would be economically irrational for a potential competitor to bring a new mumps vaccine to the relevant market," the suit claims.

The way Merck sees it, whether it misstated the vaccine's efficacy is a matter for the FDA to investigate. The company argued that the whistleblowers' claims "rest on a finding that the vaccine label is misbranded, a determination which should fall squarely under the 'scientific expertise' and 'regulatory discretion'" of the agency, the memorandum says.

But Jones didn't agree, and now it'll be up to the courts to decide--a prospect that pleases Constantine Cannon, which is representing the whistleblowers, and Robins Kaplan Miller & Ciresi, representing the direct purchasers. "This decision brings us one step closer to shining a light on Merck's deceptive business practices so that new and more effective vaccines will ultimately be developed in the future," Robins Kaplan Miller & Ciresi lawyer Kellie Lerner said in a statement.

Read the judges Memorandum

<http://assets.fiercemarkets.net/public/merckmemo.pdf>

CDC Responds to Allegation it Omitted Vaccine-Autism Study Link

by Sharyl Attkisson • August 28, 2014

The Centers for Disease Control and Prevention (CDC) is responding to a charge from one of its own senior scientists that it omitted key data in a 2004 study that would have revealed a link between autism and a commonly-required childhood vaccine, MMR (Measles, Mumps, Rubella).

The allegation was made by CDC epidemiologist William Thompson in a statement this week issued through his attorney. It states: “I regret that my coauthors and I omitted statistically significant information in our 2004 article published in the journal *Pediatrics*. The omitted data suggested that African American males who received the MMR vaccine before age 36 months were at increased risk for autism.”

It is highly unusual, if not unprecedented, for a sitting CDC senior scientist to blow the whistle on alleged scientific misconduct involving a study article that he co-authored. In this instance, the impact of the charge is magnified by more than a decade of allegations from autism advocates who say the federal government and pharmaceutical interests have worked to downplay or hide associations between vaccines and autism.

Dr. Frank DeStefano, CDC Director of Immunization Safety

A spokesman for the journal *Pediatrics* today said the publication stands by the study despite the news. “There’s a standard process that journals follow when an article is questioned,” said the spokesman. “Those discussions took place between the editors of *Pediatrics* and the authors of this study, and the editors concluded the research was appropriately conducted.” *Pediatrics* is published by the American Academy of Pediatrics, which accepts vaccine industry funding.

The Director of the CDC Immunization Safety Office, Dr. Frank DeStefano, is a co-author of the now-questioned study which has been widely-cited to dispel an MMR-autism link. DeStefano is frequently quoted as an expert who debunks vaccine-autism ties.

“I stand by the research and the conclusions in our 2004 paper, and I’ll reiterate that the evidence, thus far, the weight of the evidence, is against a causal association between vaccines and autism,” DeStefano told me in a telephone interview this week.

“Lowest Point in my Career”

Thompson is a PhD who works in the National Immunization Program at the CDC where he has been employed for 16 years. His revelations were first made public after he reportedly made wide-ranging claims and confessions in a series of telephone conversations with autism advocate and researcher Brian Hooker of Focus Autism. Hooker, also a PhD, is an assistant professor of biology and the parent of an autistic teenager. Because of the significance of Thompson’s allegations, Hooker began recording some of the conversations without Thompson’s knowledge.

“It’s the lowest point in my career that I went along with that paper,” Thompson tells Hooker in a recording played on the online Autism Media Channel. “I went along with this, we didn’t report significant findings.”

The CDC’s DeStefano acknowledges that he and his study co-authors changed their study analysis plan mid-stream, which resulted in reducing the statistical vaccine-autism link among black boys. But he says they did so for good scientific reason.

“[Vaccine] exposure around [three years of age] is just not biologically plausible to have a causal association with autism,” DeStefano says. “I mean autism would’ve already started by then...it probably starts in the womb. So I think from a biological argument, it’s implausible this was a causal association.”

Highly-Charged Issue

The issue is highly-charged for several reasons: public health officials fear that the public will panic and stop vaccinating if they believe there are links between vaccines and autism. That could lead to resurgence in serious infectious diseases.

Also, vaccination is a multi-billion dollar global industry that employs law firms and public relations agents to engage in a variety of high-powered PR efforts. These efforts include: lobbying members of Congress to prevent hearings exploring vaccine safety, holding private meetings with news executives to discourage reporting on vaccines and autism, and financing nonprofits which take favorable positions on vaccine safety issues. Because pharmaceutical companies that produce vaccines spend millions of dollars each year buying advertising on television, print and online, critics argue they may be given undue influence over content of the reporting media.

Pharmaceutical interests and their surrogates routinely falsely portray scientists and journalists who investigate vaccine safety as “anti-vaccine.” In his statement, Thompson emphasizes his safety concerns do not reflect an “anti-vaccine” mentality.

“I want to be absolutely clear that I believe vaccines have saved and continue to save countless lives,” Thompson states. “I would never suggest that any parent avoid vaccinating children of any race. Vaccines prevent serious diseases, and the risks associated with their administration are vastly outweighed by their individual and societal benefits.

“My concern has been the decision to omit relevant findings in a particular study for a particular sub group for a particular vaccine. There have always been recognized risks for vaccination and I believe it is the responsibility of the CDC to properly convey the risks associated with receipt of those vaccines.”

Subgroup Susceptibility?

Former National Institutes of Health Director Dr. Bernadine Healy broke ranks with her Institute of Medicine colleagues in 2008 in saying that public health officials have intentionally avoided researching whether subsets of children are “susceptible” to vaccine side effects because they are afraid that the answer will scare the public.

“What we’re seeing in the bulk of the population: vaccines are safe,” said Healy. “But there may be this susceptible group. The fact that there is concern, that you don’t want to know that susceptible group is a real disappointment to me. If you know that susceptible group, you can save those children. If you turn your back on the notion that there is a susceptible group... what can I say?”

“You’re saying that public health officials have turned their back on a viable area of research largely because they’re afraid of what might be found?” I asked Healy, at the time.

Healy answered, “There is a completely expressed concern that they don’t want to pursue a hypothesis because that hypothesis could be damaging to the public health community at large by scaring people. “First of all,” Healy said, “I think the public’s smarter than that. The public values vaccines. But more importantly, I don’t think you should ever turn your back on any scientific hypothesis because you’re afraid of what it might show.”

To date, the only vaccine that carries an explicit autism warning under “Adverse Reactions” on its label is Tripe-

dia's DTaP (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) vaccine. The label states that "autism" is included, along with SIDS, encephalopathy (brain damage) among other adverse events "because of the seriousness or frequency of reporting." The label states, "Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequencies or to establish a causal relationship to components of Tripedia vaccine."

The CDC's MMR vaccine information page cites the following "very rare" severe problems: "deafness, long-term seizures, coma, or lowered consciousness and permanent brain damage."

This week, in response to a query, the CDC stated that it is not currently investigating the relation between vaccines and autism spectrum disorders (ASD). "Further, CDC does not have any planned research addressing vaccines and autism," said a CDC spokesman.

"CDC believes that this topic has been thoroughly studied and no causal links have been found. Current CDC ASD related research focuses on determining how many people have ASD and understanding risk factors and causes for ASD."—CDC spokesman

In his statement, Thompson says that his colleagues and supervisors at the CDC have been entirely professional since his allegations became public. "In fact, I received a performance-based award" after the news came out, he says.

Further responding to Thompson's allegations, the CDC says, "Additional studies and a more recent rigorous review by the Institute of Medicine have found that MMR vaccine does not increase the risk

CDC: “Possibility” that vaccines rarely trigger autism

September 2014

by Sharyl Attkisson

CDC’s immunization safety director says it’s a “possibility” that vaccines rarely trigger autism but “it’s hard to predict who those children might be.” (They’re not even trying.)

A CDC senior epidemiologist stepped forward last week to say that he and his CDC colleagues omitted data that linked MMR vaccine to autism in a 2004 study. The scientist, William Thompson, said “I regret that my coauthors and I omitted statistically significant information.” A coauthor of the questioned study is Dr. Frank DeStefano, Director of the CDC Immunization Safety Office. In a telephone interview last week, DeStefano defended the study and reiterated the commonly accepted position that there’s no “causal” link between vaccines and autism. But he acknowledged the prospect that vaccines might rarely trigger autism.

“I guess, that, that is a possibility,” said DeStefano. “It’s hard to predict who those children might be, but certainly, individual cases can be studied to look at those possibilities.”

It is a significant admission from a leading health official at an agency that has worked for nearly 15 years to dispel the public of any notion of a tie between vaccines and autism. Vaccines are among the most heralded medical inventions of our time. Billions of people have been vaccinated worldwide, countless lives have been saved and debilitating injuries prevented. The possibility that vaccines may also partly be responsible for autism, in individual cases, is not something public health officials are typically eager to address. One such individual case is that of Hannah Poling.

Hannah Poling

Hannah Poling was considered normal, happy and precocious until 19 months of age when she was vaccinated against nine diseases in one doctor’s visit: measles, mumps, rubella, polio, varicella, diphtheria, pertussis, tetanus, and Haemophilus influenzae. Afterward, she developed high fevers, had screaming fits, stopped eating, didn’t respond when spoken to and began showing signs of autism. As vaccination has grown into a multi-billion dollar industry, children have gone from being inoculated against four diseases in 1953 to today’s recommended schedule of shots for 16 diseases requiring 49 doses by age 6. The government and pharmaceutical industry have said evidence shows babies’ systems can easily handle the immune boost.

In federal “vaccine court,” the U.S. government defends injury claims on behalf of vaccine makers. In 2002, Hannah’s parents—her father a neurologist, her mother a nurse and attorney—filed a claim in a specially-created federal vaccine court in which the U.S. Department of Justice defends vaccine interests. Hannah was to serve as a test case to help decide the outcome of thousands of vaccine-autism claims. The case was strong. In 2007, contemplating Hannah would win her claim, sources say the vaccine court analyzed what the broader financial impact might be. It found that a flood of similar vaccine-autism claims would quickly deplete the government’s vaccine injury compensation fund, which is supported by a small fee patients pay on each dose of vaccine.

But instead of allowing Hannah’s case to publicly serve as a precedent for other possible victims, the government took another course: it quietly settled the case and sealed the results. Other families with autistic children were never to know. Hannah’s family petitioned the court to be allowed to reveal the findings but the government fought to keep the case sealed—and prevailed. Still, news of Hannah’s case leaked out in 2008—along with the medical explanation for her vaccine-related “autistic encephalopathy [brain damage].” Vaccines prevent many diseases that once routinely killed or harmed. But can vaccines trigger autism in a small subset of vulnerable children? In a court-submitted opinion, neurologist Dr. Andrew Zimmerman, Director of Medical Research at

the Kennedy Krieger Institute, stated that he had “personally witnessed [Hannah’s] developmental regression” following “vaccine-induced fever and immune stimulation.”

Zimmerman concluded that Hannah was vulnerable to vaccine injury because she had a metabolic disorder called mitochondrial dysfunction. While vaccines are safe for most children, in Hannah, they triggered a brain injury, according to Zimmerman. Whether vaccines “caused” or “triggered” Hannah’s autism, the result was the same: but for her vaccinations, Zimmerman said, “Hannah may have led a normal full productive life.” Instead, she suffers “significant lifelong disability.”

A second underlying condition that was aggravated by vaccines, resulting in mental retardation and autism, is tuberous sclerosis or “TS,” according to a 1986 vaccine court case. According to the National Institutes of Health, TS affects 1 in every 6,000 newborns. Not all children who developed autism as a result of vaccine injuries, as determined by vaccine court, had identifiable pre-existing conditions. But I asked the CDC’s DeStefano whether it was worth trying to figure out what underlying conditions put kids at risk so they can be tested in advance and, if vulnerable, spared.

“That’s very difficult to do,” DeStefano told me. He said the CDC’s priorities are gaining a better understanding of the pathogenesis, genetics and biology of autism. “And then, I think... it’d be more feasible to try to establish if vaccines in an individual case, say a person with a certain set of genes...if we ever get to that point, then that kind of research might be fruitful.”

Not worthy of study?

But it turns out the CDC has ruled out that sort of research. A CDC spokesman told me that the agency is not “currently investigating the relation between vaccines and autism spectrum disorders (ASD). Further, CDC does not have any planned research addressing vaccines and autism.” As of May, 2010 the government had compensated 1,296 vaccine brain damage (encephalopathy/encephalitis and seizure cases) but was not tracking how many of the brain-injured children specifically ended up with autism.

“CDC believes that this topic has been thoroughly studied and no causal links have been found,” said the spokesman in an email. “Current CDC ASD related research focuses on determining how many people have ASD and understanding risk factors and causes for ASD,” said the CDC. Seven years after Hannah’s case settled, twenty-eight years after the TS case, it’s impossible to know how many similar children, if any, are out there. And the government isn’t trying to find out.

Attkisson: And is, is the pos—the current position that any potential link between vaccines and autism, secondary, any kind at all, has been entirely ruled out 100%?

DeStefano: I re, you know, I re—uh, I think every hypothesis that’s been looked at has been, uh, ruled out.
Attkisson: But, I mean, are you, are you, can I say the CDC’s position is that if anybody thinks there’s anything anymore, it’s a myth? It’s all been disproven?

DeStefano: Wouldn’t say it’s a myth, I’d say, you know, all the evidence, thus far, points to that there’s not a causal association between vaccines and autism.

Attkisson: What about secondary?

DeStefano: Sec—I don’t understand what do you mean “secondary”?

Attkisson: What about not “causal,” but “as a result of” vaccines, as in the Poling case? The medical expert found, you know, as a result of the damages she had from the vaccines, she ended up with autism. And the distinc-

tion was made in the medical expert, ‘well, that’s not ‘causal’, it’s sort of a ‘but for’ but it’s not a ‘causal.’

DeStefano: Yeah, I mean, I mean in that case, you know, she had a, I mean, you know, she had an underlying uh biological illness that uh either vaccination, or it could’ve been an infection that that would trigger some physiological stress in her, uh, seems to have, you know, could’ve, could’ve caused uh, um, manifestations that, characteristics of autism which, you, you know, appears to be what happened in her case.

Attkisson: But I mean doesn’t that, is—isn’t that a “link”? It’s not a “causal” link, but isn’t that a potential link between vaccination and autism if certain children with a “underlying biological illness” can have a “trigger” through vaccination?

DeStefano: [Unintell] as you call it, a secondary link if you wanna call it that way, w– in certain children, I mean ri—I mean, I, maybe that, but, you know, then I guess, that, that is a possibility.

Attkisson: Do you think that’s an important area of study so we could figure out which kids might have that predisposition?

DeStefano: uh, [phone noise] Yeah, I mean, I think um... You know, I think it’s something that, uh, well I mean, you know, in terms of uh... I mean, It’s hard, it’s hard to say, you know, I mean it’s like, um... I mean how how important that is. I mean, it’s a theoretical possibility, I guess the, the Poling case maybe suggested it could happen. Uh, but [unintell] cause it’s hard to predict who those children might be, but certainly, um individual cases, uh, can be studied to try to, uh, to look at those, uh, those possibilities.

Attkisson: Well I would just think—and then, then I’ll let you go in a few minutes unless you have more time—but as a parent, if my kid had whatever Poling had and we could figure that out, that would be one kid you would cull out [from vaccination] versus not worry about other kids if they don’t have that predisposition. But maybe you could identify the ones that would be vulnerable. But I haven’t seen that there’s any—is there an area of study trying to do such a thing within CDC or funded by CDC? Or NIH?

DeStefano: Well, in terms of like, you know, the area at CDC that’s that’s studying autism and possible causal relationships of autism, uh, you know, whatever they may be, uh, is in the Center the National Center for Birth Defects and Developmental Disability, and they, they do monitoring for autism prevalence and they do have, uh, studies trying to go on, you know, going on to, to look at, uh, a number of factors that could be, uh, related to, uh, increasing the risk of autism or causing autism.

Attkisson: I mean I think to sum up, you’re you’re saying what I, what I think is also the case just based on my own research: that while the government has ruled out any known “causal” link between autism and vaccines, it hasn’t ruled out the possibility, and in fact there seems to be at least one case where it’s acknowledged what I called a “secondary” link, meaning not “causal” but uh “triggered.” And the result for the parent, you know, may—to them it may be one and the same. And they may be trying to figure out which kids, you know, might have that predisposition.

DeStefano: Yeah, but you know, that’s very difficult to do. That’s almost circular reasoning, say, you know, kind of, you can’t, I mean, you know, the, the useful thing for parents who are clinically would be able to identify the kids who are gonna have, I mean, this way we’re identifying one certain child after the fact and say, you know, maybe in that one child, it was this or that that happened to him. But uh, it’s very difficult to make a causal link in in just one case.

Attkisson: Well, but isn’t that what you guys are supposed to do, figure it out? That’s a, as you know, autism is such a huge problem, even if a teeny percentage is perhaps triggered by vaccination, I would think that’d be very, very important to, to learn and try to figure out. You guys are the best at it, I’m sure somebody there can do it over time.

DeStefano: Yeah... [unintell] I think... [unintell] have a better understanding of uh of the pathogenesis of autism and the genetics and the biology and then, I think, I mean, and then, and then, with these individual cases, it’d be, you know, more feasible to try to establish if, uh, if, if vaccines in an individual case, say a person with a certain, certain set of genes or something, you know, if we ever get to that point, then that kind of research, uh, might be fruitful, you know.

Basics of the Human Immune System Prior to Introduction of Vaccines: Are Vaccines Turning Our Children's Immune Systems Inside Out?

Harold E Buttram, MD and Catherine J Frompovich

There is a universal principle referred to as "atrophy of disuse" which, as far as can be determined, applies to all physiologic processes of the human body. Although a normal full-term infant comes into the world with virtually all of the brain cells (neurons) that it will ever have, the brain continues to grow from increasing numbers of glial (connective tissue) cells and dendrite branching extensions that continue throughout life with mental activity. As an example, the story is told of two sisters who were identical twins and entered a nunnery, one gravitating into administrative work, the other into menial labor. With the passage of years the former remained mentally alert and bright, while the latter lapsed into Alzheimer's disease from brain atrophy.

As a brief review of Part 1, the human newborn comes into the world with temporary protection from residual maternal antibodies. Otherwise the infant's immune system is rudimentary, requiring a series of challenges to become fully functional, which is around three years of age. Although the so-called minor childhood diseases of earlier times were looked upon as nuisances (chickenpox and mumps) or potentially dangerous (measles and rubella), they may have evolved as friends-in-disguise by challenging and therefore uniquely activating and strengthening both epithelial and endothelial tissues, their respective organs, and lymph nodes. Those natural diseases also had the advantage of conferring permanent immunity, which is not necessarily the case with vaccines as attested to with revaccination every few years and higher percentages of infectious disease among those vaccinated.

Concerning the dangers of measles, aside from hygiene and sanitation, this largely involves personal disciplines in terms of diet, nutrition, and other health habits in which restriction/avoidance of sugar plays a prominent role along with abundant dietary sources (fresh fruits and vegetables) containing vitamins C and A. Nutrient deficiency may be an underlying reason that flu epidemics tend to occur over holidays, when people are inclined to overindulge in sweet treats and alcoholic beverages, which metabolize like sugar in the body.

There is an experimental basis for demonstrating sugar's paralyzing effects on the immune system. As demonstrated by Professor Emanuel Cheraskin at the Alabama University Medical School, blood samples were drawn from students before and after drinking a single soft drink (soda). White cells were siphoned from the blood samples and the white cells inoculated with staphylococcus microorganisms. After a period of incubation, the number of staphylococcus phagocytized (engulfed) by the white cells were counted under a microscope. The numbers of engulfed staphylococcus were reduced by more than half following consumption of the soft drink, indicating that the white cells were significantly paralyzed and crippled by that sugar-containing beverage. [1]

Also pertinent was a study conducted in Afghanistan in which 200 children with measles were divided into two groups, one of which received aspirin and Tylenol® to lower fever, the other not receiving aspirin or Tylenol®. The children receiving antipyretics had more prolonged illnesses, more diarrhea, ear infections, respiratory complications such as pneumonia and bronchitis, and higher death rates. [2]

Concerning the chickenpox (varicella) vaccine, articles by Gary Goldman seriously question the advisability of universal varicella vaccination as related to increasing subsequent occurrences of herpes zoster (shingles or zona). [3-4] The differing functions of the Th1 cellular and Th2 humoral immune systems were summarized in a review article by P. Kidd:

"The Th1 cells are hypothesized to lead the attack against intracellular pathogens such as viruses, raise the classic delayed-type to viral and bacterial antigens, and fight cancer cells. The Th2 cells are believed to emphasize protection against extracellular pathogens. On the negative side, the Th1 pathway is often portrayed as being the more aggressive of the two, and when it is overreactive, can generate organ-specific autoimmune disease (e.g. arthritis, multiple sclerosis, type 1 diabetes). The Th2 pathway is seen as underlying allergy and related IgE disease." [5]

Regarding vaccines and their propensity toward fostering allergies, Imani and Kehoe found a previously unrecognized side effect of the MMR vaccine by incubating it with a line of human plasma cells, which resulted in increased expression of allergy-related IgE antibodies accompanied by a corresponding decrease in protective IgG antibodies. Based on these findings, the authors concluded that viral vaccines might be playing a role in the increasing incidence of asthma and other allergic diseases. [6]

Much the same also holds true for a causal relationship between vaccines and the rising incidence of juvenile diabetes. In 1998 John Classen, MD, gave a presentation at a conference held by the American College of Medicine in which he reviewed 32 published articles, five authored by himself, indicating a causal relationship between vaccines and the rising incidence of insulin-dependant diabetes mellitus (IDDM). Nations represented in the papers included New Zealand, Canada, the United Kingdom, Denmark, Finland, Sweden, the USA, and Holland. Single vaccines were used including haemophilus influenza, hepatitis B, pertussis, BCG, and smallpox.

A prototype study was conducted in Finland by Classen and reported in the British Medical Journal. [7] In this study, from all children born in Finland between October 1, 1985 and August 31, 1987, approximately 116,000 were randomized as test subjects to receive four doses of haemophilus vaccine starting at three months of age, or one dose starting at 24 months. Additionally, 125,000 unvaccinated children served as controls. Each group was followed until age 10 years for development of IDDM. The incidence at seven years for those receiving four doses, those receiving one dose, and those receiving none was 261, 237, and 207 respectively with relative risks of 1.2, 1.14, and 1 for those children receiving no vaccine.

In virtually all of the reports from other countries the results were very similar, indicating a slight but consistent increase in IDDM following each of the five single vaccines listed above. Classen interpreted these results as indicating that it was not the type of vaccination that mattered so much as the immunologic impact of vaccination itself. Typically there was a 3 to 5 year delay between vaccines and onset of IDDM.

Quotations by Classen during the 1998 conference included:

"Vaccinating every child against every disease is fundamentally unsound."

"There is a 3.78-fold increased risk of insulin-dependent diabetes mellitus in children from today's vaccines."

"All autoimmune diseases are increasing in incidence. General immune (over) stimulation from vaccines is a cause of autoimmunity."

Genetic Exchanges in the World Around Us

Barbara McClintock, the 1983 Nobel Laureate “Corn Lady,” was the first to discover genetic mobility in the so-called jumping genes in the 1930s. For over 50 years she pursued solitary research with corn, uncovering some of nature’s innermost secrets about life. McClintock studied maize, a form of Indian corn, where distribution of red kernels and yellow kernels is genetically determined. What she first perceived was that some of the genes were moving from one place to another on the cell’s chromosomes (the floating threads on which genes are lined like beads on a string). She then saw patterns in the movements, with sharply differing results in the colored kernels, and realized that some genes, once moved into position, switched other genes on or off. It followed that while most genes were workers, others were controllers or managers of genes.

According to an article in World Medicine [8] scientists at the University of Geneva made the startling discovery that biological substances entering directly into the bloodstream may truly become a part of us, even a part of our genetic material. The article stated in part:

“When Japanese bacteriologists discovered that bacteria of one species transferred their own highly specific antibiotic resistance to bacteria of an entirely different species, they seemed to hit on a unique if not startling phenomenon. Dr. Maurice Stroun and Dr. Phillippe Anker, with colleagues in the Plant Physiology Department at the University of Geneva, have now accumulated a wealth of evidence that the transfer of genetic information is not confined to bacteria but also can occur between bacteria and higher plants and animals.

“Dr. Stroun and colleagues did most of their research in plants but have now turned to animals. In their latest experiments they used the isolated auricles of frogs’ hearts, [9] from which they dipped RNA extracted from the frog auricles into a bacterial suspension, resulting in a high percentage interlinkage of frog RNA with bacterial DNA.”

The article concluded that the implications of this work on “transcession” are enormous and reflect something that may be commonly taking place in human bodies. From the standpoint of future generations, the possibility that vaccines may be bringing about genetic hybridization in our children may represent far and away the greatest hazard of today’s childhood vaccine programs.

A Case On Point

During June 2011 a great number of German E.coli infections (3,406) and 39 deaths have occurred with suspicions that organically grown bean sprouts are the source of contamination. The findings have vacillated from yes, it was the sprouts to no, it was not the sprouts to now as of this writing, it IS the sprouts. However, the real issue may be more than bean sprouts, if they truly are the source of contamination and not a scapegoat. It seems the medical profession did not recognize that they were dealing with a rare strain of E.coli, O104:H4.

“What most predominantly differentiates O104 from O157 is its adoption of numerous traits not typically found congregated in one strain: Not only does it produce the noxious Shiga toxin of the virulent enterohemorrhagic strains, it also possesses defensive enteroaggregative traits –a combined mouthful of properties much more difficult to tolerate physically than verbally.”

“When people come into a hospital with bloody diarrhea, they would normally assume it’s O157 and not give antibiotics to the patients,” he said. “In this case, because it wasn’t O157, the physicians might have thought it was okay to give antibiotics, not knowing that O104 would produce the Shiga toxin.”

“This potential misunderstanding over antibiotics might at least partially explain the high rate of HUS [hemo-lytic-uremic syndrome] among the ill. Girón [Jorge Girón, Ph.D., E. coli researcher and associate professor of microbiology at the University of Florida’s Emerging Pathogens Institute] said this outbreak may necessitate new screening procedures at hospitals to account for O104 alongside O157, ensuring patients don’t receive antibiotics that could exacerbate their illness or kill them.” [Emphasis added] [11]

The above may be the classic example needed to illustrate the unknowns involved in vaccine pharmacology and morphology, and medicine’s inability or unwillingness to address that aspect of vaccinology.

Are Vaccines Sowing the Seeds of Genetic Change?

As reviewed above, the first six months of an infant’s life is a period of heightened vulnerability because of the infant’s immature and rapidly growing nervous system and highly immature immune system. It is during this time-period that 19 or 20 vaccines are routinely administered, according to officially recommended schedules, irrespective of whether the infant was born prematurely, a condition that apparently predisposes preterm infants to a series of vaccine adverse reactions. [12]

A very revealing study reported in Virus Research tends to support the hypothesis of genetic exchange associated with viral vaccines. In the study of 24 passages of a nuclear polyhedrosis virus through cell cultures, there were both insertions and deletions in the virus, [10] suggesting that the virus freely exchanged genetic material with the tissues in which it was cultured [similar to transcession discussed above].

Considering that today’s vaccines have been incubated in cell cultures of aborted fetuses, monkey kidneys, and other animal tissues, this should give any thinking person pause to consider the possible implications involved in manufacturing, injecting, and receiving vaccines.

Dr. Buttram discusses the immune system and the impact that vaccines have upon it in his book, A Commentary on Current Childhood Vaccine Programs, ISBN: 1-891485-30-X), published in 2010 by Philosophical Publishing Co., PO Box 77, Quakertown, PA 18951, phone 215-538-5300.

Catherine J Frompovich is the author of Our Chemical Lives And The Hijacking Of Our DNA available on Amazon.com here.

References:

1. Information presented at a lecture by Dr. Cheraskin in the 1970s.
 2. Ahmady, AS et al. The adverse effects of antipyretics in measles. Indian Pediatrics. Jan. 1981; 49-52.
 3. Goldman, GS. Universal varicella vaccination: Efficacy trends and effect on herpes zoster. Intern Journ Toxicol. 2005; 24: 205-213.
 4. Goldman, GS. The case against universal varicella vaccination. Intern J Toxicol, 2006; 25:313-317.
 5. Kidd, P. TH1/TH2 balance: The hypothesis, its limitations and implications in health and disease. Altern Med Rev. 2003; 8:223-246.
 6. Imani, E and Kehoe, KE. Infection of human B-lymphocytes with MMR vaccine induces IgE class switching. Journ Clin Immunol. 2001; 100(3):355-361.
 7. Classen, JB and Classen, DC. Association between type 1 diabetes and Hib vaccine, causal relation likely, British Med Journ. 1999; 319: 1133.
 8. World Medicine (Scientific News Report): Mobility of genetic material between life forms, 1971, Sept. 22nd, London: Clareville House, Oxendon St: 69-72.
 9. Anker, P and Stroun, M. Transcription of spontaneously released bacterial deoxyribonucleic acid in frog auricles, Journal of Bacteriology, 1973; 114: 114-120.
 10. Kumar, S and Miller, IK. Effects of serial passage of Autographa californica nuclear polyhydrosis virus to cell culture. Virus Research. 1987; 7: 335-349.
 11. Food Safety News, O104:H4 May Change How We Deal With E. coli <http://www.foodsafetynews.com/2011/06/e-coli-expert-weighs-in-with-facts-about-o104h4/> Accessed June 16, 2011.
 12. Pourcyrous M, Korones SB, Kristopher LA, Bada HS. Primary immunization of premature infants with gestational age <35 weeks: Cardiorespiratory complications and C-reactive protein responses associated with administration of single and multiple separate vaccines simultaneously. J Pediatrics. 2007;151, p. 171.
- See more at: <http://www.vaccinationcouncil.org/2011/06/21/risks-damage-basics-of-the-human-immune-system-prior-to-introduction-of-vaccines-are-vaccines-turning-our-childrens-immune-systems-inside-out-part-2/#sthash.SG9xMVCU.dpuf>

Government Wipes Recent Vaccine Injury Data From Website

December 30, 2015 • Sharyl Attkisson

In March, the federal government removed the latest vaccine injury court statistics—more than a year’s worth of data—from one of its publicly reported charts. It was an abrupt departure from the normal practice of updating the figures monthly.

Wiping the latest data means the “adjudication categories by alleged vaccine” chart on a government website no longer reflects the recent, sharp rise in court victories for plaintiffs who claimed their children were seriously injured or killed by one or more vaccines. Since January of 2014, the number of flu vaccine cases conceded by the government is more than double the previous eight years combined. The adjudication chart only reflects half of the current number.

Concessions Won by Flu Shot Victims since 2006
Chart shows (through 2013): 42
Actual number (through April 2015): 88

Total Flu Shot Victims Compensated Since 2006
Chart shows (through 2013): 1091
Actual number (through April 2015): 1271

Also on the rise is the number of vaccine injury cases the government has ‘conceded:’ up 55% in a little over one year. As a result of the recent website changes, neither of these trends is reflected on the current ‘adjudication’ chart.” Since its inception in 2013, the “adjudication categories by alleged vaccine” chart included monthly, updated totals.

But shortly after publishing the March 2015 chart, the government removed the 2015 and 2014 data, reverting back to outdated statistics from 2013. The chart appears on the government vaccine court website, which falls under Health Resources and Services Administration, an agency of the Department of Health and Human Services (HHS). In the unusual vaccine court, the government acts on behalf of pharmaceutical companies rather than the public, defending vaccine makers against alleged victims. Money damages are not paid by vaccine companies, but through fees collected from patients on every dose of vaccine.

Older Data Doesn’t Reflect Uptick in Awards to Vaccine Victims

HRSA says vaccine makers had no influence over the decision to revert to older data. The agency said it did so to synch up with a statistic the Centers for Disease Control (CDC) provides for the same chart that is only current through 2013: the number of vaccine doses distributed in US. “An internal decision was made to ensure that all internal data was consistent...and to update [the chart] only when all relevant data was available,” said HRSA in a statement.

Court Decisions Won By Vaccine Victims Since 2006
Chart Shows (through 2013): 159
Actual Number (through April 2015): 165

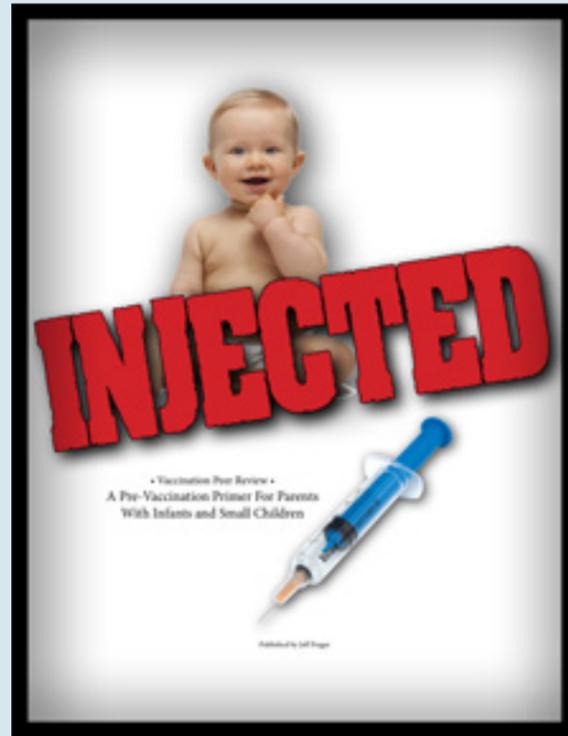
Concessions Won By Vaccine Victims Since 2006
Chart Shows (through 2013): 127
Actual Number (through April 2015): 198

Vaccine Victims Paid After Settlements Since 2006
Chart Shows (through 2013): 1388
Actual Number (through April 2015): 1488

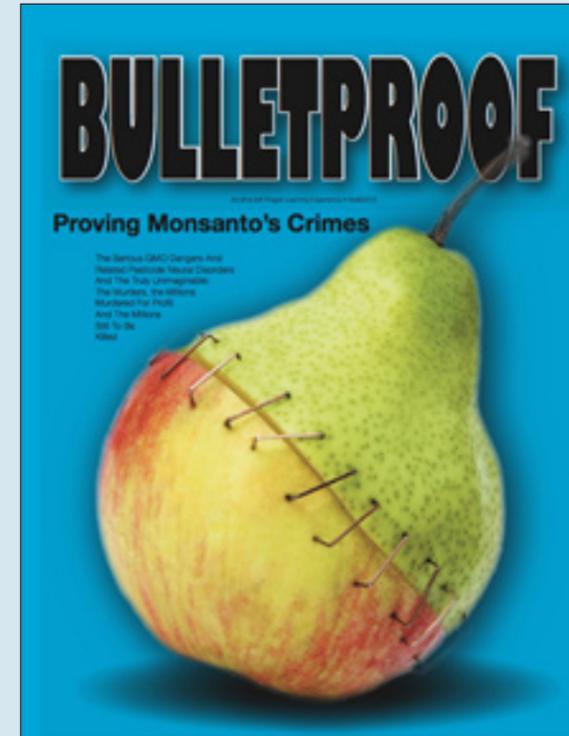
Only about one injury case for every million doses of vaccines is compensated in vaccine court. Adverse events occur more frequently, according to vaccine warning labels, but rarely end up in the little-known vaccine court. Still, vaccine court statistics can be useful in reflecting trends. Another recent change made vaccine injury data harder to find. The “adjudication categories by alleged vaccine” chart used to be the first item that showed up on the statistics page, but that has been replaced by language stating vaccines are safe and effective.

“Being awarded compensation for your claim does not necessarily mean that the vaccine caused the alleged injury,” adds the government to the statement where the adjudication chart used to be. Readers are directed to click a link to view the actual vaccine injury statistics. But clicking it only leads back to the statement that vaccines are safe and effective. To find the statistics, instead of clicking the link, readers must scroll down past it. According to the government, from 2006 to 2013, over 2.2 billion doses of vaccines were distributed in the U.S. For every 1 million doses, 1 alleged victim was compensated in vaccine court. Since 1998, over 15,916 claims have been filed in vaccine court. 4,121 were compensated, 9,904 were dismissed. The total amount paid to victims is approximately \$3.1 billion.

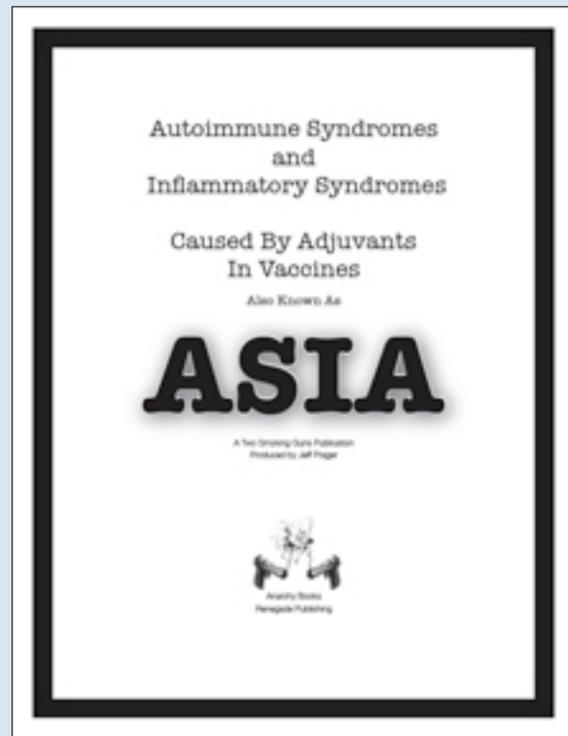
<https://sharylattkisson.com/govt-wipes-recent-vaccine-injury-data-from-website/>



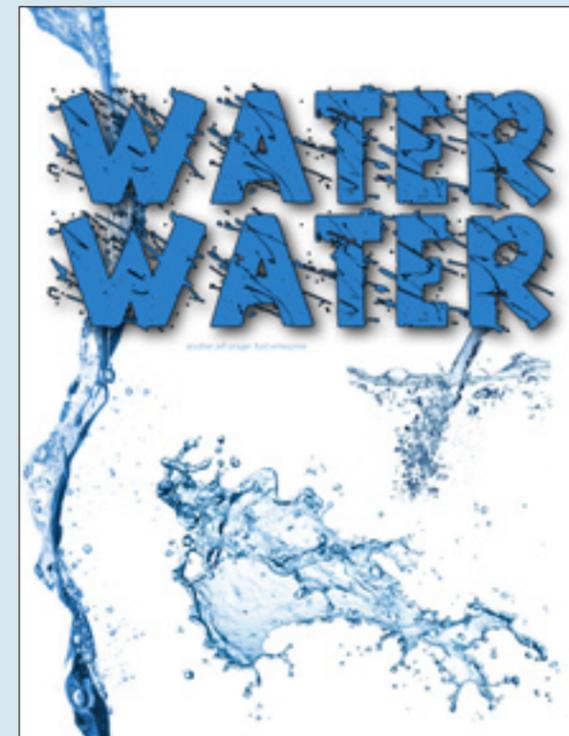
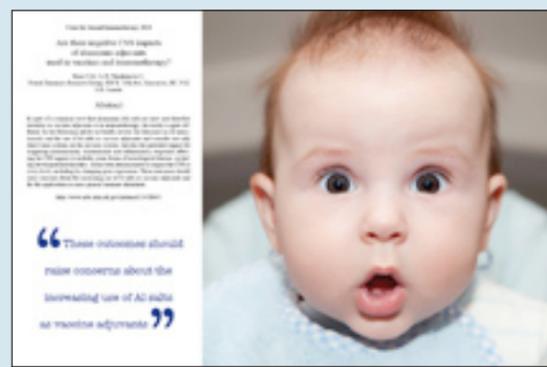
Injected • Vaccines and Genetic Mutation



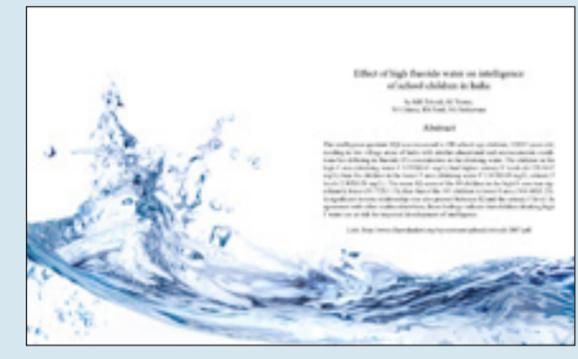
Bulletproof • An Expose On Glyphosate



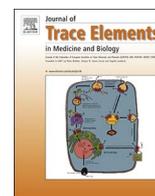
ASIA • Autoimmune And Inflammatory Disorders Caused By Vaccines



Water Water • Peer Review And Fluoridated Drinking Water



The End



Aluminium in brain tissue in autism

Matthew Mold^a, Dorcas Umar^b, Andrew King^c, Christopher Exley^{a,*}

^a The Birchall Centre, Lennard-Jones Laboratories, Keele University, Staffordshire, ST5 5BG, United Kingdom

^b Life Sciences, Keele University, Staffordshire, ST5 5BG, United Kingdom

^c Department of Clinical Neuropathology, Kings College Hospital, London, SE5 9RS, United Kingdom



ARTICLE INFO

Keywords:

Human exposure to aluminium
Human brain tissue
Autism spectrum disorder
Transversely heated atomic absorption spectrometry
Aluminium-selective fluorescence microscopy

ABSTRACT

Autism spectrum disorder is a neurodevelopmental disorder of unknown aetiology. It is suggested to involve both genetic susceptibility and environmental factors including in the latter environmental toxins. Human exposure to the environmental toxin aluminium has been linked, if tentatively, to autism spectrum disorder. Herein we have used transversely heated graphite furnace atomic absorption spectrometry to measure, for the first time, the aluminium content of brain tissue from donors with a diagnosis of autism. We have also used an aluminium-selective fluor to identify aluminium in brain tissue using fluorescence microscopy. The aluminium content of brain tissue in autism was consistently high. The mean (standard deviation) aluminium content across all 5 individuals for each lobe were 3.82(5.42), 2.30(2.00), 2.79(4.05) and 3.82(5.17) $\mu\text{g/g}$ dry wt. for the occipital, frontal, temporal and parietal lobes respectively. These are some of the highest values for aluminium in human brain tissue yet recorded and one has to question why, for example, the aluminium content of the occipital lobe of a 15 year old boy would be 8.74 (11.59) $\mu\text{g/g}$ dry wt.? Aluminium-selective fluorescence microscopy was used to identify aluminium in brain tissue in 10 donors. While aluminium was imaged associated with neurones it appeared to be present intracellularly in microglia-like cells and other inflammatory non-neuronal cells in the meninges, vasculature, grey and white matter. The pre-eminence of intracellular aluminium associated with non-neuronal cells was a standout observation in autism brain tissue and may offer clues as to both the origin of the brain aluminium as well as a putative role in autism spectrum disorder.

1. Introduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental conditions of unknown cause. It is highly likely that both genetic [1] and environmental [2] factors are associated with the onset and progress of ASD while the mechanisms underlying its aetiology are expected to be multifactorial [3–6]. Human exposure to aluminium has been implicated in ASD with conclusions being equivocal [7–10]. To date the majority of studies have used hair as their indicator of human exposure to aluminium while aluminium in blood and urine have also been used to a much more limited extent. Paediatric vaccines that include an aluminium adjuvant are an indirect measure of infant exposure to aluminium and their burgeoning use has been directly correlated with increasing prevalence of ASD [11]. Animal models of ASD continue to support a connection with aluminium and to aluminium adjuvants used in human vaccinations in particular [12]. Hitherto there are no previous reports of aluminium in brain tissue from donors who died with a diagnosis of ASD. We have measured aluminium in brain tissue in autism and identified the location of aluminium in these tissues.

2. Materials and methods

2.1. Measurement of aluminium in brain tissues

Ethical approval was obtained along with tissues from the Oxford Brain Bank (15/SC/0639). Samples of cortex of approximately 1 g frozen weight from temporal, frontal, parietal and occipital lobes and hippocampus (0.3 g only) were obtained from 5 individuals with ADI-R-confirmed (Autism Diagnostic Interview-Revised) ASD, 4 males and 1 female, aged 15–50 years old (Table 1).

The aluminium content of these tissues was measured by an established and fully validated method [13] that herein is described only briefly. Thawed tissues were cut using a stainless steel blade to give individual samples of ca 0.3 g (3 sample replicates for each lobe except for hippocampus where the tissue was used as supplied) wet weight and dried to a constant weight at 37 °C. Dried and weighed tissues were digested in a microwave (MARS Xpress CEM Microwave Technology Ltd.) in a mixture of 1 mL 15.8 M HNO_3 (Fisher Analytical Grade) and 1 mL 30% w/v H_2O_2 (BDH Aristar). Digests were clear with no fatty residues and, upon cooling, were made up to 5 mL volume using

* Corresponding author.

Table 1

Aluminium content of occipital (O), frontal (F), temporal (T) and parietal (P) lobes and hippocampus (H) of brain tissue from 5 donors with a diagnosis of autism spectrum disorder.

Donor ID	Gender	Age	Lobe	Replicate	[Al] µg/g	
A1	F	44	O	1	0.49	
				2	4.26	
				3	0.33	
				Mean (SD)	1.69 (2.22)	
				F	1	0.98
					2	1.10
					3	0.95
				Mean (SD)	1.01 (0.08)	
				T	1	1.13
			2		1.16	
			3		1.12	
			Mean (SD)	1.14 (0.02)		
			P	1	0.54	
				2	1.18	
				3	NA	
			Mean (SD)	0.86 (0.45)		
			All	Mean (SD)	1.20 (1.06)	
			A2	M	50	O
2	7.87					
3	3.49					
Mean (SD)	5.03 (2.46)					
F	1	0.86				
	2	0.88				
	3	1.65				
Mean (SD)	1.13 (0.45)					
T	1	1.31				
	2	1.02				
	3	2.73				
Mean (SD)	1.69 (0.92)					
P	1	18.57				
	2	0.01				
	3	0.64				
Mean (SD)	6.41 (10.54)					
Hip.	1	1.42				
	Mean (SD)	3.40 (5.00)				
A3	M	22	O	1	0.64	
				2	2.01	
				3	0.66	
				Mean (SD)	1.10 (0.79)	
			F	1	1.72	
				2	4.14	
				3	2.73	
			Mean (SD)	2.86 (1.22)		
			T	1	1.62	
				2	4.25	
				3	2.57	
			Mean (SD)	2.81 (1.33)		
			P	1	0.13	
				2	3.12	
				3	5.18	
			Mean (SD)	2.82 (1.81)		
			All	Mean (SD)	2.40 (1.58)	
			A4	M	15	O
2	1.66					
3	22.11					
Mean (SD)	8.74 (11.59)					
F	1	1.11				
	2	3.23				
	3	1.66				
Mean (SD)	2.00 (1.10)					
T	1	1.10				
	2	1.83				
	3	1.54				
Mean (SD)	1.49 (0.37)					
P	1	1.38				
	2	6.71				
	3	NA				
Mean (SD)	4.05 (3.77)					
Hip.	1	0.02				
	All	Mean (SD)				3.73 (6.02)

Table 1 (continued)

Donor ID	Gender	Age	Lobe	Replicate	[Al] µg/g
A5	M	33	O	1	3.13
				2	2.78
				3	1.71
			Mean (SD)	2.54 (0.74)	
			F	1	2.97
				2	8.27
				3	NA
			Mean (SD)	5.62 (3.75)	
			T	1	1.71
				2	1.64
				3	17.10
			Mean (SD)	6.82 (8.91)	
			P	1	5.53
				2	2.89
				3	NA
Mean (SD)	4.21 (1.87)				
All	Mean (SD)	4.77 (4.79)			

ultrapure water (cond. < 0.067 µS/cm). Total aluminium was measured in each sample by transversely heated graphite furnace atomic absorption spectrometry (TH GFAAS) using matrix-matched standards and an established analytical programme alongside previously validated quality assurance data [13].

2.2. Fluorescence microscopy

All chemicals were from Sigma Aldrich (UK) unless otherwise stated. Where available frontal, parietal, occipital, temporal and hippocampal tissue from 10 donors (3 females and 7 males) with a diagnosis of ASD was supplied by the Oxford Brain Bank as three 5 µm thick serial paraffin-embedded brain tissue sections per lobe for each donor (Table S1). Tissue sections mounted on glass slides were placed in a slide rack and de-waxed and rehydrated via transfer through 250 mL of the following reagents: 3 min in Histo-Clear (National Diagnostics, US), 1 min in fresh Histo-Clear, 2 min in 100% v/v ethanol (HPLC grade) and 1 min in 95, 70, 50 & 30% v/v ethanol followed by rehydration in ultrapure water (cond. < 0.067 µS/cm) for 35 s. Slides were agitated every 20 s in each solvent and blotted on tissue paper between transfers to minimise solvent carry-over. Rehydrated brain tissue sections were carefully outlined with a PAP pen for staining, in order to form a hydrophobic barrier around the periphery of tissue sections. In between staining, tissue sections were kept hydrated with ultrapure water and stored in moisture chambers, to prevent sections from drying out. Staining was staggered to allow for accurate incubation times of brain tissue sections. We have developed and optimised the fluor lumogallion as a selective stain for aluminium in cells [14] and human tissues [15]. Lumogallion (4-chloro-3-(2,4-dihydroxyphenylazo)-2-hydroxybenzene-1-sulphonic acid, TCI Europe N.V. Belgium) was prepared at ca 1 mM via dilution in a 50 mM PIPES (1,4-Piperazinediethanesulphonic acid) buffer, adjusted to pH 7.4 with NaOH. Lumogallion staining was performed via the addition of 200 µL of the staining solution to rehydrated brain tissue sections that were subsequently incubated at ambient temperature away from light for 45 min. Sections for autofluorescence analyses were incubated for 45 min in 200 µL 50 mM PIPES buffer only, pH 7.4. Following staining, glass slides containing tissue sections were washed six times with 200 µL aliquots of 50 mM PIPES buffer, pH 7.4, prior to rinsing for 30 s in ultrapure water. Serial sections numbered 1 and 2 for each lobe were incubated in 50 mM PIPES buffer, pH 7.4 or stained with 1 mM lumogallion in the same buffer, respectively, to ensure consistency across donor tissues. All tissue sections were subsequently mounted under glass coverslips using the aqueous mounting medium, Fluoromount™. Slides were stored horizontally for 24 h at 4 °C away from light, prior to analysis via fluorescence microscopy.

Stained and mounted human brain tissue sections were analysed via

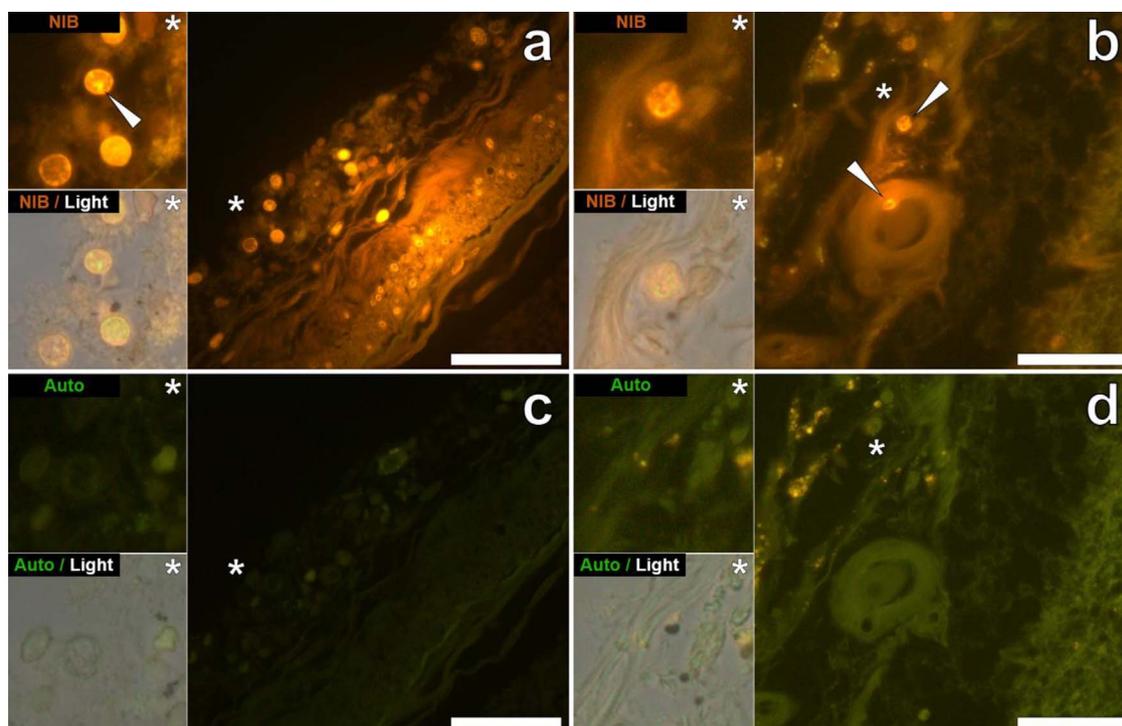


Fig. 1. Mononuclear inflammatory cells (probably lymphocytes) in leptomeningeal membranes in the hippocampus and frontal lobe of a 50-year-old male donor (A2), diagnosed with autism. Intracellular lumogallion-reactive aluminium was noted via punctate orange fluorescence emission (white arrows) in the hippocampus (a) and frontal lobe (b). A green autofluorescence emission was detected in the adjacent non-stained (5 µm) serial section (c & d). Upper and lower panels depict magnified inserts marked by asterisks, of the fluorescence channel and bright field overlay. Magnification $\times 400$, scale bars: 50 µm. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

the use of an Olympus BX50 fluorescence microscope, equipped with a vertical illuminator and BX-FLA reflected light fluorescence attachment (mercury source). Micrographs were obtained at X 400 magnification by use of a X 40 Plan-Fluorite objective (Olympus, UK). Lumogallion-reactive aluminium and related autofluorescence micrographs were obtained via use of a U-MNIB3 fluorescence filter cube (excitation: 470–495 nm, dichromatic mirror: 505 nm, longpass emission: 510 nm, Olympus, UK). Light exposure and transmission values were fixed across respective staining treatment conditions and images were obtained using the CellD software suite (Olympus, Soft Imaging Solutions, SiS, GmbH). Lumogallion-reactive regions identified through sequential screening of stained human brain tissue sections were additionally imaged on autofluorescence serial sections, to assess the contribution of the fluorophore. The subsequent merging of fluorescence and bright-field channels was achieved using Photoshop (Adobe Systems Inc. US). When determining intracellular staining the type of cells stained were estimated by their size and shape in the context of the brain area sampled and their surrounding cellular environment.

3. Results

3.1. Aluminium content of brain tissues

The aluminium content of all tissues ranged from 0.01 (the limit of quantitation) to 22.11 µg/g dry wt. (Table 1). The aluminium content for whole brains ($n = 4$ or 5 depending upon the availability of hippocampus tissue) ranged from 1.20 (1.06) µg/g dry wt. for the 44 year old female donor (A1) to 4.77 (4.79) µg/g dry wt. for a 33 year old male donor (A5). Previous measurements of brain aluminium, including our 60 brain study [13], have allowed us to define loose categories of brain aluminium content beginning with ≤ 1.00 µg/g dry wt. as pathologically benign (as opposed to 'normal'). Approximately 40% of tissues (24/59) had an aluminium content considered as pathologically-concerning (≥ 2.00 µg/g dry wt.) while approximately 67% of these tissues

had an aluminium content considered as pathologically-significant (≥ 3.00 µg/g dry wt.). The brains of all 5 individuals had at least one tissue with a pathologically-significant content of aluminium. The brains of 4 individuals had at least one tissue with an aluminium content ≥ 5.00 µg/g dry wt. while 3 of these had at least one tissue with an aluminium content ≥ 10.00 µg/g dry wt. (Table 1). The mean (SD) aluminium content across all 5 individuals for each lobe were 3.82(5.42), 2.30(2.00), 2.79(4.05) and 3.82(5.17) µg/g dry wt. for the occipital, frontal, temporal and parietal lobes respectively. There were no statistically significant differences in aluminium content between any of the 4 lobes.

3.2. Aluminium fluorescence in brain tissues

We examined serial brain sections from 10 individuals (3 females and 7 males) who died with a diagnosis of ASD and recorded the presence of aluminium in these tissues (Table S1). Excitation of the complex of aluminium and lumogallion emits characteristic orange fluorescence that appears increasingly bright yellow at higher fluorescence intensities. Aluminium, identified as lumogallion-reactive deposits, was recorded in at least one tissue in all 10 individuals. Autofluorescence of immediately adjacent serial sections confirmed lumogallion fluorescence as indicative of aluminium. Deposits of aluminium were significantly more prevalent in males (129 in 7 individuals) than females (21 in 3 individuals). Aluminium was found in both white (62 deposits) and grey (88 deposits) matter. In females the majority of aluminium deposits were identified as extracellular (15/21) whereas in males the opposite was the case with 80 out of 129 deposits being intracellular. We were only supplied with 3 serial sections of each tissue and so we were not able to do any staining for general morphology which meant that it was not always possible to determine which subtype of cell was showing aluminium fluorescence.

Aluminium-loaded mononuclear white blood cells, probably lymphocytes, were identified in the meninges and possibly in the process of

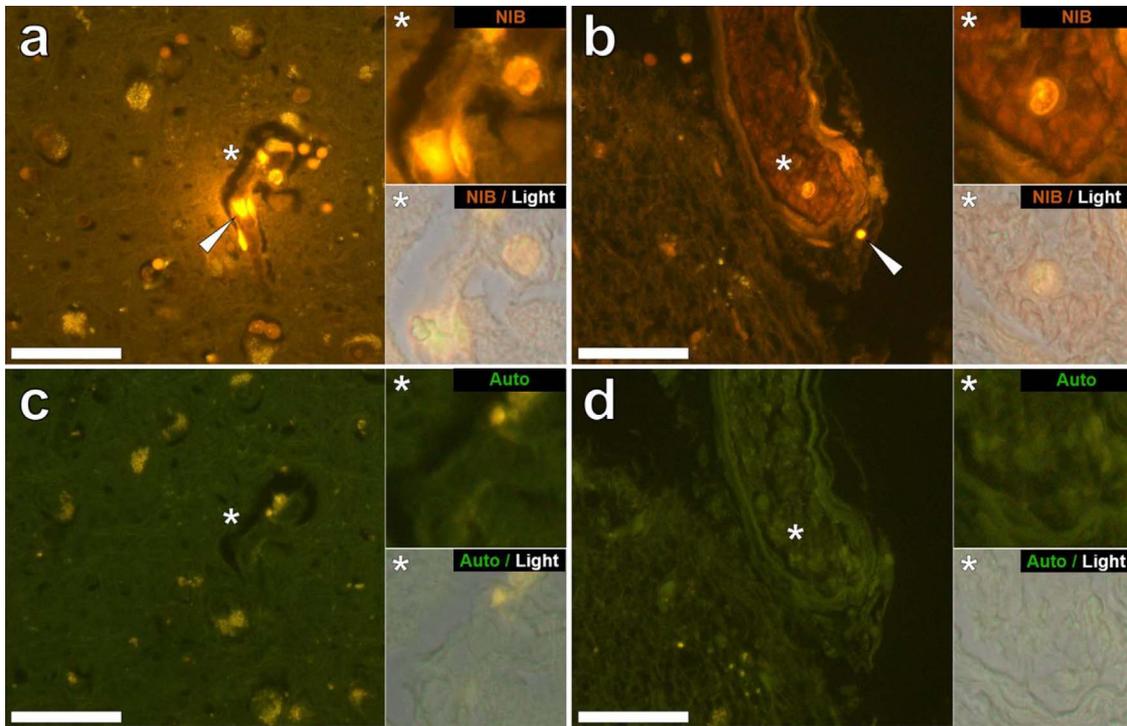


Fig. 2. Intracellular lumogallion-reactive aluminium in the vasculature of the hippocampus of a 50-year-old male donor (A2), diagnosed with autism. Aluminium-loaded inflammatory cells noted in the hippocampus in the vessel wall (white arrow) (a) and depicting punctate orange fluorescence in the lumen (b) are highlighted. An inflammatory cell in the vessel adventitia was also noted (white arrow) (b). Lumogallion-reactive aluminium was identified via an orange fluorescence emission (a & b) versus a green autofluorescence emission (c & d) of the adjacent non-stained (5 µm) serial section. Upper and lower panels depict magnified inserts marked by asterisks, of the fluorescence channel and bright field overlay. Magnification × 400, scale bars: 50 µm. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

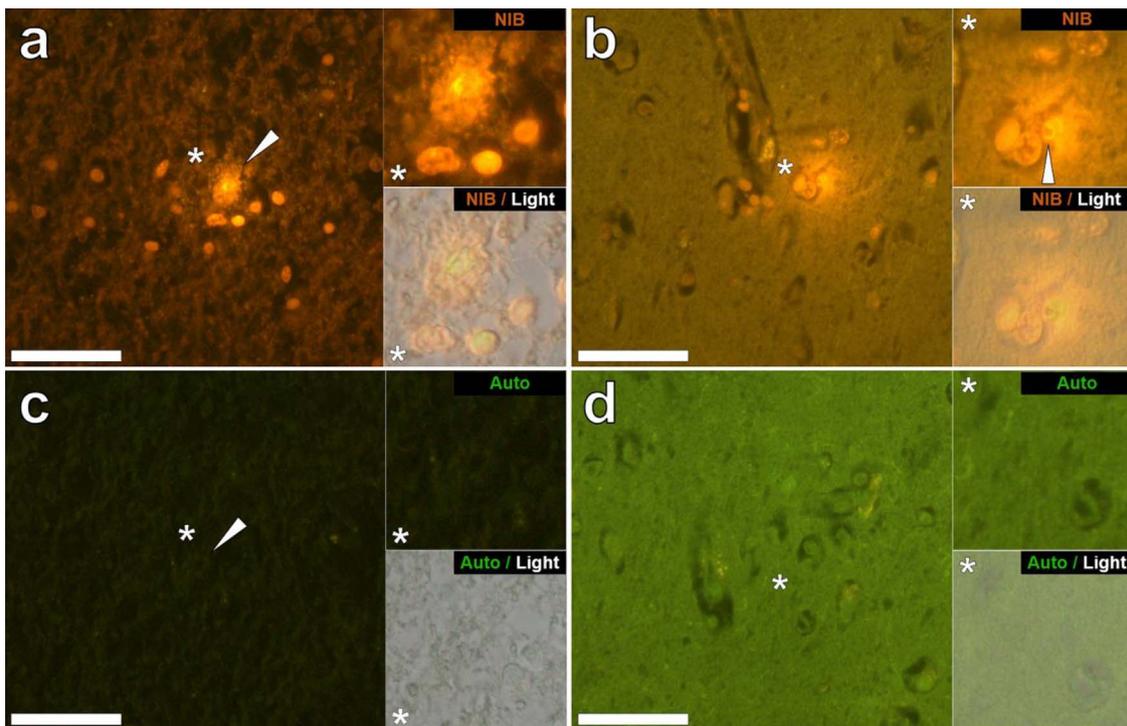


Fig. 3. Intracellular aluminium in cells morphologically compatible with glia and neurones in the hippocampus of a 15-year-old male donor (A4), diagnosed with autism. Lumogallion reactive cellular aluminium identified within glial-like cells in the hippocampus (a) and producing a punctate orange fluorescence in glia surrounding a likely neuronal cell within the parietal lobe (b) are highlighted (white arrows). Lumogallion-reactive aluminium was identified via an orange fluorescence emission (a & b) versus a green autofluorescence emission (c & d) of the subsequent non-stained (5 µm) serial section (white arrow/asterisk). Upper and lower panels depict magnified inserts marked by asterisks, of the fluorescence channel and bright field overlay. Magnification × 400, scale bars: 50 µm. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

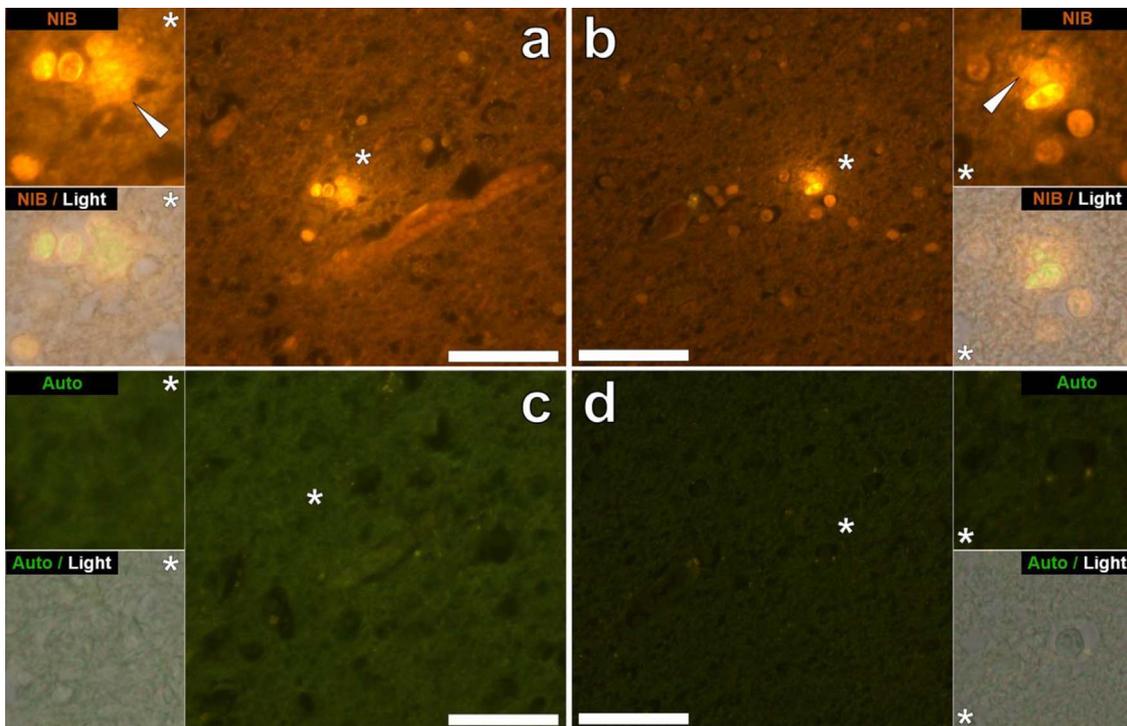


Fig. 4. Intracellular aluminium in cells morphologically compatible with microglia within the parietal and temporal lobes of 29-year-old (A8) and 15-year-old (A4) male donors, diagnosed with autism. Lumogallion-reactive extracellular aluminium (white arrows) producing an orange fluorescence emission was noted around likely microglial cells in the parietal (a) and temporal lobes (b) of donors A8 and A4 respectively. Non-stained adjacent (5 μ m) serial sections, produced a weak green autofluorescence emission of the identical area imaged in white (c) and grey matter (d) of the respective lobes. Upper and lower panels depict magnified inserts marked by asterisks, of the fluorescence channel and bright field overlay. Magnification \times 400, scale bars: 50 μ m. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

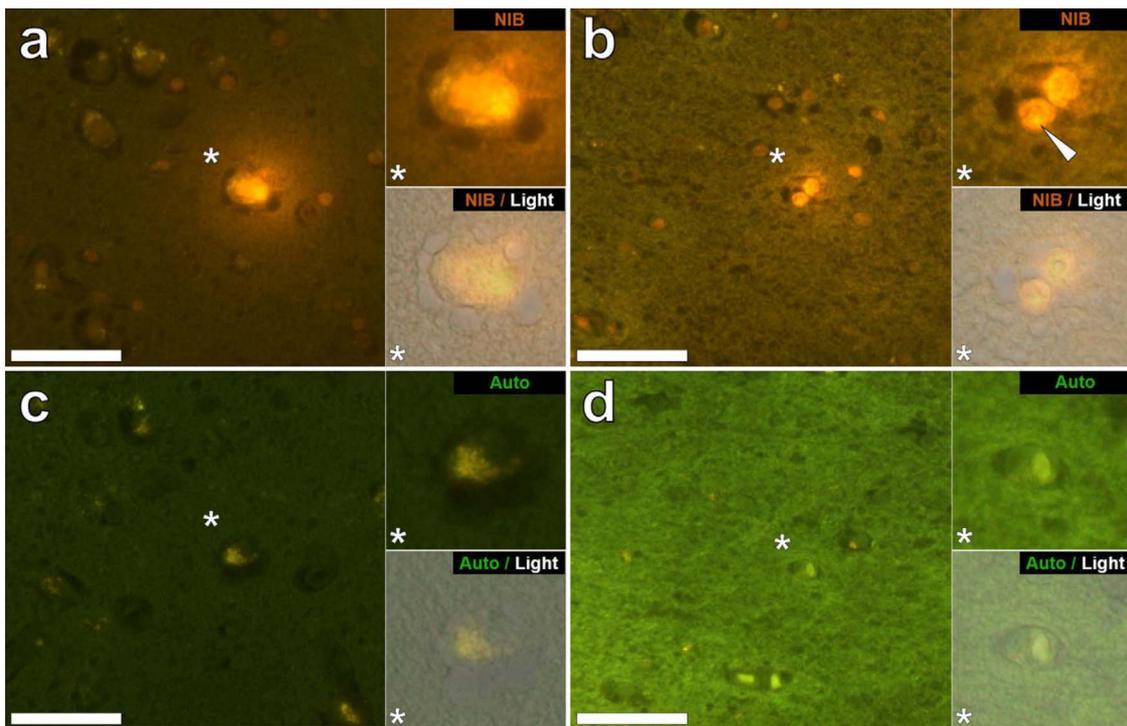


Fig. 5. Lumogallion-reactive aluminium in likely neuronal and glial cells in the temporal lobe and hippocampus of a 14-year-old male donor (A10), diagnosed with autism. Intra-neuronal aluminium in the temporal lobe (a) was identified via an orange fluorescence emission, co-deposited with lipofuscin as revealed by a yellow fluorescence in the non-stained auto-fluorescence serial (5 μ m) section (c). Intracellular punctate orange fluorescence (white arrow) was observed in glia in the hippocampus (b) producing a green autofluorescence emission on the non-stained section (d). Upper and lower panels depict magnified inserts marked by asterisks, of the fluorescence channel and bright field overlay. Magnification \times 400, scale bars: 50 μ m. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

entering brain tissue from the lymphatic system (Fig. 1). Aluminium could be clearly seen inside cells as either discrete punctate deposits or as bright yellow fluorescence. Aluminium was located in inflammatory cells associated with the vasculature (Fig. 2). In one case what looks like an aluminium-loaded lymphocyte or monocyte was noted within a blood vessel lumen surrounded by red blood cells while another probable lymphocyte showing intense yellow fluorescence was noted in the adventitia (Fig. 2b). Glial cells including microglia-like cells that showed positive aluminium fluorescence were often observed in brain tissue in the vicinity of aluminium-stained extracellular deposits (Figs. 3 and 4). Discrete deposits of aluminium approximately 1 µm in diameter were clearly visible in both round and amoeboid glial cell bodies (e.g. Fig. 3b). Intracellular aluminium was identified in likely neurones and glia-like cells and often in the vicinity of or co-localised with lipofuscin (Fig. 5). Aluminium-selective fluorescence microscopy was successful in identifying aluminium in extracellular and intracellular locations in neurones and non-neuronal cells and across all brain tissues studied (Figs. 1–5). The method only identifies aluminium as evidenced by large areas of brain tissue without any characteristic aluminium-positive fluorescence (Fig. S1).

4. Discussion

The aluminium content of brain tissues from donors with a diagnosis of ASD was extremely high (Table 1). While there was significant inter-tissue, inter-lobe and inter-subject variability the mean aluminium content for each lobe across all 5 individuals was towards the higher end of all previous (historical) measurements of brain aluminium content, including iatrogenic disorders such as dialysis encephalopathy [13,15,16–19]. All 4 male donors had significantly higher concentrations of brain aluminium than the single female donor. We recorded some of the highest values for brain aluminium content ever measured in healthy or diseased tissues in these male ASD donors including values of 17.10, 18.57 and 22.11 µg/g dry wt. (Table 1). What discriminates these data from other analyses of brain aluminium in other diseases is the age of the ASD donors. Why, for example would a 15 year old boy have such a high content of aluminium in their brain tissues? There are no comparative data in the scientific literature, the closest being similarly high data for a 42 year old male with familial Alzheimer's disease (fAD) [19].

Aluminium-selective fluorescence microscopy has provided indications as to the location of aluminium in these ASD brain tissues (Figs. 1–5). Aluminium was found in both white and grey matter and in both extra- and intracellular locations. The latter were particularly pre-eminent in these ASD tissues. Cells that morphologically appeared non-neuronal and heavily loaded with aluminium were identified associated with the meninges (Fig. 1), the vasculature (Fig. 2) and within grey and white matter (Figs. 3–5). Some of these cells appeared to be glial (probably astrocytic) whilst others had elongated nuclei giving the appearance of microglia [5]. The latter were sometimes seen in the environment of extracellular aluminium deposition. This implies that aluminium somehow had crossed the blood-brain barrier and was taken up by a native cell namely the microglial cell. Interestingly, the presence of occasional aluminium-laden inflammatory cells in the vasculature and the leptomeninges opens the possibility of a separate mode of entry of aluminium into the brain i.e. intracellularly. However, to allow this second scenario to be of significance one would expect some type of intracerebral insult to occur to allow egress of lymphocytes and monocytes from the vasculature [20]. The identification herein of non-neuronal cells including inflammatory cells, glial cells and microglia loaded with aluminium is a standout observation for ASD. For example, the majority of aluminium deposits identified in brain tissue in fAD were extracellular and nearly always associated with grey matter [19]. Aluminium is cytotoxic [21] and its association herein with inflammatory cells in the vasculature, meninges and central nervous system is unlikely to be benign. Microglia heavily loaded with

aluminium while potentially remaining viable, at least for some time, will inevitably be compromised and dysfunctional microglia are thought to be involved in the aetiology of ASD [22], for example in disrupting synaptic pruning [23]. In addition the suggestion from the data herein that aluminium entry into the brain via immune cells circulating in the blood and lymph is expedited in ASD might begin to explain the earlier posed question of why there was so much aluminium in the brain of a 15 year old boy with an ASD.

A limitation of our study is the small number of cases that were available to study and the limited availability of tissue. Regarding the latter, having access to only 1 g of frozen tissue and just 3 serial sections of fixed tissue per lobe would normally be perceived as a significant limitation. Certainly if we had not identified any significant deposits of aluminium in such a small (the average brain weighs between 1500 and 2000 g) sample of brain tissue then such a finding would be equivocal. However, the fact that we found aluminium in every sample of brain tissue, frozen or fixed, does suggest very strongly that individuals with a diagnosis of ASD have extraordinarily high levels of aluminium in their brain tissue and that this aluminium is pre-eminently associated with non-neuronal cells including microglia and other inflammatory monocytes.

5. Conclusions

We have made the first measurements of aluminium in brain tissue in ASD and we have shown that the brain aluminium content is extraordinarily high. We have identified aluminium in brain tissue as both extracellular and intracellular with the latter involving both neurones and non-neuronal cells. The presence of aluminium in inflammatory cells in the meninges, vasculature, grey and white matter is a standout observation and could implicate aluminium in the aetiology of ASD.

Competing interests

The authors declare that they have no competing interests.

Author contributions

CE designed the study, carried out tissue digests and TH GFAAS. DU carried out tissue digests and TH GFAAS. AK carried out brain neuropathology on sections prepared by MM. MM carried out all microscopy and with CE wrote the manuscript. All authors read and approved the manuscript.

Acknowledgements

The research is supported by a grant from the Children's Medical Safety Research Institute (CMSRI), a not-for-profit research foundation based in Washington DC, USA.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.jtemb.2017.11.012>.

References

- [1] A. Krishnan, R. Zhang, V. Yao, C.L. Theesfeld, A.K. Wong, et al., Genome-wide prediction and functional characterisation of the genetic basis of autism spectrum disorder, *Nat. Neurosci.* 19 (2016) 1454–1462.
- [2] L.A. Sealey, B.W. Hughes, A.N. Sriskanda, J.R. Guest, A.D. Gibson, et al., Environmental factors in the development of autism spectrum disorders, *Environ. Int.* 88 (2016) 288–298.
- [3] R. Koyama, Y. Ikegaya, Microglia in the pathogenesis of autism spectrum disorders, *Neurosci. Res.* 100 (2015) 1–5.
- [4] Q. Li, J.-M. Zhou, The microbiota-gut-brain axis and its potential therapeutic role in autism spectrum disorder, *Neuroscience* 324 (2016) 131–139.
- [5] C. Kaur, G. Rathnasamy, E.-A. Ling, Biology of microglia in the developing brain, *J.*

- Neuropathol Exp. Neurol. 76 (2017) 736–753.
- [6] M. Varghese, N. Keshav, S. Jacot-Descombes, T. Warda, B. Wicinski, et al., Autism spectrum disorder: neuropathology and animal models, *Acta Neuropathol.* 134 (2017) 537–566.
- [7] H. Yasuda, Y. Yasuda, T. Tsutsui, Estimation of autistic children by metallomics analysis, *Sci. Rep.* 3 (2013) 1199.
- [8] F.E.B. Mohamed, E.A. Zaky, A.B. El-Sayed, R.M. Elhossieny, S.S. Zahra, et al., Assessment of hair aluminium, lead and mercury in a sample of autistic Egyptian children: environmental risk factors of heavy metals in autism, *Behav. Neurol.* (2015) 545674 (Art).
- [9] M.H. Rahbar, M. Samms-Vaughn, M.R. Pitcher, J. Bressler, M. Hessabi, et al., Role of metabolic genes in blood aluminium concentrations of Jamaican children with and without autism spectrum disorder, *Int. J. Environ. Res. Public Health* 13 (2016) 1095.
- [10] A.V. Skalny, N.V. Simashkova, T.P. Klyushnik, A.R. Grabeklis, I.V. Radysh, et al., Analysis of hair trace elements in children with autism spectrum disorders and communication disorders, *Trace Elem. Med. Biol.* 177 (2017) 215–223.
- [11] L. Tomljenovic, C.A. Shaw, Do aluminium vaccine adjuvants contribute to the rising prevalence of autism? *J. Inorg. Biochem.* 105 (2011) 1489–1499.
- [12] C.A. Shaw, Y. Li, L. Tomljenovic, Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes, *J. Inorg. Biochem.* 128 (2013) 237–244.
- [13] E. House, M. Esiri, G. Forster, P. Ince, C. Exley, Aluminium, iron and copper in human brain tissues donated to the medical research council's cognitive function and ageing study, *Metallomics* 4 (2012) 56–65.
- [14] M. Mold, H. Eriksson, P. Siesjö, A. Darabi, E. Shardlow, C. Exley, Unequivocal identification of intracellular aluminium adjuvant in a monocytic THP-1 cell line, *Sci. Rep.* 4 (2014) 6287.
- [15] A. Mirza, A. King, C. Troakes, C. Exley, The identification of aluminium in human brain tissue using lumogallion and fluorescence microscopy, *J. Alzh. Dis.* 54 (2016) 1333–1338.
- [16] C. Exley, M. Esiri, Severe cerebral congophilic angiopathy coincident with increased brain aluminium in a resident of Camelford, Cornwall UK, *J. Neurol. Neurosurg. Psychiatry* 77 (2006) 877–879.
- [17] C. Exley, E.R. House, Aluminium in the human brain, *Monatsh. Chem.* 142 (2011) 357–363.
- [18] C. Exley, T. Vickers, Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report, *J. Med. Case Rep.* 8 (2014) 41.
- [19] A. Mirza, A. King, C. Troakes, C. Exley, Aluminium in brain tissue in familial Alzheimer's disease, *J. Trace Elem. Med. Biol.* 40 (2017) 30–36.
- [20] R. Shechter, O. Miller, G. Yovel, N. Rosenzweig, A. London, et al., Recruitment of beneficial M2 macrophages to injured spinal cord is orchestrated by remote brain choroid plexus, *Immunity* (38 2013) 555–569.
- [21] C. Exley, The toxicity of aluminium in humans, *Morphologie* 100 (2016) 51–55.
- [22] M.W. Salter, B. Stevens, Microglia emerge as central players in brain disease, *Nat. Med.* 23 (2017) 1018–1027.
- [23] U. Neniskyte, C.T. Gross, Errant gardeners: glial-cell-dependent synaptic pruning and neurodevelopmental disorders, *Nat. Rev. Neurosci.* 18 (2017) 658–670.



Updated aluminum pharmacokinetics following infant exposures through diet and vaccination

Robert J. Mitkus^{a,*}, David B. King^a, Maureen A. Hess^b, Richard A. Forshee^a, Mark O. Walderhaug^a

^a Office of Biostatistics and Epidemiology, USFDA Center for Biologics Evaluation and Research, 1401 Rockville Pike, HFM-210, Rockville, MD 20852, United States

^b Office of Vaccines Research and Review, USFDA Center for Biologics Evaluation and Research, 1401 Rockville Pike, HFM-405, Rockville, MD 20852, United States

ARTICLE INFO

Article history:

Received 1 July 2011

Accepted 29 September 2011

Available online 11 October 2011

Keywords:

Aluminum

Adjuvant

Safety

Pharmacokinetics

Modeling

ABSTRACT

Aluminum is a ubiquitous element that is released naturally into the environment via volcanic activity and the breakdown of rocks on the earth's surface. Exposure of the general population to aluminum occurs primarily through the consumption of food, antacids, and buffered analgesics. Exposure to aluminum in the general population can also occur through vaccination, since vaccines often contain aluminum salts (frequently aluminum hydroxide or aluminum phosphate) as adjuvants. Because concerns have been expressed by the public that aluminum in vaccines may pose a risk to infants, we developed an up-to-date analysis of the safety of aluminum adjuvants. Keith et al. [1] previously analyzed the pharmacokinetics of aluminum for infant dietary and vaccine exposures and compared the resulting body burdens to those based on the minimal risk levels (MRLs) established by the Agency for Toxic Substances and Disease Registry. We updated the analysis of Keith et al. [1] with a current pediatric vaccination schedule [2]; baseline aluminum levels at birth; an aluminum retention function that reflects changing glomerular filtration rates in infants; an adjustment for the kinetics of aluminum efflux at the site of injection; contemporaneous MRLs; and the most recent infant body weight data for children 0–60 months of age [3]. Using these updated parameters we found that the body burden of aluminum from vaccines and diet throughout an infant's first year of life is significantly less than the corresponding safe body burden of aluminum modeled using the regulatory MRL. We conclude that episodic exposures to vaccines that contain aluminum adjuvant continue to be extremely low risk to infants and that the benefits of using vaccines containing aluminum adjuvant outweigh any theoretical concerns.

Published by Elsevier Ltd.

1. Introduction

In the first year of life, infants receive vaccinations according to a schedule recommended by the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention [2]. Some of these vaccines utilize aluminum salts as adjuvants (for example, aluminum hydroxide, $\text{Al}(\text{OH})_3$, or aluminum phosphate, AlPO_4). The particular vaccines (and therefore aluminum exposures) that an infant may receive at any point in the immunization schedule may vary depending on the vaccine chosen by the health care provider, parents, and caregivers from the available FDA-licensed vaccines. Potential aluminum exposures associated with vaccine administration, however, are different from dietary exposures to aluminum, since aluminum in vaccines does not have to pass through the walls of the gastrointestinal tract, which is a significant barrier to systemic aluminum absorption. Rather, it is expected that the whole amount of aluminum in the adjuvant

will be absorbed from muscle into the blood following vaccination, albeit at some rate over time.

In an effort to evaluate the relative contribution to aluminum levels in infants from vaccines and from diet, Keith et al. [1] analyzed the pharmacokinetics of aluminum for infant dietary and vaccine exposures and compared these exposures to the level set by the Agency for Toxic Substances and Disease Registry, which is called the minimal risk level or MRL (ATSDR [29]). Exposures below this level are considered to be safe, but levels of exposure at or slightly above the MRL may also be safe due to safety factors that are built into the process of calculating the MRL. Keith et al. [1] concluded that the calculated body burden from aluminum exposures in infants from vaccines is below the MRL equivalent curve for all but a few brief periods during the first year of life. We updated the analysis of Keith et al. [1] with a current vaccination schedule, a more recent aluminum retention function from human volunteers, incorporation of infant glomerular filtration rates, an adjustment for the kinetics of aluminum efflux from the site of injection, contemporaneous MRLs, and the most recent infant body weight data for children 0–60 months of age [3].

* Corresponding author. Tel.: +1 301 827 6083.

E-mail address: Robert.Mitkus@fda.hhs.gov (R.J. Mitkus).

1.1. Exposure to aluminum

Aluminum is a ubiquitous environmental metal with no known nutritional role in humans. Because of aluminum's abundance in the environment, it is frequently consumed as an incidental component of water or food, including infant formula [4]. Aluminum is also intentionally added to food as a caking or emulsifying agent. As a result, bread made with aluminum-based baking powder can contain up to 15 mg aluminum per slice, and processed American cheese can contain as much as 50 mg aluminum per slice [5]. Another potential means of exposure to aluminum in humans can occur through vaccination. Certain vaccines may contain specific aluminum salts (primarily aluminum hydroxide and aluminum phosphate) as an adjuvant. Aluminum adjuvants are important components of vaccines, since they stimulate the immune system to respond more effectively to protein or polysaccharide antigens that have been adsorbed to the surface of insoluble aluminum particles. Specifically, these coated particles are phagocytized by cells of the innate immune system (e.g., macrophages) and activate intracytoplasmic sensors of pathogen-associated molecular patterns located within the cells, such as the nucleotide-binding domain leucine-rich repeat-containing family of sensors ([6]; Schroder and Tschopp [30]). The functional consequence of activation of this intracellular system is the activation of certain enzymatic caspases that cleave pro-interleukin (IL)-1 β to interleukin (IL)-1 β . The secretion of the mature cytokine, IL-1 β , leads to an inflammatory reaction and a downstream Th2-dependent antibody response [7], which amplify the immune response to the antigen. Adjuvanted aluminum, therefore, plays a vital role in facilitating the response that underlies the immunoprotection afforded by vaccines.

1.2. Aluminum disposition and toxicity

Dietary exposure to aluminum (usually as the citrate) results in small amounts of aluminum being absorbed from the gut (<1%) and reaching the bloodstream [4]. Following enteral absorption, aluminum is transported mainly in the plasma in association with the iron-binding protein transferrin [8]. Aluminum is distributed well throughout the body with the skeleton and lungs (due to inhalation exposures) containing the highest mass of aluminum (approximately 50% and 25% of the body burden, respectively). As for many divalent and polyvalent metals, the skeleton can be a long-term storage depot for aluminum, with the half-life of aluminum in bone being on the order of years [5]. It is anticipated that bone will serve as a stable depot for aluminum in infants, as well as adults, due to the increase in bone mass and volume that takes place during an infant's rapid growth and development. With regard to the non-skeletal compartment, the half-life of aluminum in soft tissues such as the liver is short (<2 days), which indicates very little accumulation in these organs. The majority of bioavailable aluminum is excreted shortly after exposure, primarily in the urine [5], and there appears to be little difference in the renal clearance of aluminum in infants and adults at low exposures [9]. Although aluminum accumulates in the brain as well as bone over time, the concentration of aluminum in brain is lower than that in many other tissues of the body (e.g., liver, spleen), and only 1% of whole-body aluminum is present in the brain or central nervous system at any given time [8,5].

The toxicity of aluminum depends largely on the route and length of exposure. Following single injections, occasional irritation (dermal) at the site of injection is the only adverse effect that has been reported in the published literature. Neurotoxicity in rats has been demonstrated following long-term injections of aluminum leading to aluminum overload or aluminum toxicosis [10,11]. However, the doses tested in these studies were much higher than the maximal exposures that infants might be exposed to from vaccines,

and the dosing schedules, the species of aluminum (soluble), and the routes of exposure (intraperitoneal) tested were not relevant to how infants might be exposed to aluminum through vaccination. There is no evidence for neurotoxic effects in humans who may be exposed to aluminum following single, episodic injections [12]. In addition, while aluminum hydroxide has been detected in biopsy samples of muscle obtained from some children with macrophagic myofasciitis (MMF), a rare inflammatory myopathy characterized by clinical symptoms of myalgia or arthralgia and an inflammatory infiltrate at muscle biopsy, this condition has not been shown to be caused by aluminum in vaccines [13]. The clinical symptoms that have been observed in the limited number of patients that have been diagnosed with this rare condition are considered to be due to separate, coincidental immune or neurological disorders that are unrelated to the presence of aluminum in vaccines [14,15].

2. Materials and methods

2.1. Baseline aluminum levels at birth

Rather than starting from a zero amount of aluminum in the body, we assumed a baseline level of aluminum in an infant at birth. Although whole-body aluminum levels have not been measured in human fetuses, they were measured in only one published animal study, i.e. Cranmer et al. [16], who measured "total" aluminum in fetal mice following maternal exposure to aluminum chloride or saline (control). In this study, saline-treated fetuses contained approximately 592 ppb aluminum. However, since the aluminum content of the saline was unreported and since we consider results in humans to be more relevant to human exposures, we estimated aluminum levels in newborns using the results of Moreno et al. [17], who measured background levels of aluminum in the serum of children at birth to be $0.16 \pm 0.05 \mu\text{mol/l}$, which is equivalent to a mean value of 4.32 ppb (MW, Al = 27 g). Next, we estimated levels of aluminum in whole blood to be $0.18 \mu\text{mol/l}$ (4.8 ppb), by taking into consideration published results indicating that approximately 90% of aluminum in blood resides in serum or plasma, with 10% of blood Al located in erythrocytes [5]. This value is in excellent agreement with a background blood concentration in newborns of $0.19 \pm 0.11 \mu\text{mol/l}$ reported earlier by Sedman et al. [9]. Since aluminum in blood accounts for approximately 4% of total aluminum in the body at any given time ([5] based on [18]), a blood concentration of 4.8 ppb yields a total background concentration of aluminum in newborns of 120 ppb. Because a newborn infant weighs approximately 3.2 kg (50th percentile for girls; [19]), this concentration corresponds to an estimated body burden of 384 μg , or about 0.4 mg Al, at birth. This natal body burden of aluminum is considered to be low due to the fact that the placenta partially protects the developing fetus from exposures from the mother during pregnancy [20,16,28].

2.2. Schedule of vaccination

Using the most recent recommended immunization schedule for persons aged 0–6 years [2], potential combinations of FDA-licensed routine childhood vaccines were compiled and analyzed to determine the maximum doses (*d*) of aluminum that a child might receive over the course of a year. This information was derived from FDA-approved vaccine prescribing information, and the sequence of maximum exposures was determined to be as follows: 0.25 mg at birth, 0 mg at 30 days, 1.2 mg at 60 days, 1.2 mg at 120 days, 0.975 mg at 180 days, and 0.6 mg at 365 days of age. These amounts are summarized by vaccine in Table 1. By way of comparison, Keith et al. [1] calculated aluminum exposures as 0.25 mg at birth, 1.1 mg at 60 days, 0.85 mg at 120 days, 1.1 mg at 180 days, and 0.85 at 365

Table 1
Sequence of vaccine administrations leading to maximal aluminum exposures in infants over the first year of life. Based on 2011 ACIP vaccination schedule.

Vaccine	Postnatal day of administration	Aluminum content (mg)
Hep B	0	0.25
DTaP + HepB + IPV + Hib + PCV	60	1.2
DTaP + HepB + IPV + Hib + PCV	120	1.2
DTaP + HepB + IPV + PCV	180	0.975
Hib + PCV + HepA	365	0.6

days of age using an immunization schedule which is no longer current.

2.3. Aluminum retention in children

Aluminum retention in humans has been measured in adult volunteer studies using radioactive aluminum tracers following intravenous administration [21]. Priest [5] re-analyzed the retention of aluminum in the body using longer timecourse data and reported a retention function for adults that is a three-component exponential function of time:

$$R = 29.3 \times e^{-0.595 \times t} + 11 \times e^{-0.172 \times t} + 6.5 \times e^{-0.000401 \times t} \quad (1)$$

where “R” refers to the percentage of administered aluminum in the body at time, *t*, beginning approximately one day after injection. This retention function reflects three whole-body half-lives for aluminum of 1.4, 40, and 1727 days, respectively, which mirrors aluminum residence in three compartments in the body, with long-term storage in bone most likely responsible for the longest half-life [5]. The relevant adult rate constants in this 3-compartment model were determined from Eq. (1) using the method of Gibaldi and Perrier [22] and are presented in Fig. 1.

Because glomerular filtration, the primary pathway of excretion of aluminum from the body as well as the main process of renal elimination for xenobiotics in newborns, is not fully developed at birth [23,24], it is expected that aluminum is not cleared from the blood of infants as quickly as that of adults. As a result, the elimination rate constant, *k*₁₀ (Fig. 1), would be expected to be lower in children than adults, but would also increase over time as renal function developed throughout childhood. We therefore modeled glomerular filtration in childhood based on aggregate mean creatinine clearance rates (*C*_{Cr}) measured in 122 children over the first thirteen years of life [25]. Since the data for *C*_{Cr} seemed to start out small and rise quickly and asymptotically approach a maximum between ages 5 and 13, we utilized a Michaelis–Menten function to describe the rapid increase in renal function. The functional form for *C*_{Cr} was estimated as follows:

$$C_{Cr}(t) = \hat{a} + \hat{b} \left(\frac{t}{t + \hat{c}} \right) = 50.871 + 90.044 \left(\frac{t}{t + 231.462} \right) \quad (2)$$

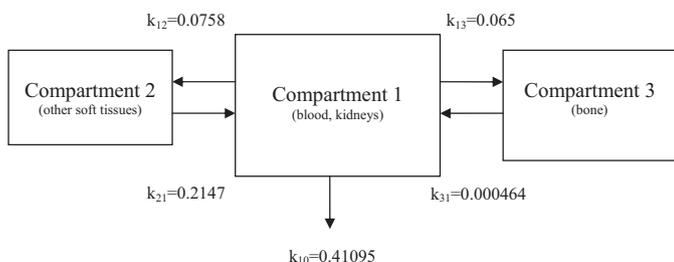


Fig. 1. Three-compartment model of aluminum disposition in adults. Rate constants were derived from the retention equation of Priest [5].

Since the horizontal asymptote of the creatinine clearance represents the adult rate of clearance, the function:

$$f(t) = \frac{\hat{a}}{\hat{a} + \hat{b}} + \frac{\hat{b}}{\hat{a} + \hat{b}} \left(\frac{t}{t + \hat{c}} \right) = 0.361 + 0.639 \left(\frac{t}{t + 231.462} \right) \quad (3)$$

which has a horizontal asymptote of unity, should roughly represent the filtration efficiency of the renal system relative to the adult efficiency. Since the primary means of aluminum removal is through the kidney, it follows that the rate of aluminum removal in children should be:

$$k_{10}(t) = \hat{k}_{10} \times f(t) = 0.41095 \left(0.361 + 0.639 \left(\frac{t}{t + 231.462} \right) \right) \quad (4)$$

where \hat{k}_{10} is the estimated elimination rate constant in adults based upon the equation from Priest [5] and *f*(*t*) represents the fraction of adult aluminum removal for children at age *t*. Upon substitution of the function from Eq. (4) into the ordinary differential equations that describe the 3-compartment model for aluminum it follows that:

$$\frac{dX_1}{dt} = -k_{10}(t)X_1 + k_{21}X_2 + k_{31}X_3 - k_{12}X_1 - k_{13}X_1 \quad (5)$$

$$\frac{dX_2}{dt} = k_{12}X_1 - k_{21}X_2 \quad (6)$$

$$\frac{dX_3}{dt} = k_{13}X_1 - k_{31}X_3 \quad (7)$$

Because this set of differential equations includes a non-constant coefficient, *k*₁₀(*t*), the exact solution is non-tractable. Therefore, we utilized numeric Runge–Kutta type methods to solve the set of differential equations numerically using the statistical program R (R Foundation for Statistical Computing [31]).

2.4. Infant body weight

Because the safe, oral daily dose of aluminum (i.e., MRL = 1 mg/kg bw/day) is expressed by ATSDR [4] as normalized to body weight, it was necessary to multiply this MRL value by infant body weight to obtain safe doses (*d*) of aluminum over the first year of life. Because infant body weight is not constant and increases rapidly after birth, it was necessary to determine the relevant mathematical functions that describe infant body weight during this time. We, therefore, modeled the most recent infant body weight data for US children 0–60 months of age [3]. We estimated the 5th and 50th percentiles of infant body weight (kg) for age (months) for males and females combined using quantile regression. The model describing the relationship between weight and age was estimated using the best-fitting polynomial functions of age, since the data indicate that this relationship is non-linear. The degree of the polynomial was determined by minimizing a cross-validation criterion, and the following functions were calculated from the NHANES [3] data:

$$BW_{5th} = 2.65899 - \left(\frac{1.86774}{(1 + age)^{0.5}} \right) + 1.59926(1 + age)^{0.5} \quad (R^2 > 0.99) \quad (8)$$

$$BW_{50th} = 3.35319 + (1.74026(1 + age)^{0.5}) + 0.618471(nl(0.1 + 0.1age)) \quad (R^2 > 0.99) \quad (9)$$

2.5. Calculations of aluminum body burdens

The ATSDR MRL of 1 mg/kg bw/day was multiplied by the relevant functions for infant body weight [Eqs. (8) and (9)] and corrected for the low absorption of aluminum from the gastrointestinal tract (0.78%; [26]), to estimate correspondingly safe oral doses (*d*) of

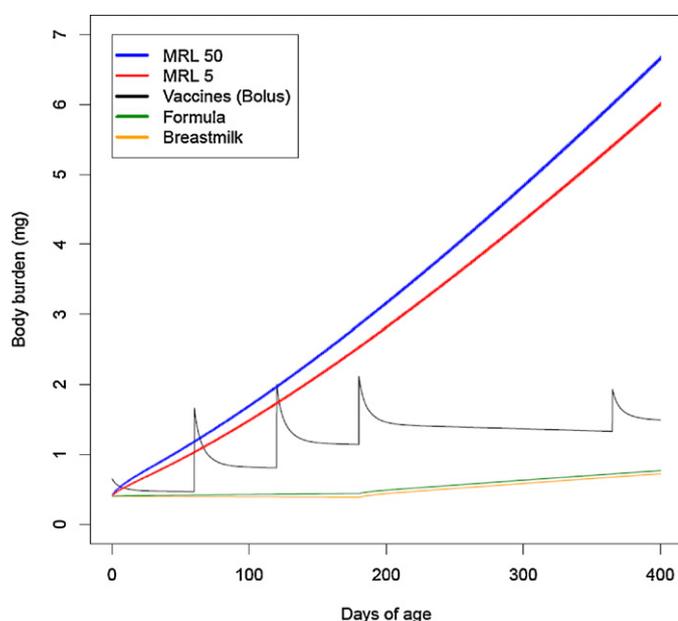


Fig. 2. Aluminum body burden contributions from diet and vaccines (100%, instantaneous absorption assumed) relative to current MRL level intake in infants. Note: the body burden of aluminum is greater than zero at birth, since infants are exposed to aluminum from their mothers *in utero*.

aluminum. The following dietary exposures of infants to aluminum, published previously by Keith et al. [1] and adjusted for 0.78% oral absorption, were utilized in our model: (1) age 0–6 months: 0.03 mg (breast milk) and 0.15 mg (formula); (2) age >6 months: 0.7 mg (breast milk or formula). Retention of aluminum following infant dietary exposures, exposures from vaccines according to the 2011 ACIP schedule, and safe doses of aluminum were then estimated over the first 400 days of life using Eqs. (1)–(7). Retention curves were generated using the publicly available statistical modeling software, R (R Foundation for Statistical Computing [31]).

3. Results and discussion

Fig. 2 shows the amount of aluminum that is retained by an infant following exposure from vaccines (assuming complete and instantaneous absorption) or the diet (formula or breast milk) throughout the first 400 days of life. The two upper curves show the amount of aluminum retained by infants of median or low birth weight, if the infant consumed the MRL of aluminum (1 mg/kg bw/day) every day over the first year of his/her life. The MRL is based on the infant's weight, so the upper curve shows the body burden of aluminum associated with infants at the median or 50th percentile weight, and the lower curve shows the level associated with infants at the 5th percentile of weight. Both curves assume intestinal absorption of 0.78% [26] and retention according to Eq. (1) that was modified to reflect glomerular filtration rates in infants. Fig. 2, as well as the equivalent curve published previously by Keith et al. [1], demonstrate that there are brief “excursions” of bodily aluminum levels above the MRL following vaccination, when complete and instantaneous absorption of aluminum from the site of injection is assumed; however, due to the rapid elimination of aluminum, the levels quickly fall back below the MRL. The curves for aluminum retention associated with formula and breastmilk show a slight change at six months that is due to the assumption that infants switch from breastmilk or formula to solid food on this date and therefore begin to receive a higher aluminum dose from baby food.

The determinations of the kinetics of aluminum retention by Priest [21,5] were based on experiments where human volunteers were given an intravenous injection of aluminum citrate. For vaccines, the injection is intramuscular, the aluminum is in an insoluble form (e.g., as the phosphate or hydroxide of aluminum), and muscle at the site of injection is considered to be a storage depot for aluminum. Over time the insoluble aluminum hydroxide or aluminum phosphate particles are solubilized by citrate ions in the interstitial fluids of muscle. After solubilization, the uptake and distribution kinetics of aluminum will likely be similar to the kinetics determined by the human volunteer studies. However, it is unlikely that the process of absorption from the site of intramuscular injection into the blood is instantaneous, as is assumed for intravenous exposures and as presumed by the retention functions used to generate Fig. 2 and by Keith et al. [1].

Flarend et al. [27] investigated the absorption into the blood of aluminum hydroxide and aluminum phosphate following intramuscular injection into New Zealand White rabbits. Two important observations were made in their experiments: (1) only a fraction of the injected aluminum was taken up from the site of injection into blood over the 28-day experimental period, and (2) absorption of neither adjuvant was instantaneous. Specifically, blood concentrations of aluminum hydroxide decreased to a minimum by the end of the experiment (reached a terminal phase), where as aluminum phosphate blood concentrations were relatively constant over the 28-day period and did not reach a terminal phase. These results likely reflected differences in the rate of absorption of each adjuvant from the site of injection and not differences in excretion, since all other experimental conditions were equivalent in each group. By comparing with the area under the curve of the blood concentration–time curve for an intravenous administration of 0.85 mg aluminum citrate, the authors determined that only 17% and 51% of injected aluminum hydroxide and aluminum phosphate, respectively, was absorbed into the blood over 28 days. If the results of the rabbit studies by Flarend et al. [27] are reflected in similar kinetics in humans, then the dose of aluminum that enters into the bloodstream after intramuscular injection of vaccines in infants is at best only one half of what has been modeled in Fig. 2.

Therefore, based on the results of [27], we assumed: (1) that only 51% (for aluminum phosphate, AP) or 17% (for aluminum hydroxide, AH) of injected aluminum would be absorbed into the blood following a single intramuscular vaccine injection over the first 28 days after exposure, and (2) that absorption of the remaining adjuvant at the site of injection would take place at a constant rate over the next 28 days for AP and 137 days for AH, rather than instantaneously, as modeled in Fig. 2. In order to make this calculation, we assumed that the rate of absorption after 28 days was the same as that during the 28-day experimental period in [27], i.e., $0.51/28 \text{ day}^{-1}$ for AP and $0.17/28 \text{ day}^{-1}$ for AH. These rates are considered to be highly conservative, since blood concentrations of AH approached zero by the end of the experiment, thereby implying a very low rate of uptake into blood, and the blood concentration–time curve for AP appeared to be entering a terminal phase 28 days post-injection. Using these assumptions for the absorption of aluminum from intramuscular injection of vaccines, we repeated our analysis.

Figs. 3 and 4 demonstrate that modeling the slower release of aluminum from the injection site eliminates the “excursions” of whole-body aluminum above MRL levels shown in Fig. 2. The body burden of aluminum is less than 50% of the oral safe level for either AP (Fig. 3) or AH (Fig. 4) at all times during the first year or so of life. Using the assumptions of slower release of aluminum adjuvant from the site of injection, the estimated level of aluminum in infants exceeds the MRL (safe) body burden at no time, and the margin of exposure between aluminum body burden from vaccine and the

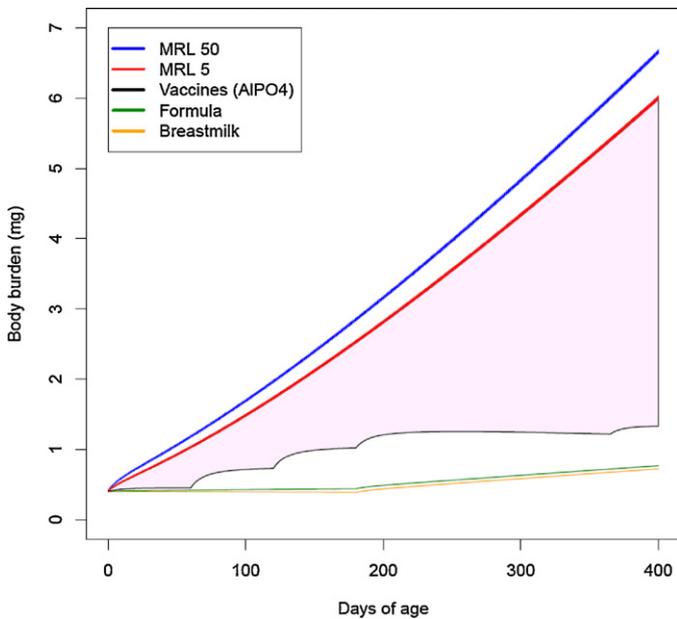


Fig. 3. Body burden contributions of aluminum from diet and vaccines (constant absorption of aluminum phosphate over 56 days based on results of Flarend et al. [27]) relative to current MRL level intake in new born infants. Margin of exposure in pink. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

MRL increases with age. It was also observed that the body burden of aluminum following injection of AH increased more gradually than that for AP. This was due to the slower rate of efflux of AH from the site of injection reported in rabbits.

Although based on the most recent data available, there are several uncertainties in our analysis. First, the published retention function for aluminum (Eq. (1)) is based on results for only one person, albeit data have been acquired from this adult for twelve years [5]. Ideally, the retention function would have been derived

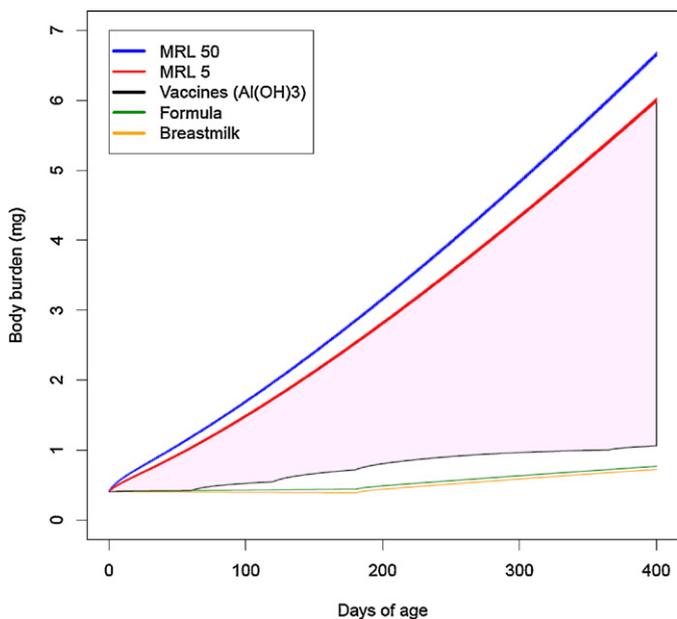


Fig. 4. Body burden contributions of aluminum from diet and vaccines (constant absorption of aluminum hydroxide over 165 days based on results of Flarend et al. [27]) relative to current MRL level intake in new born infants. Margin of exposure in pink. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

from pharmacokinetic data in infants or in more than one adult; however, an expansion of this analysis is unlikely. An infant monkey study could provide these data, however, given the present lack of evidence of harm due to the current aluminum levels, such studies may be a low priority. Second, the results of Flarend et al. [27], from which we obtained our estimate of the rate and extent of absorption of aluminum hydroxide and phosphate following intramuscular injection, are based on data from only two rabbits per adjuvant tested. The low number of animals in that study is not surprising, given that it was primarily an exploratory investigation into the disposition of injected aluminum, utilizing, at that time, a new method for detecting radioactive Al in the body (accelerator mass spectrometry). Ideally, the results of that study should be confirmed using a larger number of animals, in order to increase our confidence in the results. Nevertheless, the study clearly showed that the absorption of aluminum, at least in rabbits, is neither instantaneous nor complete up to one month following intramuscular injection [27]. We consider this behavior to be more biologically plausible than complete and instantaneous absorption from the site of injection, and more consistent with the view of muscle tissue being a storage depot for aluminum adjuvant following intramuscular vaccination. A third uncertainty in the analysis is the extent to which the use of maximum aluminum exposures (modeled here) is relevant to aluminum body burdens estimated following more typical exposures to aluminum adjuvant, which are considered to be lower. Ideally, one would like to model aluminum exposures to reflect typical exposures in the population. However, modeling body burdens following maximum exposures to aluminum provides a “worst case” scenario, since more typical exposures to aluminum will obviously lead to a lower body burden and therefore a greater margin of exposure (safety), the distance between safe and expected body burdens of aluminum. Our results indicate that body burdens following maximal exposure to aluminum adjuvant do not exceed those based on an accepted regulatory standard of safe aluminum levels, i.e., the MRL established by ATSDR.

4. Conclusions

Using the previous work of Keith et al. [1] as our starting point, we re-evaluated aluminum levels in infants using a number of updated parameters, including a current pediatric vaccination schedule, baseline aluminum levels at birth, a recent aluminum retention function from human volunteers that incorporates glomerular filtration rates in infants, an adjustment for the kinetics of aluminum efflux at the site of injection, the most recent MRL for aluminum, and up-to-date infant body weight data for children 0–60 months of age. Assuming slow release of aluminum adjuvant from the site of injection into the systemic circulation, we have demonstrated that aluminum levels in infants are well below the minimal risk level curves for either median or low-birth weight babies. We also compared the body burden of aluminum contributed by vaccines with that contributed by diet. The body burden of aluminum from vaccines is not more than 2-fold higher than that received in the diet. While the contribution of vaccines to an infant’s aluminum body burden can be slightly higher than that of the dietary contribution in our model, the fact that the primary pool where the aluminum is residing, as a long-term storage depot, is likely to be skeletal and not a more sensitive soft organ system is reassuring [5]. Although aluminum toxicosis is known to occur in humans, it is found exclusively in individuals suffering from kidney disease or in those exposed to high levels of aluminum via occupational inhalation. However, for infants, our study demonstrates that there is little risk for aluminum toxicity following immunizations administered according to ACIP recommendations even

with maximal exposures to aluminum adjuvant. For the general population of infants, who receive less than the maximal dose, the risk is even lower.

References

- [1] Keith LS, Jones DE, Chou CH. Aluminum toxicokinetics regarding infant diet and vaccinations. *Vaccine* 2002;20(Suppl. 3):S13–7.
- [2] ACIP (Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention). Policy statement – recommended childhood and adolescent immunization schedules – United States, 2011. *Pediatrics* 2011;127(2):387–8.
- [3] NHANES (National Health and Nutrition Examination Survey). Available from: <http://www.cdc.gov/nchs/nhanes/nhanes2007-2008/BMX.E.htm>; 2008 [accessed 01.03.11].
- [4] ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological profile for aluminum. Atlanta, GA; 2008.
- [5] Priest ND. The biological behaviour and bioavailability of aluminium in man, with special reference to studies employing aluminium-26 as a tracer: review and study update. *J Environ Monit* 2004;6(5):375–403.
- [6] Eisenbarth SC, Colegio OR, O'Connor W, Sutterwala FS, Flavell RA. Crucial role for the Nalp3 inflammasome in the immunostimulatory properties of aluminium adjuvants. *Nature* 2008;453(7198):1122–6.
- [7] Lindblad EB. Aluminium compounds for use in vaccines. *Immunol Cell Biol* 2004;82(5):497–505.
- [8] Yokel RA, McNamara PJ. Aluminium toxicokinetics: an updated minireview. *Pharmacol Toxicol* 2001;88(4):159–67.
- [9] Sedman AB, Klein GL, Merritt RJ, Miller NL, Weber KO, Gill WL, et al. Evidence of aluminum loading in infants receiving intravenous therapy. *N Engl J Med* 1985;312(21):1337–43.
- [10] Miu AC, Andreescu CE, Vasii R, Olteanu AI. A behavioral and histological study of the effects of long-term exposure of adult rats to aluminum. *Int J Neurosci* 2003;113(9):1197–211.
- [11] Lu ZY, Gong H, Amemiya T. Aluminum chloride induces retinal changes in the rat. *Toxicol Sci* 2002;66(2):253–60.
- [12] Krewski D, Yokel RA, Nieboer E, Borchelt D, Cohen J, Harry J, et al. Human health risk assessment for aluminium, aluminium oxide, and aluminium hydroxide. *J Toxicol Environ Health B: Crit Rev* 2007;10(Suppl. 1):1–269.
- [13] Eickhoff TC, Myers M. Workshop summary aluminum in vaccines. *Vaccine* 2002;20(Suppl. 3):S1–4.
- [14] Lach B, Cupler EJ. Macrophagic myofasciitis in children is a localized reaction to vaccination. *J Child Neurol* 2008;23(6):614–9.
- [15] Kalil RK, Monteiro Jr A, Lima MI, Silveira EB, Foltran FS, Martins CE, et al. Macrophagic myofasciitis in childhood: the role of scanning electron microscopy/energy-dispersive spectroscopy for diagnosis. *Ultrastruct Pathol* 2007;31(1):45–50.
- [16] Cranmer JM, Wilkins JD, Cannon DJ, Smith L. Fetal–placental–maternal uptake of aluminum in mice following gestational exposure: effect of dose and route of administration. *Neurotoxicology* 1986;7(2):601–8.
- [17] Moreno A, Domínguez C, Ballabriga A. Aluminum in the neonate related to parenteral nutrition. *Acta Paediatr* 1994;83(1):25–9.
- [18] ICRP (International Commission on Radiological Protection). Report on the Task Group on reference man. ICRP Publication 23; 1975.
- [19] Use of World Health Organization and CDC Growth Charts for children aged 0–59 months in the United States. *Mortal Morb Wkly Rep* 2010;59(RR-9).
- [20] Yokel RA. Toxicity of gestational aluminum exposure to the maternal rabbit and offspring. *Toxicol Appl Pharmacol* 1985;79(1):121–33.
- [21] Priest ND, Newton D, Day JP, Talbot RJ, Warner AJ. Human metabolism of aluminium-26 and gallium-67 injected as citrates. *Hum Exp Toxicol* 1995;14(3):287–93.
- [22] Gibaldi M, Perrier D. *Pharmacokinetics*. New York: Marcel Dekker; 1982.
- [23] Allegaert K, Verbesselt R, Naulaers G, van den Anker JN, Rayyan M, Debeer A, et al. Developmental pharmacology: neonates are not just small adults. *Acta Clin Belg* 2008;63(1):16–24.
- [24] Tetelbaum M, Finkelstein Y, Nava-Ocampo AA, Koren G. Back to basics: understanding drugs in children: pharmacokinetic maturation. *Pediatr Rev* 2005;26(9):321–8.
- [25] Schwartz GJ, Feld LG, Langford DJ. A simple estimate of glomerular filtration rate in full-term infants during the first year of life. *J Pediatr* 1984;104(6):849–54.
- [26] Greger JL, Baier MJ. Excretion and retention of low or moderate levels of aluminium by human subjects. *Food Chem Toxicol* 1983;21(4):473–7.
- [27] Flarend RE, Hem SL, White JL, Elmore D, Suckow MA, Rudy AC, et al. In vivo absorption of aluminium-containing vaccine adjuvants using 26Al. *Vaccine* 1997;15(12–13):1314–8.
- [28] Borak J, Wise Sr JP. Does aluminum exposure of pregnant animals lead to accumulation in mothers or their offspring? *Teratology* 1998;57(3):127–39.
- [29] ATSDR (Agency for Toxic Substances and Disease Registry). Toxicological profile for aluminum. Atlanta, GA; 1999.
- [30] Schroder K, Tschopp J. The Inflammasomes. *Cell* 2010;140(6):821–32.
- [31] R Foundation for Statistical Computing. 2011. Available from: <http://www.r-project.org>.



Glyphosate pathways to modern diseases VI: Prions, amyloidoses and autoimmune neurological diseases

Anthony Samsel¹ and Stephanie Seneff^{2,*}

¹ Samsel Environmental and Public Health Services, Deerfield, NH 03037, USA

² Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA 02139, USA

Usage of the herbicide glyphosate on core crops in the USA has increased exponentially over the past two decades, in step with the exponential increase in autoimmune diseases including autism, multiple sclerosis, inflammatory bowel disease, type 1 diabetes, coeliac disease, neuromyelitis optica and many others. In this paper we explain how glyphosate, acting as a non-coding amino acid analogue of glycine, could erroneously be integrated with or incorporated into protein synthesis in place of glycine, producing a defective product that resists proteolysis. Whether produced by a microbe or present in a food source, such a peptide could lead to autoimmune disease through molecular mimicry. We discuss similarities in other naturally produced disease-causing amino acid analogues, such as the herbicide glufosinate and the insecticide L-canavanine, and provide multiple examples of glycine-containing short peptides linked to autoimmune disease, particularly with respect to multiple sclerosis. Most disturbing is the presence of glyphosate in many popular vaccines including the measles, mumps and rubella (MMR) vaccine, which we have verified here for the first time. Contamination may come through bovine protein, bovine calf serum, bovine casein, egg protein and/or gelatin. Gelatin sourced from the skin and bones of pigs and cattle given glyphosate-contaminated feed contains the herbicide. Collagen, the principal component of gelatin, contains very high levels of glycine, as do the digestive enzymes: pepsin, trypsin and lipase. The live measles virus could produce glyphosate-containing haemagglutinin, which might induce an autoimmune attack on myelin basic protein, commonly observed in autism. Regulatory agencies urgently need to reconsider the risks associated with the indiscriminate use of glyphosate to control weeds.

Keywords: autism, autoimmune disease, collagen, glycine, glyphosate, multiple sclerosis, protein misfolding, vaccines

1. INTRODUCTION

At first glance, multiple sclerosis (MS) and autism appear to have little in common, aside from the fact that both are neurological diseases. Autism is a condition with prenatal or early childhood onset, characterized by repetitive behaviours, impaired social interaction and cognitive impairment. The male:female ratio for autism is 4:1, while multiple sclerosis is twice as common in women as in men; its first symptoms usually begin in early adulthood to involve impaired lower limb mobility, although in later stages it affects both mental and physical capabilities. Both conditions are, however, associated with inflammatory autoimmune features [1, 2], and both diseases are viewed as having an environmental and a genetic component [3–6].

A study comparing a population of 658 MS patients with the general population found an association between MS and increased rates of asthma, inflammatory bowel disease (IBD), type 1 diabetes mellitus, pernicious anaemia and autoimmune thyroid disease [7], all of which

have also been linked to autism [8–11]. These conditions are all considered to be *autoimmune diseases*, which can be triggered through molecular mimicry, where an antibody responding to a foreign protein that resembles a native protein becomes sensitized to the native protein as well [12]. A paper by Shoenfeld and Aron-Maor in 2000 developed the argument that both autism and MS may be examples of an autoimmune reaction via mimicry following exposure to an antigenic stimulus, possibly from an infection or through vaccination [13]. They further propose specifically that myelin basic protein (MBP) and other proteins constituting the myelin sheath are attacked by the immune system in both autism and MS. This has been recognized by many others in autism [14, 15] and MS [16–20]. In 1982, Weizman et al. reported a cell-mediated autoimmune response to human MBP in 76% of the autistic children studied [16]. Immune sensitization to the myelin sheath proteins could arise either through mimicry as a consequence of exposure of the immune system to a foreign antigen with a similar peptide sequence that is

* Corresponding author. E-mail: seneff@csail.mit.edu

resistant to clearance, or because the proteins themselves have been altered in some way that renders them defective, exposed and/or resistant to proteolysis.

Unlike DNA synthesis, protein synthesis is highly prone to error [21, 22]. It appears that biological systems have adopted a strategy of allowing coding errors to survive during active synthesis, but use protein misfolding as a criterion to mark a defective peptide for degradation and recycling through ubiquitination. It is estimated that 15% of average-length proteins will have at least one misincorporated amino acid. Typically, 10–15% of random substitutions disrupt protein function, mostly because of misfolding [22]. Such destabilization causes protein–protein aggregation, and can lead to multiple neurological diseases and amyloidoses. Drummond et al. propose that early-forming toxic oligomers of amyloidogenic proteins are enriched with missense errors [22].

Glyphosate is the active ingredient in the pervasive herbicide Roundup and in many other formulations of herbicides used to control weeds on agricultural, residential and public land worldwide. A recent study based in Germany involving 399 urine samples from adults not involved in agricultural work revealed glyphosate residues above the detection limit in the urine of 32% of the subjects, and residues of AMPA, a metabolite, in 40% [23]. In a paper published in 2014, Swanson et al. showed a remarkable correlation between the rising rate of glyphosate usage on corn (maize) and soy crops in the USA and an alarming rise in a number of different chronic diseases [24]. Additional strong correlations for other conditions and diseases are provided in two follow-on papers [25, 26]. While correlation does not necessarily mean causation, causation becomes much more likely if a plausible mechanism can be found. Swanson et al. found a remarkable 0.98 correlation coefficient between the rise in autism rates in the USA and the use of glyphosate on crops (P -value $\leq 9.6 \times 10^{-6}$). The correlation for multiple sclerosis was not as high, but still highly significant at 0.83 (P -value $\leq 1.1 \times 10^{-5}$). IBD had a correlation coefficient of 0.94 (P -value $\leq 7.1 \times 10^{-8}$) (see Table 1 for other diseases).

Table 1. Correlations between time trends in several diseases and conditions recorded by the US Centers for Disease Control (CDC) with glyphosate usage on corn (maize) and soy crops reported by the USDA. Data reproduced from [23] and [25].

Disease	Correlation coefficient (R)	P -value
Autism (prevalence)	0.98	9.6×10^{-6}
MS (deaths)	0.83	1.1×10^{-5}
IBD	0.94	7.1×10^{-8}
Anaemia	0.90	1.8×10^{-4}
Diabetes (prevalence)	0.97	9.2×10^{-9}
Thyroid cancer (incidence)	0.99	7.6×10^{-9}

IBD, especially among children, is an emerging global epidemic [27] that is linked to autism [28, 29]. Impairment of intestinal barrier function is a core feature of IBD [30]. Increased intestinal permeability promotes infiltration of unmetabolized peptides into the lymph system and general circulation. This provides an opportunity for an immune antigenic response, which by molecular mimicry can lead to an attack on crucial proteins in the brain and spinal column. Disturbances of collagen texture are a major factor leading to the onset of diverticular disease and IBD along with the disturbed wound-healing mechanisms seen in the pathogenesis of anastomatic leakage following large bowel surgery [31].

In a recent paper [32], we suggested that glyphosate, a non-coding amino acid analogue of glycine, could substitute for glycine in error during protein synthesis. Such misincorporation and disruption of proteostasis could explain the strong correlations observed between glyphosate usage and multiple modern diseases. *In this paper, we show that this could be one of the most important mechanisms by which glyphosate could induce multiple autoimmune diseases.*

A prime site for initiation of the disease process is the colon, where misfolded collagen, resistant to degradation, could lead to an autoimmune disease and, subsequently, a leaky gut. Autoantibodies against type VII collagen have been detected in up to 68% of IBD patients [33]. Glycine is the most common amino acid in collagen, making up one fourth of the residues in the protein. Proline is also a very common component of collagen and, as we discuss later in this paper, proline resists hydrolysis. Incomplete collagen degradation by matrix metalloproteinases in the gut could lead to the accumulation of short pro–gly–pro peptides that are resistant to proteolysis. These could then induce the infiltration of neutrophils or the activation of resident immune cells to induce an inflammatory response [34].

An unpublished study conducted by Monsanto and submitted to the US Environmental Protection Agency (EPA) traced the accumulation of radiolabeled glyphosate in various tissues of rats following low-dose oral administration (10 mg/kg body weight) [35]. By far the highest accumulation was found in the bones (Table 11 in [36]). Radioactive levels in the colon were 4–6 times as high as those in the stomach and small intestine.

The production of novel non-coding amino acids by plants and microbes wards off predators. The toxicity of these products may be due to the fact that they replace coding analogues during protein synthesis. Examples include: azetidine-2-carboxylic acid (Aze), a proline analogue [37, 38]; glufosinate, a glutamate analogue that is also a popular herbicide [39]; β -N-methylamino-L-alanine

(BMAA), an analogue of serine [40]; and L-canavanine, a natural analogue of L-arginine that is exploited as an insecticide [41, 42].

A remarkable true-life story involving a 119-day Alaskan wilderness experiment conducted by Christopher McCandless was recounted in the book *Into the Wild* by Jon Krakauer (later made into a popular movie) [43]. McCandless was thought to have died in the wilderness from starvation; however, Krakauer always suspected a toxin in the seeds of the wild potato, *Hedysarum alpinum*, which formed a staple of his diet in his last month of life. Krakauer had originally suspected a poisonous alkaloid but, through later research, was able to identify a significant level of L-canavanine in the wild potato seeds and published a paper on this analysis with several other authors in 2016 [42].

A key factor in L-canavanine's toxicity is its ability to insinuate itself into peptides in place of L-arginine. L-canavanine can be assimilated into essentially any protein to create aberrant canavanyl proteins that can disrupt many fundamentally important biochemical reactions across a broad spectrum of organisms [41, 44]. L-canavanine is exploited in agriculture as a potent insecticide against the tobacco hornworm [45], although the tobacco budworm has developed tolerance with a unique enzyme, canavanine hydrolase, which can quickly metabolize it [46]. Larvae exposed to L-canavanine incorporate it into the protein lysozyme, resulting in a 48% loss in catalytic activity [41]. Furthermore, dipterocins B and C of *Protoformia terranova*, but not dipterocin A, are negatively impacted by L-canavanine. The distinction is that dipterocin A has histidine at position 38 instead of the L-arginine found in the other two dipterocins. Presciently, with respect to glyphosate, Rosenthal wrote: "These insect studies support the view that the biological effects of canavanine result from its incorporation into a protein, resulting in an alteration in protein conformation that leads ultimately to impairment of protein function" [41].

2. SHIKIMATE PATHWAY INHIBITION REVISITED

The shikimate pathway enzyme, 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) is believed to be the main target of glyphosate's toxicity to plants [47]. A 1991 paper by Padgett et al. describes studies to gain insight into the mechanism by which glyphosate disrupts EPSPS [47]. Surprisingly, it is not understood exactly how glyphosate binds to the active site.

The microbes *Klebsiella pneumoniae*, *Escherichia coli* [47, 48] and *Agrobacterium sp.* strain CP4 [48, 49] have all evolved to produce versions of EPSPS that are glyphosate-resistant. The CP4 variant has been widely exploited by importing it into genetically modified

glyphosate-resistant crops [48]. Insight can be gained by investigating the alterations to the peptide sequence that afforded resistance. All three mutations involved replacing a glycine residue at the active site with alanine [47, 48]. In the case of *E. coli*, the mutated enzyme is about 72 times *less* efficient than the wild-type enzyme, but 69 times *more* efficient in the presence of glyphosate. Changing the DNA code from glycine to alanine completely disables glyphosate's inhibiting effects on the enzyme [48].

Substitution of gly-96 at the active site in *E. coli* by serine leads to a version of the enzyme that is unable to bind PEP, most likely due to steric hindrance. The authors speculated that the hydroxymethyl group of serine displaces the phosphate of PEP and functions as a nucleophile. In fact, this mutated enzyme achieves a kind of reverse reaction, breaking EPSP down into shikimate-3-phosphate and pyruvate via hydrolysis.

We propose that substitution of gly-96 (gly-100 in the CP4 variant) by glyphosate during protein synthesis could explain its disruption of the enzyme's function. One can expect that the highly reactive and bulky glyphosate molecule, if substituted for gly-96, would behave more like serine than alanine. An additional disruptive factor is glyphosate's chelation of manganese, which would disrupt the catalytic action of EPSPS. A cell containing both wild-type and glyphosate-substituted forms of the enzyme would arguably circuitously convert PEP to pyruvate via EPSP without producing ATP from ADP; i.e., would waste the energy in the phosphate bond, as shown in Fig. 1, and end up with excess pyruvate and a deficiency in EPSP.

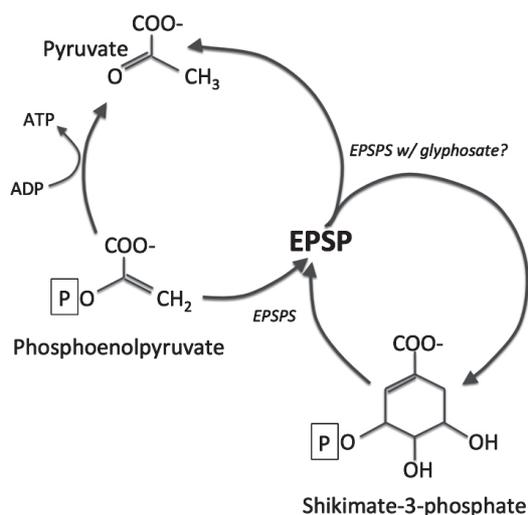


Figure 1. Diagram of the hypothetical pathway by which glyphosate substitution for glycine in EPSPS could result in the synthesis of pyruvate from PEP without generating ATP; i.e., wasting the energy in the phosphate group, as discussed in the text.

3. GLYPHOSATE AS A GLYCINE ANALOGUE

While glyphosate's main mechanism of toxicity to plants is considered to be disruption of the shikimate pathway, it is also likely that it disrupts other biological pathways where glycine is either a substrate or a ligand, due to the fact that it is a glycine analogue. It has been proposed that, through glycine mimicry, glyphosate's rôle as a ligand to NMDA receptors in the brain could explain its known ability to activate NMDA receptors and cause neuronal damage [49, 50]. In [51], acute exposure of rat hippocampal slices to Roundup (0.00005–0.1%) for 30 minutes caused oxidative stress and neuronal cell death, which was attributed to NMDA receptor activation. Glyphosate also interferes with the synthesis of porphyrin, a precursor to haem, by disrupting the first step in the pathway where glycine is substrate [52].

N-substituted glycine "peptoids" are an attractive class of synthetic molecules that can be constructed by linking component N-substituted glycines at sequential nitrogen–carbon bonds; they are directly analogous to the linking of amino acids into peptides [53]. Glyphosate is of course an N-substituted glycine, where the nitrogen side chain is a methyl phosphonyl group. Part of the attraction of peptoids is that they are highly resistant to proteolysis, just as is the amino acid proline, in which the carbon side chain circles back and binds to the peptide nitrogen. Impaired ability to break down proline-rich gliadin has been proposed as a contributing factor in coeliac disease and gluten intolerance [54]. This can explain why common cereals with high proline contents are especially problematic to gluten-sensitive individuals [55, 56].

Glyphosate is probably particularly problematic when it substitutes for N-terminal glycines in proteins where these glycines are highly conserved and play a significant rôle. Several proteins rely on an N-terminal glycine for anchoring to the plasma membrane (e.g., endothelial nitric oxide synthase (eNOS) [57]) or to the cytoskeleton (e.g., Kelch-like ECH-associated protein 1 (KEAP1) [58]). Protein N-myristoylation and prenylation depend on an amide bond to the N-terminal glycine residue [59]. For example, myristoylated G proteins involved in many signaling mechanisms depend on an N-terminal glycine residue [59]. This would be disrupted if the nitrogen atom has a side chain through glyphosate substitution for the terminal glycine.

N-nitrosoamino acids form a reasonable model for N-nitrosoglyphosate, a carcinogenic derivative of glyphosate that was of concern to the EPA during Monsanto's early studies. N-nitrosoproline is particularly relevant because proline, like glyphosate, has an extra carbon atom bound to the nitrogen atom. With respect to non-coding amino acids, and especially the incorporation

of N-nitrosoamino acids into peptides and proteins, R.C. Massey remarked: "In addition to their presence as free N-nitrosoamino acids, species such as N-nitrosoproline (NPRO) and N-nitroso-4-hydroxyproline (HONPRO) may exist in a peptide- or protein-bound form as a result of N-nitrosation of an N-terminal imino acid residue" [62]. Tricker et al. [63] and Kubacki et al. [64] devised high performance liquid chromatography–thermal energy analyser (HPLC–TEA) techniques for analysis of multiple dipeptides with a nitrosylated N-terminal, including N-nitrosopropylalanine (NPROALA), N-nitrosopropyl-4-hydroxyproline (NPROHOPRO) and N-nitrosopropylglycine (NPROGLY) [63, 64]. Tricker notes that the average recoveries for NPROALA, NPROHOPRO and NPROGLY, 200 µg of which was added to cured meat, were between 69 and 88%. Tricker also used the method to analyse the nitroso-tripeptide N-nitrosopropylglycylglycine [65].

Nitrosamines of glyphosate (N-phosphonomethylglycine), its salts and esters include: N-nitrosoglyphosate (NNG) (Monsanto CP 76976), N-nitrosoiminodiacetic acid (NNIDA), N-nitrosoglyphosate sodium salt (NNGNa), N-nitrosoglyphosate isopropylamine ester (NNGIPA), N-nitrosoglyphosate potassium salt (NNGK), the metabolite N-nitrosoAMPA (NNAMPA), the metabolites N-nitrosodimethyl amine (NDMA) and N-nitrosarcosine (NSAR), which occur in glyphosate products or may be generated *in vivo* or in soils and waterways. N-nitroso compounds derived from secondary amines are considered carcinogenic.

Monsanto glyphosate documents reveal analysis and quantification of five nitrosamines of concern [61]. Out of six lots of Roundup analysed for NNG, four lots contained NNG residues of 0.61 to 0.78 ppm and two lots had residues from 0.22 to 0.40 ppm NNG. Analysis of six lots of Monsanto Rodeo revealed NNG residues in the range 0.13–0.49 ppm.

Recently, a powerful metatranscriptome study on bacterial gene expression following glyphosate treatment was conducted on microbes growing within the rhizosphere of glyphosate-tolerant corn [66]. RNA transcript abundance was compared between control and glyphosate-treated samples in order to characterize which protein genes were upregulated or downregulated. While they found many changes in gene expression, most striking to us was the upregulation of genes involved in both protein synthesis and protein hydrolysis. The ribosomal proteins L16p (L10e) and Firmicutes ribosomal L7Ae family proteins involved in the synthesis of the ribosomal large subunit increased 1.4- and two-fold, respectively, and the small subunit ribosomal protein S11p (S14e) increased 1.5-fold. Upregulation of genes involved in protein degradation was even more dramatic. For

example, transcripts for a proteasome β 2 subunit (EC 3.4.25.1) increased 4.3-fold and aminopeptidase YpdF increased threefold. An explanation could be an increase in the number of proteins that fail to fold properly due to glyphosate substitution for glycine in the protein. These authors also suggested a potential shift towards an increase in glyphosate-tolerant bacteria, a point that will become important later in this paper.

These results are corroborated by a study on pea plants grown in hydroponic culture, which revealed that glyphosate induced a significant increase in two major systems for proteolytic degradation: the ubiquitin-26 S proteasome system and papain-like cysteine proteases [67]. It also increased the total free amino acid content and decreased the soluble protein in the root system.

4. GLYPHOSATE-CONTAMINATED COLLAGEN AND PROTEOLYSIS RESISTANCE

We mentioned in the Introduction the gly-pro-gly peptide sequence that is common in collagen and linked to autoimmune disease. There are several enzymes in multiple organisms that are devoted to the proteolysis of peptide sequences containing proline, particularly the gly-pro sequence. These include enzymes that detach a terminal proline, enzymes that detach a dipeptide sequence where the second residue is a proline molecule and the first one is often glycine, and enzymes that break apart the X-pro dipeptide to release two free amino acids, one of which is proline. Certain pathogens have special modified versions of these enzymes, and there are genetic diseases related to pathologies in these enzymes. Substitution of glyphosate for glycine in this sequence is likely to cause extra stress to the enzymes that break down these sequences, potentially leading to autoimmune disease.

Prolyl aminopeptidase is an enzyme that detaches a terminal proline residue from a peptide. The enzyme is expressed predominantly by pathogenic bacteria in the gut, in particular *Serratia marcescens*, a common pathogen in the gut as well as in the urinary tract; it is often multiply antibiotic-resistant and is a serious threat in hospital-acquired infection [34]. This enzyme is especially important to the pathogens for degrading collagen, providing amino acids as fuel. It is conceivable that the pathogens are able to degrade glyphosate-contaminated peptides terminating in proline whereas the human form of the enzyme is not. It is intriguing that the *S. marcescens* version of prolyl aminopeptidase is unusual in having extra space at the active site [34], which could potentially accommodate the larger glyphosate molecule adjacent to the terminal proline residue. This might also contribute to glyphosate's observed effect on the gut microbiome: excessive growth of pathogens.

Multiple strains of the toxic mould *Aspergillus* secrete an X-prolyl dipeptidyl aminopeptidase (X-PDAP) that is important for digesting collagen because it can separate out an X-pro pair to bypass the difficult step of breaking the X-pro bond. Research has shown that this enzyme is essential for hydrolysing proline-containing peptides [69, 70]. It is likely that it becomes even more essential when X is glyphosate, as the peptoid sequence glyphosate-proline is likely almost impossible to break. Since gly-pro is a very common sequence in collagen, glyphosate-pro is likely to impede the breakdown of collagen fragments, which may then encourage *Aspergillus* infection in both plants and animals. Glyphosate has been shown to increase the growth rate of *Aspergillus* [71].

The most disturbing question is, what happens in the absence of pathogens that can effectively clear collagen peptides contaminated with glyphosate? As we will see later in this paper, antibodies to collagen are linked to antibodies to vaccines. A genetic defect in the enzyme prolylase, which can break apart the very common gly-pro dipeptide to release the individual amino acids, leads to a severe disease with mental deficiencies and multiple skin lesions [72]. Intriguingly, a common plant pathogen, *Xanthomonas campestris*, which causes blight on multiple plant species has a unique variant of prolylase with two mutations, a substitution of tyrosine for gly-385 and valine for tyr-387, two highly conserved residues in the peptide sequence [73]. Is it possible that swapping out glycine affords protection from glyphosate substitution for this residue? We hypothesize that peptides derived from multiple proline and glyphosate-contaminated proteins, which are highly resistant to proteolysis, are causing an autoimmune epidemic that is an important contributor to autism and other autoimmune disorders.

5. BMAA AND ALS IN GUAM

β -N-methylamino-L-alanine (BMAA) is another noncoding amino acid and an analogue of serine [40]. BMAA is synthesized by cyanobacteria, the microbes responsible for the toxic algal blooms that occur in lakes experiencing an accumulation of nitrogen and phosphate nutrients following hot, rainy weather [74]. An *in vitro* study by Dunlop et al. in 2013 demonstrated that BMAA can be misincorporated into human proteins, causing protein misfolding that could lead to neurological diseases [40].

BMAA has, in fact, been linked to several neurodegenerative diseases, including Parkinson's, Alzheimer's and amyotrophic lateral sclerosis (ALS) [75]. A 2013 study linked an ALS cluster in Chesapeake Bay to consumption of BMAA-contaminated crabs [76]. A study in France investigated an ALS cluster near a lagoon that supplied oysters and mussels to the local

population. The authors demonstrated that the shellfish were contaminated with BMAA, but also remarked that there was intensive chemical-based agriculture in the region [77]. Interestingly, cyanobacteria have been found to be remarkably resistant to glyphosate [78, 79], and this could contribute to the recent record-setting algal blooms in the Great Lakes region, where glyphosate is extensively used on genetically modified (GM) Roundup-Ready crops [80].

One likely molecule that could be adversely affected by BMAA is the glutamate transporter, whose defective expression has been linked to ALS [81]. Glutamate excitotoxicity in motor neurons is associated with ALS, and this could be caused by an impaired glutamate transport system. Ordinarily, astrocytes quickly clear glutamate from the synapse, following its release by neurons, and the transporter is essential for this clearance. A conserved serine-rich motif in the glutamate transporter forms a reentrant loop, similar to a structure found in many ion channels [82]. This loop is crucial for the enzyme's proper function, and would be disrupted by substitution of BMAA for serine.

An interesting detective story has evolved around an epidemic of a complex neurological condition termed amyotrophic lateral sclerosis–Parkinsonism dementia complex (ALS–PDC), which reached epidemic proportions during a short interval after World War II among the native Chamorro people on the small island of Guam in the South Pacific. At the peak of the epidemic, the natives had a hundredfold increased risk to ALS and Parkinson's disease compared to the risk in the general human population.

A plausible explanation for this epidemic relates to a popular native food source: seeds from the cycad trees [83–85]. Cycad seeds contain BMAA, likely derived from associated cyanobacteria. However, what is especially interesting is that the BMAA becomes concentrated in the skin of fruit bats that feed on the cycad seeds. Fruit bats were a popular delicacy among the natives, who ate every part of them, including the skin. Increased access to firearms from the USA during the war may have made it easier to kill the bats, on which the natives then feasted, ultimately leading to the natives' near-extinction through the accumulation of BMAA in their brains [86]. Meanwhile the near-extermination of the bats through the hunting removed the presumed source of the epidemic [83].

However, the warfare also led to the accumulation of many toxic chemicals in the soil, which could have encouraged the proliferation of cyanobacteria, which are especially resilient in the face of stressors. The bats' demise was undoubtedly hastened by the accumulation of

excess BMAA in their tissues. A measurement of the amount of BMAA in three dried specimens of fruit bats from Guam taken from a museum in Berkeley found concentrations between 1200 and 7500 µg/g, which indicates up to hundredfold bioamplification over the level in the seeds of the cycad tree [87].

There have been inconsistent results in measuring the levels of BMAA in different tissue samples, but this has been explained recently by the realization that any BMAA incorporated into proteins may be missed in analysis without sufficient proteolysis. Ince et al. wrote: "When the insoluble, protein-containing fraction following TCA (trichloroacetic acid) extraction is further hydrolysed to release BMAA from protein, there is a further pool of protein-bound BMAA that is present in a ratio of between 60:1 and 120:1 compared with the pool of free BMAA" [84, p. 348]. We believe that this point has great significance when it comes to glyphosate: we highly suspect that different methodologies used to measure glyphosate contamination in any situation where there is a significant protein-bound component may yield different results depending on the degree to which protein hydrolysis is carried out.

6. GLYPHOSATE CONTAMINATION IN COLLAGEN, ENZYMES, GELATIN AND VACCINES

Gelatin is commonly used as an excipient stabilizer in vaccines, particularly the live virus vaccines. Gelatin is derived from animal skin and bone, especially of pigs and cattle; they may be fed glyphosate-contaminated forages, including GM Roundup-Ready corn and soy feed, which are sometimes supplemented with GM Roundup-Ready beet pulp. Gelatin is mainly derived by partial hydrolysis from the collagen in skin and bone. 26% of the amino acids in collagen are glycine; proline and hydroxyproline together make up 18% [88]; and glutamate constitutes 6%. All three of these components are problematic. The proline could be substituted by Aze from the sugar beet, the glycine could be substituted by residual glyphosate in the feed, and glutamate is a neurotransmitter but known to be neurotoxic at high concentrations; it works together with glycine to excite NMDA receptors in the brain. The vaccine virus may incorporate some of the noncoding amino acids into its own proteins to produce versions of them that resist proteolysis and induce autoimmunity through molecular mimicry.

One of us (Samsel) analysed a number of animal protein products for glyphosate. These included the bones of pigs, cows, horses' hooves, bees and bee products, collagen and gelatin products, vitamins, protein powders, enzymes and vaccines. Results are shown in Tables 2 and 3. Both high performance liquid

chromatography with tandem mass spectrometry (HPLC–MSMS) and enzyme-linked immunosorbent assay (ELISA) methods were utilized. It has been shown that both HPLC and ELISA are comparable in terms of accuracy and precision for detection and quantification of glyphosate in water-based analysis and including Nanopure, tap and river waters. Water-based solvents for

glyphosate demonstrate a detection limit of 0.6 ng/mL and a linear functional range of 1–25 ng/mL [200]. However, HPLC was not able to achieve detection below 5 ppb;¹ hence, in cases including water-based vaccines, analysis using numerous sample runs was made including using two independent labs to test the same samples.

Table 2. Residues of glyphosate found in animal-based products that were reported to the US Food and Drug Administration (FDA) by Samsel Environmental & Public Health Services. The limit of detection for glyphosate using hot water extraction is 0.075 parts per billion (ppb).¹

Protein substrate	Type	Test date	Glyphosate residue (ppb) ¹
GELATIN	JELL-O ORANGE #07 JAN 2018 DB02 02:36	29 July 2016	9.00
GELATIN	POWER-MAX PROTEIN POWDER ADVANCED NUTRITION	29 July 2016	14.94
GELATIN	DISNEY GUMMIES VITAMINS	9 August 2016	8.27
GELATIN	FLINTSTONES GUMMIES VITAMINS	9 August 2016	5.32
ORAGEL	CHILDREN'S ORAGEL 7.5% BENZOCAINE FORMULA	26 September 2016	2.81

HPLC–MSMS was also later used, where the method detection limit (MDL) permitted, for additional confirmation and quantification of glyphosate in digestive enzymes and collagens. Spiked sample recoveries were done for all samples tested. Freshly prepared glyphosate standard solutions were run as controls and results were calculated based on a standard curve.

In 1989, Monsanto researchers conducted an experiment on exposure of bluegill sunfish to ¹⁴C-radiolabeled glyphosate [89]. One of us (Samsel) obtained the (unpublished) report from the EPA through the Freedom of Information Act. The researchers had found that, with EDTA extraction, the amount of radiolabel in tissue samples was much higher than the amount of detected glyphosate. They decided to apply a digestive enzyme, proteinase K, and discovered that this “caused a substantial improvement in extractability”. It brought the yield from 17–20% in the case of EDTA to 57–70% following digestion with proteinase K. They summed up as follows: “Proteinase K hydrolyses proteins to amino acids and small oligopeptides, suggesting that a significant portion of the ¹⁴C activity residing in the bluegill sunfish tissue was tightly associated with *or incorporated into protein*” (present authors’ emphasis). In this context it is important to recall that a 60- to 120-fold higher detection level of BMAA was obtained following protein hydrolysis of contaminated proteins [84].

Since Monsanto found bioaccumulation of glyphosate in all animal tissues, with the highest levels in the bones and marrow [35, 36], one would expect that all tissues derived from animals fed a diet containing glyphosate residues and used for food by people around the globe would be contaminated. Knowing that the bioaccumulation of glyphosate would be evident in the vast majority of animals raised for market and fed a contaminated diet, as well as their products; and suspecting the possibility of contamination of even the digestive enzymes derived from these animals, one of us (Samsel) decided to analyse random samples.

Results from various gelatin-based products, along with the results for several different vaccines (discussed later) were reported to the FDA by Samsel Environmental & Public Health Services in August 2016. Table 2 shows results for glyphosate residues found in these gelatin-based products. The highest level found in a gelatin sample was almost 15 ppb.¹

Having found glyphosate in animal gelatins, analysing the collagen at the source was a logical next step. Tissues from pork and cattle obtained from a local supermarket, commercially available collagen sourced from industrially-raised swine and oxen, as well as the purified digestive enzymes pepsin, lipase and trypsin, derived from pigs, were selected for evaluation. Three methods of laboratory analysis were used to determine if

¹ Parts per (US) billion. To put this into perspective, 1 ppb = 1 µg/kg, and 1 µg of glyphosate (N-phosphonomethylglycine) contains 3.561×10^{12} molecules of the substance, each one of which could integrate with a protein.

glyphosate was present in porcine pepsin and in the glycine-rich collagen from the tissues of pigs and cattle, protein sources that are regularly consumed by Americans. The results are given in Table 3.

Glyphosate integration with enzymes is a serious consideration, as glyphosate may serve as an enzyme inhibitor like other phosphonates [90–92]. Inhibition and immobilization of enzymes may occur via three basic categories: covalent linkage; adsorption on a carrier; or entrapment within macromolecules [93].

Inhibition of enzymes may be reversible or irreversible. Types of reversible enzyme inhibition include competitive, noncompetitive and uncompetitive. *Irreversible* inhibitors covalently bond to the functional groups of the active site, thus permanently inactivating catalytic activity. Irreversible inhibition includes two types: group-specific inhibition and “suicide” inhibition.

The importance of fully functional digestive enzymes cannot be understated. They are essential for metabolic function, as they convert food into nutrients and other molecules that are then available to cells for tissue and organ growth, maintenance and repair. The precursor trypsinogen, produced in the pancreas, is enzymatically transformed into the serine protease trypsin. Trypsin catalyses the hydrolysis of proteins into peptides and provides substrates for further enzymatic hydrolysis for protein absorption.

Pepsin, a primary protease of digestion, is also responsible for the metabolism of dietary protein.

Pepsin’s cleavage of peptide bonds is responsible for the availability of the aromatic amino acids phenylalanine, tyrosine and tryptophan. It is also responsible for the cleavage and release of several other amino acids, including valine, glycine, histamine, glutamine, alanine and leucine.

Lipase participates in cell signaling, inflammation and metabolism. Pancreatic lipase is the catalyst for the hydrolysis of dietary lipids, which include fats, oils, cholesterol esters and triglycerides [94]. Triglyceride triester is metabolized for utilization as glucose and three fatty acids. Glyphosate integration into and inhibition of lipase could induce excessive bioaccumulation of fatty material in the blood vessels, gut, liver, spleen and other organs, as well as mimic lysosomal acid lipase deficiency. It would also allow for an increase in triglycerides in the blood, leading to numerous disease cascades, including malabsorption, fatty liver disease, jaundice, failure to thrive in infants, calcification of the adrenal gland, anaemia, hypercholesterolaemia, biliary dysfunction, decreased HDL, increased LDL, blood clots, fat-enlarged hepatocytes and liver fibrosis and failure. Samsel found that radiolabeled glyphosate was not detectable by HPLC–MSMS in samples of lipase deliberately spiked for analysis, suggesting that glyphosate may irreversibly inhibit lipase. On the other hand, pepsin and trypsin had good spike recoveries, demonstrating reversibility as glyphosate was released from the protein.

Table 3. Integration of glyphosate residues in various proteins, assessed using three testing methods.^a

Protein substrate (Method)	Type	Glyphosate residue (ppb)
Bone (ELISA)	Bovine leg	11.56
Bone marrow (ELISA)	Bovine leg marrow	4.22
Bone (ELISA)	Porcine foot	9.81
Skin (ELISA)	Porcine	0.325
Gelatin (ELISA)	Bovine, Sigma Aldrich, gel strength 225 Type B	2.04
Collagen (ELISA)	Bovine I & III	120.18
Collagen (GC-MS)	Bovine I & III	130 µg/kg
Collagen (HPLC-MSMS)	Bovine I & III	95 µg/kg
Pepsin (ELISA)	Purified porcine enzyme	< 40.00
Pepsin (GC-MS)	Purified porcine enzyme	430 µg/kg
Pepsin (HPLC-MSMS)	Purified porcine enzyme	290 µg/kg
Trypsin (ELISA)	Purified porcine enzyme	61.99
Lipase (ELISA)	Purified porcine enzyme	24.43
Bee bread (HPLC-MSMS)	Bee bread	2300 µg/kg
Bees (HPLC-MSMS)	<i>Apis mellifera</i>	< 10 µg/kg trace
Honey & comb (HPLC-MSMS)	Honey	< 10 µg/kg trace

^a The trace amount found in the bee substrates appeared as a small peak, which directly corresponded to glyphosate, complete with retention time and molecular features confirming contamination using HPLC–MSMS.

Table 3 shows results for various bovine and porcine products, including enzymes, bone, bone marrow, skin, collagen and gelatin. Acid hydrolysis was used on the bovine and porcine skin, bones and marrow, which were shaken and digested with 0.15 M hydrochloric acid for 24 h. The analysis methods were ELISA, gas chromatography–mass spectrometry (GC–MS) and HPLC–MSMS. All of the tested products were contaminated, with the highest level detected being 430 µg/kg in porcine pepsin (via GC–MS).

Additional evidence of glyphosate accumulation was found by Samsel in 2015 in the bodies of dead bees, bee bread and honey from bee hives suspected of colony collapse disorder (CCD), and these are also shown in the table. Colony collapse disorder (CCD) is an ever-increasing problem threatening pollination of crops globally. It may share a similar aetiology to that of Alzheimer’s disease with regard to learning and memory within the bee’s brain. Integration of glyphosate with the structural proteins and enzymes of the bee may affect protein folding and function. Additionally, glyphosate may also affect the digestive enzymes and bacterial homeostasis within the digestive system, which in turn may affect the quality of the honey produced. Glyphosate in bees may become part of their chitin, which has a structural function, in their bodies, analogous to glyphosate becoming part of the collagens of humans and other animals.

The results in Table 3 show ubiquitous contamination of the bee and bee products. Honey is derived from nectar and is the source of carbohydrates in the bee diet, whereas pollen turned into bee bread supplies the fats and proteins. Royal jelly, made from the secretions of the glands found in the hypopharynx of the worker bees, is fed to the queen and developing larvae [96].

Results for nineteen different vaccines, from five manufacturers, are shown in Table 4. Some vaccines do not contain live viruses and do not involve gelatin in their preparation, but many involve the use of eggs, bovine calf serum, fetal bovine serum or bovine proteins [95]. Engerix Hepatitis B vaccine is manufactured through a novel procedure, which involves culturing genetically engineered *Saccharomyces cerevisiae* yeast cells that carry the surface antigen gene of the hepatitis B virus. The procedures result in a product that can contain up to 5% yeast proteins, which could be a source of glyphosate if the yeast is grown on broths or media that utilize glyphosate-contaminated nutrient sources such as animal or plant proteins.

Vaccines that tested negative for glyphosate included Merck’s Hep-B vaccine, most of the pneumococcal vaccines and the sterile diluent included as a control. Gelatin is not listed as an ingredient in any of these vaccines, nor is bovine serum. In contrast, all of the vaccines that listed gelatin as an excipient tested positive for glyphosate, and nearly all of them also included bovine serum (including Varicella, MMR-II, MMRV and Zoster).

It is significant that MMR-II consistently contained the highest levels of glyphosate, significantly more than any of the other vaccines. This vaccine uses up to 12% hydrolysed gelatin as an excipient–stabilizer; as well as foetal bovine serum albumin, human serum albumin and residual chick embryo; all of which are contaminated by glyphosate during animal production.

7. EVIDENCE FOR A ROLE FOR COLLAGEN IN VACCINE ADVERSE REACTIONS

Post-vaccination allergic reactions to MMR and varicella vaccines have been linked to the gelatin excipient, and confirmed through observation of induced gelatin-specific IgE antibodies [97–100]. 24 out of 26 children with allergic reactions to vaccines (e.g., anaphylactic shock) had anti-gelatin IgE ranging from 1.2 to 250 µg/mL. Seven were allergic to gelatin-containing foods. A pool of 26 control children all tested negative for anti-gelatin IgE [99]. A study from 2009 that looked at gelatin sensitivity in children who were sensitive to cows’ milk, beef and/or pork as determined by IgE antibody levels [101] found that 16% of beef-sensitized children and 38% of pork-sensitized children had IgE antibodies to beef- or pork-derived gelatins that were cross-reactive with each other.

In a published case study, a 2-month-old baby developed Kawasaki disease one day after receiving its first dose of Infanrix (DTaP-IPV-Hib) and Prevenar, a pneumococcal conjugate vaccine [102]. Kawasaki disease is an acute, multisystemic vasculitis whose occurrence very early in life is extremely rare. Extensive tests for the presence of infection with multiple bacteria and viruses were all negative. We suggest that glyphosate contamination in one or both of the vaccines may have contributed to the vasculitis through glyphosate uptake into common proteins such as collagen in the vasculature to induce the autoimmune reaction.

Kelso (1993) reported the case of a 17-year-old girl who experienced anaphylaxis within minutes of receiving an MMR vaccine [98]. The girl described the event as “kind of like what happens when I eat Jell-O²”. Further testing found gelatin to be the component of the vaccine

² Jell-O is a proprietary brand of gelatin-based desserts, popular in the USA, and manufactured by Kraft Foods, part of the Kraft Heinz Company, headquartered in Chicago.

Table 4. Glyphosate levels in vaccines determined by ELISA reported to the US CDC, NIH, FDA and UN WHO of the Americas in September 2016 by Samsel Environmental & Public Health Services.^a

Vaccine undiluted	Manufacturer	Lot number Exp date	Test date Lab #	Glyphosate residue (ppb)	% Recovery in spiked sample
DTaP ADACEL	SANOFI PASTEUR	58160-820-43	7-15-2016	0.109	82%
DTaP	SANOFI PASTEUR	NDC 3-30-2018 C50418A	LAB #1 5-11-2016	< 0.075	81%
DTaP ADACEL	SANOFI PASTEUR	9-2-2018 NDC 58160-820-43	LAB #1 7-12-2016	ND	-
HEPATITIS-B	MERCK	3-30-2018 LO16427	LAB #2 5-11-2016	< 0.075	97%
HEPATITIS ENGERIX-B	GLAXOSMITH- KLINE	4-13-2017 NDC 58160-820-43	LAB #1 7-15-2016	0.337	73%
INFLUENZA FLUZONE QUAD	SANOFI PASTEUR	6-1-2018 6762	LAB #1 7-15-2016	0.170	95%
INFLUENZA	NOVARTIS	6-30-2016 1573 3P	LAB #1 5-11-2016	0.227	106%
Pneumococcal PNEUMOVAX 23	MERCK	05/2016 700281601	LAB #1 9-19-2016	0.112	118%
MMR II	MERCK	5-18-2017 7002151400	LAB #1 7-15-2016	3.740	-
MMR II	MERCK	9-9-2017 009545	LAB #1 5-11-2016	2.963	-
MMR II	MERCK	3-19-2017 7002151400	LAB #1 9-19-2016	3.154	-
MMR II	MERCK	9-9-2017 7002151400	LAB #1 7-12-2016	2.90	-
MMRV PROQUAD	MERCK	9-9-2017 7002305700	LAB #2 9-19-2016	0.659	103%
MMRV PROQUAD	MERCK	9-12-2017 7002305700	LAB #1 7-15-2016	0.512	86%
MRV PROQUAD	MERCK	9-12-2017 7002305700	LAB #1 7-12-2016	0.43	-
Pneumococcal PNEUMOVAX 23	MERCK	9-12-2017 700281601	LAB #2 7-15-2016	< 0.075	77%
Pneumococcal PREVNAR 13	WYETH	5-18-2017 73332	LAB #1 5-11-2016	< 0.075	82%
Pneumococcal PNEUMOVAX 23	MERCK	07/2017 7002681601	LAB #1 7-12-2016	ND	-
STERILE DILUENT	MERCK, SHARP & DOHME	5-18-2017 LO 40058	LAB #2 7-15-2016	< 0.075	97%
VARICELLA VARIVAX	MERCK	5-11-2018 7002025000	LAB #1 7-15-2016	0.556	84%
MVARICELLA VARIVAX	MERCK	2-8-2018 7002025000	LAB #1 7-12-2016	0.41	-
ZOSTER ZOSTAVAX	MERCK	2-8-2018 7002502401	LAB #2 9-19-2016	0.620	95%
ZOSTER ZOSTAVAX	MERCK	6-1-2017 7002602401	LAB #1 7-15-2016	0.558	98%
ZOSTER ZOSTAVAX	MERCK	6-1-2017 7002602401	LAB #1 7-12-2016	0.42	-
ZOSTER ZOSTAVAX	MERCK	6-1-2017 7002602401	LAB #2 7-12-2016	0.42	-

^a Limits of detection for glyphosate in vaccines in parts per billion (ppb):¹ 0.075 (LAB #1); 0.15 (LAB #2).

to which the girl was allergic. The connexion may be to misfolded proteins, which include the collagens and associated partially hydrolysed gelatins. Indeed, both Jell-O and vaccines have been contaminated by glyphosate, as we reported in the previous section.

Puppies immunized with the rabies vaccine and a multivalent canine vaccine were compared to unvaccinated

control puppies [103]. The vaccinated puppies, but not the unvaccinated ones, developed autoantibodies to their own collagen. A follow-up study where either just the rabies vaccine or just the multivalent vaccine was administered produced a similar result. The authors suggested that this could explain issues of joint pain that are currently common among dogs, particularly as they age.

8. MULTIPLE SCLEROSIS (MS)

8.1 Sugar beet and MS

The world obtains 30% of its sugar supply from beet sugar. While sugar cane is grown in tropical regions, sugar beet requires a temperate climate. The highest incidences of MS worldwide are in the USA, Canada and western Europe [5], where most of the beet sugar is produced. MS rates are higher in the northern states of the USA compared to the south, corresponding to the distribution of sugar beet cultivation. MS rates in Canada are highest in the Alberta prairie region, at the centre of the Canadian sugar beet industry [104]. Studies on migrants have shown that those who move from a low-risk to a high-risk area tend to adopt high-risk only if they migrated during childhood [105]. This implicates local environmental factors acting before adolescence. Tokachi province in Japan hosts only 0.3% of the population, but produces 45% of the sugar beet consumed in Japan [37]; this province has the highest rate of MS among all Asian populations [106].

A fascinating proposition how sugar beet could cause MS implicates a unique noncoding amino acid that is produced by sugar beet, namely Aze. Both proline and Aze have a unique structure for an amino acid: the side chain loops back round to connect up to the nitrogen atom. In the case of Aze, there are only 3 carbons in the ring instead of the 4 carbons in proline (Fig. 2). It has been shown experimentally that Aze can be inserted by mistake into proteins in place of proline [38].

Myelin basic protein (MBP) is an essential protein for maintaining the myelin sheath, and it interacts with actin, tubulin, calmodulin and SH3 domains [107]. It

assembles actin filaments and microtubules, binds actin filaments and SH3 domains to membrane surfaces, and participates in signal transduction in oligodendrocytes and myelin. A central proline-rich region in MBP is functionally significant [108–110] and, in particular, is a binding site for Fyn-SH3, a key regulatory protein [111]. Proline substitutions of the SH3 ligand decrease its affinity for the Fyn-SH3 domain [108]. Fyn is localized to the cytoplasmic leaflet of the oligodendrocyte plasma membrane, where it participates in numerous signaling pathways during development of the central nervous system [112, 113]. Phosphorylation at a polyproline structure in the Fyn-binding region of MBP affects its structure.

A study using recombinant murine MBP inserted into *E. coli* strains demonstrated conclusively that Aze makes its way into MBP, substituting for up to three of the eleven possible proline sites. Molecular modeling of a proline-rich region of the recombinant MBP illustrated that misincorporation of Aze at any site would cause a severe bend in the polypeptide chain, and that multiple Aze substitutions would completely disrupt the structure of MBP [114, 115].

A possible concern regarding Aze is that over 90% of the sugar beet grown in the USA and Canada is genetically engineered to resist glyphosate. Therefore, the crops are exposed to significant amounts of glyphosate. The electronic *Code of Federal Regulations e-CFR 180.364 Glyphosate; Tolerances for Residues*, allows up to 25 ppm residue of glyphosate in dried sugar beet pulp. In 1999, Monsanto realized that its GM sugar beet crop well exceeded the upper limit established by the EPA for glyphosate residues. They requested, and were granted, a 125-fold increase in the upper residue limit for dried beet pulp (from 0.2 to 25 ppm). At the same time, the upper limit for fresh beet was increased fiftyfold to 10 ppm.

Glyphosate has been shown to increase the risk of root rot in sugar beet, caused by fungi [116]. Aze has been demonstrated to have antifungal activity [117]. Plants tend to increase synthesis of toxins under stress conditions, and it is plausible that an increased potential for root rot would result in increased synthesis of Aze. This is especially likely given that plants increase proline synthesis under a variety of different stress conditions [118]. However, to our knowledge, whether glyphosate causes an increase in either proline or Aze synthesis in sugar beet has not been investigated.

Consumption of milk worldwide is strongly correlated with MS risk (Spearman's correlation test = 0.836; $P < 0.001$) [119]. For the past several decades, cows' feed has been supplemented with either beet

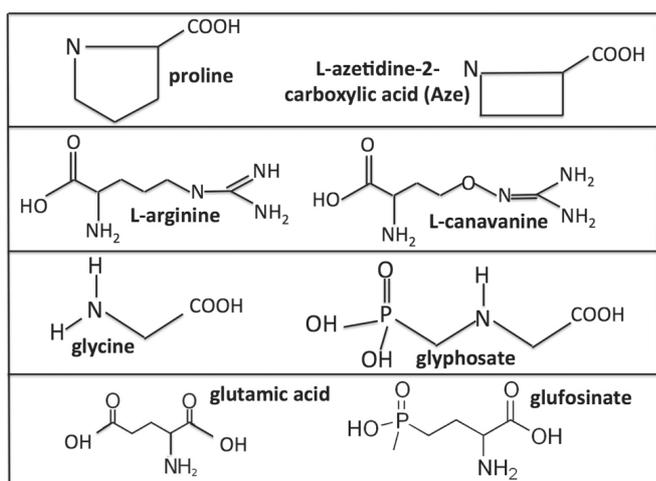


Figure 2. Molecular structures of the coding amino acids proline, L-arginine, glycine and glutamic acid; and their respective noncoding analogues Aze, L-canavanine, glyphosate and glufosinate.

molasses or sugar beet pulp, left as a residue after the sugar has been extracted [120]. Aze has been experimentally found in three sugar beet by-products that are fed to farm animals: sugar beet molasses, and both shredded and pelleted sugar beet pulp [38]. Casein is relatively enriched in proline [121]. If cows are exposed to Aze from the sugar beet, it will likely get inserted by mistake into casein, causing it to resist proteolysis. MBP's critical proline-rich sequence is vulnerable to misincorporation of Aze. The characteristic plaques of MS show loss of MBP within lesions in axon sheaths [107]. It is unclear whether this autoimmune reaction would arise through molecular mimicry from antibodies to unmetabolized peptides from casein or as a direct result of improperly folded MBP due to Aze insertion.

Glyphosate, an analogue of glycine, can be expected to be found in all tissues, including the milk of all mammals consuming glyphosate residues in the diet. Radiolabeled glyphosate studies conducted with lactating goats found ^{13}C and ^{14}C residues of glyphosate (N-phosphonomethylglycine), N-acetylglyphosate and other radiolabeled metabolites in milk. Monsanto found daily average ^{14}C residue levels from 19 to 86 ppb, with levels falling after five days of depuration to 6 ppb prior to sacrifice for organ examination. Results disseminated by Monsanto indicate that lactating animals (goats) fed a diet containing glyphosate and AMPA can be expected to have measured residue levels in edible tissues and milk [122]. In 2007 Dupont, in a similar study, examined the metabolism of N-acetylglyphosate in lactating goats. Detectable residues of N-acetylglyphosate, glyphosate and AMPA were detected in milk and other tissues. Milk, liver and kidney each contained 0.03% of the administered dose. Individual daily radiolabeled residues in the milk ranged from 0.030 to 0.036 $\mu\text{g/g}$ [123].

Lactobacillus plays an important rôle in metabolizing casein in the human gut. A detailed study of the prolyl aminopeptidase from *Lactobacillus* revealed that it is a member of the class of α/β hydrolases. Multiple sequence alignment has revealed three distinct highly conserved regions in this family and all three contain at least two highly conserved glycines [124] that would be vulnerable to displacement by glyphosate. The motif gly-x-ser-x-gly-gly characterizes the domain surrounding the catalytic serine residue of prolyl oligopeptidases in general. The glycine residues in this motif contribute to the correct positioning of the catalytic serine with respect to its substrate. A second glycine-rich domain appears essential to activity, as it likely corresponds to the oxyanion hole. The function of the third highly conserved glycine-rich domain, with the motif asp-x-x-gly-x-gly-x-ser, remains unknown. *Lactobacillus*

spp. are also highly dependent on manganese to protect them from oxidative damage, hence glyphosate's preferential chelation of manganese likely harms *Lactobacillus* [125].

An examination of collagen in the jugular veins of MS patients undergoing surgical reconstruction revealed an abnormal collagen structure, characterized by thin, loosely packed type III fibres [126]. Collagen is rich in proline. If too many of the prolines in procollagen are displaced by Aze, the polypeptide does not fold into a stable triple-helical conformation, which is a prerequisite for normal secretion of procollagen [127]. This reduces the release of procollagen and the misfolded molecules are subjected to proteolysis for recycling, resulting in the useless expenditure of energy for building and degrading procollagen molecules. Those that are released can be expected to produce defective collagen matrices. Collagen is even more highly enriched in glycine than in proline, as its core structure consists of a triple peptide repeat, where glycine is always the third residue of the triplet, and proline and hydroxyproline often occupy the other two positions [128]. Glyphosate substitution for glycine in structural proteins; i.e., collagen, elastin, fibronectin and laminin; would contribute to disrupted folding as well as defective strength and elasticity.

Conserved prolines also play a crucial rôle in ion channel gating, the regulation of hypoxia-inducible factor (HIF) and embryogenesis; in fact, substituting Aze for proline is a technique used to test whether a particular proline residue is critical to the protein's proper functioning [37].

8.2 Rôle of *Acinetobacter* and *Pseudomonas aeruginosa* in MS

A series of papers by Ebringer et al. have suggested an important rôle for the Gram-negative bacteria *Acinetobacter* and *Pseudomonas aeruginosa* in MS [129–131] as well as a proposed link to prion diseases. Their most recent paper in *Medical Hypotheses* presents the evidence to support this idea from multiple dimensions [130]. First, MS patients were shown to have elevated levels of antibodies to these two microbes but not to the common gut microbe *E. coli* [132, 116]. They have autoantibodies to MBP and myelin oligodendrocyte glycoprotein (MOG) [131]. MS patients are also prone to sinusitis and *Acinetobacter* is one of the most common microbes found in nasal sinuses. Ebringer et al. also proposed that the increased prevalence of sinusitis in colder climates may explain the geographical distribution of MS in more northerly latitudes [130]. *P. aeruginosa* causes upper respiratory infections and it is among the microbes that have developed multiple antibiotic

resistance in recent years, presenting a huge problem in hospital infection [133]. *Acinetobacter* has also become resistant to multiple antibiotics [134].

The number of microbial species that can metabolize glyphosate is quite small. A 1996 study showed that *Acinetobacter* is able to fully metabolize both glyphosate and AMPA and utilize these molecules as a source of phosphorus [135]. A study of agricultural soil heavily polluted with glyphosate identified only three species capable of degrading glyphosate when exposed at a level of 1000 ppm: *Pseudomonas putida*, *P. aeruginosa* and *Acetobacter faecalis* [136]. Another study on marine species identified *Pseudomonas* as being among the rare microbial species that can utilize the phosphonate in glyphosate as a source of phosphorus [137]. It can be predicted that *Pseudomonas* and *Acinetobacter* species in the nasal or digestive tracts would have a substantial advantage over other microbes if they can degrade glyphosate. On the other hand, they would also be heavily exposed if they actively take it up, and it would not be unreasonable to assume that some of the glyphosate might end up in their synthesized proteins by mistake in place of glycine. Both *Pseudomonas aeruginosa* and *Acinetobacter* strains have recently become a serious problem in hospitals, and a public health issue, due to their multiple-antibiotic resistance [138]. Glyphosate has been

shown to induce generic antibiotic resistance in other microbial species, including *E. coli* and *Salmonella*, through the induction of a generic capability to export toxic chemicals through efflux pumps [139].

A PEP transferase enzyme synthesized by *Acinetobacter calcaceticus* has sequence homology with a bovine prion sequence, and antibodies against synthetic peptides containing the structurally related sequences were found to be significantly elevated in cattle with bovine spongiform encephalopathy (BSE) compared to negative controls [140]. Ebringer et al. (2005) [129] link MS to BSE, also known as “mad cow disease”, and to the related human disease, Creutzfeldt–Jakob disease (CJD). Cows suffering from BSE manifest hindquarters paralysis early after onset, similar to the mobility issues afflicting MS patients at onset. Ebringer et al. found elevated levels of antibodies to both *Acinetobacter* and *Pseudomonas*, along with autoantibodies to both white and grey matter components, in BSE-affected animals, as is also the case for MS [129].

Of particular note are the molecular similarities they identified between certain peptides found in these two microbes and peptides in MOG and MBP that are known to be allergenic. Strikingly, all three of the microbial sequences they identified and all three of their human protein analogues contain conserved glycines (Table 5).

Table 5. Amino acid sequences of three peptides from *Acinetobacter* and *Pseudomonas* and the corresponding human peptides from MBP that they mimic.^a

Microbe	<i>Acinetobacter</i>	<i>Acinetobacter</i>	<i>Pseudomonas</i>
Protein	3-OACT-A	4-CMLD	Gamma-CMLD
Peptide	Leu-Tyr-Arg-Ala-Gly-Lys	Ser-Arg-Phe-Ala-Tyr-Gly	Thr-Arg-His-Ala-Tyr-Gly
MBP	Leu-Tyr-Arg-Asp-Gly-Lys	Ser-Arg-Phe-Ser-Tyr-Gly	Ser-Arg-Phe-Ser-Tyr-Gly

^a Note that all six peptides have a glycine residue.

MOG is strongly implicated in the disease pathology of MS; autoantibodies recognizing MOG have been found in the CNS of MS patients [141]. One of the major encephalitogenic peptides in MOG is the sequence from residue 92 to residue 106, which contains a highly conserved glycine near its centre [142].

Both diabetes and MS are associated with abnormal T-cell immunity to proteins found in cow’s milk [143]. In a study conducted in dairy cows by Monsanto in 1973, ¹⁴C-radiolabeled glyphosate was studied in the distribution of residues in milk, urine, faeces and other tissues of the lactating cow. Glyphosate contamination of milk ranged from 9 to 15 ppb with the highest accumulation in the kidney and rumen fluid (201 ppb and 109 ppb, respectively) [201]. An epitope of bovine serine albumin found in milk that is linked to MS but not to diabetes is BSA193. It shows

structural homology with exon 2 of MBP through the peptide sequence GLCHMYK. Note that the first peptide in this sequence is glycine. Exon 2 is a target peptide in both MS autoimmunity and in experimental autoimmune encephalitis (EAE), an animal model of MS [144–146]. Exon 2 of MBP is implicated in remyelination [144]. Its expression is largely restricted to the developing brain and to areas of myelin reconstruction, notably MS lesions [147].

The gly-ser-gly-lys tetrapeptide is highly conserved among MBPs from multiple species [148]. The serine in this sequence is the site of attachment of polyphosphoinositide. The highly conserved nature of this sequence suggests that the phospholipidation of MBP is important biologically. Substitution of glyphosate for either of the glycines would likely disrupt this modification.

9. MMR VACCINE AND AUTISM

In this section, we make a case for a direct link between the measles, mumps, and rubella (MMR) vaccine and autism, via autoantibody induction through molecular mimicry. In a paper provocatively titled, “Peptide cross-reactivity: the original sin of vaccines”, Kanduc makes the point that massive cross-reactivity between antigens in vaccines and similar sequences in human proteins makes it almost inevitable that vaccines lead to autoimmune disease through molecular mimicry [149]. Reported post-vaccination autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis, inflammatory myopathies, multiple sclerosis, Guillain-Barré syndrome and vasculitis [150].

It is becoming increasingly acknowledged that autism may be an autoimmune disease. Family members of autistic children have a significant increased risk to other known autoimmune diseases such as hypothyroidism, rheumatic fever and multiple sclerosis [151]. Several studies on both humans and monkeys have revealed a potential link between maternal antibodies directed against specific foetal brain proteins and a future autism diagnosis in the foetus [152–155]. Furthermore, it has already been demonstrated that vaccines are capable of inducing autoimmune antibodies against proteins in the brain. The narcolepsy epidemic in Europe following an aggressive immunization campaign against the H1N1 'flu virus was eventually conclusively resolved as being attributed to autoimmune reactions to the hypocretin receptor through molecular mimicry from a peptide in the surface-exposed region of the influenza nucleoprotein A that was present in the H1N1 vaccine [156] (hypocretin is an important regulator of sleep).

Much controversy surrounds the concept that the MMR vaccine may be contributing to the autism epidemic in the USA and elsewhere. In an immune-compromised child, the live measles virus from the vaccine is capable of infecting the brain and sustaining a chronic measles infection, resulting in loss of neurons, eosinophilic intranuclear inclusions and gliosis, a condition termed “subacute measles encephalitis”. This can result in a seizure disorder and developmental delay in language and motor skills (as was clearly observed in a case study involving an HIV-positive 2-year-old boy [157]).

Singh et al. have published a series of papers over the past two decades [14, 158–160] proposing that there is a subpopulation among the autism community who can be characterized as suffering from “autoimmune autistic disorder” [14]. The 1998 study by Singh et al. found that 90% of measles-IgG-positive autistic sera were also positive for anti-MBP antibodies, supporting the hypothesis that a virus-induced autoimmune response may be

causal in autism [158]. A follow-on serologic study of antibodies to viruses associated with autism published in 2003 revealed a statistically significantly elevated level of measles antibody in children with autism compared to their siblings ($P = 0.0001$) or to unrelated children ($P = 0.003$), but not with antibodies to mumps or rubella [159]. In a later study, 60% of 125 autistic children had significantly elevated levels of antibodies to measles haemagglutinin unique to the MMR strain of the virus, compared to the 92 control children [160]. Over 90% of the children who had elevated antibody levels also tested positive for MBP autoantibodies. It was suggested that this could be linked to virus-induced autoimmunity through mimicry.

In fact, there is a sequence homology of 78% between a peptide sequence from MBP (EISFKLGQEGRDSRSGTP) and one found in a measles virus protein, MP3 (EISDNLGQEGRASTSGTP) [161, Table 2, p. 7]. Three of the matches between these two sequences are glycines. Measles virus-neutralizing antibodies are mainly directed to haemagglutinin, implying that it is essential for acquired immunity from the vaccine [162]; yet over-production, particularly if the virus penetrates the blood–brain barrier, runs the risk of inducing an autoimmune response to the myelin sheath. In fact, high measles antibody titres have been previously linked to MS [163].

Gonzalez-Granow et al. found high titres of autoantibodies in both the IgG and IgA classes specific to MBP in the serum of patients with autism [15]. The IgA antibodies in particular were shown to act as serine proteinases to degrade MBP *in vitro*. They also induced a decrease in long-term potentiation in perfused rat hippocampi. Reduced long-term potentiation in the hippocampus is a feature of autism, as has been clearly demonstrated in studies using mouse models of autism [164].

Dr Andrew Wakefield was the first to reveal a possible connexion between MMR and autism. His controversial *Lancet* paper, published in 1998 and then later retracted, proposed that this vaccine caused an acute reaction in children with gut dysbiosis (abdominal pain, diarrhoea, food intolerances, bloating etc.) [9]. The paper reported on a group of 12 children who had experienced developmental delay following an MMR vaccine and who were diagnosed with autism. These children suffered from rash, fever, delirium and seizures following the vaccination with MMR. He and several colleagues later published additional papers elaborating the hypothesis that dysbiosis in the gut, combined with impaired protein hydrolysis, leads to autoimmune lesions in the duodenum that are associated with extensive colonic lymphoid hyperplasia. The release of undigested peptides

into the vasculature across a leaky gut barrier and, ultimately, from the vasculature across a leaky blood–brain barrier, could induce encephalopathy [165–167].

In an epidemiological study from 1998, encephalopathy was clearly demonstrated as an acute reaction to measles vaccine, where 48 cases were found following vaccination, with no cases identified after administration of either monovalent mumps or rubella [168]. Among these 48 children, eight died, and the remainder experienced mental regression, chronic seizures, movement disorders and sensory deficits in the subsequent months.

The FDA’s vaccine adverse event reporting system (VAERS) database is a valuable tool for uncovering trends in vaccine adverse reactions. Our earlier studies on VAERS comparing MMR with an age-matched, equal-sized distribution of all other vaccines showed a significant association of MMR with autism ($P < 0.007$) [169]. This was puzzling, because MMR has never contained either aluminium or mercury, the two prime candidates for the kind of neurological damage that might lead to autism [170–174]. Strong associations also appeared with fever and rash. In that paper, we proposed that the adverse reaction might be caused by the acetaminophen administered to the child to try to curb the seizures.

Since glyphosate usage on crops has gone up dramatically since the GM Roundup Ready crops were

first introduced in 1996, we decided it would be worthwhile to compare the early data on MMR in VAERS with the later data. We defined a cutoff date on 1 January 2003, such that the events where MMR was included as an administered vaccine could be separated into “early” and “late”, based on whether they were before or after that date. Each dataset represented a 13-year interval. We found 10 639 events in the early set and 19 447 events in the late set; thus, the raw number of events nearly doubled in the later years.

We also tabulated the frequency of different adverse reactions in the two sets, and used a standard statistical analysis to compute the significance of any differences observed: we randomly down-sampled both sets as needed such that there was an identical total count and an identical distribution over age in the two datasets. Results were surprising: many symptoms associated with atopy or with an allergic reaction were significantly higher in the later set, and “hospitalization” was highly significantly overrepresented in the later set [Table 6]. Other overrepresented symptoms included seizures, dyspnea, hyperventilation, asthma, eczema, autism, hives, anaphylactic [shock], and irregular heart rate. Interestingly, the early set had more frequent occurrences of joint pain and arthritis, suggesting that the toxic elements in the vaccine impacted the joints rather than the brain.

Table 6. Frequency of various adverse reactions to MMR before and after January 2003 [US FDA, VAERS]. The P -values were computed according to a χ^2 goodness-of-fit test.

More common before 2003			
Reaction	Count < 2003	Count \geq 2003	P -value
Arthritis	52	18	0.045
Joint pain	175	75	0.012
More common after 2002			
Reaction	Count < 2003	Count \geq 2003	P -value
Hospital	132	423	0.00041
Seizures	314	534	0.0055
Dyspnea	139	279	0.0086
Hives	444	654	0.011
Anaphylactic	28	91	0.017
Eczema	10	47	0.028
Autism	105	184	0.031
Hyperventilation	18	57	0.035
General infection	77	136	0.044
Asthma	22	58	0.046
Immunoglobulin G	0	17	0.048
Ear infection	32	72	0.048
Heart rate irregular	11	39	0.049

To our knowledge, there have been no significant changes to the formulation of MMR since its introduction. The explanation for the significant changes in adverse reactions must, therefore, lie in external factors, one of which is likely to be glyphosate. We suggest that both chronic exposure to glyphosate from food, water and air and direct exposure to glyphosate residues in the vaccine are relevant factors. A child with a disrupted gut microbiome due to chronic glyphosate exposure will also suffer from a leaky blood–brain barrier, and this will lead to a much greater possibility of measles antigenic proteins entering the brain and causing anaphylaxis and seizures.

The measles virus is a member of the family of paramyxoviruses, which have two highly-conserved glycine residues at positions 3 and 7 in the hydrophobic fusion peptide (FP) region of the viral fusion-mediating glycoproteins [175]. This FP region is the most highly conserved region of the glycoproteins, and it plays a critical rôle in destabilizing the membrane of the host cell to gain entry. Substitutions of other amino acids for either the G3A or G7A glycines caused increases in both cell–cell fusion and the reactivity of the protein to antibodies, leading to both a higher infection rate and increased chances for an autoimmune reaction. Glyphosate substitution is likely to do the same, as well as leading to a form of the protein that would resist proteolysis.

The FPs of both the influenza virus and human immunodeficiency virus (HIV) gp41 contain numerous glycine residues at regular intervals, with glycine overall making up 29 and 26%, respectively, of the total peptide sequence [175]. Optic neuritis, an immune-mediated demyelinating injury of the optic nerve, has been recognized as a side effect of the influenza vaccine that can lead to blindness [176].

10. OTHER AUTOIMMUNE DISEASES

10.1 Neuromyelitis optica and aquaporin

Neuromyelitis optica is a rare severe inflammatory demyelinating disorder of the central nervous system, which is related to multiple sclerosis but distinctly different and manifested mainly by paralysis and optic nerve damage [177, 178]. It has been conclusively demonstrated that this condition is caused by an autoimmune reaction to aquaporin-4, which is highly expressed in the astrocyte membrane [177, 178].

Aquaporins are important membrane proteins, which can transport water molecules through pores into the cell while excluding protons [179]. They are highly expressed by astrocytes, one of whose rôles is to mediate water flow among the vasculature, the

cerebrospinal fluid and the lymph system [178]. Thus, aquaporins are implicated in brain oedema [180]. Plants produce aquaporins as well, and mimicry between plant and human aquaporins has been proposed as a mechanism for the development of an autoimmune sensitivity to this protein [181]. Plants considered to show aquaporin mimicry notably include corn and soy as well as tomato, tobacco and spinach [182].

Autoimmune sensitivity to aquaporin has also been found in association with MS [182]. Vojdani et al. found significant elevations in antibodies against both human and plant aquaporin 4, in addition to antibodies against MB, MOG and S100 calcium-binding protein B (S100B) in patients suffering from MS.

Among the aquaporins, aquaporin-6 is unique in that it operates as an anion channel instead of as a water channel. Analysis of the peptide sequence in comparison to other aquaporins reveals that aquaporin-6 has an asparagine substituted in place of a glycine at residue 60. This one small difference completely changes the way the molecule behaves in the membrane. A glycine at this position is conserved among all the other aquaporins. Furthermore, aquaporins are constructed of α -helices, and there are three sites where the helices cross. Highly conserved glycine residues are found at all three sites [57, 183].

Aquaporin is also found in bacteria, although homology with human aquaporin is only about 20%. The bacterial aquaporin is a 27 kDa trypsin-resistant protein called aquaporin-Z, which was originally described in *E. coli* [184]. Sequence analysis conducted by Ren et al. [185] revealed four regions where homology was considerably stronger (90%, 60%, 50% and 45% respectively). They convincingly showed cross immunoreactivity between the human and bacterial versions of the protein. Antibodies to aquaporin Z bind to astrocytes, activate complement, and cause death.

Ren et al. [185] identified all the residues where the bacterial and human peptides were identical (Fig. 1 in [185]). A tally of counts reveals that glycine was by far the most common among these matched residues, representing 14 of the total 66 matches. The second most common amino acid was lysine with 8 matches. Alanine, isoleucine and valine had 7, 5 and 4 matches respectively, and all other amino acids had less than four.

Thus, it appears that glyphosate-substituted trypsin-resistant aquaporin from both gut microbes and from GM glyphosate-resistant corn and soy foods are plausible sources of antigens that could induce neuromyelitis optica and contribute to the disease process in MS through misincorporation.

10.2 Type 1 diabetes

Type 1 diabetes is considered a genetic disease, but its incidence has been increasing by 3–4% worldwide every year in the recent past [186, 168]. Although an environmental component is highly suspected, environmental factors have not yet been identified. An increased incidence of type 1 diabetes is associated with both MS [187] and autism [188]. The disease is characterized by an autoimmune reaction to various proteins expressed in the pancreatic islet cells. Specifically, antibodies against glutamic acid decarboxylase (GAD65) are often found [189]. Cross-reactivity with proteins from foods and microbes in the gut are both possibilities.

One microbe that may be inducing antibody production through mimicry is *Mycobacterium avium paratuberculosis* (MAP). Blast analysis revealed 75% homology between a previously identified antigenic region of GAD65 [190] and a MAP heat-shock protein (HSP65) [189]. The specific 16-residue matched sequence in HSP65 centrally contains a pair of glycines which could be substituted by glyphosate to cause resistance to proteolysis. This microbe has been linked to numerous other human diseases including ulcerative colitis, irritable bowel syndrome, sarcoidosis, Hashimoto's thyroiditis, MS and autism [188]. With respect to MS and autism, cross-reactivity between HSP65 and MBP through mimicry may provide the link.

Patients with type-1 diabetes commonly have an antibody reaction to bovine serum albumin, a component of cows' milk [191]. The hypothesized explanation is an autoimmune reaction to a beta-cell specific surface protein through mimicry.

Insulin-derived amyloidosis is a condition that can develop following long-term insulin therapy, whereby an "insulin ball" develops at the site of injection. This hard mass has been analysed and found to contain accumulations of insulin fibrils reminiscent of amyloid β -plaque in the Alzheimer's brain. Insulin amyloidosis is more common for animal (cows and pigs)-derived than human-derived insulin products. Nowadays, cows and pigs are chronically exposed to glyphosate in their feed. The rôle of glycine residues in proteins may indeed be to protect from aggregation into amyloid fibrils [192]. Substitution of glyphosate for any of these conserved glycines would therefore tend to promote amyloidosis.

Glutamic acid and glycine are by far the largest component amino acids of bovine proinsulin and make up 25% of the amino acid residues in the molecule [193]. The same is true for human insulin, which differs very little from the animal versions. The herbicide glufosinate is a natural noncoding amino acid analogue of glutamic

acid (Fig. 2). Substitution of either glufosinate for glutamic acid or glyphosate for glycine in insulin is likely to impair its function, and may also lead to amyloidosis.

The widespread appearance of glyphosate-resistant weeds among the glyphosate-resistant crops has forced some farmers to turn to glufosinate as the herbicide of choice [194]. Glufosinate-tolerant corn and soybean have been available on the US market since their approval by the USDA in 1995 and 1996, respectively. A tri-resistant form of soybean tolerant of glyphosate, glufosinate, and 2,4-D was approved by the FDA in September 2014. Dual resistance to glufosinate and glyphosate in corn was approved in November 2015.

10.3 Coeliac disease

Coeliac disease and, more generally, gluten intolerance, have reached epidemic proportions in the USA in the past decade [195]. Wheat grown there is being routinely sprayed with glyphosate for staging and desiccation just before harvest. This practice clears the field of weeds prior to harvest and planting of the next crop, but increases the amount of residual glyphosate in the grain. The practice has been increasing in popularity in step with the increase in gluten intolerance. Glyphosate is systemic in the plant and enters the seed as the plant dies, hence eventually ending up in wheat-based foods.

Proline residues make up 20% of the first 100 amino acids of both α - and γ -gliadins [54]. Related proteins from rye and barley are also unusually proline-rich [56]. As we implied earlier, proline is inaccessible to most digestive proteases because the bond between the peptide nitrogen atom and the side group complicates hydrolytic attack. As a consequence, specialized prolyl aminopeptidases detach the amino-terminal proline from a peptide. These enzymes depend on manganese as a catalyst, and manganese is one of the metals most dramatically affected by glyphosate chelation [125]. Unhydrolysed gliadin peptides bind to HLA-DQ molecules (receptors on antigen-presenting cells) and trigger pathogenic T-cell responses [196]. Genetic variants of HLA-DQ are linked to both coeliac disease and type 1 diabetes [197, 198].

Analysis of the X-ray crystal structure of a human cytosolic prolyl aminopeptidase worked out in 2008 revealed that it is a dimer with a dependency on two manganese ions as the catalytic centres [199]. The full sequence of the catalytic domains of six prolyl peptidases from both human and microbial species is shown in Fig. 6 in ref. 199. Six of the twenty sites of fully conserved residues across all species were glycine residues, three were histidine, two were tyrosine and two were proline. The remaining seven were seven different amino acids.

11. CONCLUSION

In this paper, we have shown that widespread misincorporation of glyphosate for glycine during protein synthesis could explain the aetiology of multiple autoimmune diseases that are currently increasing in incidence in the USA. Misincorporation is plausible by analogy with multiple known toxins produced by organisms in defence against pathogens, including Aze, BMAA, L-canavanine and glufosinate, which work in a similar manner. We have shown that proteins from foods such as milk, wheat and sugar beet, as well as peptides derived from microbes resident in the gut or nasal tract or introduced iatrogenically through vaccination, are all potential causes of autoimmune disease induced through molecular mimicry. It is highly significant that two microbes linked to MS through molecular mimicry are among the very few microbes that can fully metabolize glyphosate. Using the VAERS database, we have shown that severe adverse reactions to the MMR vaccine have increased significantly over the past decade in step with the increased use of glyphosate. Glyphosate in MMR may originate from growth of the live virus on culture materials derived from glyphosate-exposed animals and/or from gelatin used as an excipient stabilizer. We have confirmed the presence of glyphosate contamination in MMR and in many other vaccines where the live virus is cultured in eggs, bovine protein or gelatin, or where animal products are used as an excipient component. Notably, some vaccines prepared without live culture on gelatin were free of glyphosate contamination. Substitution of glyphosate for glycine during protein synthesis could yield a peptide that resists proteolysis, making it more likely to induce an immune response. Furthermore, enzymes involved in proteolysis are likely to be disrupted due to their confirmed contamination with glyphosate. A non-exhaustive list of possible diseases that can be attributed to this mechanism include autism, multiple sclerosis, type 1 diabetes, coeliac disease, inflammatory bowel disease and neuromyelitis optica.

ACKNOWLEDGMENT

This research is supported in part by Quanta Computers, Taiwan, under the auspices of the Qmulus program.

REFERENCES

- Ashwood, P. & van de Water, J. Is autism an autoimmune disease? *Autoimmun. Rev.* **3** (2004) 557–562.
- Gulcher, J.R., Vartanian, T. & Stefansson, K. Is multiple sclerosis an autoimmune disease? *Clin. Neurosci.* **2** (1994) 246–252.
- Hertz-Picciotto, I., Croen, L.A., Hansen, R., Jones, C.R., van de Water, J. & Pessah, I.N. The CHARGE study: An epidemiologic investigation of genetic and environmental factors contributing to autism. *Environ. Health Perspectives* **114** (2006) 1119–1125.
- London, E.A. The environment as an etiologic factor in autism: a new direction for research. *Environ. Health Perspectives* **108** (Suppl. 3) (2000) 401–404.
- Milo, R. & Kahana, E. Multiple sclerosis: Geoepidemiology, genetics and the environment. *Autoimmunity Rev.* **9** (2010) A387–A394.
- Koch-Henriksen, N. & Sorensen P.S. The changing demographic pattern of multiple sclerosis epidemiology. *Lancet Neurol.* **9** (2010) 520–532.
- Edwards, L.J. & Constantinescu, C.S. A prospective study of conditions associated with multiple sclerosis in a cohort of 658 consecutive outpatients attending a multiple sclerosis clinic. *Multiple Sclerosis* **10** (2004) 575–581.
- Kotey, S., Ertel, K. & Whitcomb, B. Co-occurrence of autism and asthma in a nationally-representative sample of children in the United States. *J. Autism Devl Disorders* **44** (2014) 3083–3088.
- Wakefield, A.J., Murch, S.H., Anthony, A., Linnell, J., Casson, D.M., Malik, M., Berelowitz, M., Dhillon, A.P., Thomson, M.A., Harvey, P., Valentine, A., Davies, S.E. & Walker-Smith, J.A. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* **351** (1998) 637–641 (retracted).
- Seneff, S., Davidson, R.M. & Liu, J. Is cholesterol sulfate deficiency a common factor in preeclampsia, autism, and pernicious anemia? *Entropy* **14** (2012) 2265–2290.
- Gillberg, C., Gillberg, C. & Kopp, S. Hypothyroidism and autism spectrum disorders. *J. Child Psychol. Psychiat.* **33** (1992) 531–542.
- Miyazawa, M. Molecular mimicry and mechanisms of autoantibody production. *Nihon Rinsho* **55** (1997) 1370–1376 [in Japanese].
- Shoenfeld, Y.F. & Aron-Maor, A. Vaccination and autoimmunity/vaccinosis: A dangerous liaison? *J. Autoimmunity* **14** (2000) 1–10.
- Singh, V.K. Phenotypic expression of autoimmune autistic disorder (AAD): a major subset of autism. *Ann. Clin. Psychiat.* **21** (2009) 148–161.
- Gonzalez-Gronow, M., Cuchacovich, M., Francos, R., Cuchacovich, S., Blanco, A., Sandoval, R., Gomez, C.F., Valenzuela, J.A., Ray, R. & Pizzo, S.V. Catalytic autoantibodies against myelin basic protein (MBP) isolated from serum of autistic children impair *in vitro* models of synaptic plasticity in rat hippocampus. *J. Neuroimmunol.* **287** (2015) 1–8.
- Weizman, A., Weizman, R., Szekely, G.A., Wijzenbeak, H. & Livni, E. Abnormal immune response to brain tissue antigen in the syndrome of autism. *Am. J. Psychiatr.* **139** (1982) 1462–1465.
- Herroelen, L., de Keyser, J. & Ebinger, G. Central nervous system demyelination after immunization with recombinant Hepatitis B vaccine. *Lancet* **338** (1991) 1174–1175.
- Genain, C.P., Cannella, B., Hauser, S.L. & Raine, C.S. Identification of autoantibodies associated with myelin damage in multiple sclerosis. *Nature Med.* **5** (1999) 170–175.
- Fredman, P., Vedeler, C.A., Nyland, H., Aarli, J.A. & Svennerholm, L. Antibodies in sera from patients with

- inflammatory demyelinating polyradiculoneuropathy reactive with ganglioside LM1 and sulfate of peripheral nerve myelin. *J. Neurol.* **238** (1991) 75–79.
20. Steinman, L. Multiple sclerosis: A two-stage disease. *Nature Immunol.* **2** (2001) 762–764.
 21. Drummond, D.A. & Wilke, C.O. The evolutionary consequences of erroneous protein synthesis. *Nature Rev. Genetics* **10** (2009) 715–724.
 22. Drummond, D.A. & Wilke, C.O. Mistranslation-induced protein misfolding as a dominant constraint on coding-sequence evolution. *Cell* **134** (2008) 341–352.
 23. Conrad, A., Schröter-Kermani, C., Hoppe, H.W., Rütger, M., Pieper, S. & Kolossa-Gehring, M. Glyphosate in German adults—time trend (2001 to 2015) of human exposure to a widely used herbicide. *Intl J. Hyg. Environ. Health* **220** (2017) 8–16.
 24. Swanson, N.L., Leu, A., Abrahamson, J. & Wallet, B. Genetically engineered crops, glyphosate and the deterioration of health in the United States of America. *J. Org. Syst.* **9** (2014) 6–37.
 25. Hoy, J., Swanson, N. & Seneff, S. The high cost of pesticides: Human and animal diseases. *Poultry Fish. Wildlife Sci.* **3** (2015) 132.
 26. Seneff, S., Swanson, N. & Li, C. Aluminum and glyphosate can synergistically induce pineal gland pathology: connection to gut dysbiosis and neurological disease. *Agric. Sci.* **6** (2015) 42–70.
 27. Malmborg, P. & Hildebrand, H. The emerging global epidemic of paediatric inflammatory bowel disease—causes and consequences. *J. Intern. Med.* **279** (2016) 241–258.
 28. Boorom, K.F. Is this recently characterized gastrointestinal pathogen responsible for rising rates of inflammatory bowel disease (IBD) and IBD associated autism in Europe and the United States in the 1990s? *Med. Hypotheses* **69** (2007) 652–659.
 29. Horvath, K., Papadimitriou, J.C., Rabsztyrn, A., Drachenberg, C. & Tildon, J.T. Gastrointestinal abnormalities in children with autistic disorder. *J. Pediatrics* **135** (1999) 559–563.
 30. Michielan, A. & D’Inca, R. Intestinal permeability in inflammatory bowel disease: pathogenesis, clinical evaluation, and therapy of leaky gut. *Mediators Inflammation* **2015** (2015) 628157.
 31. Stumpf, M., Krones, C.J., Klinge, U., Rosch, R., Junge, K. & Schumpelick, V. Collagen in colon disease. *Hernia* **10** (2006) 498–501.
 32. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases V: Amino acid analogue of glycine in diverse proteins. *J. Biol. Phys. Chem.* **16** (2016) 9–46.
 33. Hundorfean, G., Neurath, M.F. & Sitaru, C. Autoimmunity against type VII collagen in inflammatory bowel disease. *J. Cell Molec. Med.* **14** (2010) 2393–2403.
 34. Koelink, P.J., Overbeek, S.A., Braber, S., Morgan, M.E., Henricks, P.A., Roda, A., Verspaget, H.W., Wolfkamp, S.C., te Velde, A.A., Jones, C.W., Jackson, P.L., Blalock, J.E., Sparidans, R.W., Kruijtz, J.A., Garssen, J., Folkerts, G. & Kraneveld, A.D. Collagen degradation and neutrophilic infiltration: a vicious circle in inflammatory bowel disease. *Gut* **63** (2014) 578–587.
 35. Ridley, W.P. & Mirly, K. The metabolism of glyphosate in Sprague Dawley rats. Part I. Excretion and tissue distribution of glyphosate and its metabolites following intravenous and oral administration (unpublished study MSL-7215 conducted by Monsanto’s Environmental Health Laboratory and submitted to the EPA July 1988) (MRID#407671-01) (1988).
 36. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases IV: cancer and related pathologies. *J. Biol. Phys. Chem.* **15** (2015) 121–159.
 37. Rubenstein, E. Misincorporation of the proline analog azetidine-2-carboxylic acid in the pathogenesis of multiple sclerosis: a hypothesis. *J. Neuropathol. Exp. Neurol.* **67** (2008) 1035–1040.
 38. Rubenstein, E., McLaughlin, T., Winant, R.C., Sanchez, A., Eckart, M., Krasinska, K.M. & Chien, A. Azetidine-2-carboxylic acid in the food chain. *Phytochemistry* **70** (2009) 100–104.
 39. Hoerlein, G. Glufosinate (phosphinothricin), a natural amino acid with unexpected herbicidal properties. *Rev. Environ. Contamination Toxicol.* **138** (1994) 73–145.
 40. Dunlop, R.A., Cox, P.A., Banack, S.A. & Rodgers, K.J. The non-protein amino acid BMAA is misincorporated into human proteins in place of L-serine causing protein misfolding and aggregation. *PLoS ONE* **8** (2013) e75376.
 41. Rosenthal, G.A. The biochemical basis for the deleterious effects of L-canavanine. *Phytochemistry* **30** (1990) 1055–1058.
 42. Krakauer, J., Long, Y., Kolbert, A., Thanedar, S. & Southard, J. Presence of L-canavanine in *Hedysarum alpinum* seeds and its potential rôle in the death of Chris McCandless. *Wilderness Environ. Med.* **26** (2015) 36–42.
 43. Krakauer, J. *Into the Wild*. New York: Anchor Books (1996).
 44. Rosenthal, G.A. Biochemical basis for the deleterious effects of L-canavanine. *Phytochemistry* **30** (1991) 1055–1058.
 45. Dahlman, D.L. & Rosenthal, G.A. Non-protein amino acid-insect interactions I. Growth effects and symptomology of L-canavanine consumption by tobacco hornworm, *Manduca sexta* (L.). *Comparative Biochem. Physiol. A* **51** (1975) 33–36.
 46. Melangeli, C., Rosenthal, G.A. & Dalmank, D.L. The biochemical basis for l-canavanine tolerance by the tobacco budworm *Heliothis virescens* (Noctuidae). *Proc. Natl Acad. Sci. USA* **94** (1997) 2255–2260.
 47. Padgett, S.R., Re, D.B., Gasser, C.S., Eichholtz, D.A., Frazier, R.B., Hironaka, C.M., Levine, E.B., Shah, D.M., Fraley, R.T. & Kishore, G.M. Site-directed mutagenesis of a conserved region of the 5-enolpyruvylshikimate-3-phosphate synthase active site. *J. Biol. Chem.* **266** (1991) 22364–22369.
 48. Eschenburg, S., Healy, M.L., Priestman, M.A., Lushington, G.H. & Schonbrunn, E. How the mutation glycine 96 to alanine confers glyphosate insensitivity to 5-enolpyruvyl shikimate-3-phosphate synthase from *Escherichia coli*. *Planta* **216** (2002) 129–135.
 49. Funke, T., Han, H., Healy-Fried, M.L., Fischer, M. & Schonbrunn, E. Molecular basis for the herbicide resistance of Roundup Ready crops. *Proc. Natl Acad. Sci. USA* **103** (2006) 13010–13015.

50. Beecham, J.E. & Seneff, S. The possible link between autism and glyphosate acting as glycine mimetic—a review of evidence from the literature with analysis. *J. Molec. Genet. Med.* **9** (2015) 187.
51. Cattani, D., de Liz Oliveira Cavalli, V.L., Heinz Rieg, C.E., Domingues, J.T., Dal-Cim, T., Tasca, C.I., Mena Barreto Silva, F.R. & Zamoner, A. Mechanisms underlying the neurotoxicity induced by glyphosate-based herbicide in immature rat hippocampus: involvement of glutamate excitotoxicity. *Toxicology* **320** (2014) 34–45.
52. Kitchen, L.M., Witt, W.W. & Rieck, C.E. Inhibition of δ -aminolevulinic acid synthesis by glyphosate. *Weed Sci.* **29** (1981) 571–577.
53. Zuckermann, R.N., Martin, E.J., Spellmeyer, D.C., Stauber, G.B., Shoemaker, K.R., Kerr, J.M., Figliozzi, G.M., Goff, D.A., Siani, M.A., Simon, R.J. et al. Discovery of nanomolar ligands for 7-transmembrane G-protein-coupled receptors from a diverse N-(substituted)glycine peptoid library. *J. Med. Chem.* **37** (1994) 2678–2685.
54. Hausch, F., Shan, L., Santiago, N.A., Gray, G.M. & Khosla, C. Intestinal digestive resistance of immunodominant gliadin peptides. *Am. J. Physiol. Gastrointestinal Liver Physiol.* **283** (2002) G996–G1003.
55. Schuppan, D. Current concepts of celiac disease pathogenesis. *Gastroenterology* **119** (2000) 234–242.
56. Wieser, H. Relation between gliadin structure and coeliac toxicity. *Acta Paediatr. (Suppl.)* **412** (1996) 3–9.
57. Liu, J. & Sessa, W.C. Identification of covalently bound amino-terminal myristic acid in endothelial nitric oxide synthase. *J. Biol. Chem.* **269** (1994) 11691–11694.
58. Kang, M.-I., Kobayashi, A., Wakabayashi, N., Kim, S.-G. & Yamamoto, M. Scaffolding of Keap1 to the actin cytoskeleton controls the function of Nrf2 as key regulator of cytoprotective phase 2 genes. *Proc. Natl Acad. Sci. USA* **101** (2004) 2046–2051.
59. Aicart-Ramos, C., Valero, R.A. & Rodriguez-Crespo, I. Protein palmitoylation and subcellular trafficking. *Biochim. Biophys. Acta* **1808** (2011) 2981–2994.
60. Kleuss, C. & Krause, E. G α s is palmitoylated at the N-terminal glycine. *EMBO J.* **22** (2003) 826–832.
61. Hirsch, R.H., Augustin, D.J. Nitrosamine analyses of Roundup herbicide, Rodeo herbicide, MON 0139 and Polado Technical (unpublished study RD835). St Louis, Missouri: Monsanto Agricultural Company (4 November 1987).
62. Massey, R.C. Analysis of N-nitroso compounds in foods and human body fluids. In: *Nitrosamines Toxicology and Microbiology* (ed. M.H. Hill), p. 26, section 2.4.4. VCH (1988).
63. Tricker, A.R., Perkins, M.J., Massey, R.C. & McWeeny, D.J. Some nitrosoamino acids in bacon adipose tissue and their contribution to the total N-nitroso compound concentration. *Z. Lebensmittel Untersuchung Forschung* **180** (1985) 379–383.
64. Kubacki, S.J., Havery, D.C. & Fazio, T. Nonvolatile N-nitrosamine investigations: methods for the determination of N-nitrosoamino acids and preliminary results of the development of a method for the determination of nitrosopeptides N-terminal in proline. In: *N-Nitroso Compounds: Occurrence, Biological Effects and Relevance to Human Cancer* (eds I.K. O’Neill, R.C. von Borstel, C.T. Miller, J. Long & H. Bartsch), No. 57, pp. 145–158. Lyons: International Agency for Research on Cancer (1984).
65. Tricker, A.R., Perkins, M.J., Massey, R.C. & McWeeny, D.J. Characterization studies on insoluble total N-nitroso compounds in bacon adipose connective tissue. *Food Additives Contaminants* **3** (1986) 153–159.
66. Newman, M.M., Lorenz, N., Hoilett, N., Lee, N.R., Dick, R.P., Liles, M.R., Ramsier, C. & Kloepper, J.W. Changes in rhizosphere bacterial gene expression following glyphosate treatment. *Sci. Total Environ.* **553** (2016) 32–41.
67. Zulet, A., Gil-Monreal, M., Villamor, J.G., Zabalza, A., van der Hoorn, R.A. & Royuela, M. Proteolytic pathways induced by herbicides that inhibit amino acid biosynthesis. *PLoS ONE* **8** (2013) e73847.
68. Nakajima, Y., Ito, K., Sakata, M., Xu, Y., Nakashima, K., Matsubara, F., Hatakeyama, S. & Yoshimoto, T. Unusual extra space at the active site and high activity for acetylated hydroxyproline of prolyl aminopeptidase from *Serratia marcescens*. *J. Bacteriol.* **188** (2006) 1599–1606.
69. Beauvais, A., Monod, M., Wyniger, J., Debeaupuis, J.P., Grouzmann, E., Brakch, N., Svab, J., Hovanessian, A.G. & Latgé, J.P. Dipeptidyl-peptidase IV secreted by *Aspergillus fumigatus*, a fungus pathogenic to humans. *Infection Immunity* **65** (1997) 3042–3047.
70. Byun, T., Kofod, L., Blinkovsky, A. Synergistic action of an X-prolyl dipeptidyl aminopeptidase and a non-specific aminopeptidase in protein hydrolysis. *J. Agric. Food Chem.* **49** (2001) 2061–2063.
71. Barberis, C.L., Carranza, C.S., Chiacchiera, S.M., Magnoli, C.E. Influence of herbicide glyphosate on growth and aflatoxin B1 production by *Aspergillus* section Flavi strains isolated from soil on in vitro assay. *J. Environ. Sci. Health B* **48** (2013) 1070–1079.
72. Freij, B.J., Levy, H.L., Dudin, G., Mutasim, D., Deeb, M., Der Kaloustian, V.M. Clinical and biochemical characteristics of prolidase deficiency in sibs. *Am. J. Med. Genet.* **19** (1984) 561–571.
73. Kumar, A., Are, V.N., Ghosh, B., Agrawal, U., Jamdar, S.N., Makde, R.D., Sharma, S.M. Crystallization and preliminary X-ray diffraction analysis of Xaa-Pro dipeptidase from *Xanthomonas campestris*. *Acta Crystallogr. F. Struct. Biol. Commun.* **70** (2014) 1268–1271.
74. Davis, T.W., Berry, D.L., Boyer, G.L. & Gobler, C.J. The effects of temperature and nutrients on the growth and dynamics of toxic and non-toxic strains of *Microcystis* during cyanobacteria blooms. *Harmful Algae* **8** (2009) 715–725.
75. Al-Sammak, M.A., Rogers, D.G. & Hoagland, K.D. Acute α -N-methylamino-L-alanine toxicity in a mouse model. *J. Toxicol.* **2015** (2015) 739–746.
76. Field, N.C., Metcalf, J.S., Caller, T.A., Banack, S.A., Cox, P.A. & Stommel, E.W. Linking β -N-methylamino-L-alanine exposure to sporadic amyotrophic lateral sclerosis in Annapolis, MD. *Toxicol.* **70** (2013) 179–183.
77. Masseret, E., Banack, S., Boumédiène, F., Abadie, E., Brient, L., Pernet, F., Juntas-Morales, R., Pageot, N., Metcalf, J., Cox, P. & Camu, W. French Network on ALS Clusters Detection and Investigation. Dietary BMAA exposure in an amyotrophic lateral sclerosis cluster from southern France. *PLoS ONE* **8** (2013) e83406.

78. Powell, H.A., Kerby, N.W. & Rowell, P. Natural tolerance of cyanobacteria to the herbicide glyphosate. *New Phytol.* **119** (1991) 421–426.
79. Forlani, G., Pavan, M., Gramek, M., Kafarski, P. & Lipok, J. Biochemical bases for a widespread tolerance of cyanobacteria to the phosphonate herbicide glyphosate. *Plant Cell Physiol.* **49** (2008) 443–456.
80. Michalak, A.M., Anderson, E.J., Beletsky, D., Boland, S., Bosch, N.S., Bridgeman, T.B., Chaffin, J.D., Cho, K., Confesor, R., Daloglu, I., DePinto, J.V. et al. Record-setting algal bloom in Lake Erie caused by agricultural and meteorological trends consistent with expected future conditions. *Proc. Natl Acad. Sci. USA* **110** (2013) 6448–6452.
81. Foran, E. & Trotti, D. Glutamate transporters and the excitotoxic path to motor neuron degeneration in amyotrophic lateral sclerosis. *Antioxidant Redox Signaling* **11** (2009) 1587–1602.
82. Slotboom, D.J., Sobczak, I., Konings, W.N. & Lolkema, J.S. A conserved serine-rich stretch in the glutamate transporter family forms a substrate-sensitive reentrant loop. *Proc. Natl Acad. Sci. USA* **96** (1999) 14282–14287.
83. Cox, P.A. & Sacks, O.W. Cycad neurotoxins, consumption of flying foxes, and ALS-PDC disease in Guam. *Neurology* **58** (2002) 956–959.
84. Ince, P.G. & Codd, G.A. Return of the cycad hypothesis does the amyotrophic lateral sclerosis/parkinsonism dementia complex (ALS/PDC) of Guam have new implications for global health? *Neuropathol. Appl. Neurobiol.* **31** (2005) 345–353.
85. Steele, J.C. & McGeer, P.L. The ALS/PDC syndrome of Guam and the cycad hypothesis. *Neurology* **70** (2008) 1984–1990.
86. Monson, C.S., Banack, S.A. & Cox, P.A. Conservation implications of Chamorro consumption of flying foxes as a possible cause of Amyotrophic Lateral Sclerosis Parkinsonism dementia complex in Guam. *Conservation Biol.* **17** (2003) 678–686.
87. Banack, S.A. & Cox, P.A. Biomagnification of cycad neurotoxins in flying foxes: implications for ALS-PDC in Guam. *Neurology* **61** (2003) 387–389.
88. Eastoe, J.E. The amino acid composition of mammalian collagen and gelatin. *Biochem. J.* **61** (1955) 589–600.
89. Ridley, W.P. & Chott, K.A. Uptake, depuration and bioconcentration of C-14 glyphosate to bluegill sunfish (*Lepomis macrochirus*) Part II: Characterization and quantitation of glyphosate and its metabolites. St Louis, Missouri: Monsanto Agricultural Company (unpublished study) (August 1989).
90. Yang, K.W., Brandt, J.J., Chatwood, L.L., Crowder, M.W. Phosphoramidate and phosphothioate dipeptides as potential inhibitors of VanX. *Bioorg. Med. Chem. Lett.* **10** (2000) 10850–10857.
91. Perlikowska, R., Fichna, J., do-Rego J.C., Gach, K., Janecka, A. Kinetic studies of novel inhibitors of endomorphin degrading enzymes. *Med. Chem. Res.* **21** (2012) 1445–1450.
92. Kramer, G.J., Mohd, A., Schwager, S.L.U., Masuyer, G., Acharya, K.R., Sturrock, E.D. & Bachmann, B.O. Interkingdom pharmacology of angiotensin-I converting enzyme inhibitor phosphonates produced by Actinomycetes. *ACS Med. Chem. Lett.* **5** (2014) 346–351.
93. Rubin, B. & Dennis, E. *Lipases, Part B: Enzyme Characterization and Utilization* (vol. 286). Academic Press (1997).
94. Chapus, C., Rovey, M., Sarda, L. & Verger, R. Minireview on pancreatic lipase and colipase. *Biochimie* **70** (1988) 1223–1234.
95. *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 13th edn, Appendix B. Centers for Disease Control and Prevention (2015).
96. Graham, J. (ed.). *The Hive and the Honey Bee* (rev. edn). Watertown, Wisconsin: Dadant & Sons (1992).
97. Pool, V., Braun, M.M., Kelso, J.M., Mootrey, G., Chen, R.T., Yunginger, J.W., Jacobson, R.M., Gargiullo, P.M. & VAERS Team. US Vaccine Adverse Event Reporting System. Prevalence of anti-gelatin IgE antibodies in people with anaphylaxis after measles-mumps rubella vaccine in the United States. *Pediatrics* **110** (2002) e71.
98. Kelso, J.M., Jones, R.T. & Yunginger, J.W. Anaphylaxis to measles, mumps, and rubella vaccine mediated by IgE to gelatin. *J. Allergy Clin. Immunol.* **91** (1993) 867–872.
99. Sakaguchi, M., Nakayama, T. & Inouye, S. Food allergy to gelatin in children with systemic immediate-type reactions, including anaphylaxis, to vaccines. *J. Allergy Clin. Immunol.* **98** (1996) 1058–1061.
100. Sakaguchi, M., Yamanaka, T., Ikeda, K., Sano, Y., Fujita, H., Miura, T. & Inouye S. IgE-mediated systemic reactions to gelatin included in the varicella vaccine. *J. Allergy Clin. Immunol.* **9** (1997) 263–264.
101. Bogdanovic, J., Halsey, N.A., Wood, R.A. & Hamilton, R.G. Bovine and porcine gelatin sensitivity in milk and meat-sensitized children. *J. Allergy Clin. Immunol.* **124** (2009) 1108–1110.
102. Ece, I., Akbayram, S., Demiroren, K. & Uner, A. Is Kawasaki Disease a side effect of vaccination as well? *J. Vaccines Vaccination* **5** (2014) 234.
103. Hogenesch, H., Azcona-Olivera, J., Scott-Moncrieff, C., Snyder, P.W. & Glickman, L.T. Vaccine-induced autoimmunity in the dog. *Adv. Vet. Med.* **41** (1999) 733–747.
104. Beck, C.A., Metz, L.M., Svenson, L.W. & Patten, S.B. Regional variation of multiple sclerosis prevalence in Canada. *Multiple Sclerosis* **11** (2005) 516–519.
105. Gale, C.R. & Martyn, C.N. Migrant studies in multiple sclerosis. *Prog. Neurobiol.* **47** (1995) 425–448.
106. Houzen, H., Niino, M., Kikuchi, S., Fukazawa, T., Nogoshi, S., Matsumoto, H. & Tashiro, K. The prevalence and clinical expression of MS in northern Japan. *J. Neurol. Sci.* **211** (2003) 49–53.
107. Boggs, J.M. Myelin basic protein: a multifunctional protein. *Cell Molec. Life Sci.* **63** (2006) 1945–1961.
108. Smith, G.S., De Avila, M., Paez, P.M., Spreuer, V., Wills, M.K., Jones, N., Boggs, J.M. & Harauz, G. Proline substitutions and threonine pseudophosphorylation of the SH3 ligand of 18.5-kDa myelin basic protein decrease its affinity for the Fyn-SH3 domain and alter process development and protein localization in oligodendrocytes. *J. Neurosci. Res.* **90** (2012) 28–47.
109. Harauz, G. & Libich, D.S. The classic basic protein of myelin conserved structural motifs and the dynamic molecular barcode involved in membrane adhesion and protein-protein interactions. *Current Protein Peptide Sci.* **10** (2009) 196–215.

110. Homchaudhuri, L., Polverini, E., Gao, W., Harauz, G. & Boggs, J.M. Influence of membrane surface charge and post-translational modifications to myelin basic protein on its ability to tether the Fyn-SH3 domain to a membrane in vitro. *Biochemistry* **48** (2009) 2385–2393.
111. Machold, R., Hayashi, S., Rutlin, M., Muzumdar, M.D., Nery, S., Corbin, J.G., Gritli-Linde, A., Dellovade, T., Porter, J.A., Rubin, L.L., Dudek, H., McMahon, A.P. & Fishell, G. Sonic hedgehog is required for progenitor cell maintenance in telencephalic stem cell niches. *Neuron* **39** (2003) 937–950.
112. Manié, S.N., Astier, A., Haghayeghi, N., Canty, T., Druker, B.J., Hirai, H. & Freedman, A.S. Regulation of integrin-mediated p130(Cas) tyrosine phosphorylation in human B cells. A role for p59(Fyn) and SHP2. *J. Biol. Chem.* **272** (1997) 15636–15641.
113. Resh, M.D. Fyn, a Src family tyrosine kinase. *Intl J. Biochem. Cell Biol.* **30** (1998) 1159–1162.
114. Bessonov, K., Vassall, K.A. & Harauz, G. Parameterization of the proline analogue Aze (azetidine-2-carboxylic acid) for molecular dynamics simulations and evaluation of its effect on homo-pentapeptide conformations. *J. Molec. Graphics Modelling* **39** (2013) 118–125.
115. Bessonov, K., Bamm, V.V. & Harauz, G. Misincorporation of the proline homologue Aze (azetidine-2-carboxylic acid) into recombinant myelin basic protein. *Phytochemistry* **71** (2010) 502–507.
116. Kiewnick, S., Jacobsen, B.J., Braun-Kiewnick, A., Eckhoff, J.L.A. & Bergman, J.W. Integrated control of Rhizoctonia crown and root rot of sugar beet with fungicides and antagonistic bacteria. *Plant Diseases* **85** (2001) 718–722.
117. Bach, B., Gregson, R.P., Holland, G.S., Quinn, R.J. & Reichelt, J.L. L-Azetidine-2-carboxylic acid, the antidermatophyte constituent of two marine sponges. *Experientia* **34** (1978) 688.
118. Hayat, S., Hayat, Q., Alyemeni, M.N., Wani, A.S., Pichtel, J. & Ahmad, A. Role of proline under changing environments: a review. *Plant Signaling Behaviour* **7** (2012) 1456–1466.
119. Malosse, D., Perron, H., Sasco, A. & Seigneurin, J.M. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: A worldwide study. *Neuroepidemiology* **11** (1992) 304–312.
120. Huhtanen, P. The effects of barley, unmolassed sugar-beet pulp and molasses supplements on organic matter, nitrogen and fiber digestion in the rumen of cattle given a silage diet. *Animal Feed Sci. Technol.* **20** (1988) 259–278.
121. Gordon, W.G., Semmett, W.F. & Alanine, M.B. Glycine and proline contents of casein and its components. *J. Am. Chem. Soc.* **72** (1950) 4282–4282.
122. Bodden, R.M., Patanella, J.E., Feng, P. *Metabolism Study of Synthetic ¹³C/¹⁴C- Labeled Glyphosate and AMPA In Lactating Goats*, vols 1 & 2 (unpublished study). St. Louis, Missouri: Monsanto Company (February 1988).
123. Lowrie, C. Metabolism of [¹⁴C]-N-Acetylgllyphosate (IN-MCX20) in the Lactating Goat (Charles River Laboratories Project no. 210583, submitted by E.I. du Pont de Nemours and Company) (Report No DuPont-19796) (2007).
124. Morel, F., Gilbert, C., Geourjon, C., Frot-Coutaz, J., Portalier, R. & Atlan, D. The prolyl aminopeptidase from *Lactobacillus delbrueckii* subsp. *bulgaricus* belongs to the u/v hydrolase fold family. *Biochim. Biophys. Acta* **1429** (1999) 501–505.
125. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases III: Manganese neurological diseases and associated pathologies. *Surg. Neurol. Intern.* **6** (2015) 45.
126. Coen, M., Menegatti, E., Salvi, F., Mascoli, F., Zamboni, P., Gabbiani, G. & Bochaton-Piallat, M.L. Altered collagen expression in jugular veins in multiple sclerosis. *Cardiovasc. Pathol.* **22** (2013) 33–38.
127. Tan, E.M., Ryhänen, L. & Uitto, J. Proline analogues inhibit human skin fibroblast growth and collagen production in culture. *J. Investigative Dermatol.* **80** (1983) 261–267.
128. Bhattacharjee, A. & Bansal, M. Collagen structure: the madras triple helix and the current scenario. *IUBMB Life* **57** (2005) 161–172.
129. Ebringer, A., Rashid, T. & Wilson, C. Bovine spongiform encephalopathy, multiple sclerosis, and Creutzfeldt-Jakob disease are probably autoimmune diseases evoked by *Acinetobacter* bacteria. *Ann. NY Acad. Sci.* **1050** (2005) 417–428.
130. Ebringer, A., Rashid, T. & Wilson, C. The role of *Acinetobacter* in the pathogenesis of multiple sclerosis examined by using Popper sequences. *Med. Hypotheses* **78** (2012) 763–769.
131. Hughes, L.E., Smith, P.A., Bonell, S., Natt, R.S., Wilson, C., Rashid, T., Amor, S., Thompson, E.J., Croker, J. & Ebringer, A. Cross-reactivity between related sequences found in *Acinetobacter* sp., *Pseudomonas aeruginosa*, myelin basic protein and myelin oligodendrocyte glycoprotein in multiple sclerosis. *J. Neuroimmunol.* **144** (2003) 105–115.
132. Hughes, L.E., Bonell, S., Natt, R.S., Wilson, C., Tiwana, H., Ebringer, A., Cunningham, P., Chamoun, V., Thompson, E.J., Croker, J. & Vowles, J. Antibody responses to *Acinetobacter* spp. and *Pseudomonas aeruginosa* in multiple sclerosis: prospects for diagnosis using the myelin *Acinetobacter* neurofilament antibody index. *Clin. Diagnostic Lab. Immunol.* **8** (2001) 1181–1188.
133. Lister, P.D., Wolter, D.J. & Hanson, N.D. Antibacterial-resistant *Pseudomonas aeruginosa*: Clinical impact and complex regulation of chromosomally encoded resistance mechanisms. *Clin. Microbiol. Rev.* **22** (2009) 582–610.
134. Karageorgopoulos, D.E. & Falagas, M.E. Current control and treatment of multidrug-resistant *Acinetobacter baumannii* infections. *Lancet Infectious Diseases* **8** (2008) 751–762.
135. Chung, N.-J., Han, H.-J., Lee, H.-H., Rhie, H.-G. & Lee, H.-S. Degradation of phosphonate herbicide glyphosate by *Acinetobacter lwoffii* HN401. *Molecules Cells* **6** (1996) 239–245.
136. Olawale, A.K. & Akintobi, O.A. Biodegradation of glyphosate pesticide by bacteria isolated from agricultural soil. *Report Opinion* **3** (2011) 124–128.
137. Moore, J.K., Braymer, H.D. & Larson, A.D. Isolation of a *Pseudomonas* sp. which utilizes the phosphonate herbicide glyphosate. *Appl. Environ. Microbiol.* **46** (1983) 316–320.
138. Landman, D., Quale, J.M., Mayorga, D., Adediji, A., Vangala, K., Ravishankar, J., Flores, C. & Brooks, S.

- Citywide clonal outbreak of multiresistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in Brooklyn, NY: The preantibiotic era has returned. *Arch. Intern. Med.* **162** (2002) 1515–1520.
139. Kurenbach, B., Marjoshi, D., Amabile-Cuevas, C.F., Ferguson, G.C., Godsoe, W., Gibson, P. & Heinemann, J.A. Sublethal exposure to commercial formulations of the herbicides dicamba, 2,4-dichlorophenoxyacetic acid, and glyphosate cause changes in antibiotic susceptibility in *Escherichia coli* and *Salmonella enterica* serovar typhimurium. *nBio* **6** (2015) e00009.
140. Wilson, C., Hughes, L., Rashid, T., Cunningham, P., Bansal, S., Ebringer, A. & Ettelaie, C. Antibodies to prion and *Acinetobacter* peptide sequences in bovine spongiform encephalopathy. *Vet. Immunol. Immunopathol.* **98** (2004) 1–7.
141. O'Connor, K.C., Appel, H., Bregoli, L., Call, M.E., Catz, I., Chan, J.A., Moore, N.H., Warren, K.G., Wong, S.J., Hafler, D.A. & Wucherpfennig, K.W. Antibodies from inflamed central nervous system tissue recognize myelin oligodendrocyte glycoprotein. *J. Immunol.* **175** (2005) 1974–1982.
142. Clements, C.S., Reid, H.H., Beddoe, T., Tynan, F.E., Perugini, M.A., Johns, T.G., Bernard, C.C. & Rossjohn, J. The crystal structure of myelin oligodendrocyte glycoprotein, a key autoantigen in multiple sclerosis. *Proc. Natl Acad. Sci. USA* **100** (2003) 11059–11064.
143. Winer, S., Astsaturov, I., Cheung, R.K., Schrade, K., Gunaratnam, L., Wood, D.D., Moscarello, M.A., O'Connor, P., McKerlie, C., Becker, D.J. & Dosch, H.M. T cells of multiple sclerosis patients target a common environmental peptide that causes encephalitis in mice. *J. Immunol.* **166** (2001) 4751–4756.
144. Segal, B.M., Raine, C.S., McFarlin, D.E., Voskul, R.R. & McFarland, H.F. Experimental allergic encephalomyelitis induced by the peptide encoded by exon 2 of the MBP gene, a peptide implicated in remyelination. *J. Neuroimmunol.* **51** (1994) 7–19.
145. Fritz, R.B. & Zhao, M.L. Encephalitogenicity of myelin basic protein exon-2 peptide in mice. *J. Neuroimmunol.* **51** (1994) 1–6.
146. Voskuhl, R.R., Robinson, E.D., Segal, B.M., Tranquill, L., Camphausen, K., Albert, P.S., Richert, J.R. & McFarland, H.F. HLA restriction and TCR usage of T lymphocytes specific for a novel candidate autoantigen, X2 MBP, in multiple sclerosis. *J. Immunol.* **153** (1994) 4834–4844.
147. Capello, E.R., Voskuhl, R.R., McFarland, H.F. & Raine, C.S. 1997. Multiple sclerosis: re-expression of a developmental gene in chronic lesions correlates with remyelination. *Ann. Neurol.* **41** (1997) 797–805.
148. Chang, P.C., Yang, J.C., Fujitaki, J.M., Chiu, K.C. & Smith, R.A. Covalent linkage of phospholipid to myelin basic protein: identification of serine-54 as the site of attachment. *Biochemistry* **25** (1986) 2682–2686.
149. Kanduc, D. Peptide cross-reactivity: the original sin of vaccines. *Frontiers Biosci.* **4** (2012) 1393–1401.
150. Orbach, H., Agmon-Levin, N. & Zandman-Goddard, G. Vaccines and autoimmune diseases of the adult. *Discovery Med.* **9** (2010) 90–97.
151. Sweeten, T.L., Bowyer, S.L., Posey, D.J., Halberstadt, G.M. & McDougle, C.J. Increased prevalence of familial autoimmunity in probands with pervasive developmental disorders. *Pediatrics* **112** (2003) e420–e424.
152. Brimberg, L., Sadiq, A., Gregersen, P.K. & Diamond, B. Brain-reactive IgG correlates with autoimmunity in mothers of a child with an autism spectrum disorder. *Molec. Psychol.* **18** (2013) 1171–1177.
153. Bauman, M.D., Iosif, A. M., Ashwood, P., Braunschweig, D., Lee, A., Schumann, C.M. et al. Maternal antibodies from mothers of children with autism alter brain growth and social behavior development in the rhesus monkey. *Transl. Psychiat.* **3** (2013) e278.
154. Atladóttir, H.O., Pedersen, M.G., Thorsen, P., Mortensen, P.B., Deleuran, B., Eaton, W.W. & Parner, E.T. Association of family history of autoimmune diseases and autism spectrum disorders. *Pediatrics* **124** (2009) 687–694.
155. Braunschweig, D., Krakowiak, P., Duncanson, P., Boyce, R., Hansen, R.L., Ashwood, P. et al. Autism-specific maternal autoantibodies recognize critical proteins in developing brain. *Transl. Psychiat.* **3** (2013) e277.
156. Ahmed, S.S., Volkmoth, W., Duca, J., Corti, L., Pallaoro, M., Pezzicoli, A., Karle, A., Rigat, F., Rappuoli, R., Narasimhan, V., Julkunen, I., Vuorela, A., Vaarala, O., Nohynek, H., Laghi Pasini, F., Montomoli, E., Trombetta, C., Adams, C.M., Rothbard, J. & Steinman, L. Antibodies from vaccine-associated narcolepsy sera cross-reacted with both influenza nucleoprotein and hypocretin receptor 2. *Sci. Translational Med.* **7** (2015) 294ra105.
157. Poon, T.P., Tchertkoff, V. & Win, H. Subacute measles encephalitis with AIDS diagnosed by fine needle aspiration biopsy. A case report. *Acta Cytol.* **42** (1998) 729–733.
158. Singh, V.K., Lin, S.X. & Yang, V.C. Serological association of measles virus and human herpes virus-6 with brain autoantibodies in autism. *Clin. Immunol. Immunopathol.* **89** (1998) 105–108.
159. Singh, V.K. & Jensen, R.L. Elevated levels of measles antibodies in children with autism. *Pediat. Neurol.* **28** (2003) 292–294.
160. Singh, V.K., Lin, S.X., Newell, E. & Nelson, C. Abnormal measles-mumps-rubella antibodies and CNS autoimmunity in children with autism. *J. Biomed. Sci.* **9** (2002) 359–364.
161. Oldstone, M.B.A. (ed.). *Molecular Mimicry: Infection-Inducing Autoimmune Disease*. Springer (2006).
162. de Swart, R.L., Yüksel, S. & Osterhaus, A.D.M.E. Relative contributions of measles virus hemagglutinin- and fusion protein-specific serum antibodies to virus neutralization. *J. Virol.* **79** (2005) 11547–11551.
163. Alter, M. Is multiple sclerosis an age-dependent host response to measles? *Lancet* **28** (1976) 456–457.
164. Kaphzan, H., Hernandez, P., Jung, J., Cowansage, K.K., Deinhardt, K., Chao, M.V., Abel, T. & Klann, E. Reversal of impaired hippocampal long-term potentiation and contextual fear memory deficits in Angelman syndrome model mice by ErbB inhibitors. *Biol. Psychiat.* **72** (2012) 182–190.
165. Kawashima, H., Mori, T., Kashiwagi, Y., Takekuma, K., Hoshika, A. & Wakefield, A. Detection and sequencing of measles virus from peripheral mononuclear cells from patients with inflammatory bowel disease and autism. *Digestive Diseases Sci.* **45** (2000) 723–729.

166. Torrente, F., Ashwood, P., Day, R., Machado, N., Furlano, R.I., Anthony, A., Davies, S.E., Wakefield, A.J., Thomson, M.A., Walker-Smith, J.A. & Murch, S.H. Small intestinal enteropathy with epithelial IgG and complement deposition in children with regressive autism. *Molec. Psychol.* **7** (2002) 375–382.
167. Wakefield, A.J., Puleston, J.M., Montgomery, S.M., Anthony, A., O’Leary, J.J. & Murch, S.H. Review article: the concept of entero-colonic encephalopathy, autism and opioid receptor ligands. *Alimentary Pharmacol. Therapeut.* **16** (2002) 663–674.
168. Weibel, R.E., Caserta, V., Benor, D.E. & Evans, G. Acute encephalopathy followed by permanent brain injury or death associated with further attenuated measles vaccines: A review of claims submitted to the national vaccine injury compensation program. *Pediatrics* **101** (1998) 383–387.
169. Seneff, S., Davidson, R.M. & Liu, J. Empirical data confirm autism symptoms related to aluminum and acetaminophen exposure. *Entropy* **14** (2012) 2227–2253.
170. Dufault, R., Schnoll, R., Lukiw, W.J., LeBlanc, B., Cornett, C., Patrick, L., Wallinga, D., Gilbert, S.G. & Crider, R. Mercury exposure, nutritional deficiencies and metabolic disruptions may affect learning in children. *Behavioral Brain Functions* **5** (2009) 44.
171. Sharpe, M.A., Gist, T.L. & Baskin, D.S. B-lymphocytes from a population of children with autism spectrum disorder and their unaffected siblings exhibit hypersensitivity to thimerosal. *J. Toxicol.* **2013** (2013) 801517.
172. Shaw, C.A., Kette, S.D., Davidson, R.M. & Seneff, S. Aluminum’s role in CNS-immune system interactions leading to neurological disorders. *Immunome Res.* **9** (2013) 069.
173. Shaw, C.A., Seneff, S., Kette, S.D., Tomljenovic, L., Oller, J.W., Jr. & Davidson, R.M. Aluminum-induced entropy in biological systems: implications for neurological disease. *J. Toxicol.* **2014** (2014) 491316.
174. Tomljenovic, L. & Shaw, C.A. Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations. *Lupus* **21** (2012) 223–230.
175. Russell, C.J., Jardetzky, T.S. & Lamb, R.A. Conserved glycine residues in the fusion peptide of the paramyxovirus fusion protein regulate activation of the native state. *J. Virol.* **78** (2004) 13727–13742.
176. Kawasaki, A., Purvin, V.A. & Tang, R. Bilateral anterior ischemic optic neuropathy following influenza vaccination. *J. Neuroophthalmol.* **18** (1998) 56–59.
177. Papadopoulos, M.C. & Verkman, A.S. Aquaporin 4 and neuromyelitis optica. *Lancet Neurol.* **11** (2012) 535–544.
178. Roemer, S.F., Parisi, J.E., Lennon, V.A., Benarroch, E.E., Lassmann, H., Bruck, W., Mandler, R.N., Weinshenker, B.G., Pittock, S.J., Wingerchuk, D.M. & Lucchinetti, C.F. Pattern-specific loss of aquaporin-4 immunoreactivity distinguishes neuromyelitis optica from multiple sclerosis. *Brain* **130** (2007) 1194–1205.
179. Liu, K., Kozono, D., Kato, Y., Agre, P., Hazama, A. & Yasui, M. Conversion of aquaporin 6 from an anion channel to a water-selective channel by a single amino acid substitution. *Proc. Natl Acad. Sci. USA* **102** (2005) 2192–2197.
180. Zador, Z., Bloch, O., Yao, X. & Manley, G.T. Aquaporins: role in cerebral edema and brain water balance. *Prog. Brain Res.* **161** (2007) 185–194.
181. Vaishnav, R.A., Liu, R., Chapman, J., Roberts, A.M., Ye, H., Rebolledo-Mendez, J.D., Tabira, T., Fitzpatrick, A.H., Achiron, A., Running, M.P. & Friedland, R.P. Aquaporin 4 molecular mimicry and implications for neuromyelitis optica. *J. Neuroimmunol.* **260** (2013) 92–98.
182. Vojdani, A., Mukherjee, P.S., Berookhim, J. & Kharrazian, D. Detection of antibodies against human and plant aquaporins in patients with multiple sclerosis. *Autoimmune Diseases* **2015** (2015) 905208.
183. Schneider, D., Liu, Y., Gerstein, M. & Engelman, D.M. Thermostability of membrane protein helix-helix interaction elucidated by statistical analysis. *FEBS Lett.* **523** (2002) 231–236.
184. Borgnia, M.J., Kozono, D., Calamita, G., Maloney, P.C. & Agre, P. Functional reconstitution and characterization of AqpZ, the *E. coli* water channel protein. *J. Molec. Biol.* **291** (1999) 1169–1179.
185. Ren, Z., Wang, Y., Duan, T., Patel, J., Liggett, T., Loda, E., Brahma, S., Goswami, R., Grouse, C., Byrne, R., Stefoski, D., Javed, A., Miller, S.D. & Balabanov, R. Cross-immunoreactivity between bacterial aquaporin-Z and human aquaporin-4: potential relevance to neuromyelitis optica. *J. Immunol.* **189** (2012) 4602–4611.
186. Tuomilehto, J. The emerging global epidemic of type 1 diabetes. *Current Diabetes Rep.* **13** (2013) 795–804.
187. Tetley, P., Simpson, S. Jr., Taylor, B.V. & van der Mei, I.A.F. The co-occurrence of multiple sclerosis and type 1 diabetes: Shared aetiologic features and clinical implication for MS aetiology. *J. Neurol. Sci.* **348** (2015) 126–131.
188. Dow, C.T. *Mycobacterium paratuberculosis* and autism: is this a trigger? *Med. Hypotheses* **77** (2011) 977–981.
189. Naser, S.A., Thanigachalam, S., Dow, S.T. & Collins, M.T. Exploring the role of *Mycobacterium avium* subspecies *paratuberculosis* in the pathogenesis of type 1 diabetes mellitus: a pilot study. *Gut Pathogens* **5** (2013) 14.
190. Capitani, G., De Biase, D., Gut, H., Ahmed, S. & Grutter, M.G. Structural model of human GAD65: prediction and interpretation of biochemical and immunogenic features. *Proteins* **59** (2005) 7–14.
191. Karjalainen, J., Martin, J.M., Knip, M., Ilonen, J., Robinson, B.H., Savilahti, E., Akerblom, H.K. & Dosch, H.M. A bovine albumin peptide as a possible trigger of insulin-dependent diabetes mellitus. *N. Engl. J. Med.* **327** (1992) 302–307.
192. Parrini, C., Taddei, N., Ramazzotti, M., Degl’Innocenti, D., Ramponi, G., Dobson, C.M. & Chiti, F. Glycine residues appear to be evolutionarily conserved for their ability to inhibit aggregation. *Structure* **13** (2005) 1143–1151.
193. Nolan, C., Margoliash, E., Peterson, J.D. & Steiner, D.F. The structure of bovine proinsulin. *J. Biol. Chem.* **246** (1971) 2780–2795.
194. Green, J.M. & Castle, L.A. Transitioning from single to multiple herbicide-resistant crops. In: *Glyphosate Resistance in Crops and Weeds: History, Development, and Management* (ed. V.K. Nandula), ch. 4, p. 112. Wiley (2010).
195. Samsel, A. & Seneff, S. Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance. *Interdisciplinary Toxicol.* **6** (2013) 159–184.

196. Janssen, G., Christis, C., Kooy-Winkelaar, Y., Edens, L., Smith, D., van Veelen, P. & Koning, F. Ineffective degradation of immunogenic gluten epitopes by currently available digestive enzyme supplements. *PLoS ONE* **10** (2015) e0128065.
197. Todd, J.A., Bell, J. & McDevitt, H.O. HLA-DQ beta gene contributes to susceptibility and resistance to insulin-dependent diabetes mellitus. *Nature* **329** (1987) 599–604.
198. Hogberg, L., Falth-Magnusson, K. & Grodzinsky, E. Familial prevalence of coeliac disease: a twenty-year follow-up study. *Scand. J. Gastroenterol.* **38** (2003) 61–65.
199. Li, X., Lou, Z., Li, X., Zhou, W., Ma, M., Cao, Y., Geng, Y., Bartlam, M., Zhang, X.C. & Rao, Z. Structure of human cytosolic X-prolyl aminopeptidase: a double Mn(II)-dependent dimeric enzyme with a novel three-domain subunit. *J. Biol. Chem.* **283** (2008) 22858–22866.
200. Rubio, F., Veldhuis, L.J., Clegg, S., Fleeker, J.R., & Hall, J.C. Comparison of a direct ELISA and an HPLC method for glyphosate determinations in water. *J. Agric. Food Chem.* **51** (2003) 691–696.
201. Jenkins, D.H., Grapenthien, N. & Keplinger, M.L. Milk and tissue residue study with N-phosphonomethylglycine (CP 67573) (unpublished study) prepared by Industrial Biotest Laboratories, Inc., submitted by Monsanto to US EPA, Washington, DC EPA MRID #0178 06004 (16 October 1973).

State of health of unvaccinated children

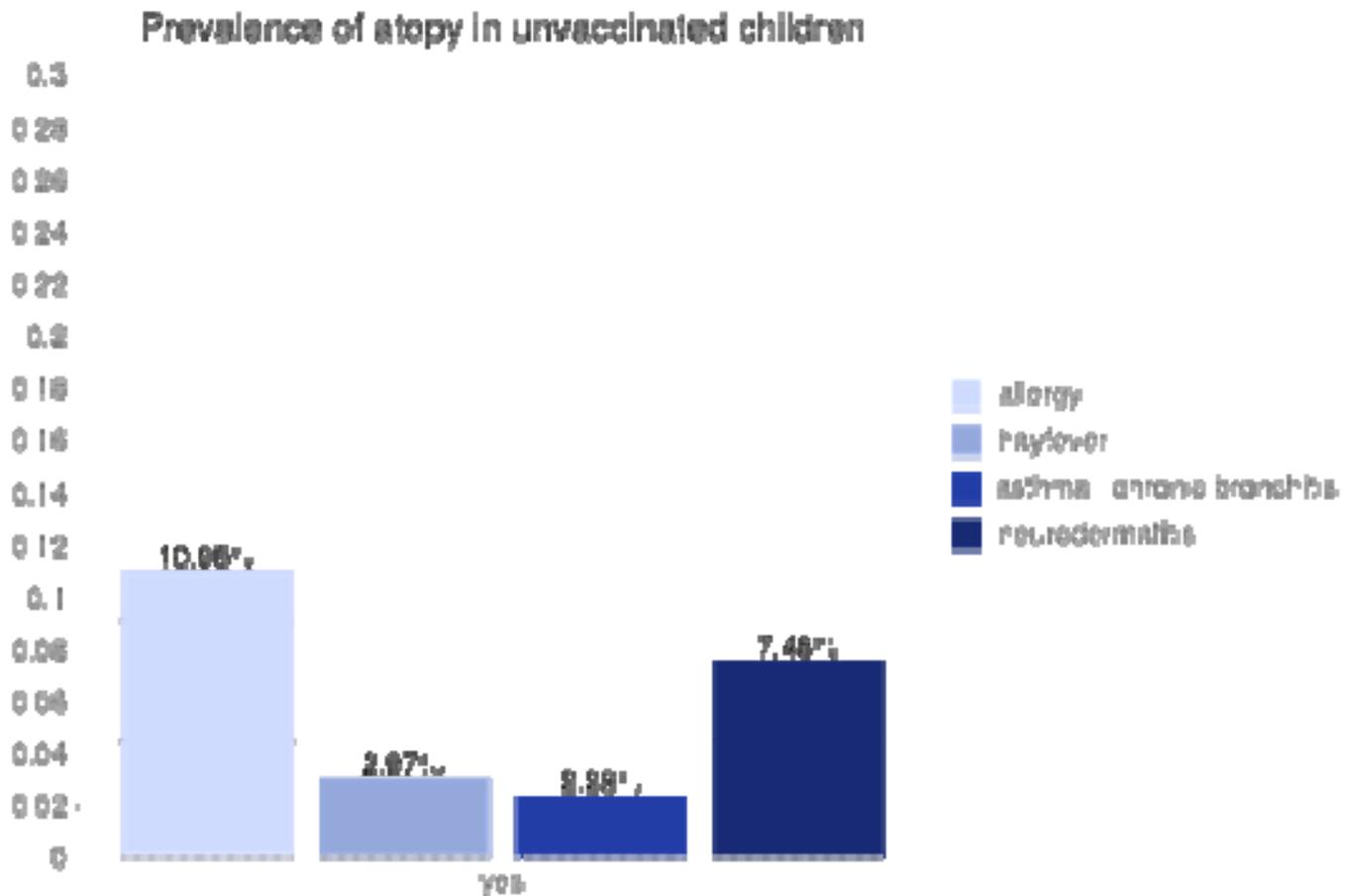
Illnesses in unvaccinated children

The results of our survey with currently 11921 participants show that unvaccinated children are far less affected by common diseases than vaccinated children. Due to the fact that the majority of children in the survey are between 0 and 2 years of age and some diseases generally do not appear in this age group, the results are subdivided into different age groups (you can see that by clicking on the chart). Information about country, gender, age, age distribution, breastfeeding, preferred treatment can be found [here](#).

Atopic diseases among unvaccinated children

Asthma, hayfever and [neurodermatitis](#) are seen very frequently today. A recent German study with 17461 children between 0-17 years of age ([KIGGS](#)) showed that 4.7% of these children suffer from asthma, 10.7% of these children from hayfever and 13.2% from [neurodermatitis](#). These numbers differ in western countries, i.e. the [prevalence](#) of asthma among children in the US is 6% whereas it is 14-16% in Australia (Australia's Health 2004, AIHW)

The [prevalence](#) of asthma among unvaccinated children in our study is around 2.5%, hayfever 3% and [neurodermatitis](#) 7%. According to the KIGGS study more than 40% of children between the ages of 3 and 17 years were sensitized against at least one allergen tested (20 common allergens were tested) and 22.9% had an allergic disease. Although we did not perform a bloodtest, around 10% stated that their children had an allergy.

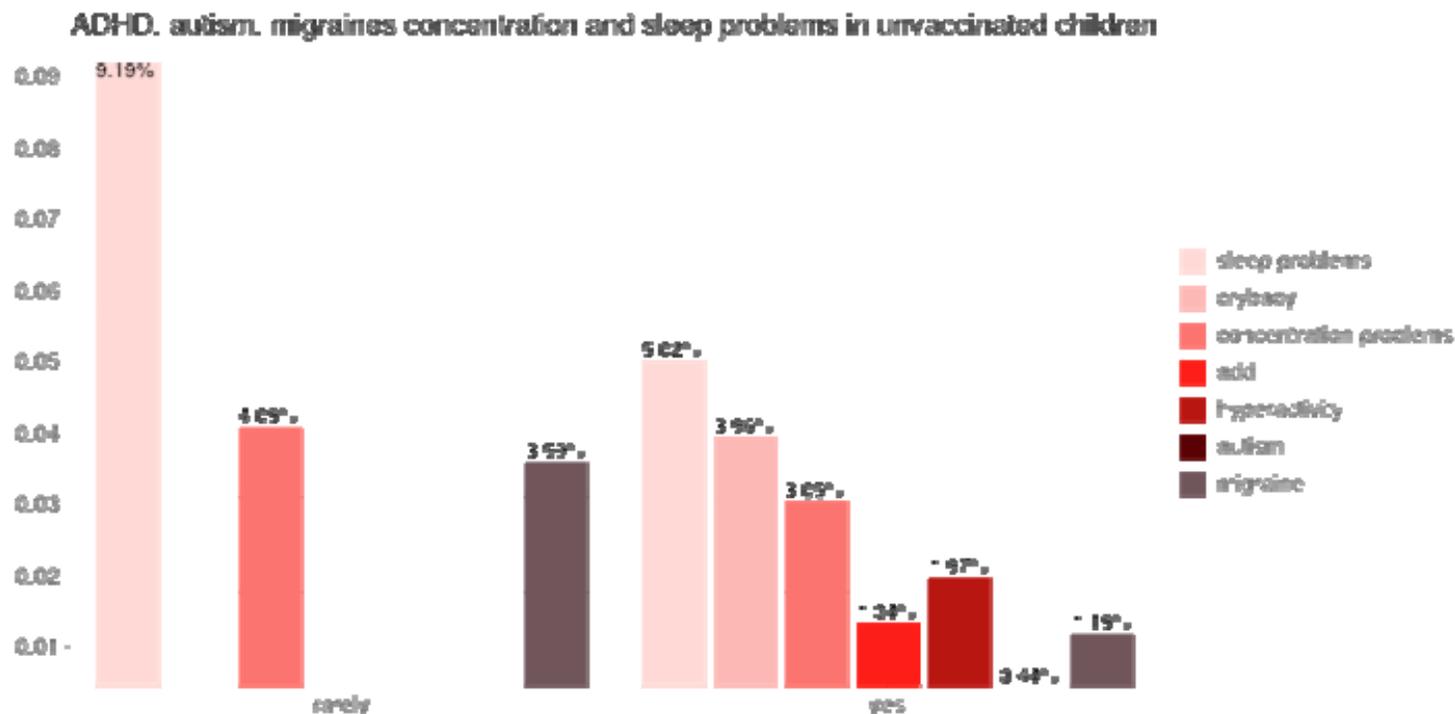


By clicking on the graphic you can see the age distribution of the selected diseases.

If you want to compare the results with the results of the survey on our German website impfschaden.info go [here](#).

ADS, Hyperactivity, Autism, Sleeping problems, concentration problems and migraine

ADS and Hyperaktivität is between 1 and 2 % in our survey, the [prevalence](#) of ADHD in Germany is 7,9% and another 5,9% which were not yet diagnosed, but were borderline cases(KIGGS).



By clicking on the graphic you can see the age distribution of the selected diseases.

There are also autism cases in unvaccinated children. Among all participants there were 4 severe autism cases.

Of these 4 children one tested very high for metals(mercury, aluminum, arsenic), in another case the mother was tested very high for mercury.

The [CDC](#) estimates that about 1 in 88 (1,1%) children has been identified with an autism spectrum disorder (ASD)(Autism and Developmental Disabilities Monitoring (ADDM) Network). ASDs are almost 5 times more common among boys (1 in 54; 1,8%) than among girls(1 in 252;0,39%).(Jon Baio, [Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008, March 30, 2012 / 61\(SS03\);1-19](#))

Otitis media, Sinusitis, Herpes, Warts, Polyps and fungal infections

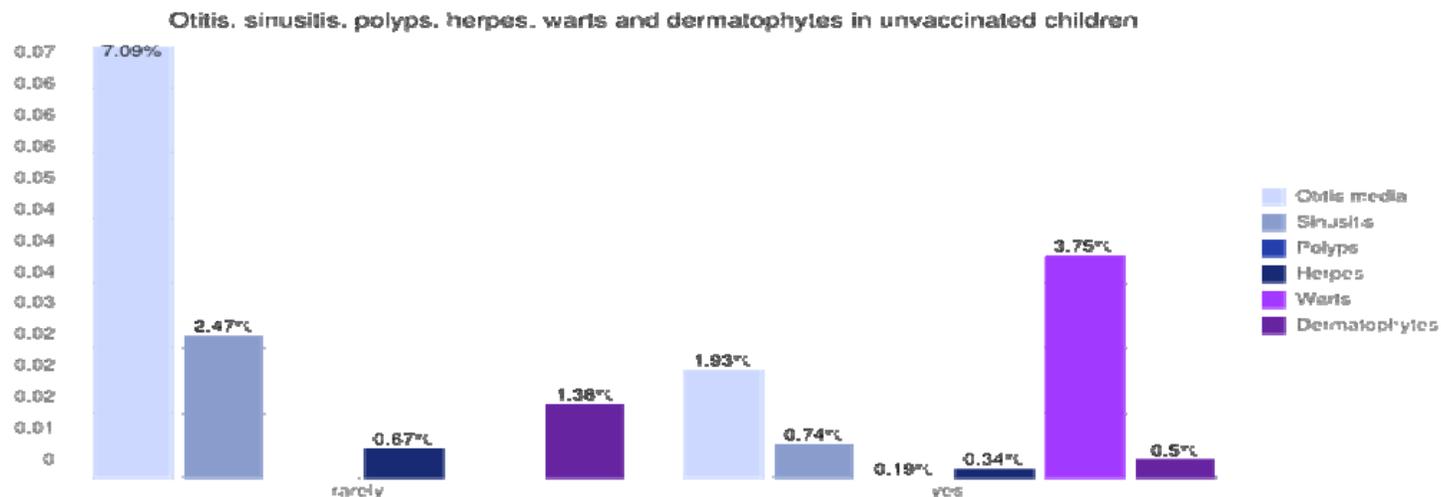
KIGGS showed that 12.8% of the children in Germany had herpes and 11% suffer from otitis media (an inflammation of the middle ear). If you compare this to unvaccinated children you can see that herpes among unvaccinated children is very rare (less than 0.5%).

The [prevalence](#) of sinusitis in young children has gone up as high as 32% (*Albegger KW. Banale Entzündungen der Nase und der Nasennebenhöhlen. In: Berendes J, Link JR, Zöllner F, eds. Hals, Nasen-, OhrenHeilkunde in Praxis und Klinik. Band I. Obere und untere Luftwege. Stuttgart: G Thieme Verlag, 1979: 11.1–11.32.*)

In our survey less than 1% of the children have problems with sinusitis, in around 2% it happened only once or rarely.

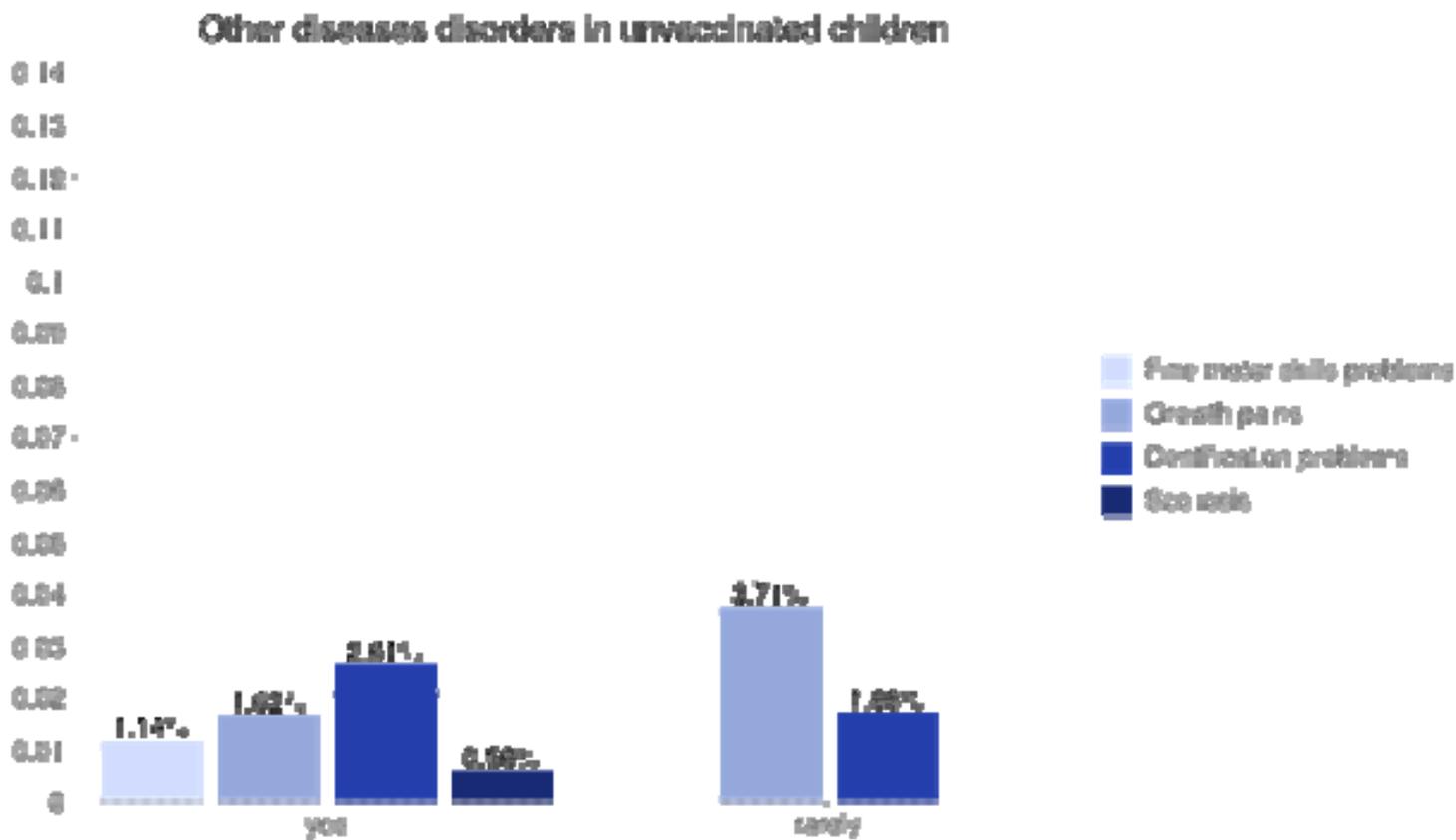
In young kids under the age of 3 warts are very rare. Above the age of three years however the [prevalence](#) is rising. In the ages between 4 and 6 years, 5-10% of the kids have warts, in the age group 16-18, 15-20% have warts. (http://www.netdokter.at/health_center/dermatologie/warzen.htm)

Only 3% of unvaccinated children in our survey have warts.



By clicking on the graphic you can see the age distribution of the selected diseases.

Fine motor skill problems, dentification problems, growth pains and scoliosis



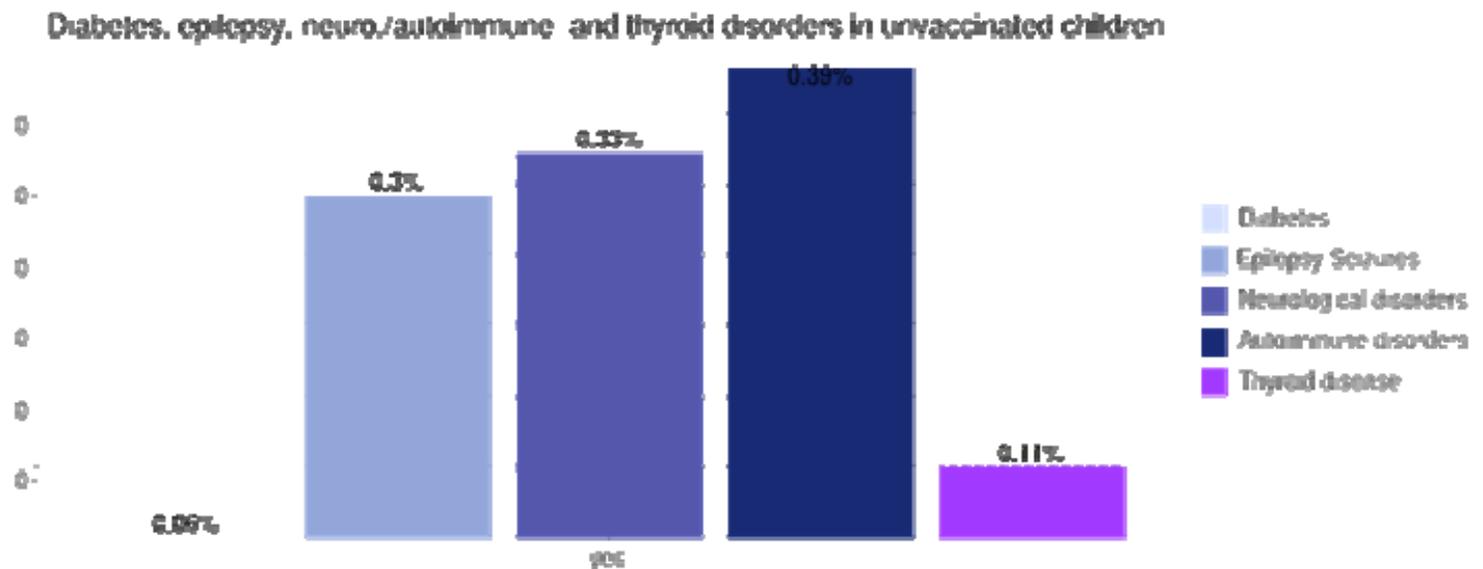
By clicking on the graphic you can see the age distribution of the selected diseases.

Diabetes, Epilepsy and seizures, neurological and autoimmune diseases, thyroid disorders

The national institute of health in the USA states that 23.5 % Americans suffer from autoimmune disease. This is a [prevalence](#) of more than 7% of children.

Diabetes affects 0.2% of the children under 20 years of age in the USA (National Diabetes Fact Sheet)

The KIGGS study showed prevalences of epilepsy with 3.6%, [prevalence](#) of Diabetes in Germany with 0.1% and diseases of the thyroid gland with 1.7%.



By clicking on the graphic you can see the age distribution of the selected diseases.

Other disorders and diseases

As we included open questions in our survey we evaluated the [prevalence](#) (of the first 10070 participants) of some other disorders and illnesses. Unvaccinated children show very low prevalences of the following disorders:

Dyslexia

Speech delay/articulation problems

Sensory Processing disorder

Anxiety

Depression

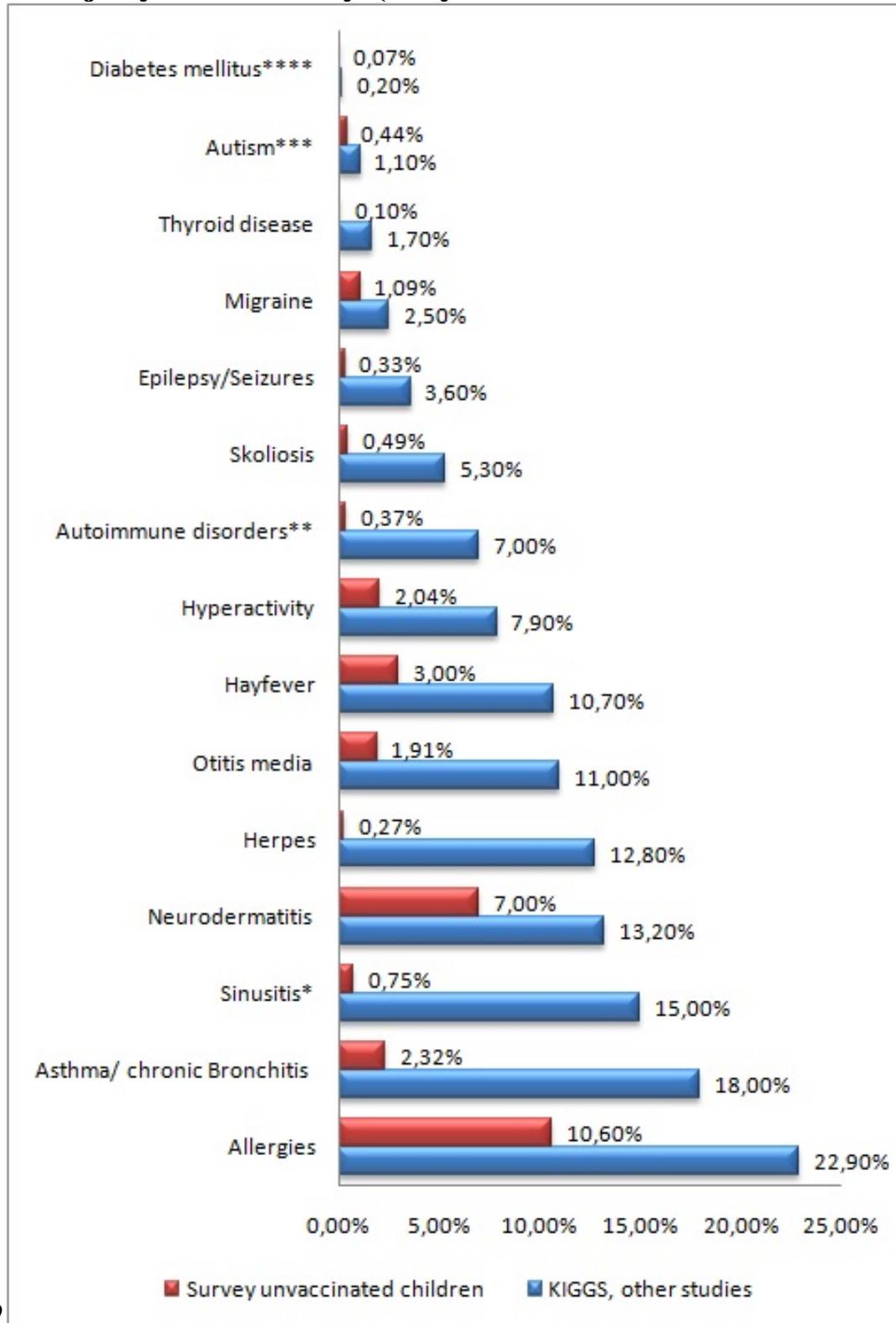
Bedwetting

Celiac disease

Gluten sensitivity

GERD (Gastroesophageal reflux disease)

Direct comparison KIGGS study (and other studies) and vaccineinjury.info-survey (July



2012

* http://thorax.bmj.com/content/55/suppl_2/S20.full.pdf

** National Institutes of Health

***Jon Baio, [Prevalence](#) of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008, March 30,

Quotes from parents about the state of health of their unvaccinated children

Lots of parents gave some additional information of their children. Here are some typical quotes:

"I am 27 years old and am completely unvaccinated. I am very healthy and only get a cold maybe once every year or two."

"My son is mostly vaxxed, my daughter not. They both were exposed to a recently vaccinated family member and me and my son contracted whooping cough. His lasted much longer than mine (he has various health issues primarily caused by vaccine) which was expected. My unvaccinated daughter coughed once the entire length of our illness and the second time we were exposed - same situation- she wasn't affected at all."

"I am one of 10 children from the same mother and father. None of us were vaccinated. Our ages are 38-59. We were all allowed to have childhood diseases to boost our immune systems. Most of our children were not vaccinated either. Most of all none of the non-vaccinated children in our family have major illness."

"I will put the health of my three unvaccinated children up against the health of a vaccinated child any day of the week and twice on Sunday."

"My 3 year old child is in a 5 year old class, and is even advanced for that grade. She has not been near as sick as a lot of her friends. She is considered very advanced for her age. Her two oldest siblings had both been injured by vaccinations and have been recovering for the last 6.5 years."

"My two boys are both uncircumcised, unvaccinated, including no vitamin K shot at birth, and no PKU newborn blood screening, and no painful procedure of any kind. I gave birth drug-free and naturally in an upright kneeling position, after walking throughout my entire labor and transition. Both boys are extremely healthy, intelligent, kind, and beautiful. I breastfed my older son until he turned 4 years, and I'm currently breastfeeding my 2 year old."

"My 3 vaccinated children were sick often during their first 2 years, suffered from ear infections repeatedly for which the doctor was constantly prescribing antibiotics, which would never work on the 1st round. They'd go through 3 separate rounds of antibiotics before the infection would be gone, meanwhile they'd develop diarrhea and candida diaper rash. They got every "bug" that was going around and strep and tonsillitis on several occasions. They all have skin conditions which the doctor has diagnosed as keratosis pylaris. My unvaccinated child has never been sick beyond a slight, short-lived cold. Never had an ear infection and has no skin issues either."

"We chose not to vaccinate for various reasons, and have never tried to create an antiseptic environment for the children. We live on a small mid-western farm and the children seldom wear shoes in the warmer months (warmer than freezing) so that is most of the time. They are subject to occasional cuts from various metals, glass, etc. and have not had any infections to speak of. Not only that, but they get bitten by various animals, cats, mice, (they're always catching mice) garden snakes, and the like, insects of all kinds, with no adverse affects. All but the first were home-birth, all were breast fed, and none of the last 8 have ever seen a doctor, (or MacDonalds)."

"I fully vaccinated his sister. She died at age 5 mos 14 days after suffering many symptoms of mercury poisoning including eczema, milk allergy and hypotonic-hyporesponsive episodes as well as dilated pupils. Her death was labeled "SIDS". I know it was vaccine induced. I also suffered a severe reaction to smallpox vaccine and have other family history of severe vaccine reactions. My unvaxed son has never needed an antibiotic, never had an ear infection, and has not seen a doctor since he was 2 and that was for an eye issue that resolved itself."

"He has never had an ear infection or serious illness that required medication and he turned 2 in Dec 2010. Vaccinated kids I know, including my 8 year old, were always sick. Croup, eczema, RSV, Scarlet fever, strep, roseola, thrush, asthma, food allergies, other allergies, and most of all ear infection after ear infection. Comparing my daughter's health records she was on antibiotics over 14 times her first 2 years of life. She was SOOO sick all the time...doc said it was normal and compared to friends kids it was. Everyone had sick kids ALL the time. It is considered normal in kids under 3. She was not in daycare...so that argument of picking it up at daycare does not work. I could not take her anywhere of she was sick. Even pneumonia!"

"Amazed at the overall health compared to all the kids her age, she gets the same cold/flu and has extremely mild symptoms compared to the other kids who are experiencing severe infections resulting in urgent care visits and prescriptions. All of the milestones were met early is able to read words before 2 1/2 years of age."

"My father is a MD and when time came for my daughter vaccination he asked me for the schedule and after reading it recommended to me not to do it. I myself when kid, was asthmatic and my dad was worried about the effects of the vaccines on her. She is a super healthy teen, never has been on antibiotic, resists all flu season without a problem and her immune system is super strong. Her brother is just the same"

"When she was a baby, I was kicked out of 2 pediatrician offices due to them thinking we were neglectful. One of them threatened to go to authorities. We wound up with a pediatrician who thought it was her obligation to care for her even more than her other patients due to our non-vaccine status. When Sarah was 18, her doctor said she was healthier than most of her patients, but a little underweight."

"We have three incredibly healthy children in our family that have all grown into highly effective professionals. The children have never had headaches, nosebleeds, vaginal infections, gut issues... none of the common ailments that people believe are normal, but are actually signs of disease."

"My son was born out of hospital at a nurse midwife birthing center 6 min. from a major medical facility, all natural and he has been breastfed up to 2+ yrs of life. He's an incredibly astute young toddler with a very active imagination and great sense of humor. He knows his alphabet and is approaching learning to put together words already. He's amazing and I attribute it to his lack of medical "care" involvement. I'm a health care professional and very attuned to the faults in our system here in the US."

"Trust in strong immune system. Use natural foods diet, homeopathy, vitamin C and herbs to strengthen immunity. Child has had chicken pox, swine flu and whooping cough without serious complications."

"She(17 years) is very healthy, and most are shocked that she never had an ear infection in her lifetime."

"S. is 21 now in 4th year of university. He is extremely bright and healthy man. He was always the healthiest child in his classes through grade school and high school. rarely even a cold. maybe once a year a 3 days cold. he has never taken an antibiotic, steroid or other allopathic medicine. i would give him an A+ in over all health."

"I am actually a 63 year old Baby Boomer who has never had any of those childhood vaccinations, simply because we lived in such a rural, remote area, "they" could not effectively get to me, and my mother, with her naive intuition didn't want them to "hurt me." Wow. Understatement. My heart aches for kids today. Stories like mine, of people never vaccinated, growing up and living a life of health and vigor, are ignored. It might be helpful to open up the survey to broader age groups."

"I didn't start J. on vaccines until she was 3 because i wanted her to be able to talk well first. The thought of having to inject something that could cause death into your child scared me but i thought it was required. She wasn't nearly as sickly or mentally handicapped as my son that HAD to receive each vaccine on time because we lived on a military installation. But her health doesn't even compare to our son who never received any vaccinations as he's never been on any antibiotics in his 9 yrs!"

"My first child has the most vaccines. The second has some. The last had none. The overall healthiest with the least problems is the one who got no vaccines. I have my masters degree in Nursing. I read all sorts of stuff cause I really wanted to believe vaccines are safe and ok but they are not. So my intensive research swayed me the other way."

"J. is our eighth child and the first to remain almost completely undamaged by the medical system. We did not even allow any newborn testing (such as PKU, etc...), nor did we allow a hearing screening, or vitamin k, or even the antibiotics in the eyes. He did not leave our sight in the hospital, because we did not trust the nurses to respect our desire to protect him from testing, vaccines, etc.... In fact, we would have avoided the hospital altogether if I did not have to deliver by c-section. J. is more alert and healthier than any of our other children. He is almost two and has not needed medical care yet. He is rarely sick, and has never had an ear infection. If fourteen years ago, before we had our first child, our pediatrician (or anyone for that matter) had given us a list of vaccine ingredients, including an understanding as to how they are made, and perhaps the opportunity to view the warning label (although the ingredi ent list would have done it for me), we would have NEVER vaccinated any of our children, ever. It should be mandatory that ingredients and warning labels be read by parents before a doctor is allowed to administer a vaccine. We are lied to and deceived by our government and our medical doctors/establishment. We did not question our doctors, because we were raised to believe that they existed for our good and we were to trust them. Well, we have paid the price, along with countless others. We stopped vaccinating three years ago. Shortly after my seventh child was born. She had only a few vaccines, but still a few too many. Several of my other children also came out only partially vaccinated. When I first learned of the ingredients of vaccines and how they were made, I was devastated and in shock that I had been so foolish to believe the doctors and cause such irreversible harm to my children. I am still grieved about it. People need to be told the truth!"

For more stories go to: <http://www.vaccineinjury.info/results-unvaccinated/personal-stories.html>

Studies Prove Without Doubt That Unvaccinated Children Are Healthier Than Their Vaccinated Peers

As doctors, parents and concerned citizens we consistently strive to do what is best for the children in our lives. As of late, with the passage of SB277 in California, the mainstream media has been trying to convince everyone that the vaccinated child is somehow a healthier individual and lives a more “disease” free life versus their unvaccinated counterpart.

But, is this the truth?

A 20 year old study from the 1990’s has recently surfaced that compares unvaccinated children to vaccinated children. The study concludes that those who were vaccinated were more likely to suffer from the following illnesses:

- asthma
- eczema
- ear infections
- hyperactivity
- and many other chronic conditions.

There was a 10-fold increase in cases of tonsillitis in the children who were vaccinated and a 100% absence of tonsillitis in those unvaccinated.

In 1992, the [Immunization Awareness Society](#) (IAS) conducted a survey to examine the health of New Zealand’s children. Unsurprisingly, the results of their study indicated that unvaccinated children were far healthier than vaccinated children.

Questionnaires were given out to IAS members, their friends and their associates asking various health questions. A total of 245 families returned their questionnaires, giving the researchers a total of 495 children surveyed. Of these children, 226 were vaccinated and 269 were unvaccinated.

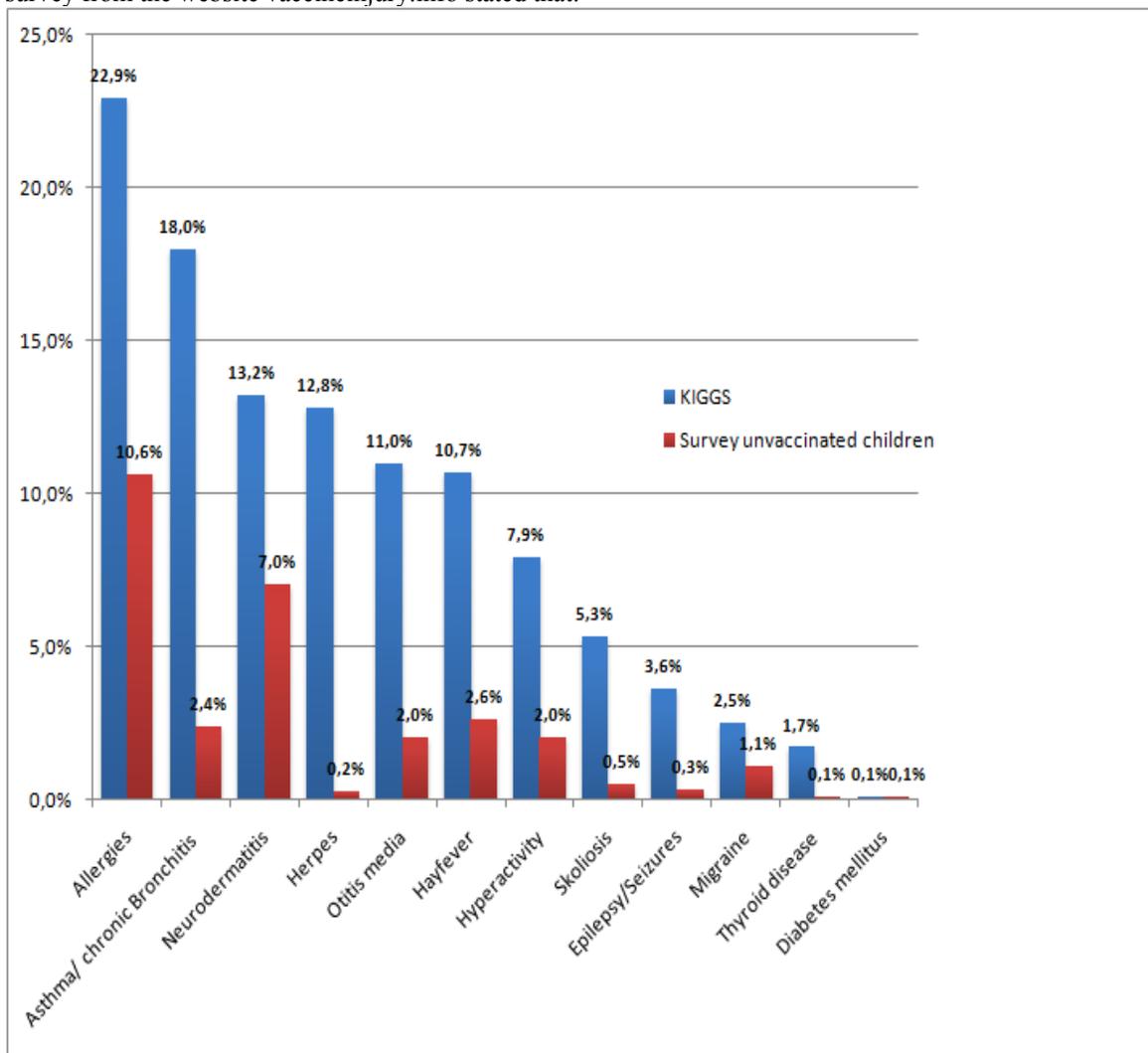
Healthy Children and Ethics

The ages of the children ranged between the ages of two weeks – 46 years (obviously some friends were older with older children). Of the children studied, 273 were males and 216 were females. (Six children were unclassified.) Sue Claridge, who reported on the study, wrote: *“Respondents were asked to provide the year of birth, gender, vaccinations received, whether or not the child suffered from a range of chronic conditions (asthma, eczema, ear infections/glue ear, recurring tonsillitis, hyperactivity, diabetes or epilepsy) whether or not he or she needed grommets, had had a tonsillectomy, or were shown to develop motor skills (walking, crawling, sitting-up etc.). Parents also provided information on breastfeeding and bottle feeding and when a child was weaned if breastfed.”* During the study, another interesting fact emerged. Researchers discovered that 92 percent of the children requiring a tonsillectomy operation had received the measles vaccination, indicating that the vaccination for measles may have made some of the children more susceptible to tonsillitis. The study also revealed that 81 of the families had both vaccinated and unvaccinated children. Many of these families had vaccinated their older children but had grown more reluctant to vaccinate their younger children, due to their growing concerns regarding vaccine safety. Researchers concluded that: *“While this was a very limited study, particularly in terms of the numbers of*

unvaccinated children that were involved and the range of chronic conditions investigated, it provides solid scientific evidence in support of considerable anecdotal evidence that unvaccinated children are healthier than their vaccinated peers.” [1] Although governments from around the world have continually stated that studying vaccinated versus unvaccinated children would be unethical, the New Zealand researchers are not the only group of researchers to study comparisons.

Vaccinated Children 5 Times More Likely To Suffer From A Range Of Diseases

In September 2011, German researchers carrying out a longitudinal study surveyed a total of 8000 unvaccinated children from the ages of 0 –19. As with the New Zealand study, researchers collected their data by conducting a survey using questionnaires. [2] Results showed that vaccinated children were up to five times more likely to suffer from a variety of diseases and disorders than unvaccinated children. Their results were compared to another German study (KiGGS), which examined a larger sample group consisting of 17,461 participants between the ages of 0 –17. Dr. Andreas Bachair, a German classical homeopathic practitioner, responsible for collecting the results of the survey from the website vaccineinjury.info stated that:



“Asthma, hay fever and neurodermatitis are seen very frequently today. A recent German study with 17461 children between 0-17 years of age (KIGGS) showed that 4.7% of these children suffer from asthma, 10.7% of these children from hay fever and 13.2% from neurodermatitis. These numbers differ in western countries, i.e. the prevalence of asthma among children in the US is 6% whereas it is 14-16% in Australia (Australia’s Health 2004, AIHW). The prevalence of asthma among unvaccinated children in our study is around 2.5%, hay fever, 3%, and

neurodermatitis, 7%. According to the KIGGS study more than 40% of children between the ages of 3 and 17 years were sensitized against at least one allergen tested (20 common allergens were tested) and 22.9% had an allergic disease. Although we did not perform a blood test, around 10% stated that their children had an allergy.” [3] (As this study is a longitudinal study, the number of children being studied has since risen to 13,222. To join the study, you can fill in the questionnaire provided by clicking on the link listed as the third reference at the end of this article.) Although there were four cases of autism reported among unvaccinated children, Dr. Bachair reported that: “Of these 4 children one tested very high for metals (mercury, aluminium, arsenic); in another case the mother was tested very high for mercury.” However, this number pales into insignificance when we compare it to the 1 in 88 children currently being reported as autistic by the CDC. [4]

Other Conditions Found To Be Almost Non-Existent In Unvaccinated Children

Dr. Andreas Bachair continued her report by stating that their study found the prevalence of sinusitis, warts, skin problems and middle ear infections were also much lower in the unvaccinated children, as were the cases of diabetes and epilepsy. She went on to say that the results demonstrated that the prevalence of many conditions in the unvaccinated children were also significantly lower. These were: “Other disorders and diseases As we included open questions in our survey we evaluated the prevalence (of the first 10,070 participants) of some other disorders and illnesses. Unvaccinated children show very low prevalences of the following disorders:

- *Dyslexia: 0.21%*
- *Speech delay/articulation problems: 0.38%*
- *Sensory Processing disorder: 0.28%*
- *Anxiety: 0.25%*
- *Depression: 0.12%*
- *Bedwetting: 0.12%*
- *Celiac disease: 0.12%*
- *Gluten sensitivity: 0.41%*
- *GERD (Gastroesophageal reflux disease): 0.06%”*

Dr. Bachair concluded her amazing and intuitive paper by adding a number of statements from parents, which I believe really added weight to her overall findings.

No study of health outcomes of vaccinated people versus unvaccinated has ever been conducted in the U.S. by CDC or any other agency in the 50 years or more of an accelerating schedule of vaccinations (now over 60 doses of 14 vaccines given before kindergarten, 26 doses in the first year). Most data collected by CDC is contained in the Vaccine Adverse Event Reporting System (VAERS) database. The VAERS is generally thought to contain only 3 to 5 percent of reportable incidents. This is simply because only some immediate reactions are reported by doctors; but many are not admitted to be reactions to the vaccine. Most importantly, the VAERS numbers are only *immediate reactions*, which would take place within a few hours to a few weeks. Long-term vaccine-induced diseases and disorders are not recognized by parents or doctors when these conditions develop perhaps a few months to five years or more and would never be realized to come from multiple vaccinations. In other words, many children and adults have diseases and disorders that are vaccine induced and they never suspect they are from the vaccines, as this study indicates.

Conclusion

We find it amazing that despite mainstream media and leading government agencies stressing repeatedly that studies comparing vaccinated children to unvaccinated children cannot take place for ethical reasons, groups around the world are taking it upon themselves to do these studies anyway.

While surveys of this kind are often dismissed as being purely epidemiological and passed off as little more than stamp collecting, we believe that studies of this nature should not be dismissed out of hand. After all, many stamp collections contain just one stamp that is worth far more than its weight in gold.

These studies show without doubt that unvaccinated children are healthier than their vaccinated peers and, for this reason, these studies should be given careful consideration by all parents and professionals studying vaccination safety.

References

1. <http://www.viewbix.com/v/Unvaccinated-Children-Healthier...>
2. <http://healthimpactnews.com/2011/new-study-vaccinated-children-have-2-to-5-times-more-diseases...>
3. <http://www.vaccineinjury.info/vaccinations-in-general/health-unvaccinated-children...>
4. <http://www.cdc.gov/ncbddd/autism/data.html>



SO YOU WANT TO

TAKE YOUR LEGISLATORS BACK TO SCHOOL

Vaccines, Herd Immunity, & the Immunocompromised

LEVI QUACKENBOSS

Super!

HERE'S YOUR TABLE OF CONTENTS

TALKING POINTS	SECTION
Finding Your Legislator	01
Herd Immunity	02
The Immunocompromised	03
Pertussis Vaccine Explained	04
Measles and Mumps	05
The Unvaxed Get Sick More?	06
Injury is Just One in a Million	07
Time to Testify	08
Resources	09

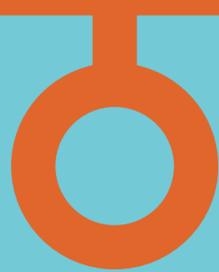


01



WHERE ARE YOUR LEGISLATORS?

We have both federal and state legislators. Federal legislators make up Congress: the House of Representatives and the Senate. However, you'll ordinarily be speaking with your **state legislators** regarding state legislation, not federal.



Every state has a "find my legislator" function in their legislative website.

GOOGLE "FIND MY LEGISLATOR" WITH YOUR STATE'S NAME.

Each state has two legislative houses: one is the house of representatives or assembly, and the other is the senate. You want the contact information for your reps in **both houses**.

02

HERD IMMUNITY.

The greatest accomplishment that can never be achieved through vaccination.



People generally aren't ready to hear there's no such thing as herd immunity. However...

YOU NEED TO POLITELY ASK YOUR LEGISLATOR TO "RECONSIDER WHAT THEY'VE LEARNED ABOUT HERD IMMUNITY" IN LIGHT OF SOME FACTS.

Start with a point your legislator can relate to, such as when they were vaccinated as an infant: most likely between 1950 and 1980.

03

WHAT ABOUT PROTECTING THE IMMUNOCOMPROMISED KIDS?



We assume there is a subset of vulnerable children who "can't be vaccinated," but the CDC doesn't treat these children like you think they would.



The CDC recognizes three types of immunocompromised people.*

- 1. THOSE LIVING WITH HIV**
- 2. THE SEVERELY IMMUNOCOMPROMISED WITHOUT HIV**
- 3. THOSE WITH IMMUNE DEFICITS LIKE SPLEEN OR KIDNEY FAILURE**

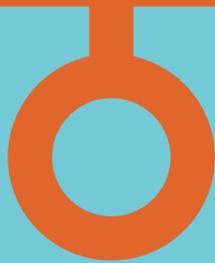
An immunocompromised person has an impaired immune system, and they get sick easier than the average person.

04



LEGISLATORS CARE ABOUT THE WHOOPING COUGH VACCINE.

3 to 16 infants under 1 year old have died of whooping cough in America each year since 2012, and their deaths make headlines. While that is an extraordinarily small number, this is a very emotional issue.



Each time a child tragically dies from pertussis, we all hear, "Thanks, anti-vaxxers."

BUT IS THIS TRUE? ARE PEOPLE WHO DON'T VACCINATE TO BLAME FOR PERTUSSIS INFECTIONS IN OTHERS?

No. And the CDC has known this for years. Only pediatricians and journalists place the blame on unvaccinated people.

There is no such thing as vaccine-induced herd immunity to whooping cough.

FOR TWO REASONS.

First, we can never obtain lifetime immunity to bacteria. How many times do susceptible kids come down with a strep infection? Endless. Bacteria mutate. Even a natural pertussis infection provides immunity for only 20 years.

Second, the vaccine cannot contribute to herd immunity because it doesn't prevent an infection from occurring in the vaccinated person. Any immunity would come from infection after vaccine failure, not the vaccination itself.

The idea that the current vaccine is "the best defense we've got" is irrelevant when it comes to taking away parents' rights to decline an ineffective, symptom-reducing vaccine for their children.



05



MEASLES AND MUMPS.

Legislators are scared of the measles, and lately, mumps. How terrible were these diseases in the 1960s?

We often hear that measles causes secondary infections.

BEFORE THE MEASLES VACCINE WAS LICENSED, JUST OVER 20% OF CASES WERE EVEN REPORTED.

Of the reported cases, about 6 in 100 suffered from "respiratory complications." This refers to pneumonia, which would be treated today with antibiotics. Adjusted upward for known under-reporting, that number would be 6 in 450 cases.

06

ARE UNVACCINATED CHILDREN MORE LIKELY TO BECOME INFECTED WITH DISEASE?



The CDC claims that unvaccinated children are 8 times more likely to develop a whooping cough infection than vaccinated children.

Is it true that parents put their unvaccinated kids at risk?

NO. THEY AREN'T AT ANY MORE RISK THAN VACCINATED KIDS.

This is an attempt to paint non-vax parents in a negative light, while allowing the lobbyist and legislator to have the appearance of caring about the wellbeing of all children.

07

THE RISK OF VACCINE INJURY IS JUST ONE IN A MILLION, RIGHT?



We often hear public health experts claim that vaccine injuries only happen once per million doses.



Where does this "one in a million" number come from?

SURELY THERE IS SOMEONE MONITORING MILLIONS OF CHILDREN.

No, there isn't. We have the Vaccine Adverse Events Reporting System (VAERS), which is a passive reporting system most doctors refuse to use. The FDA admits that fewer than 1% of adverse events end up reported to VAERS because parents don't know it exists.*

08



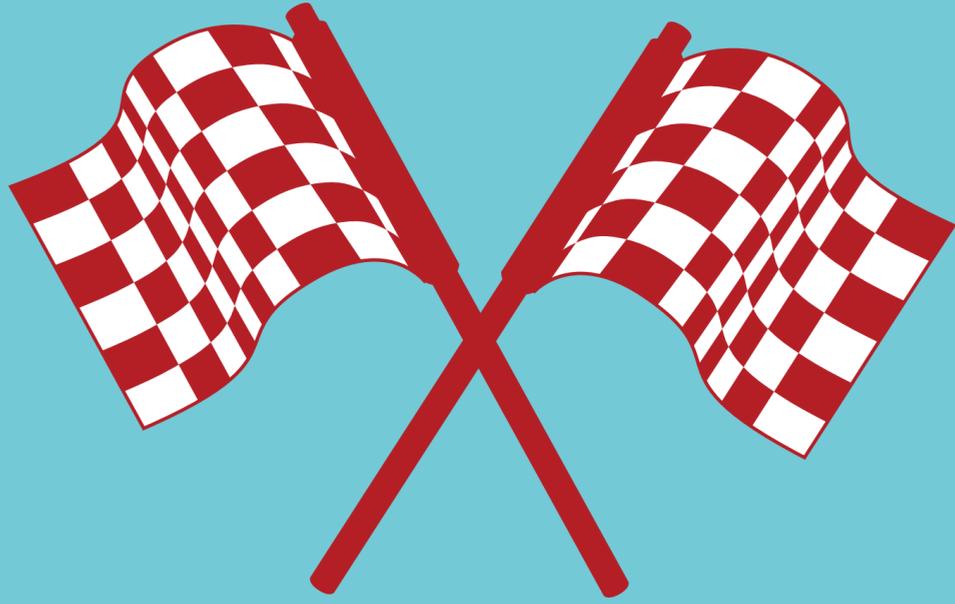
TIME TO TESTIFY

Most states allow residents to testify against or in support of bills being heard by a committee.

Call the committee staff two days in advance to ask if you must sign up ahead of time.

MOST STATES WILL ALLOW YOU TO SIGN UP THE DAY OF THE HEARING.

Not every state allows everyone to testify. California only provides residents with the opportunity to state whether they support or oppose a bill, and staff will mute the microphone if the speaker goes beyond that.



Levi Quackenboss

THE END

THANKS FOR YOUR
SUPPORT ON PATREON

TEN LITTLE KNOWN FACTS ABOUT THE VACCINATION PROGRAM IN THE UNITED STATES



1) Vaccine 'science' is unsettled

There are numerous scientific peer-reviewed papers exposing the dangers of vaccines as well as the "herd immunity myth". [See the [International Medical Council on Vaccination](#).] There is evidence the Center for Disease Control (CDC) has intentionally kept this information away from public health workers, physicians, legislators and the general public.

[See: [Health Hazards of Disease Prevention](#), [Deadly Immunity](#) by Robert Kennedy, Jr., [Science for Sale](#) by Dr David Lewis, Red Ice Creations [interview with researcher scientist Dr. Brian Hooker](#).]

2) Harvard Study concludes "safe and effective drugs" are a myth

A 2013 Harvard Study exposed the epidemic of corruption in governmental agencies due to Big Pharma influence and money.

[See: [Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs](#)]

3) All participating in vaccination program are exempted from liability

Those manufacturing, ordering and administering vaccines have all been exempted from liability should the drug cause injury, illness or even death. There is no incentive to ensure vaccines are safe, or even effective.

[See [Supreme Court decision Bruesewitz versus Wyeth](#)]

4) Patients and parents never given full disclosure

Vaccine package inserts are intentionally substituted with a sales pitch created by the CDC and the American Academy of Pediatrics (AAP) that falsely touts the benefits of vaccines and hides the truth about their health risks, including seizures, denying parents/patients full disclosure. [See: AAP's [Refusal to Vaccinate](#) document.]

5) CDC vaccination recommendations not science based

Vaccine schedules have been established by the CDC and are promoted by public health departments, the AAP and various organizations. CDC vaccine recommendations are not science-based as many of their reports have been altered to hide pertinent and damning information. [See former CDC scientist [Dr. David Lewis' book Science for Sale](#)]

6) CDC is a private for-profit corporation 'doing business'

The CDC is not a government health advocacy organization. It is a corporation listed on Dun and Bradstreet and headquartered in the STATE OF GEORGIA, with strong ties to the pharmaceutical industry. Therefore, their recommendations are influenced by the 'fiscal' health of their corporation.

7) State public health institutions are private for-profit corporations 'doing business'

Medical clinic records are frequently reviewed by STATE public health departments, which are also for-profit corporations listed on Dun and Bradstreet, who receive monetary compensation from the CDC to perform this function. Therefore, state public health departments' recommendations and actions are influenced by the 'fiscal' health of their own corporation.

8) American Academy of Pediatrics is a private for-profit corporation 'doing business'

The AMERICAN ACADEMY OF PEDIATRICS is not health advocacy organization. It is a trade association/corporation (listed on Dun and Bradstreet) head-quartered in the STATE OF ILLINOIS, whose monetary compensation from vaccine manufacturers contributes to the 'fiscal' health of its corporation.

9) Physicians get more money for each 'fully vaccinated' child

Physicians (who are intentionally misinformed by the CDC and Big Pharma and who cannot be sued for vaccine injuries) are paid higher insurance reimbursement rates for each "fully vaccinated" child.

10) Profits, not science, motivate vaccine mandates

LEGISLATORS for the STATE have passed corporate statutes mandating certain vaccines for attendance in educational institutions. As the LEGISLATORS have no medical training and can be easily influenced by drug company lobbyists and/or the CDC, INC, their statutes are not scientifically motivated.

[See retired pharmacist and lobbyist Kristine Severyn's [Profits, Not Science, Motivate Vaccine Mandates](#)]

(NaturalNews) An ongoing study out of Germany comparing disease rates among vaccinated and unvaccinated children points to a pretty clear disparity between the two groups as far as illness rates are concerned. As reported by the group *Health Freedom Alliance*, children who have been vaccinated according to official government schedules are up to five times more likely to contract a preventable disease than children who developed their own immune systems naturally without vaccines.

Released as its own preliminary study back in September 2011, the survey includes data on 8,000 unvaccinated children whose overall disease rates were compared to disease rates among the general population, the vast majority of which has been vaccinated. And in every single disease category, unvaccinated children fared far better than vaccinated children in terms of both disease prevalence and severity. In other words, the evidence suggests that vaccines are neither effective nor safe.

"No study of health outcomes of vaccinated people versus unvaccinated has ever been conducted in the U.S. by CDC or any other agency in the 50 years or more of an accelerating schedule of vaccinations (now over 50 doses of 14 vaccines given before kindergarten, 26 doses in the first year)," wrote Louis Rain back in 2011 for *Health Freedom Alliance* about the survey.

As disclosed at *VaccineInjury.info*, vaccinated children are nearly twice as likely as unvaccinated children to develop neurodermatitis, for instance, a skin disorder marked by chronic itching and scratching. Similarly, [vaccinated children](#) are about two-and-a-half times as likely, based on current data, to develop a pattern of migraine headaches compared to unvaccinated children.

The numbers are even more divergent for asthma and chronic bronchitis, where vaccinated children are about eight times more likely than [unvaccinated](#) children to develop such respiratory problems. Vaccinated children are also far more likely to develop hyperactivity, hayfever, and thyroid disease, with their likelihood three times, four times, and a shocking 17 times higher, respectively, compared to unvaccinated children.

You can view the complete data, as it currently exists, here:
<http://journal.livingfood.us>

Autism extremely rare among unvaccinated children

Where the gloves really come off on the issue, however, is with autism, the long-held point of contention in the vaccine safety debate. According to the data, only four of the 8,000 unvaccinated [children](#) that were included in the 2011 release of the study responded as having severe autism, which is a mere half of one percent of the overall population. Meanwhile the autism rate among the general population, as tabulated in the German KiGGS study used for comparison, is about 1.1 percent.

This means that vaccinated children are about 2.5 times more likely to develop severe autism compared to unvaccinated children, a shocking find when considering the medical establishment vehemently denies any link whatsoever between vaccines and autism. And as it turns out, the four unvaccinated children who reported severe autism all tested high for heavy metals, including mercury, which further indicts vaccines and their disease-causing adjuvants.

Though this correlation does not necessarily conclude causation, the overall disparity of [disease](#) rates between vaccinated and unvaccinated children at the very least points to a very strong connection that cannot be denied or dismissed. Even after accounting for bias, as the survey's authors have tried to do over the years, the data continues to show much higher disease rates among vaccinated children compared to unvaccinated children.

In a similar but unrelated study conducted back in the 1990s, researchers found that the death rate among vaccinated children for infection with diphtheria, tetanus, and whooping cough (pertussis) is also twice as high, on average, compared to unvaccinated children.

Sources for this article include:

<http://journal.livingfood.us>

<http://mnhopkins.blogspot.se>

Learn more:

http://www.naturalnews.com/038647_vaccinated_children_disease_risk_unvaccinated.html#ixzz2HoBCPwL4

Topic: [Vaccination: All](#)



Vaccination: All

02/22/2015

[Vaccination: Influenza](#)
[Vaccination: Diphtheria-Pertussis-Tetanus](#)
[Vaccination: Mumps-Measles-Rubella \(MMR\)](#)
[Vaccination: BCG \(Tuberculosis\)](#)
[Vaccination: Haemophilus Influenzae](#)
[Vaccination: Anthrax](#)
[Vaccination: Varicella \(Chicken pox\)](#)
[Vaccination: Polio](#)
[Vaccination: Plasmid DNA Vaccines](#)
[Vaccination: HPV \(Gardasil\)](#)
[Vaccination: Tetanus](#)
[Vaccination: Rabies](#)
[Vaccination: Rotavirus](#)
[Vaccination: Adult Rubella](#)
[Vaccination: Anti-Fertility](#)
[Vaccination: BCG \(Tuberculosis\)](#)
[Vaccination: Animal Model](#)
[Vaccination: Abortion](#)
[Vaccination: Combinations](#)
[Vaccination: Hepatitis B](#)
[Vaccination: Varicella Zoster \(Shingles\)](#)
[Vaccination: GMO Vaccines](#)
[Vaccination: Hexavalent](#)
[Vaccination: Japanese Encephalitis Virus Vaccine](#)
[Vaccination: Lyme disease](#)
[Vaccination: Measles](#)
[Vaccination: Oral Polio Vaccine, Bivalent](#)
[Vaccination: Oral Polio Vaccine](#)
[Vaccination: Nasal](#)
[Vaccination: Pertussis](#)
[Vaccination: Rabies](#)
[Vaccination: Smallpox](#)
[Vaccination: Tetanus](#)
[Vaccination: Pneumococcal](#)
[Vaccination: Plasmid DNA Vaccines](#)
[Vaccination: Yellow Fever](#)
Allow full anonymous view
[Thimerosal](#)
[Contraceptive Vaccines](#)
[Diploid Cell Vaccines](#)
[Edible Vaccines](#)
[GMO Vaccines](#)
[Live Attenuated Vaccines](#)
[Plant Vaccines](#)
[Simian virus 40 \(SV40\)](#)
[Vaccine Adjuvant](#)
[Antibody Theory Of Vaccinology](#)
[Adventitious Viruses](#)
[Vaccine Contamination](#)



361

Evidence Density Group

4702

1424624266

Facebook Like Info

39

24
8
71
1333056298
0

29206

Additional Research

- [Thimerosal](#)
- [Contraceptive Vaccines](#)
- [Diploid Cell Vaccines](#)
- [Edible Vaccines](#)
- [GMO Vaccines](#)
- [Live Attenuated Vaccines](#)
- [Plant Vaccines](#)
- [Simian virus 40 \(SV40\)](#)
- [Vaccine Adjuvant](#)
- [Antibody Theory Of Vaccinology](#)
- [Adventitious Viruses](#)
- [Vaccine Contamination](#)

What is Cumulative Knowledge, and Why Should it Interest Me?

Cumulative Knowledge is determined by ascribing a numerical value to all the articles indexed on our database. The [GreenMedInfo.com](#) algorithm appraises a study's overall evidentiary power and quality by generating a numerical value. This "Cumulative Knowledge" score incorporates variables such as study type, with the following types listed in descending order by their power: Meta-Analysis, Human Study, Human: Case Study, Animal:Transgenic, Animal, In Vitro, Review, and Commentary. The cumulative total will provide you an idea about the depth and quality of information that this topic has accumulated on our site. For instance, if you downloaded a document on "**Cancers: All**", you might see "**Curcumin**" with a **Cumulative Knowledge** of **677** and **Resveratrol** with a **Cumulative Knowledge** of **175**. This does not mean that **Curcumin** is better, but just that we have gathered more quality research on the Substance **Curcumin**. [Click here to read a more in depth explanation](#)

How are Topics and Articles Sorted in this PDF?

Articles in this document are placed within their respective **Topic** category. If you download a document on the Disease "**Cancers: All**" and are interested in all articles pertaining to the Substance "**Curcumin**" with regard to "**Cancers: All**", you will find them under the "**Curcumin**" sub-section underneath the **Cumulative Knowledge** section. **Topics** are sorted based on their **Cumulative Knowledge** in relation to the main topic of the download. In the previous example, it would be in relation to "**Cancers: All**". Articles are then sorted based on the articles **Published Date**. **Articles** are sorted in a descending fashion, which means that the most recent articles are displayed first. **Articles** may appear more than once in this document. For each **Topic** that an **Article** contains, it will be displayed in that sub-section. For example, if an **Article** contains the **Substances** "**Pterostilbene**" and "**Resveratrol**", the article will be displayed under each **Topic**.

Related Topics

This Topic includes articles from the following related Topics : [Vaccination: Abortion](#), [Vaccination: Adult Rubella](#), [Vaccination: Animal Model](#), [Vaccination: Anthrax](#), [Vaccination: Anti-Fertility](#), [Vaccination: BCG \(Tuberculosis\)](#), [Vaccination: Combinations](#), [Vaccination: Diphtheria-Pertussis-Tetanus](#), [Vaccination: GMO Vaccines](#), [Vaccination: HPV \(Gardasil\)](#), [Vaccination: Haemophilus](#)

[Influenzae, Vaccination: Hepatitis B, Vaccination: Hexavalent, Vaccination: Influenza, Vaccination: Japanese Encephalitis Virus Vaccine, Vaccination: Lyme disease, Vaccination: Measles, Vaccination: Mumps-Measles-Rubella \(MMR\), Vaccination: Nasal, Vaccination: Oral Polio Vaccine, Vaccination: Oral Polio Vaccine, Bivalent, Vaccination: Pertussis, Vaccination: Plasmid DNA Vaccines, Vaccination: Pneumococcal, Vaccination: Polio, Vaccination: Rabies, Vaccination: Rotavirus, Vaccination: Smallpox, Vaccination: Tetanus, Vaccination: Varicella \(Chicken pox\), Vaccination: Varicella Zoster \(Shingles\), Vaccination: Yellow Fever](#)

Quick Summary: 219 Diseases

Name	Cumulative Knowledge	Article Count
Vaccine-induced Toxicity	2123	301
Measles	439	47
Influenza	215	19
Chickenpox	203	21
Sudden Infant Death Syndrome (SIDS)	178	24
Hepatitis B	168	26
Infant Mortality	167	16
Whooping Cough	153	15
Pertussis	148	21
Rubella	147	17
Autism Spectrum Disorders	140	21
Autism	138	17
Guillain-Barre Syndrome	138	31
Thrombocytopenia	126	13
Multiple Sclerosis	125	33
Pregnancy: Vaccination	123	13
Autoimmune Diseases	122	49
Asthma	121	9
Influenza A	120	9
Vaccination: Abortion	109	33
Myelitis	107	14
Herpes Zoster	103	11
Varicella	100	10
Demyelinating Diseases	99	16
Purpura: Thrombocytopenic	97	14
Mercury Poisoning	95	10
Mumps	93	8
Infant Infections	90	7
Anthrax	84	12
Pneumococcal Infections	82	10
H1N1 Infection	81	9
Myopericarditis	80	8
Upper Respiratory Infections	80	6
Poliomyelitis	72	16
Systemic Lupus Erythematosus	68	19
Arthritis	66	9
Hemolytic Anemia	66	5
Vasculitis	66	22
Allergies	63	4
Human Papillomavirus (HPV)	62	17
Hypersensitivity	61	4
Allergies: Childhood	60	3
Elderly: Age Specific Diseases	60	3
Intussusception	60	6
Myocarditis	60	6
Pericarditis	60	6
Swine Flu Associated Virus	60	9
Immune Dysregulation: TH1/TH2 imbalance	51	6

Birth Defects	50	5
Erythema	50	5
Pneumonia	50	4
Childhood Infections	46	6
Optic Neuritis	46	6
Non-polio acute flaccid paralysis (NPAFP)	44	8
Child Mortality	43	7
Ear Infection	42	6
Arthritis: Juvenile Idiopathic	40	4
Cold and Flu: Infants & Children	40	2
Cystic Fibrosis	40	3
Elevated CRP	40	4
Encephalitis	40	4
Encephalopathy: Acute Necrotizing	40	4
Gulf War Syndrome	40	4
HPV	40	4
Infant Chemical Exposures	40	2
Infection: In Infants & Children	40	2
Meningitis: Viral	40	4
Abortion: Spontaneous	38	20
Rheumatoid Arthritis	38	17
Rabies	35	5
Smallpox	32	5
Acute Autoimmune Neuropathy	30	3
C-Reactive Protein	30	3
Cataract	30	3
Corticosteroid-Induced Toxicity	30	3
Febrile Seizures	30	3
Lyme Disease	30	3
Neuropathy: Small Fiber	30	3
Premature Birth	30	3
Vaccinia virus	30	3
Polio	27	5
Glomerulonephritis	26	4
Lupus Erythematosus: Systemic	26	4
Seizures	26	4
Macrophagic myofasciitis	25	14
Tetanus	23	3
Animal Diseases: Infectious	22	11
Alopecia	20	2
Anemia: Aplastic	20	2
Arthritis: Juvenile Chronic	20	2
Arthritis: Juvenile Rheumatoid	20	2
Arthritis: Rheumatoid	20	2
Atopic Disease	20	1
Autoimmune inflammatory polyneuropathy (PN)	20	2
CRP	20	2
Cardiovascular Diseases	20	2
Cervical Cancer	20	2
Diabetes Mellitus: Type 2	20	2
Dravet syndrome	20	2
Gastroenteritis	20	2
Gastrointestinal Diseases	20	2
Haemophilus influenzae	20	2
Hearing Loss: Sudden	20	1
Hepatitis	20	2
Herpes: Ocular	20	2

Hypersensitivity: Immediate	20	1
Iatrogenic Disease	20	2
Infant Neurological Development	20	2
Inflammation	20	2
Inflammatory Bowel Diseases	20	2
Influenza B	20	1
Joint Diseases	20	2
Liver Disease	20	2
Pancytopenia	20	2
Pharyngeal Diseases	20	2
Pre-Eclampsia	20	2
Pregnancy Complications	20	2
Preterm Birth: Prevention	20	2
Shingles	20	2
Stroke: Prevention	20	2
Syncope	20	2
Thromboembolism	20	2
Ulcerative Colitis	20	2
Uveitis	20	2
Viremia	20	2
Animal Diseases: Porcine Circovirus Type 2 (PCV2)	17	9
Chronic Fatigue Syndrome	16	4
Guillain Barre Syndrome: Miller Fisher Variant	16	3
Animal Diseases: Smithburn Rift Valley Fever	12	6
Inflammatory Myopathy	12	12
Mycoplasma Infections	11	2
Aging	10	1
Allergic Rhinitis	10	1
Anaphylaxis	10	6
Breast Augmentation Complications	10	1
Cholera	10	1
Diarrhea	10	1
Empyema	10	1
Encephalitis: Japanese	10	1
Fever	10	1
Hepatitis C	10	1
Malaria	10	1
Miscarriage	10	1
Miscarriage: Medical Intervention	10	1
Narcolepsy	10	1
Orchitis	10	1
Parapertussis	10	1
Parapneumonic Empyema	10	1
Pregnancy: Flu	10	1
Respiratory Diseases	10	1
Rotavirus Infections	10	1
Silicone Implant Toxicity	10	1
Tuberculosis	10	1
Dermatomyositis	8	4
Acute Inflammatory Demyelinating Polyradiculoneuropathy	6	2
Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE)	6	2
Aphthosis: Buccal	6	2
Bell's Palsy	6	2
Chorioretinitis	6	2

Diabetes Mellitus: Type 1	6	2
Epilepsy	6	2
Hydranencephaly	6	3
Lipoatrophy	6	2
Lupus Erythematosus: Cutaneous	6	2
Miller Fisher Syndrome	6	2
Pneumonitis	6	2
Polyradiculoneuropathy: Acute Inflammatory	6	2
Rhabdomyolysis	6	2
Rift Valley Fever	6	3
Statin-Induced Pathologies	6	2
Simian virus 40 (SV40)	5	1
Acute Flaccid Paralysis	4	4
Amygdala: Damage/Abnormalities	4	2
Animal Diseases: Scrapie	4	2
Animal Diseases: Simian Immunodeficiency Virus (SIV)	4	2
Infertility	4	2
Liver Damage	4	2
Neuritis: Brachial Plexus	4	4
Neurodevelopmental Disorders	4	2
Polio: Vaccine-Related	4	2
Retroviruses	4	3
Glyphosate Toxicity	3	1
Hemophilus influenzae	3	1
Herpes Zoster Keratitis	3	1
Incontinentia Pigmenti	3	1
Leukemia Cutis	3	1
Morphea profunda	3	1
Ovarian Failure	3	1
Parkinsonian Disorders	3	1
Pseudolymphoma	3	1
Psychiatric Disorders	3	1
Shoulder Injuries	3	1
Aluminum Toxicity	2	2
Brain Inflammation	2	2
Epstein-Barr Virus Infections	2	2
Myasthenia Gravis	2	2
Neuromuscular Diseases	2	2
Neuropathies	2	2
Oxidative Stress	2	1
Peripheral Neuropathies	2	2
Polyarteritis Nodosa	2	2
Prostate Cancer	2	1
Sarcoma	2	2
Tumors	2	2
Urinary Tract Infections	2	2
Yellow Fever	2	2
Attention Deficit Disorder	1	1
Attention Deficit Disorder with Hyperactivity	1	1
Encephalomyelitis	1	1
Encephalopathies	1	1
Endogenous avian retrovirus (EAV-0)	1	1
Excitotoxicity	1	1
Immune Disorders: B-Cell Over-Activity	1	1
Infertility: Female	1	1
Mental Retardation	1	1

Mitochondrial Diseases	1	1
Myopathy: Inflammatory	1	1
Neuromyelitis Optica	1	1
Spongiform Encephalopathies: Transmissible	1	1

Quick Summary: 8 Adverse Pharmacological Actions

Name	Cumulative Knowledge	Article Count
Tumor necrosis factorα (TNFα) up-regulation	40	4
Immunotoxic	36	5
Immunosuppressive	20	2
Interleukin-6 up-regulation	20	2
Teratogenic	20	2
Neurotoxic	13	2
Myotoxicity	6	2
Hepatotoxic	4	2

Quick Summary: 39 Problematic Actions

Name	Cumulative Knowledge	Article Count
Vaccination: All	3990	542
Vaccination: Diphtheria-Pertussis-Tetanus	835	100
Vaccination: Hepatitis B	823	120
Vaccination: Influenza	695	87
Vaccination: Mumps-Measles-Rubella (MMR)	624	82
Vaccination: Measles	447	55
Vaccination: Varicella (Chicken pox)	363	55
Vaccination: Pertussis	293	36
Vaccination: Polio	262	38
Vaccination: HPV (Gardasil)	223	37
Vaccination: Tetanus	175	32
Vaccination: Smallpox	132	15
Vaccination: Anthrax	124	16
Vaccination: Combinations	120	12
Vaccination: Pneumococcal	112	13
Vaccination: Haemophilus Influenzae	96	22
Vaccination: Animal Model	86	40
Vaccination: BCG (Tuberculosis)	86	10
Vaccination: Rotavirus	86	23
Vaccination: Adult Rubella	74	17
Vaccination: Diphtheria	60	5
Vaccination: Oral Polio Vaccine	43	5
Vaccination: Oral Polio Vaccine, Bivalent	43	5
Vaccination: Lyme disease	42	15
Vaccination: Rabies	22	19
Brachytherapy	20	2
Vaccination: Yellow Fever	15	6
Vaccination: Hexavalent	12	4
Obstetric Interventions	10	1
Vaccination: Cholera	10	1
Vaccination: Japanese Encephalitis Virus Vaccine	10	1
Vaccination: Nasal	9	3
Vaccination: Plasmid DNA Vaccines	6	4
Vaccination: GMO Vaccines	4	3
Vaccination: Varicella Zoster (Shingles)	3	1
Genetically Modified Organisms	2	2
Vaccination: Anti-Fertility	2	2
Vaccination: Conjugate Vaccines	1	1
Vaccination: Streptococcus Pneumoniae	1	1

Category: Diseases

Topic: Vaccine-induced Toxicity

[38,787 adverse events including infant death \(highest in 1-3 month olds\) after vaccination were reported between 1991-1994. \(The authors speciously claim SIDS and not vaccination caused these deaths\).](#) - GMI Summary

Pubmed Data : J Pediatr. 1997 Oct;131(4):529-35. PMID: [9386653](#)

Article Published Date : Oct 01, 1997

Authors : M M Braun, S S Ellenberg

Study Type : Meta Analysis

Additional Links

Diseases : [Hearing Loss: Sudden](#) : CK(30) : AC(3), [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents.](#) - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies](#) : CK(520) : AC(96), [Allergies: Childhood](#) : CK(70) : AC(5), [Asthma](#) : CK(918) : AC(140), [Hypersensitivity](#) : CK(64) : AC(15), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Tetanus](#) : CK(61) : AC(8)

[Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem.](#) - GMI Summary

Pubmed Data : Am J Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B](#) : CK(219) : AC(37), [Infant Chemical Exposures](#) : CK(165) : AC(24), [Mercury Poisoning](#) : CK(172) : AC(45), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Over 1,000 confirmed cases of vaccine-induced thrombocytopenia were reported between 1990-2008.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Nov 29. Epub 2010 Nov 29. PMID: [21126606](#)

Article Published Date : Nov 29, 2010

Authors : Emily Jane Woo, Robert P Wise, David Menschik, Sean V Shadomy, John Iskander, Judy Beeler, Frederick Varricchio, Robert Ball

Study Type : Meta Analysis

Additional Links

Diseases : [Thrombocytopenia](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Over 600 cases of sudden infant death syndrome following vaccination were reported from 1990-1997. - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2001 Jun-Jul;10(4):279-85. PMID: [11760487](#)

Article Published Date : Jun 01, 2001

Authors : L E Silvers, S S Ellenberg, R P Wise, F E Varricchio, G T Mootrey, M E Salive

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

The risk of adverse events from the pertussis outweighed the risk of pertussis infection during the period of 1970-83 in children living in non-deprived circumstances in Britain. - GMI Summary

Pubmed Data : Dev Biol Stand. 1985;61:395-405. PMID: [3835080](#)

Article Published Date : Jan 01, 1985

Authors : G T Stewart

Study Type : Meta Analysis

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

There is a highly statistically significant correlation between increasing number of vaccine doses and increasing infant mortality rates. - GMI Summary

Pubmed Data : Hum Exp Toxicol. 2011 May 4. Epub 2011 May 4. PMID: [21543527](#)

Article Published Date : May 04, 2011

Authors : Neil Z Miller, Gary S Goldman

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Thimerosal-containing vaccines are associated with autism prevalence and measles-containing vaccines are associated with serious neurological disorders. - GMI Summary

Pubmed Data : Med Sci Monit. 2004 Mar;10(3):PI33-9. Epub 2004 Mar 1. PMID: [14976450](#)

Article Published Date : Mar 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Vaccination in infants less than 3 months is associated with an increased risk of sudden infant death syndrome. - GMI Summary

Pubmed Data : Fundam Clin Pharmacol. 1995;9(3):263-70. PMID: [7557822](#)

Article Published Date : Jan 01, 1995

Authors : A P Jonville-Bera, E Autret, J Laugier

Study Type : Meta Analysis

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-](#)

[Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccination is associated with a rare autoimmune neurological condition transverse myelitis.](#) - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1198-204. PMID: [19880568](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, S Kivity, M Szyper-Kravitz, Y Shoenfeld

Study Type : Meta Analysis

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination is associated with an increased risk for hemolytic anemia.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7394-7. Epub 2009 Sep 18. PMID: [19766577](#)

Article Published Date : Dec 09, 2009

Authors : Allison L Naleway, Edward A Belongia, James G Donahue, Burney A Kieke, Jason M Glanz,

Study Type : Meta Analysis

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

["Chart-confirmed guillain-barre syndrome after 2009 H1N1 influenza vaccination among the Medicare population, 2009-2010."](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2013 Sep 15 ;178(6):962-73. Epub 2013 May 6. PMID: [23652165](#)

Article Published Date : Sep 14, 2013

Authors : Laura L Polakowski, Sukhminder K Sandhu, David B Martin, Robert Ball, Thomas E Macurdy, Riley L Franks, Jonathan M Gibbs, Garner F Kropp, Armen Avagyan, Jeffrey A Kelman, Christopher M Worrall, Guoying Sun, Rebecca E Kliman, Dale R Burwen

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A measles outbreak was reported in a highly vaccinated population, San Diego, 2008](#) - GMI Summary

Pubmed Data : Pediatrics. 2010 Apr ;125(4):747-55. Epub 2010 Mar 22. PMID: [20308208](#)

Article Published Date : Mar 31, 2010

Authors : David E Sugeran, Albert E Barskey, Maryann G Delea, Ismael R Ortega-Sanchez, Daoling Bi, Kimberly J Ralston, Paul A Rota, Karen Waters-Montijo, Charles W Lebaron

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A modified self-controlled case series method links multidose vaccinations to sudden unexpected death.](#) - GMI Summary

Pubmed Data : Stat Med. 2011 Mar 15;30(6):666-77. Epub 2010 Nov 30. PMID: [21337361](#)

Article Published Date : Mar 15, 2011

Authors : Ronny Kuhnert, Hartmut Hecker, Christina Poethko-Müller, Martin Schlaud, Mechtild Vennemann, Heather J Whitaker, C Paddy Farrington

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Acute necrotizing encephalopathy secondary to diphtheria, tetanus toxoid and whole-cell pertussis vaccination has been reported.](#) - GMI Summary

Pubmed Data : [Pediatr Radiol. 2010 Jul;40\(7\):1281-4. Epub 2010 Jan 30. PMID: 20119724](#)

Article Published Date : Jul 01, 2010

Authors : Hale Aydin, Esra Ozgul, Ahmet Muhtesem Agildere

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing : CK\(20\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Adverse effects of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine in 6- to 7-year-old children.](#) - GMI Summary

Pubmed Data : [Pediatr Neonatol. 2011 Feb;52\(1\):38-41. Epub 2011 Feb 17. PMID: 21385656](#)

Article Published Date : Feb 01, 2011

Authors : Sung-Hsi Wei, Yen-Nan Chao, Song-En Huang, Tsuey-Feng Lee, Luan-Yin Chang

Study Type : Human Study

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Adverse events following smallpox vaccination with ACAM2000 in a military population have been reported.](#) - GMI Summary

Pubmed Data : [Arch Dermatol. 2010 Jun;146\(6\):656-61. PMID: 20566929](#)

Article Published Date : Jun 01, 2010

Authors : Thomas M Beachkofsky, Scott C Carrizales, Jeffrey J Bidinger, David E Hrncir, Darren E Whittemore, Chad M Hivnor

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Among female infants, those who receive both BCG and DTP vaccines experience higher mortality than those who receive only one of the two vaccines.](#) - GMI Summary

Pubmed Data : [Trop Med Int Health. 2005 Oct;10\(10\):947-55. PMID: 16185228](#)

Article Published Date : Oct 01, 2005

Authors : Lawrence H Moulton, Lakshmi Rahmathullah, Neal A Halsey, R D Thulasiraj, Joanne Katz, James M Tielsch

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[An association between Pandemrix vaccination and narcolepsy has been observed in Finland and Sweden](#) - GMI Summary

Pubmed Data : [Euro Surveill. 2014 ;19\(17\):15-25. Epub 2014 May 1. PMID: 24821121](#)

Article Published Date : Dec 31, 2013

Authors : D O'Flanagan, A S Barret, M Foley, S Cotter, C Bonner, C Crowe, B Lynch, B Sweeney, H Johnson, B McCoy, E Purcell

Study Type : Human Study

Additional Links

Diseases : [Narcolepsy](#) : CK(21) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

[An Italian study found that 61% of women experienced an adverse event after the administration of the first dose of HPV vaccine.](#) - GMI Summary

Pubmed Data : Recent Prog Med. 2013 Jun ;104(6):262-6. PMID: [23801230](#)

Article Published Date : May 31, 2013

Authors : Stefania Spila-Alegiani, Roberto Da Cas, Cristina Giambi, Roberto Raschetti, Stefania Salmaso

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

[Autistic children have elevated levels of measles antibodies indicating that measles vaccination may be causing autoimmunity in these children.](#) - GMI Summary

Pubmed Data : Pediatr Neurol. 2003 Apr;28(4):292-4. PMID: [12849883](#)

Article Published Date : Apr 01, 2003

Authors : Vijendra K Singh, Ryan L Jensen

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax](#) : CK(43) : AC(6), [Birth Defects](#) : CK(204) : AC(39), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Anthrax](#) : CK(62) : AC(8)

Adverse Pharmacological Actions : [Teratogenic](#) : CK(318) : AC(62)

[Breastfeeding attenuates reductions in energy intake induced by a mild immunologic stimulus represented by DPTH immunization.](#) - GMI Summary

Pubmed Data : J Nutr. 2002 Jun;132(6):1293-8. PMID: [12042449](#)

Article Published Date : Jun 01, 2002

Authors : Mardya López-Alarcón, Cutberto Garza, Jean-Pierre Habicht, Lourdes Martínez, Virginia Pegueros, Salvador Villalpando

Study Type : Human Study

Additional Links

Substances : [Breast Milk](#) : CK(428) : AC(49)

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Therapeutic Actions : [Breastfeeding](#) : CK(739) : AC(77)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor](#) : CK(1021) : AC(365)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-](#)

[Breastfeeding is associated with a decreased incidence of fever after immunizations.](#) - GMI Summary

Pubmed Data : Pediatrics. 2010 Jun;125(6):e1448-52. Epub 2010 May 17. PMID: [20478932](#)

Article Published Date : Jun 01, 2010

Authors : Alfredo Pisacane, Paola Continisio, Orsola Palma, Stefania Cataldo, Fabiola De Michele, Ugo Vairo

Study Type : Human Study

Additional Links

Substances : [Breast Milk : CK\(428\) : AC\(49\)](#)

Diseases : [Fever : CK\(77\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Children vaccinated with MMR before age 10 are at significantly higher risk of multiple sclerosis.](#) - GMI Summary

Pubmed Data : Eur J Epidemiol. 2009;24(9):541-52. Epub 2009 Jul 26. PMID: [19633994](#)

Article Published Date : Jan 01, 2009

Authors : Cecilia Ahlgren, Kjell Torén, Anders Odén, Oluf Andersen

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24. PMID: [18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications : CK\(32\) : AC\(4\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Silicone Implant Toxicity : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Silicone Implants : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures : CK\(83\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Congenital malformation is a possible consequence of rubella vaccination during pregnancy.](#) - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[CRP level in infants is elevated in the 48 hours following immunization. - GMI Summary](#)

Pubmed Data : J Pediatr. 2007 Aug ;151(2):167-72. Epub 2007 Jun 22. PMID: [17643770](#)

Article Published Date : Aug 01, 2007

Authors : Massaro Pourcyrous, Sheldon B Korones, Kristopher L Arheart, Henrietta S Bada

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Multiple Vaccines : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. - GMI Summary](#)

Pubmed Data : Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18. PMID: [21093496](#)

Article Published Date : Jan 10, 2011

Authors : J Agergaard, E Nante, G Poulstrup, J Nielsen, K L Flanagan, L Østergaard, C S Benn, P Aaby

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Diphtheria-tetanus-peteruss vaccines increase child mortality in rural Guinea-Bissau. - GMI Summary](#)

Pubmed Data : Int J Epidemiol. 2004 Apr;33(2):374-80. PMID: [15082643](#)

Article Published Date : Apr 01, 2004

Authors : Peter Aaby, Henrik Jensen, Joaquim Gomes, Manual Fernandes, Ida Maria Lisse

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[DPT vaccines have been associated with recurrent seizures. - GMI Summary](#)

Pubmed Data : Am J Dis Child. 1984 Oct;138(10):908-11. PMID: [6206715](#)

Article Published Date : Oct 01, 1984

Authors : J V Murphy, L D Sarff, K M Marquardt

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Seizures : CK\(135\) : AC\(33\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau. - GMI Summary](#)

Pubmed Data : [Vaccine](#). 2007 Jan 26;25(7):1265-9. Epub 2006 Oct 18.

Article Published Date : Jan 25, 2007

Authors : Peter Aaby, Sidu Biai, Jens Erik Veirum, Morten Sodemann, Ida Lisse, May-Lill Garly, Henrik Ravn, Christine Stabell Benn, Amabelia Rodrigues

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Combinations](#) : CK(20) : AC(2)

[Even though 95% of the children had measles antibodies after vaccination, vaccine efficacy was not more than 68%. - GMI Summary](#)

Pubmed Data : J Infect Dis. 1990 Nov ;162(5):1043-8. PMID: [2230232](#)

Article Published Date : Oct 31, 1990

Authors : P Aaby, K Knudsen, T G Jensen, J Thårup, A Poulsen, M Sodemann, M C da Silva, H Whittle

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Antibody Theory Of Vaccinology](#) : CK(75) : AC(5), [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Measles](#) : CK(157) : AC(16)

[Evidence exists demonstrating that diphtheria-tetanus-pertussis \(DTP\) vaccines increase mortality in children. - GMI Summary](#)

Pubmed Data : Trop Med Int Health. 2007 Jan;12(1):15-24. PMID: [17207144](#)

Article Published Date : Jan 01, 2007

Authors : Peter Aaby, Christine Stabell Benn, Jens Nielsen, Ida Maria Lisse, Amabelia Rodrigues, Henrik Jensen

Study Type : Human Study

Additional Links

Diseases : [Child Mortality](#) : CK(64) : AC(8), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth. - GMI Summary](#)

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP](#) : CK(30) : AC(3), [Elevated CRP](#) : CK(82) : AC(8), [Pre-Eclampsia](#) : CK(299) : AC(33), [Pregnancy: Vaccination](#) : CK(92) : AC(16), [Pregnancy Complications](#) : CK(168) : AC(20), [Preterm Birth: Prevention](#) : CK(111) : AC(9), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation](#) : CK(14) : AC(3), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#) : CK(42) : AC(4)

[Hair mercury in breast-fed infants exposed to thimerosal-preserved vaccines indicates significant levels of exposure. - GMI Summary](#)

Pubmed Data : Eur J Pediatr. 2007 Sep;166(9):935-41. Epub 2007 Jan 20. PMID: [17237965](#)

Article Published Date : Sep 01, 2007

Authors : Rejane C Marques, José G Dórea, Márlon F Fonseca, Wanderley R Bastos, Olaf Malm

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning](#) : CK(172) : AC(45), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Therapeutic Actions : [Breastfeeding](#) : CK(739) : AC(77)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination may contribute to autoimmune demyelinating complications due to immunological cross-reactivity between Hepatitis B virus surface antigen and myelin basic protein.](#) - GMI Summary

Pubmed Data : Clin Dev Immunol. 2005 Sep;12(3):217-24. PMID: [16295528](#)

Article Published Date : Sep 01, 2005

Authors : Dimitrios-Petrou Bogdanos, Heather Smith, Yun Ma, Harold Baum, Giorgina Mieli-Vergani, Diego Vergani

Study Type : Human Study

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Demyelinating Diseases](#) : CK(1309) : AC(247), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2), [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination was statistically associated with gastrointestinal reactions including: hepatitis, gastrointestinal disease and liver function test abnormalities.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2002 Nov-Dec;49(48):1571-5. PMID: [12397738](#)

Article Published Date : Nov 01, 2002

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Gastrointestinal Diseases](#) : CK(38) : AC(14), [Hepatitis](#) : CK(64) : AC(24), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine is associated with an increased risk of liver problems in U.S. children less than 6 years old, 1993 and 1994.](#) - GMI Summary

Pubmed Data : Epidemiology. 1999 May;10(3):337-9. PMID: [10230847](#)

Article Published Date : May 01, 1999

Authors : M A Fisher, S A Eklund

Study Type : Human Study

Additional Links

Diseases : [Liver Disease](#) : CK(112) : AC(31), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine is associated with an increased risk of multiple sclerosis.](#) - GMI Summary

Pubmed Data : Neurology. 2004 Sep 14;63(5):838-42. PMID: [15365133](#)

Article Published Date : Sep 14, 2004

Authors : Miguel A Hernán, Susan S Jick, Michael J Olek, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Hepatitis B vaccine may have a possible association with the development of uveitis in some patients.](#) - GMI Summary

Pubmed Data : Cutan Ocul Toxicol. 2010 Mar;29(1):26-9. PMID: [19947819](#)

Article Published Date : Mar 01, 2010

Authors : Frederick W Fraunfelder, Eric B Suhler, Frederick T Fraunfelder

Study Type : Human Study

Additional Links

Diseases : [Uveitis](#) : CK(73) : AC(11), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis C prevalence in Southern Italy may be due to iatrogenic transmission through the Salk Polio vaccine 1956-1965.](#) - GMI Summary

Pubmed Data : J Med Virol. 2003 May;70(1):49-50. PMID: [12629643](#)

Article Published Date : May 01, 2003

Authors : Maurizio Montella, Anna Crispo, Maria Grimaldi, Vincenzo Tridente, Mario Fusco

Study Type : Human Study

Additional Links

Diseases : [Hepatitis C](#) : CK(413) : AC(65), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[High antibody titres against predicted Mycoplasma surface proteins do not prevent sequestration in infected lung tissue in the course of experimental contagious bovine pleuropneumonia.](#) - GMI Summary

Pubmed Data : Vet Microbiol. 2014 Aug 6 ;172(1-2):285-93. Epub 2014 May 5. PMID: [24880898](#)

Article Published Date : Aug 05, 2014

Authors : Elise Schieck, Anne Liljander, Carl Hamsten, Nimmo Gicheru, Massimo Scacchia, Flavio Sacchini, Martin Heller, Christiane Schnee, Anja Sterner-Kock, Andreas Hlinak, Jan Naessens, Jane Poole, Anja Persson, Joerg Jores

Study Type : Human Study

Additional Links

Diseases : [Mycoplasma Infections](#) : CK(2) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Antibody Theory Of Vaccinology](#) : CK(75) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[High titre measles vaccination increases female mortality in those receiving immunization in West Africa.](#) - GMI Summary

Pubmed Data : Int J Epidemiol. 1996 Jun;25(3):665-73. PMID: [8671571](#)

Article Published Date : Jun 01, 1996

Authors : K M Knudsen, P Aaby, H Whittle, M Rowe, B Samb, F Simondon, J Sterne, P Fine

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Measles](#) : CK(157) : AC(16)

[Human Papilloma Virus \(HPV\) vaccine is associated with demyelinating events.](#) - GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, II Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [HPV](#) : CK(31) : AC(4), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [HPV Vaccine](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

In the US the highest number of cases of Guillain-Barre syndrome are associated with influenza and hepatitis B vaccines. - GMI Summary

Pubmed Data : J Clin Neuromuscul Dis. 2009 Sep;11(1):1-6. PMID: [19730016](#)

Article Published Date : Sep 01, 2009

Authors : Nizar Souayah, Abu Nasar, M Fareed K Suri, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Incidence of adverse reactions to vaccines in pediatric populations are under-reported and may be as high as 43.4% for certain vaccine combinations. - GMI Summary

Pubmed Data : Clin Drug Investig. 2004;24(8):457-63. PMID: [17523706](#)

Article Published Date : Jan 01, 2004

Authors : Pilar Carrasco-Garrido, Carmen Gallardo-Pino, Rodrigo Jiménez-García, Miguel A Tapias, Angel Gil de Miguel

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster (shingles) cases managed in the same time period. - GMI Summary

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Shingles : CK\(472\) : AC\(35\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events. - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Cardiovascular Diseases : CK\(5342\) : AC\(665\)](#), [Diabetes Mellitus: Type 2 : CK\(3603\) : AC\(359\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Interleukin-6 upregulation : CK\(26\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination may increase the risk of Guillain-Barré Syndrome. - GMI Summary](#)

Pubmed Data : Kidney Int. 2008 Dec;74(11):1461-7. Epub 2008 Sep 24. PMID: [18592444](#)

Article Published Date : Dec 01, 2008

Authors : C I Blanco-Marchite, L Buznego-Suárez, M A Fagúndez-Vargas, M Méndez-Llitas, P Pozo-Martos

Study Type : Human Study

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant : CK\(13\) : AC\(2\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza vaccines may be causing vasculitis. - GMI Summary](#)

Pubmed Data : J Ethnopharmacol. 2000 Aug;71(3):457-63. PMID: [19734734](#)

Article Published Date : Aug 01, 2000

Authors : Rainer Birck, Isabelle Kaelsch, Peter Schnuelle, Luis Felipe Flores-Suárez, Rainer Nowack

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccines were not shown to be effective among children 6 to 59 months of age during 2 influenza seasons. - GMI Summary](#)

Pubmed Data : Anticancer Res. 2009 Nov;29(11):4629-32. PMID: [18838647](#)

Article Published Date : Nov 01, 2009

Authors : Peter G Szilagyi, Gerry Fairbrother, Marie R Griffin, Richard W Hornung, Stephanie Donauer, Ardythe Morrow, Mekibib Altaye, Yuwei Zhu, Sandra Ambrose, Kathryn M Edwards, Katherine A Poehling, Geraldine Lofthus, Michol Holloway, Lyn Finelli, Marika Iwane, Mary Allen Staat,

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Injection site reactions occur in 28% of those who receive the anthrax vaccine, with women having twice the incidence of reaction versus men. - GMI Summary](#)

Pubmed Data : Pharmacoepidemiol Drug Saf. 2007 Mar ;16(3):259-74. PMID: [17245803](#)

Article Published Date : Mar 01, 2007

Authors : Michael M McNeil, I-Shan Chiang, John T Wheeling, Yujia Zhang

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Gender Differences : CK\(63\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Live attenuated influenza vaccines may cause shedding of the virus in children 6-59 months. - GMI Summary

Pubmed Data : Vaccine. 2011 Apr 20. Epub 2011 Apr 20. PMID: [21513761](#)

Article Published Date : Apr 20, 2011

Authors : Raburn M Mallory, Tingting Yi, Christopher S Ambrose

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders. - GMI Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Measles-mumps-rubella vaccine that is given in the second year of life is associated with an increased risk of immune thrombocytopenia purpura. - GMI Summary

Pubmed Data : Pediatrics. 2008 Mar;121(3):e687-92. PMID: [18310189](#)

Article Published Date : Mar 01, 2008

Authors : Eric K France, Jason Glanz, Stanley Xu, Simon Hambidge, Kristi Yamasaki, Steve B Black, Michael Marcy, John P Mullooly, Lisa A Jackson, James Nordin, Edward A Belongia, K Hohman, Robert T Chen, Robert Davis,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Noticeable adverse reactions to the HPV vaccine occurred in 22% of those polled. - GMI Summary

Pubmed Data : Aten Primaria. 2010 Dec 14. Epub 2010 Dec 14. PMID: [21163554](#)

Article Published Date : Dec 14, 2010

Authors : M Amparo Torrecilla Rojas, Miguel Pedregal González, Fermín García Rodríguez, Josefa Ruiz Fernández

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary. - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#), [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Pertussis vaccination may activate a genetic predisposition for encephalopathy in susceptible individuals.](#) - GMI Summary

Pubmed Data : Cytotechnology. 2002 Nov;40(1-3):139-49. PMID: [20447868](#)

Article Published Date : Nov 01, 2002

Authors : Anne M McIntosh, Jacinta McMahon, Leanne M Dibbens, Xenia Iona, John C Mulley, Ingrid E Scheffer, Samuel F Berkovic

Study Type : Human Study

Additional Links

Diseases : [Dravet syndrome : CK\(30\) : AC\(3\)](#), [Encephalitis : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pertussis vaccine has been linked to hypotonic-hyporesponsive episodes \(HHE\) in infants and children.](#) - GMI Summary

Pubmed Data : Drug Saf. 2002;25(2):85-90. PMID: [11888351](#)

Article Published Date : Jan 01, 2002

Authors : Michael S Gold

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pneumococcal conjugate vaccination is associated with higher levels of serious adverse respiratory events and nonrespiratory events in infants 6 weeks to 6 months of age.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Jun;28(6):455-62. PMID: [19483514](#)

Article Published Date : Jun 01, 2009

Authors : Marilla G Lucero, Hanna Nohynek, Gail Williams, Veronica Tallo, Eric A F Simões, Socorro Lupisan, Diozele Sanvictores, Simon Forsyth, Taneli Puumalainen, Juanita Ugpo, Marites Lechago, Margaret de Campo, Erma Abuzejo-Ladesma, Lydia Sombrero, Antti Nissinen, Anu Soinen, Petri Ruutu, Ian Riley, Helen P Mäkelä

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Respiratory Diseases : CK\(174\) : AC\(29\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Rates of intussusception associated with rotavirus vaccines may be significantly underestimated.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2009 Nov 1;200 Suppl 1:S264-70. PMID: [19817607](#)

Article Published Date : Nov 01, 2009

Authors : Margaret M Cortese, Mary Allen Staat, Geoffrey A Weinberg, Kathryn Edwards, Marilyn A Rice, Peter G Szilagyi, Caroline B Hall, Daniel C Payne, Umesh D Parashar

Study Type : Human Study

Additional Links

Diseases : [Intussusception](#) : CK(30) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)
Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Rotavirus](#) : CK(33) : AC(6)

[Rotavirus vaccination has been associated with increased risk for gastroenteritis and intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2004 Apr;113(4):e353-9. PMID: [15060267](#)

Article Published Date : Apr 01, 2004

Authors : Penina Haber, Robert T Chen, Lynn R Zanardi, Gina T Mootrey, Roseanne English, M Miles Braun,

Study Type : Human Study

Additional Links

Diseases : [Gastroenteritis](#) : CK(96) : AC(11), [Intussusception](#) : CK(30) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Rotavirus](#) : CK(33) : AC(6)

[Rotavirus vaccinations have a history of causing adverse effects such as intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2001 Jun;107(6):E97. PMID: [11389295](#)

Article Published Date : Jun 01, 2001

Authors : L R Zanardi, P Haber, G T Mootrey, M T Niu, M Wharton

Study Type : Human Study

Additional Links

Diseases : [Intussusception](#) : CK(30) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Rotavirus](#) : CK(33) : AC(6)

[Serious adverse events associated with whole cell pertussis vaccine, e.g. sudden infant death syndrome and encephalopathy, may have occurred in metabolically vulnerable children.](#) - GMI Summary

Pubmed Data : Pharmazie. 2007 Apr;62(4):299-304. PMID: [19660877](#)

Article Published Date : Apr 01, 2007

Authors : Kumanan Wilson, Beth Potter, Douglas Manuel, Jennifer Keelan, Pranesh Chakraborty

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Smallpox vaccine caused iatrogenic vaccinia in children in Russia.](#) - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr(2):40-5. PMID: [11548257](#)

Article Published Date : Mar 01, 2001

Authors : G G Onishchenko, V I Markov, V N Ustiushin, S V Borisevich, G I Kuznetsova, S Ia Loginova, A M Berezhnoi, N T Vasil'ev, V A Maksimov, A A Makhlaï

Study Type : Human Study

Additional Links

Diseases : [Smallpox](#) : CK(23) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vaccinia virus](#) : CK(22) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Smallpox](#) : CK(71) : AC(8)

[Sudden Infant Death syndrome mortality rate in the period zero to three days following DTP was found to be 7.3 times higher than in the period 30 days after immunization.](#) - GMI Summary

Pubmed Data : Am J Public Health. 1987 Aug;77(8):945-51. PMID: [3496805](#)

Article Published Date : Aug 01, 1987

Authors : A M Walker, H Jick, D R Perera, R S Thompson, T A Knauss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Symptomatic Gulf War Syndrome is strongly associated with the presence of autoantibodies to squalene, an adjuvant used in vaccines.](#) - GMI Summary

Pubmed Data : Exp Mol Pathol. 2000 Feb;68(1):55-64. PMID: [10640454](#)

Article Published Date : Feb 01, 2000

Authors : P B Asa, Y Cao, R F Garry

Study Type : Human Study

Additional Links

Diseases : [Gulf War Syndrome : CK\(33\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The anthrax vaccine is one of the most reactogenic vaccines reported in the Vaccine Adverse Events Reporting System \(VAERS\) database.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2004 May-Jun;51(57):762-7. PMID: [15143911](#)

Article Published Date : May 01, 2004

Authors : Mark R Geier, David A Geier

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects.](#) - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

[There has been a five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine.](#) - GMI Summary

Pubmed Data : [Pediatr Infect Dis J. 2008 Nov;27\(11\):1030-2. PMID: 18845981](#)

Article Published Date : Nov 01, 2008

Authors : Debra J Hendrickson, Dean A Blumberg, Jesse P Joad, Sanjay Jhawar, Ruth J McDonald

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Empyema : CK\(10\) : AC\(1\)](#), [Parapneumonic Empyema : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[There is a positive association between autism prevalence and childhood vaccination uptake across the U.S. population.](#) - GMI Summary

Pubmed Data : [J Toxicol Environ Health A. 2011 Jan ;74\(14\):903-16. PMID: 21623535](#)

Article Published Date : Jan 01, 2011

Authors : Gayle DeLong

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[There is evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD.](#) - GMI Summary

Pubmed Data : [Transl Neurodegener. 2013 ;2\(1\):25. Epub 2013 Dec 19. PMID: 24354891](#)

Article Published Date : Dec 31, 2012

Authors : David A Geier, Brian S Hooker, Janet K Kern, Paul G King, Lisa K Sykes, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Mercury : CK\(131\) : AC\(17\)](#), [Thimerosal : CK\(367\) : AC\(23\)](#)

[There were 69 reports of Guillain-Barré Syndrome \(GBS\) after Gardasil vaccination that occurred in the United States between 2006 and 2009.](#) - GMI Summary

Pubmed Data : [Vaccine. 2010 Sep 23. Epub 2010 Sep 23. PMID: 20869467](#)

Article Published Date : Sep 23, 2010

Authors : Nizar Souayah, P A Michas-Martin, Abu Nasar, Nataliya Krivitskaya, Hussam A Yacoub, Hafiz Khan, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Thirty-five percent of children with juvenile idiopathic arthritis experienced flare of the disease after vaccination.](#) - GMI Summary

Pubmed Data : [Clin Exp Rheumatol. 2012 Mar 15. Epub 2012 Mar 15. PMID: 22513085](#)

Article Published Date : Mar 15, 2012

Authors : Natasa Toplak, Vesna Subelj, Tanja Kveder, Sasa Cucnik, Katarina Prosenec, Alenka Trampus-Bakija, Ljupco Todorovski, Tadej Avcin

Study Type : Human Study

Additional Links

Diseases : [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Timing of routine immunisations \(earlier = increased\) and subsequent hay fever risk.](#) - GMI Summary

Pubmed Data : Arch Dis Child. 2005 Jun ;90(6):567-73. PMID: [15908618](#)

Article Published Date : May 31, 2005

Authors : S A Bremner, I M Carey, S DeWilde, N Richards, W C Maier, S R Hilton, D P Strachan, D G Cook

Study Type : Human Study

Additional Links

Diseases : [Allergic Rhinitis : CK\(340\) : AC\(40\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Vaccination for DPT, Hepatitis B and influenza has been reported to be associated with the development of erythema multiforme in an infant.](#) - GMI Summary

Pubmed Data : Indian J Dermatol Venereol Leprol. 2008 May-Jun;74(3):251-3. PMID: [18583795](#)

Article Published Date : May 01, 2008

Authors : Sarvjit Kaur, Sanjeev Handa

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Vaccinated children and adults may serve as reservoirs for silent pertussis infection and become potential transmitters to unprotected infants.](#) - GMI Summary

Pubmed Data : Emerg Infect Dis. 2000 Sep-Oct;6(5):526-9. PMID: [10998384](#)

Article Published Date : Sep 01, 2000

Authors : I Srugo, D Benilevi, R Madeb, S Shapiro, T Shohat, E Somekh, Y Rimmar, V Gershtein, R Gershtein, E Marva, N Lahat

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) :](#)

[Vaccination can precipitate lupus erythematosus.](#) - GMI Summary

Pubmed Data : Semin Arthritis Rheum. 1999 Dec;29(3):131-9. PMID: [10622677](#)

Article Published Date : Dec 01, 1999

Authors : S A Older, D F Battafarano, R J Enzenauer, A M Krieg

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Vaccination is associated with thrombocytopenic purpura in children.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Feb 26;25(10):1838-40. Epub 2006 Nov 9. PMID: [17126957](#)

Article Published Date : Feb 26, 2007

Authors : J Rajantie, B Zeller, I Treutiger, S Rosthøj,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination-associated adverse events occur in approximately 1 of every 6 toddlers receiving measles-mumps-rubella vaccine dose 1, with high fever occurring in 1 of 20](#) - GMI Summary

Pubmed Data : Pediatrics. 2006 Oct;118(4):1422-30. PMID: [17015532](#)

Article Published Date : Oct 01, 2006

Authors : Charles W LeBaron, Daoling Bi, Bradley J Sullivan, Carol Beck, Paul Gargiullo

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Whole cell pertussis vaccines may have been causing serious neurological disorders.](#) - GMI Summary

Pubmed Data : Brain Dev. 2004 Aug;26(5):296-300. PMID: [15165669](#)

Article Published Date : Aug 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Infant Neurological Development : CK\(46\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Zinc supplementation has a beneficial effect on malaise, one of the influenza vaccine associated adverse events, and decrease serum TNF- \$\alpha\$ levels.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2011 Apr 21. Epub 2011 Apr 21. PMID: [21514808](#)

Article Published Date : Apr 21, 2011

Authors : S Songül Yalçın, Defne Engür-Karasınav, Dursun Alehan, Kadriye Yurdakök, Süheyla Ozkutlu, Turgay Coşkun

Study Type : Human Study

Additional Links

Substances : [Zinc : CK\(880\) : AC\(128\)](#)

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A case of extensive ulcerating vasculitis following a BCG vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Plast Reconstr Aesthet Surg. 2009 Aug;62(8):e286-9. Epub 2007 Dec 31. PMID: [18166508](#)

Article Published Date : Aug 01, 2009

Authors : A Ghattaura, K A Eley, E Molenaar, G Smith

Study Type : Human: Case Report

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#)

[A case of Leukemia Cutis arising at the site of injection of a Tetanus Booster has been reported.](#) - GMI Summary

Pubmed Data : Actas Dermosifiliogr. 2010 Oct;101(8):727-9. PMID: [20965018](#)

Article Published Date : Oct 01, 2010

Authors : R M Guinovart, J M Carrascosa, C Ferrándiz

Study Type : Human: Case Report

Additional Links

Diseases : [Leukemia Cutis : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Acute immune thrombocytopenic purpura as adverse reaction to oral polio vaccine \(OPV\).](#) - GMI Summary

Pubmed Data : Hum Vaccin Immunother. 2013 Jun 4 ;9(8). Epub 2013 Jun 4. PMID: [23807364](#)

Article Published Date : Jun 03, 2013

Authors : Cheng-Qiang Jin, Hai-Xin Dong, Zhuo-Xiang Sun, Jian-Wei Zhou, Cui-Yun Dou, Shu-Hua Lu, Rui-Rui Yang

Study Type : Human: Case Report

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#)

[Acute transverse myelitis after influenza vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Neuroimaging. 1996 Oct;6(4):248-50. PMID: [8903080](#)

Article Published Date : Oct 01, 1996

Authors : R Bakshi, J C Mazziotta

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : [CK\(39\)](#) : [AC\(5\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2011 Jan;45(1):e8. Epub 2010 Dec 28. PMID: [21189364](#)

Article Published Date : Jan 01, 2011

Authors : Sabrina Montagnani, Marco Tuccori, Giuseppe Lombardo, Arianna Testi, Stefania Mantarro, Elisa Ruggiero, Corrado Blandizzi

Study Type : Human: Case Report

Additional Links

Diseases : [Hemolytic Anemia](#) : [CK\(75\)](#) : [AC\(5\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Autoimmunity following hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 Feb ;21(2):146-52. PMID: [22235045](#)

Article Published Date : Jan 31, 2012

Authors : Y Zafrir, N Agmon-Levin, Z Paz, T Shilton, Y Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases](#) : [CK\(5523\)](#) : [AC\(880\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

Adverse Pharmacological Actions : [Immunotoxic](#) : [CK\(254\)](#) : [AC\(48\)](#)

[Case report: a shoulder injury related to vaccine administration.](#) - GMI Summary

Pubmed Data : J Am Board Fam Med. 2012 Nov ;25(6):919-22. PMID: [23136333](#)

Article Published Date : Oct 31, 2012

Authors : Matthew G Barnes, Christopher Ledford, Karen Hogan

Study Type : Human: Case Report

Additional Links

Diseases : [Shoulder Injuries](#) : [CK\(23\)](#) : [AC\(2\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Deep morphea after vaccination in two young children has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Dermatol. 2006 Sep-Oct;23(5):484-7. PMID: [17014648](#)

Article Published Date : Sep 01, 2006

Authors : Antonio Torrelo, José Suárez, Isabel Colmenero, Daniel Azorín, Antonio Perera, Antonio Zambrano

Study Type : Human: Case Report

Additional Links

Diseases : [Morphea profunda](#) : [CK\(3\)](#) : [AC\(1\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#)

[Delayed focal lipomatrophy after AS03-adjuvanted influenza A \(H1N1\) 2009 vaccine has been reported.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Dec 17. Epub 2010 Dec 17. PMID: [21172376](#)

Article Published Date : Dec 17, 2010

Authors : Emilie Javelle, Benjamin Soulier, Christian Brosset, Solène Lorcy, Fabrice Simon

Study Type : Human: Case Report

Additional Links

Diseases : [Lipoatrophy : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Diabetes Mellitus: Type 1 : CK\(1197\) : AC\(235\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussi eres

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine associated with dermatomyositis has been reported.](#) - GMI Summary

Pubmed Data : Rheumatol Int. 2008 Apr;28(6):609-12. Epub 2007 Nov 23. PMID: [18034245](#)

Article Published Date : Apr 01, 2008

Authors : Arie Altman, Martine Szyper-Kravitz, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Immune-mediated myelitis following hepatitis B vaccination has been reported.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2012 Apr 1. Epub 2012 Apr 1. PMID: [22498789](#)

Article Published Date : Apr 01, 2012

Authors : Joerg-Patrick Stübgen

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : [CK\(39\)](#) : [AC\(5\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

[In 1985 twin boys simultaneously succumbed to sudden unexpected deaths two to three hours after vaccination with diphtheria, tetanus, and pertussis vaccine \(DTP\).](#) - GMI Summary

Pubmed Data : Arch Dis Child. 1987 Jul;62(7):754-9. PMID: [3498443](#)

Article Published Date : Jul 01, 1987

Authors : S C Roberts

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\)](#) : [CK\(138\)](#) : [AC\(18\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : [CK\(282\)](#) : [AC\(31\)](#)

[Influenza vaccination did not reduce the risk of subsequent hospital admission among patients with vaccine failure. These findings do not support the hypothesis that vaccination mitigates influenza illness severity.](#) - GMI Summary

Pubmed Data : Vaccine. 2014 Jan 16 ;32(4):453-7. Epub 2013 Nov 26. PMID: [24291201](#)

Article Published Date : Jan 15, 2014

Authors : Huong Q McLean, Jennifer K Meece, Edward A Belongia

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Additional Keywords : [Vaccine Failure](#) : [CK\(244\)](#) : [AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Measles vaccine and glyphosate-induced parkinsonism has been reported.](#) - GMI Summary

Pubmed Data : Arq Neuropsiquiatr. 2003 Jun ;61(2B):381-6. Epub 2003 Jul 28. PMID: [12894271](#)

Article Published Date : Jun 01, 2003

Authors : Maria do Desterro Leiros da Costa, Lílian Regina Gonçalves, Egberto Reis Barbosa, Luiz Alberto Bacheschi

Study Type : Human: Case Report

Additional Links

Diseases : [Glyphosate Toxicity](#) : [CK\(29\)](#) : [AC\(14\)](#), [Parkinsonian Disorders](#) : [CK\(15\)](#) : [AC\(4\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Measles](#) : [CK\(157\)](#) : [AC\(16\)](#)

Problem Substances : [Glyphosate](#) : [CK\(403\)](#) : [AC\(130\)](#)

Adverse Pharmacological Actions : [Neurotoxic](#) : [CK\(1116\)](#) : [AC\(188\)](#)

[Optic neuritis following hepatitis B vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2009 Nov;72(11):594-7. PMID: [19948437](#)

Article Published Date : Nov 01, 2009

Authors : Muferet Erguven, Sirin Guven, Umit Akyuz, Olcay Bilgiç, Fuat Laloglu

Study Type : Human: Case Report

Additional Links

Diseases : [Optic Neuritis](#) : [CK\(23\)](#) : [AC\(3\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

Possible systemic lupus erythematosus following HPV immunization has been reported. - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):158-61. PMID: [22235047](#)

Article Published Date : Jan 01, 2012

Authors : Hf Soldevilla, Sfr Briones, Sv Navarra

Study Type : Human: Case Report

Additional Links

Diseases : [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardisil\) : CK\(105\) : AC\(13\)](#)

The psychic reactions following injections of bacterial vaccines. - GMI Summary

Pubmed Data : Int Arch Allergy Appl Immunol. 1950 ;1(3):226-43. PMID: [14794265](#)

Authors : J ILAVSKY

Study Type : Human: Case Report

Additional Links

Diseases : [Psychiatric Disorders : CK\(71\) : AC\(10\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Vaccination as a probable cause of incontinentia pigmenti reactivation has been reported. - GMI Summary

Pubmed Data : Pediatr Dermatol. 2010 Jan-Feb;27(1):62-4. PMID: [20199413](#)

Article Published Date : Jan 01, 2010

Authors : Ali Alikhan, Andrew D Lee, Donald Swing, Christie Carroll, Gil Yosipovitch

Study Type : Human: Case Report

Additional Links

Diseases : [Incontinentia Pigmenti : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows. - GMI Summary

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Chevillie

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce autoimmune demyelination.](#) - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rubella](#) : CK(54) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Fatal adverse pulmonary reaction in calves after inadvertent intravenous vaccination has been reported.](#) - GMI Summary

Pubmed Data : Vet Pathol. 2005 Jul;42(4):492-5. PMID: [16006609](#)

Article Published Date : Jul 01, 2005

Authors : J D Ramsay, C L Williams, E Simko

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Animal Model](#) : CK(41) : AC(17)

[Hepatitis B vaccine alters the expression of 144 genes in the mouse liver within 1 day of vaccination, 7 of which are related to inflammation and metabolism.](#) - GMI Summary

Pubmed Data : Mol Biol Rep. 2011 Jun 21. Epub 2011 Jun 21. PMID: [21691704](#)

Article Published Date : Jun 21, 2011

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine induces cell death in liver cells and mouse liver.](#) - GMI Summary

Pubmed Data : Apoptosis. 2012 Jan 17. Epub 2012 Jan 17. PMID: [22249285](#)

Article Published Date : Jan 17, 2012

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Changchun Li, Mengjin Zhu, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Liver Damage](#) : CK(648) : AC(226), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

Adverse Pharmacological Actions : [Hepatotoxic](#) : CK(301) : AC(85)

[Maturation changes in amygdala volume and the binding capacity of an opioid antagonist in the amygdala was significantly altered in infant macaques receiving the vaccine schedule.](#) - GMI Summary

Pubmed Data : Acta Neurobiol Exp (Wars). 2010 ;70(2):147-64. PMID: [20628439](#)

Article Published Date : Dec 31, 2009

Authors : Laura Hewitson, Brian J Lopresti, Carol Stott, N Scott Mason, Jaime Tomko

Study Type : Animal Study

Additional Links

Diseases : [Amygdala: Damage/Abnormalities : CK\(12\) : AC\(1\)](#), [Neurodevelopmental Disorders : CK\(124\) : AC\(13\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Problem Substances : [Thimerosal : CK\(367\) : AC\(23\)](#)

[Newborn primates receiving mercury-containing hepatitis B vaccines exhibit neurodevelopmental delays. - GMI Summary](#)

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(19):1298-313. PMID: [20711932](#)

Article Published Date : Jan 01, 2010

Authors : Laura Hewitson, Lisa A Houser, Carol Stott, Gene Sackett, Jaime L Tomko, David Atwood, Lisa Blue, E Railey White

Study Type : Animal Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Post-infection rabies vaccination increases mortality in mice. - GMI Summary](#)

Pubmed Data : Comp Immunol Microbiol Infect Dis. 1988;11(2):139-42. PMID: [2972508](#)

Article Published Date : Jan 01, 1988

Authors : J Blancou, D Sitte

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%. - GMI Summary](#)

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies. - GMI Summary](#)

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does. - GMI Summary](#)

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The mercury containing vaccine adjuvant known as thimerosal has immunosuppressive and autoimmune effects in mice.](#) - GMI Summary

Pubmed Data : Toxicol Appl Pharmacol. 2005 Apr 15;204(2):109-21. PMID: [15808517](#)

Article Published Date : Apr 15, 2005

Authors : S Havarinasab, B Häggqvist, E Björn, K M Pollard, P Hultman

Study Type : Animal Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The use of animal cells in the production of vaccines may cause infection by endogenous retroviruses associated with chronic fatigue and prostate cancer.](#) - GMI Summary

Pubmed Data : Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8. PMID: [20378372](#)

Article Published Date : May 01, 2010

Authors : Takayuki Miyazawa

Study Type : Animal Study

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Prostate Cancer : CK\(1024\) : AC\(311\)](#), [Retroviruses : CK\(7\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly.](#) - GMI Summary

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The vaccine adjuvant thimerosal induces adverse changes in the cerebellum of mice, lending plausibility to the association between autism and low-dose mercury exposure.](#) - GMI Summary

Pubmed Data : Cell Biol Toxicol. 2009 Apr 9. PMID: [19357975](#)

Article Published Date : Apr 09, 2009

Authors : Takeshi Minami, Eriko Miyata, Yamato Sakamoto, Hideo Yamazaki, Seiji Ichida

Study Type : Animal Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[There is evidence that a DNA vaccine exhibits anti-fertility properties.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jul 12 ;29(31):4933-9. Epub 2011 May 17. PMID: [21596079](#)

Article Published Date : Jul 12, 2011

Authors : Meng-Fei Yu, Wen-Ning Fang, Gao-Feng Xiong, Ying Yang, Jing-Pian Peng

Study Type : Animal Study

Additional Links

Diseases : [Infertility : CK\(576\) : AC\(109\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Plasmid DNA Vaccines : CK\(3\) : AC\(2\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25.](#) - GMI Summary

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escjadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced scrapie has been reported in animals.](#) - GMI Summary

Pubmed Data : J Gen Virol. 2003 Apr;84(Pt 4):1047-52. PMID: [12655108](#)

Article Published Date : Apr 01, 2003

Authors : Gianluigi Zanusso, Cristina Casalone, Pierluigi Acutis, Elena Bozzetta, Alessia Farinazzo, Matteo Gelati, Michele Fiorini, Gianluigi Forloni, Man Sun Sy, Salvatore Monaco, Maria Caramelli

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Animal Diseases: Scrapie : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

["Adverse events associated with 17D-derived yellow fever vaccination--United States, 2001-2002."](#) - GMI Summary

Pubmed Data : MMWR Morb Mortal Wkly Rep. 2002 Nov 8 ;51(44):989-93. PMID: [12455906](#)

Article Published Date : Nov 08, 2002

Study Type : Review

Additional Links

Diseases : [Brain Inflammation : CK\(86\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

["Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations."](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):223-30. PMID: [22235057](#)

Article Published Date : Jan 01, 2012

Authors : L Tomljenovic, Ca Shaw

Study Type : Review

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum : CK\(166\) : AC\(43\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

"Viral nucleic acids in live-attenuated vaccines: detection of minority variants and an adventitious virus." - GMI Summary

Pubmed Data : J Virol. 2010 Jun ;84(12):6033-40. Epub 2010 Apr 7. PMID: [20375174](#)

Article Published Date : May 31, 2010

Authors : Joseph G Victoria, Chunlin Wang, Morris S Jones, Crystal Jaing, Kevin McLoughlin, Shea Gardner, Eric L Delwart

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Adventitious Viruses : CK\(18\) : AC\(9\)](#), [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Acute disseminated encephalomyelitis (ADEM) may be caused by vaccination. - GMI Summary

Pubmed Data : J Clin Neurosci. 2008 Dec;15(12):1315-22. Epub 2008 Oct 30. PMID: [18976924](#)

Article Published Date : Dec 01, 2008

Authors : William Huynh, Dennis J Cordato, Elias Kehdi, Lynette T Masters, Chris Dedousis

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Encephalomyelitis : CK\(12\) : AC\(7\)](#), [Neuromyelitis Optica : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Adjuvants in vaccines may trigger innate cells response by toll-like receptors, thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity. - GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Immune Disorders: B-Cell Over-Activity : CK\(2\) : AC\(2\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#)

Aluminium-containing adjuvants in vaccines may be causing autoimmune conditions such as chronic fatigue syndrome and the inflammatory myopathy known as macrophagic myofasciitis. - GMI Summary

Pubmed Data : Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11. PMID: [19004564](#)

Article Published Date : Feb 01, 2009

Authors : Christopher Exley, Louise Swarbrick, Rhomain K Gherardi, Francois-Jérôme Authier

Study Type : Commentary

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Myopathy: Inflammatory : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Autism spectrum disorders are associated with vaccination, heavy metal toxicity and excitotoxicity. - GMI Summary

Pubmed Data : Altern Ther Health Med. 2008 Nov-Dec;14(6):46-53. PMID: [19043938](#)

Article Published Date : Nov 01, 2008

Authors : Russell L Blaylock

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Excitotoxicity : CK\(57\) : AC\(34\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[DTP vaccination may contribute to urinary tract disease and sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : Reprod Biomed Online. 2010 Jul;21(1):100-8. Epub 2010 Mar 30. PMID: [15356430](#)

Article Published Date : Jul 01, 2010

Authors : Joseph Prandota

Study Type : Commentary

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Urinary Tract Infections : CK\(338\) : AC\(47\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women.](#) - GMI Summary

Pubmed Data : Am J Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Feline injection site-associated sarcoma is a serious problem associated with malignancy.](#) - GMI Summary

Pubmed Data : Vet Microbiol. 2006 Oct 5;117(1):59-65. PMID: [16769184](#)

Article Published Date : Oct 05, 2006

Authors : Jolle Kirpensteijn

Study Type : Review

Additional Links

Diseases : [Sarcoma : CK\(42\) : AC\(26\)](#), [Tumors : CK\(199\) : AC\(116\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[From 1990 to the present, the number of cases \(n = 31\) and deaths \(n = 12\) from the yellow fever vaccine in travelers has exceeded the reports of YF \(n = 6\) acquired by natural infection.](#) - GMI Summary

Pubmed Data : Expert Rev Vaccines. 2012 Apr ;11(4):427-48. PMID: [22551029](#)

Article Published Date : Apr 01, 2012

Authors : Thomas P Monath

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Yellow Fever : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis. - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccinations is associated with autoimmune hazards. - GMI Summary

Pubmed Data : Autoimmun Rev. 2005 Feb;4(2):96-100. PMID: [15722255](#)

Article Published Date : Feb 01, 2005

Authors : Marc Girard

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

HIV-1/AIDS may have been caused by contaminated polio vaccines grown in SIV infected chimpanzee kidney cells during the late 1950's. - GMI Summary

Pubmed Data : Mol Nutr Food Res. 2010 Jan 28. Epub 2010 Jan 28. PMID: [11405924](#)

Article Published Date : Jan 28, 2010

Authors : E Hooper

Study Type : Commentary

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

In 2011, there were an extra 47,500 new cases of non-polio acute flaccid paralysis (NPAFP); Clinically indistinguishable from polio paralysis but twice as deadly, the incidence of NPAFP was directly proportional to doses of oral polio received. - GMI Summary

Pubmed Data : Indian J Med Ethics. 2012 Apr-Jun;9(2):114-7. PMID: [22591873](#)

Article Published Date : Apr 01, 2012

Authors : Neetu Vashisht, Jacob Puliyel

Study Type : Review

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Infection and vaccines are triggers for autoimmune disease. - GMI Summary

Pubmed Data : Autoimmunity. 2005 May;38(3):235-45. PMID: [16126512](#)

Article Published Date : May 01, 2005

Authors : Vered Molina, Yehuda Shoenfeld

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)
Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Measles vaccination in developing countries has resulted in higher infant mortality rates.](#) - GMI Summary

Pubmed Data : BMJ. 1993 Nov 20;307(6915):1294-5. PMID: [8257878](#)

Article Published Date : Nov 20, 1993

Authors : A J Hall, F T Cutts

Study Type : Review

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Over 40,000 cases of AFP are reported annually since 2007 regardless of the number of actual polio cases.](#) - GMI Summary

Pubmed Data : BMC Public Health. 2012 ;12:229. Epub 2012 Mar 22. PMID: [22439606](#)

Article Published Date : Jan 01, 2012

Authors : Rie R Yotsu, Katharine Abba, Helen Smith, Abhijit Das

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#), [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Review: possible adverse effects that are associated with smallpox vaccination.](#) - GMI Summary

Pubmed Data : MMWR Recomm Rep. 2003 Feb 21;52(RR-4):1-28. PMID: [12617510](#)

Article Published Date : Feb 21, 2003

Authors : Joanne Cono, Christine G Casey, David M Bell,

Study Type : Review

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Rotavirus vaccines have been found contaminated with porcine circovirus.](#) - GMI Summary

Pubmed Data : Biologicals. 2012 Mar 6. Epub 2012 Mar 6. PMID: [22402185](#)

Article Published Date : Mar 06, 2012

Authors : Sarah M Gilliland, Lindsay Forrest, Heather Carre, Adrian Jenkins, Neil Berry, Javier Martin, Philip Minor, Silke Schepelmann

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[The epidemic of autism may be linked to both vaccinations and mitochondrial diseases.](#) - GMI Summary

Pubmed Data : Clin Exp Pharmacol Physiol. 2004 Dec;31 Suppl 2:S51-3 PMID: [19043939](#)

Article Published Date : Dec 01, 2004

Authors : Stephanie F Cave

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Mercury Poisoning](#) : CK(172) : AC(45), [Mitochondrial Diseases](#) : CK(157) : AC(57), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Diseases that are Linked](#) : CK(2142) : AC(272)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis](#) : CK(53) : AC(15), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Hepatitis B](#) : CK(219) : AC(37), [Neuritis: Brachial Plexus](#) : CK(1) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Tetanus](#) : CK(61) : AC(8)

[The number of elective abortions following vaccination during pregnancy may be under-reported and could be substantial.](#) - GMI Summary

Pubmed Data : Vaccine. 2008 May 2;26(19):2428-32. Epub 2008 Mar 17. PMID: [18406499](#)

Article Published Date : May 02, 2008

Authors : Soju Chang, Robert Ball, M Miles Braun

Study Type : Review

Additional Links

Diseases : [Abortion: Spontaneous](#) : CK(204) : AC(29), [Vaccination: Abortion](#) : CK(40) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Transmissible spongiform encephalopathies may be passed iatrogenically through vaccines.](#) - GMI Summary

Pubmed Data : Dev Biol (Basel). 2001;106:455-9; discussion 460-1, 465-75. PMID: [11761262](#)

Article Published Date : Jan 01, 2001

Authors : N R Cashman

Study Type : Commentary

Additional Links

Diseases : [Spongiform Encephalopathies: Transmissible](#) : CK(2) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Vaccination against novel H1N1 may accelerate atherogenesis \(heart disease\).](#) - GMI Summary

Pubmed Data : Med Microbiol Immunol. 2009 Oct 23. PMID: [19851782](#)

Article Published Date : Oct 23, 2009

Authors : Sucharit Bhakdi, Karl Lackner, Hans-Wilhelm Doerr

Study Type : Commentary

Additional Links

Diseases : [H1N1 Infection](#) : CK(468) : AC(88), [Swine Flu Associated Virus](#) : CK(145) : AC(32), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Vaccination for contraception.](#) - GMI Summary

Pubmed Data : Aust N Z J Obstet Gynaecol. 1994 Jun;34(3):320-9. PMID: [7848209](#)

Article Published Date : Jun 01, 1994

Authors : W R Jones

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anti-Fertility : CK\(1\) : AC\(1\)](#)

[Vaccination may be contributing to autoimmune disease.](#) - GMI Summary

Pubmed Data : J Autoimmun. 2000 Feb;14(1):1-10. PMID: [10648110](#)

Article Published Date : Feb 01, 2000

Authors : Y Shoenfeld, A Aron-Maor

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Vaccination proponents have suggested that breastfeeding should be delayed in order to prevent immune factors within breast milk from inactivating vaccine-associated antibody titer elevations and vaccine potency.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2010 Oct;29(10):919-923. PMID: [20442687](#)

Article Published Date : Oct 01, 2010

Authors : Sung-Sil Moon, Yuhuan Wang, Andi L Shane, Trang Nguyen, Pratima Ray, Penelope Dennehy, Luck Ju Baek, Umesh Parashar, Roger I Glass, Baoming Jiang

Study Type : Commentary

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccine-derived poliovirus may become pathogenic in complex viral ecosystems, through frequent recombination events and mutations.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2012 May 1 ;205(9):1363-73. Epub 2012 Mar 29. PMID: [22457288](#)

Article Published Date : May 01, 2012

Authors : Marie-Line Joffret, Sophie Jégouic, Maël Bessaud, Jean Balanant, Coralie Tran, Valerie Caro, Barbara Holmblat, Richter Razafindratsimandresy, Jean-Marc Reynes, Mala Rakoto-Andrianarivelo, Francis Delpeyroux

Study Type : Review

Additional Links

Diseases : [Polio](#) : CK(19) : AC(8), [Polio: Vaccine-Related](#) : CK(1) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Polio](#) : CK(94) : AC(15)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder](#) : CK(134) : AC(12), [Attention Deficit Disorder with Hyperactivity](#) : CK(242) : AC(31), [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Child Mortality](#) : CK(64) : AC(8), [Infant Mortality](#) : CK(249) : AC(25), [Mental Retardation](#) : CK(71) : AC(7), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Thimerosal](#) : CK(3) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Measles

["The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate."](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2012 ;2:CD004407. Epub 2012 Feb 15. PMID: [22336803](#)

Article Published Date : Dec 31, 2011

Authors : Vittorio Demicheli, Alessandro Rivetti, Maria Grazia Debalini, Carlo Di Pietrantonj

Study Type : Meta Analysis

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Mumps](#) : CK(41) : AC(1), [Rubella](#) : CK(54) : AC(4)

Additional Keywords : [Rubella](#) : CK(54) : AC(4), [Vaccine Safety](#) : CK(21) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

["A history of prior vaccination is not always associated with immunity nor with the presence of specific antibodies."](#) - GMI Summary

Pubmed Data : Clin Invest Med. 1988 Aug ;11(4):304-9. PMID: [3168353](#)

Article Published Date : Jul 31, 1988

Authors : L Sekla, W Stackiw, G Eibisch, I Johnson

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8)

Additional Keywords : [Antibody Theory Of Vaccinology](#) : CK(75) : AC(5), [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Measles](#) : CK(157) : AC(16)

[A 1993 outbreak of measles in a highly immunised Australian population.](#) - GMI Summary

Pubmed Data : Aust J Public Health. 1994 Sep ;18(3):249-52. PMID: [7841251](#)

Article Published Date : Aug 31, 1994

Authors : A Herceg, I Passaris, C Mead

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Measles](#) : CK(157) : AC(16)

[A low measles vaccine efficacy rate may explain the less-than-expected gains attributable to vaccination. - GMI Summary](#)

Pubmed Data : BMC Int Health Hum Rights. 2009 ;9 Suppl 1:S6. Epub 2009 Oct 14. PMID: [19828064](#)

Article Published Date : Dec 31, 2008

Authors : Robert J Ledogar, John Fleming, Neil Andersson

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A major measles epidemic occurred in 1989 in the region of Quebec despite a 99% vaccine coverage. - GMI Summary](#)

Pubmed Data : Can J Public Health. 1991 May-Jun;82(3):189-90. PMID: [1884314](#)

Article Published Date : Apr 30, 1991

Authors : N Boulianne, G De Serres, B Duval, J R Joly, F Meyer, P Déry, M Alary, D Le Hénaff, N Thériault

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak at a college with a prematriculation immunization requirement. - GMI Summary](#)

Pubmed Data : Am J Public Health. 1991 Mar ;81(3):360-4. PMID: [1994745](#)

Article Published Date : Feb 28, 1991

Authors : B S Hersh, L E Markowitz, R E Hoffman, D R Hoff, M J Doran, J C Fleishman, S R Preblud, W A Orenstein

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak in Montana in 1985 indicates vaccine failure. - GMI Summary](#)

Pubmed Data : Am J Epidemiol. 1987 Sep ;126(3):438-49. PMID: [3618578](#)

Article Published Date : Aug 31, 1987

Authors : R M Davis, E D Whitman, W A Orenstein, S R Preblud, L E Markowitz, A R Hinman

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[An outbreak of measles occurred in a high school with a documented vaccination level of 98 per cent. - GMI Summary](#)

Pubmed Data : Am J Public Health. 1987 Apr ;77(4):434-8. PMID: [3826461](#)

Article Published Date : Mar 31, 1987

Authors : B M Nkowane, S W Bart, W A Orenstein, M Baltier

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Despite a high coverage with measles vaccines in parts of west Africa, epidemics of measles occur with reduced severity in an increasing proportion of older children who have been vaccinated.](#) - GMI Summary

Pubmed Data : Lancet. 1999 Jan 9 ;353(9147):98-102. PMID: [10023894](#)

Article Published Date : Jan 08, 1999

Authors : H C Whittle, P Aaby, B Samb, H Jensen, J Bennett, F Simondon

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population.](#) - GMI Summary

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)

Article Published Date : Dec 31, 2013

Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Brachytherapy : CK\(10\) : AC\(1\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Even though 95% of the children had measles antibodies after vaccination, vaccine efficacy was not more than 68%.](#) - GMI Summary

Pubmed Data : J Infect Dis. 1990 Nov ;162(5):1043-8. PMID: [2230232](#)

Article Published Date : Oct 31, 1990

Authors : P Aaby, K Knudsen, T G Jensen, J Thårup, A Poulsen, M Sodemann, M C da Silva, H Whittle

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[High titre measles vaccination increases female mortality in those receiving immunization in West Africa.](#) - GMI Summary

Pubmed Data : Int J Epidemiol. 1996 Jun;25(3):665-73. PMID: [8671571](#)

Article Published Date : Jun 01, 1996

Authors : K M Knudsen, P Aaby, H Whittle, M Rowe, B Samb, F Simondon, J Sterne, P Fine

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[High-titer measles vaccination before 9 months of age has been linked to increased female mortality.](#) - GMI Summary

Pubmed Data : Semin Pediatr Infect Dis. 2003 Jul;14(3):220-32. PMID: [12913835](#)

Article Published Date : Jul 01, 2003

Authors : Peter Aaby, Henrik Jensen, Francois Simondon, Hilton Whittle

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[In a measles outbreak from March 1991 to April 1992 in Rio de Janeiro 76.4% of those suspected to be infected had received measles vaccine before their first birthday. - GMI Summary](#)

Pubmed Data : Rev Soc Bras Med Trop. 1995 Oct-Dec;28(4):339-43. PMID: [8668833](#)

Article Published Date : Sep 30, 1995

Authors : S A de Oliveira, W N Soares, M O Dalston, M T de Almeida, A J Costa

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles outbreak in a fully immunized secondary-school population with up to 99 percent vaccination. - GMI Summary](#)

Pubmed Data : N Engl J Med. 1987 Mar 26 ;316(13):771-4. PMID: [3821823](#)

Article Published Date : Mar 25, 1987

Authors : T L Gustafson, A W Lievens, P A Brunell, R G Moellenberg, C M Buttery, L M Sehulster

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles, mumps, and rubella catch up immunisation in a measles epidemic did not appear to confer protection and was associated with a variety of new side effects of the vaccine. - GMI Summary](#)

Pubmed Data : BMJ. 1995 Jun 24 ;310(6995):1629-32. PMID: [7795447](#)

Article Published Date : Jun 23, 1995

Authors : R J Roberts, Q D Sandifer, M R Evans, M Z Nolan-Farrell, P M Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Passive acquired immunity against measles in infants born to naturally infected and vaccinated mothers. - GMI Summary](#)

Pubmed Data : Med Sci Monit. 2003 Dec ;9(12):CR541-6. PMID: [14646978](#)

Article Published Date : Nov 30, 2003

Authors : Leszek Szenborn, Annedore Tischer, Jerzy Pejcz, Zbigniew Rudkowski, Marta Wójcika

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Passive immunity against measles is superior in infants of mothers who experienced naturally acquired measles infection versus those who were vaccinated.](#) - GMI Summary

Pubmed Data : Vaccine. 1997 Apr-May;15(6-7):620-3. PMID: [9178461](#)

Article Published Date : Mar 31, 1997

Authors : G De Serres, J R Joly, M Fauvel, F Meyer, B Mâsse, N Boulianne

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Health Myths Explored : CK\(22\) : AC\(4\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Primary and secondary vaccine failure may explain the 1992 measles epidemic in Cape Town.](#) - GMI Summary

Pubmed Data : S Afr Med J. 1994 Mar ;84(3):145-9. PMID: [7740350](#)

Article Published Date : Feb 28, 1994

Authors : N Coetzee, G D Hussey, G Visser, P Barron, A Keen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein \(the protective coating of the nerves\) contributing to the pathogenesis of autism.](#) - GMI Summary

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[The occurrence of secondary vaccine failure and vaccine-modified measles in the United States may lead to underreporting of measles cases and result in overestimation of vaccine efficacy in h](#) - GMI Summary

Pubmed Data : JAMA. 1990 May 9 ;263(18):2467-71. PMID: [2278542](#)

Article Published Date : May 08, 1990

Authors : M B Edmonson, D G Addiss, J T McPherson, J L Berg, S R Circo, J P Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[There is evidence that measles vaccine recipients can shed measles vaccine.](#) - GMI Summary

Pubmed Data : J Clin Microbiol. 1995 Sep ;33(9):2485-8. PMID: [7494055](#)

Article Published Date : Aug 31, 1995

Authors : P A Rota, A S Khan, E Durigon, T Yuran, Y S Villamarzo, W J Bellini

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. - GMI Summary](#)

Pubmed Data : Am J Clin Nutr. 2004 Jul ;80(1):193-8. PMID: [15213048](#)

Article Published Date : Jun 30, 2004

Authors : Laura E Caulfield, Mercedes de Onis, Monika Blössner, Robert E Black

Study Type : Human Study

Additional Links

Diseases : [Diarrhea : CK\(544\) : AC\(73\)](#), [Malaria : CK\(89\) : AC\(30\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Additional Keywords : [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Case report: an outbreak of measles among persons with prior evidence of immunity, New York City, 2011. - GMI Summary](#)

Pubmed Data : Clin Infect Dis. 2014 May ;58(9):1205-10. Epub 2014 Feb 27. PMID: [24585562](#)

Article Published Date : Apr 30, 2014

Authors : Jennifer B Rosen, Jennifer S Rota, Carole J Hickman, Sun B Sowers, Sara Mercader, Paul A Rota, William J Bellini, Ada J Huang, Margaret K Doll, Jane R Zucker, Christopher M Zimmerman

Study Type : Human: Case Report

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[In this animal study measles vaccine did not prevent infection or disease against wild type MeV. - GMI Summary](#)

Pubmed Data : MBio. 2014 ;5(2):e01047. Epub 2014 Apr 15. PMID: [24736226](#)

Article Published Date : Dec 31, 2013

Authors : Wen-Hsuan W Lin, Chien-Hsiung Pan, Robert J Adams, Beth L Laube, Diane E Griffin

Study Type : Animal Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles vaccination in developing countries has resulted in higher infant mortality rates. - GMI Summary](#)

Pubmed Data : BMJ. 1993 Nov 20;307(6915):1294-5. PMID: [8257878](#)

Article Published Date : Nov 20, 1993

Authors : A J Hall, F T Cutts

Study Type : Review

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-](#)

[spectrum disorder.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Topic: [Influenza](#)

[Influenza vaccination for healthcare workers who work with the elderly has no effect on laboratory-proven influenza, pneumonia or deaths from pneumonia.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD005187. Epub 2010 Feb 17. PMID: [20166073](#)

Article Published Date : Jan 01, 2010

Authors : Roger E Thomas, Tom Jefferson, Toby J Lasserson

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is a lack of evidence for the effectiveness of influenza vaccines in adults aged 65 years or older.](#) - GMI Summary

Pubmed Data : Lancet Infect Dis. 2011 Oct 25. Epub 2011 Oct 25. PMID: [22032844](#)

Article Published Date : Oct 25, 2011

Authors : Michael T Osterholm, Nicholas S Kelley, Alfred Sommer, Edward A Belongia

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is no solid evidence available supporting the belief that vaccines are effective in preventing influenza in the elderly.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD004876. Epub 2010 Feb 17. PMID: [20166072](#)

Article Published Date : Jan 01, 2010

Authors : Tom Jefferson, Carlo Di Pietrantonj, Lubna A Al-Ansary, Eliana Ferroni, Sarah Thorning, Roger E Thomas

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[We concluded that there is no credible evidence that vaccination of healthy people under the age of 60, who are healthcare workers caring for the elderly, affects influenza complications in those cared for.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2006 ;3:CD005187. Epub 2006 Jul 19. PMID: [16856082](#)

Article Published Date : Jan 01, 2006

Authors : R E Thomas, T Jefferson, V Demicheli, D Rivetti

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#)

Additional Keywords : [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Annual influenza vaccination hampers the development of virus-specific CD8\(+\) T cell responses necessary to protect against influenza infection.](#) - GMI

Summary

Pubmed Data : J Virol. 2011 Nov ;85(22):11995-2000. Epub 2011 Aug 31. PMID: [21880755](#)

Article Published Date : Nov 01, 2011

Authors : Rogier Bodewes, Pieter L A Fraaij, Martina M Geelhoed-Mieras, Carel A van Baalen, Harm A W M Tiddens, Annemarie M C van Rossum, Fiona R van der Klis, Ron A M Fouchier, Albert D M E Osterhaus, Guus F Rimmelzwaan

Study Type : Human Study

Additional Links

Diseases : [Cystic Fibrosis](#) : [CK\(523\)](#) : [AC\(78\)](#), [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

Adverse Pharmacological Actions : [Immunosuppressive](#) : [CK\(156\)](#) : [AC\(26\)](#)

[Influenza vaccination may increase the risk of Guillain-Barré Syndrome.](#) - GMI

Summary

Pubmed Data : Kidney Int. 2008 Dec;74(11):1461-7. Epub 2008 Sep 24. PMID: [18592444](#)

Article Published Date : Dec 01, 2008

Authors : C I Blanco-Marchite, L Buznego-Suárez, M A Fagúndez-Vargas, M Méndez-Llatas, P Pozo-Martos

Study Type : Human Study

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant](#) : [CK\(13\)](#) : [AC\(2\)](#), [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#)

[Influenza vaccines were not shown to be effective among children 6 to 59 months of age during 2 influenza seasons.](#) - GMI Summary

Pubmed Data : Anticancer Res. 2009 Nov;29(11):4629-32. PMID: [18838647](#)

Article Published Date : Nov 01, 2009

Authors : Peter G Szilagyi, Gerry Fairbrother, Marie R Griffin, Richard W Hornung, Stephanie Donauer, Ardythe Morrow, Mekibib Altaye, Yuwei Zhu, Sandra Ambrose, Kathryn M Edwards, Katherine A Poehling, Geraldine Lofthus, Michol Holloway, Lyn Finelli, Marika Iwane, Mary Allen Staat,

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections](#) : [CK\(275\)](#) : [AC\(29\)](#), [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy](#) : [CK\(104\)](#) : [AC\(2\)](#), [Autoimmune Diseases](#) : [CK\(5523\)](#) : [AC\(880\)](#), [Guillain-Barre Syndrome](#) : [CK\(84\)](#) : [AC\(14\)](#), [Influenza](#) : [CK\(656\)](#) : [AC\(99\)](#), [Swine Flu Associated Virus](#) :

[CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Widening influenza vaccine coverage is not correleated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussières

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[H1N1 vaccination has been linked to possible new-onset seizure.](#) - GMI Summary

Pubmed Data : Pharmacotherapy. 2011 Jan;31(1):113. PMID: [21182364](#)

Article Published Date : Jan 01, 2011

Authors : [No authors listed]

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Seizures : CK\(135\) : AC\(33\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination did not reduce the risk of subsequent hospital admission among patients with vaccine failure. These findings do not support the hypothesis that vaccination mitigates influenza illness severity.](#) - GMI Summary

Pubmed Data : Vaccine. 2014 Jan 16 ;32(4):453-7. Epub 2013 Nov 26. PMID: [24291201](#)

Article Published Date : Jan 15, 2014

Authors : Huong Q McLean, Jennifer K Meece, Edward A Belongia

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Chickenpox](#)

[Administration of varicella vaccine before the age of 15 months, and the](#)

prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease. - GMI Summary

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Mullooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#), [Corticosteroid-Induced Toxicity : CK\(78\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Approximately 1 in every 5 children who receives 1 dose of varicella vaccine may develop varicella disease, also known as breakthrough disease, if exposed to varicella-zoster virus. - GMI Summary

Pubmed Data : J Infect Dis. 2008 Mar 1 ;197 Suppl 2:S127-31. PMID: [18419385](#)

Article Published Date : Feb 29, 2008

Authors : Sandra S Chaves, John Zhang, Rachel Civen, Barbara M Watson, Tina Carbajal, Dana Perella, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster (shingles) cases managed in the same time period. - GMI Summary

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Shingles : CK\(472\) : AC\(35\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Loss of vaccine-induced immunity to varicella over time. - GMI Summary

Pubmed Data : N Engl J Med. 2007 Mar 15 ;356(11):1121-9. PMID: [17360990](#)

Article Published Date : Mar 14, 2007

Authors : Sandra S Chaves, Paul Gargiullo, John X Zhang, Rachel Civen, Dalya Guris, Laurene Mascola, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Varicella vaccination in South Korea, despite high compliance rates (via mandatory vaccination), has not eradicated the disease. - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2014 May ;21(5):762-8. Epub 2014 Mar 26. PMID: [24671555](#)

Article Published Date : Apr 30, 2014

Authors : Sung Hee Oh, Eun Hwa Choi, Seon Hee Shin, Yun-Kyung Kim, Jin Keun Chang, Kyong Min Choi, Jae Kyun Hur, Kyung-Hyo Kim, Jae Youn Kim, Eun Hee Chung, Soo Young Lee, Su Eun Park, Sungho Cha,

Kwang-Nam Kim, Sang Hyuk Ma, Byung Wook Eun, Nam Hee Kim, Dae Sun Jo, Bo Youl Choi, Shin Ah Kim

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been associated with viremia and streptococcal toxic shock syndrome.](#) - GMI Summary

Pubmed Data : Med J Aust. 2009 Apr 20;190(8):451-3. PMID: [19374621](#)

Article Published Date : Apr 20, 2009

Authors : Claire M Italiano, Cheryl S Toi, Simon P Chan, Dominic E Dwyer

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Viremia : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to cause chronic, acyclovir-resistant herpes zoster infection in an immunosuppressed child.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2003 Oct 1;188(7):954-9. Epub 2003 Sep 26. PMID: [14513413](#)

Article Published Date : Oct 01, 2003

Authors : Myron J Levin, Karen M Dahl, Adriana Weinberg, Roger Giller, Amita Patel, Philip R Krause

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Acyclovir-Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to viral meningitis in an immunocompetent child.](#) - GMI Summary

Pubmed Data : Ann Emerg Med. 2009 Jun;53(6):792-5. Epub 2008 Nov 22. PMID: [19028409](#)

Article Published Date : Jun 01, 2009

Authors : Sujit Iyer, Manoj K Mittal, Richard L Hodinka

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Undefined : CK\(14\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine may be associated with aplastic anemia in children.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Aug;28(8):746-8. PMID: [19633522](#)

Article Published Date : Aug 01, 2009

Authors : Paola Angelini, Fotini Kavadas, Navneet Sharma, Susan E Richardson, Graham Tipples, Chaim Roifman, Yigal Dror, Yehuda Nofech-Mozes

Study Type : Human Study

Additional Links

Diseases : [Anemia: Aplastic : CK\(30\) : AC\(3\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others - Article 2.](#) - GMI

Summary

Pubmed Data : J Infect Dis. 1997 Oct;176(4):1072-5. PMID: [9333170](#)

Article Published Date : Oct 01, 1997

Authors : P LaRussa, S Steinberg, F Meurice, A Gershon

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others.](#) - GMI Summary

Pubmed Data : Homeopathy. 2009 Apr;98(2):77-82. PMID: [9255208](#)

Article Published Date : Apr 01, 2009

Authors : M B Salzman, R G Sharrar, S Steinberg, P LaRussa

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[A chickenpox outbreak occurred in a school in which 97% of students without a prior history of chickenpox were vaccinated.](#) - GMI Summary

Pubmed Data : Pediatrics. 2004 Mar ;113(3 Pt 1):455-9. PMID: [14993534](#)

Article Published Date : Feb 29, 2004

Authors : Barna D Tugwell, Lore E Lee, Hilary Gillette, Eileen M Lorber, Katrina Hedberg, Paul R Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Sudden Infant Death Syndrome \(SIDS\)](#)

[Over 600 cases of sudden infant death syndrome following vaccination were reported from 1990-1997.](#) - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2001 Jun-Jul;10(4):279-85. PMID: [11760487](#)

Article Published Date : Jun 01, 2001

Authors : L E Silvers, S S Ellenberg, R P Wise, F E Varricchio, G T Mootrey, M E Salive

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination in infants less than 3 months is associated with an increased risk of sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : Fundam Clin Pharmacol. 1995;9(3):263-70. PMID: [7557822](#)

Article Published Date : Jan 01, 1995

Authors : A P Jonville-Bera, E Autret, J Laugier

Study Type : Meta Analysis

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-](#)

[Serious adverse events associated with whole cell pertussis vaccine, e.g. sudden infant death syndrome and encephalopathy, may have occurred in metabolically vulnerable children.](#) - GMI Summary

Pubmed Data : Pharmazie. 2007 Apr;62(4):299-304. PMID: [19660877](#)

Article Published Date : Apr 01, 2007

Authors : Kumanan Wilson, Beth Potter, Douglas Manuel, Jennifer Keelan, Pranesh Chakraborty

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing : CK\(20\) : AC\(2\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Sudden infant death syndrome and DTP vaccine timing may be linked.](#) - GMI Summary

Pubmed Data : Otol Neurotol. 2002 Jul;23(4):447-51. PMID: [6835859](#)

Article Published Date : Jul 01, 2002

Authors : L J Baraff, W J Ablon, R C Weiss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Sudden Infant Death syndrome mortality rate in the period zero to three days following DTP was found to be 7.3 times higher than in the period 30 days after immunization.](#) - GMI Summary

Pubmed Data : Am J Public Health. 1987 Aug;77(8):945-51. PMID: [3496805](#)

Article Published Date : Aug 01, 1987

Authors : A M Walker, H Jick, D R Perera, R S Thompson, T A Knauss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[A case of sudden infant death associated with hexavalent immunization has been reported.](#) - GMI Summary

Pubmed Data : Forensic Sci Int. 2008 Aug 6;179(2-3):e25-9. Epub 2008 Jun 6. PMID: [18538957](#)

Article Published Date : Aug 06, 2008

Authors : Stefano D'Errico, Margherita Neri, Irene Riezzo, Giuseppina Rossi, Cristoforo Pomara, Emanuela Turillazzi, Vittorio Fineschi

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[In 1985 twin boys simultaneously succumbed to sudden unexpected deaths two to three hours after vaccination with diphtheria, tetanus, and pertussis vaccine \(DTP\).](#) - GMI Summary

Pubmed Data : Arch Dis Child. 1987 Jul;62(7):754-9. PMID: [3498443](#)

Article Published Date : Jul 01, 1987

Authors : S C Roberts

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Simultaneous sudden infant death syndrome has been reported in twins two days after receiving mutple vaccinations.](#) - GMI Summary

Pubmed Data : J Forensic Leg Med. 2007 Feb;14(2):87-91. PMID: [17654772](#)

Article Published Date : Feb 01, 2007

Authors : Yasemin Balci, Mehmet Tok, B Kenan Kocaturk, Cinar Yenilmez, Coşkun Yirulmaz

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Sudden infant death syndrome \(SIDS\) shortly after hexavalent vaccination has been reported.](#) - GMI Summary

Pubmed Data : Virchows Arch. 2006 Jan;448(1):100-4. Epub 2005 Oct 18. PMID: [16231176](#)

Article Published Date : Jan 01, 2006

Authors : Giulia Ottaviani, Anna Maria Lavezzi, Luigi Maturri

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

[DTP vaccination may contribute to urinary tract disease and sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : Reprod Biomed Online. 2010 Jul;21(1):100-8. Epub 2010 Mar 30. PMID: [15356430](#)

Article Published Date : Jul 01, 2010

Authors : Joseph Prandota

Study Type : Commentary

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Urinary Tract Infections : CK\(338\) : AC\(47\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Topic: Hepatitis B

Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem. - GMI Summary

Pubmed Data : Am J Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Infant Chemical Exposures : CK\(165\) : AC\(24\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

When polled 5% of nonpediatricians would not use Haemophilus influenzae type b vaccine if they had a child born in 2004. - GMI Summary

Pubmed Data : Pediatrics. 2005 Nov;116(5):e623-33. PMID: [16263976](#)

Article Published Date : Nov 01, 2005

Authors : Klara M Posfay-Barbe, Ulrich Heininger, Christoph Aebi, Daniel Desgrandchamps, Bernard Vaudaux, Claire-Anne Siegrist

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Acute hepatitis B can occur in those who are vaccinated against it and who are exposed through unprotected sexual contact and iatrogenically. - GMI Summary

Pubmed Data : Postgrad Med J. 2006 Mar;82(965):207-10. PMID: [16517803](#)

Article Published Date : Mar 01, 2006

Authors : G Rosner, Y Lurie, L Blendis, Z Halpern, R Oren

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Iatrogenic Disease : CK\(62\) : AC\(7\)](#)

Additional Keywords : [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations. - GMI Summary

Pubmed Data : Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24. PMID: [18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications : CK\(32\) : AC\(4\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Silicone Implant Toxicity : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Silicone Implants : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination with or without hepatitis B immunoglobulin at birth to babies born of HBsAg-positive mothers prevents overt HBV transmission but may not prevent occult HBV infection in babies: a randomized controlled trial.](#) - GMI Summary

Article Published Date : Oct 31, 2013

Authors : C Pande, S K Sarin, S Patra, A Kumar, S Mishra, S Srivastava, K Bhutia, E Gupta, C K Mukhopadhyay, A K Dutta, S S Trivedi

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Additional Keywords : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Hepatitis Viruses : CK\(1\) : AC\(1\)](#)

[Hepatitis B vaccine is associated with an increased risk of multiple sclerosis.](#) - GMI Summary

Pubmed Data : Neurology. 2004 Sep 14;63(5):838-42. PMID: [15365133](#)

Article Published Date : Sep 14, 2004

Authors : Miguel A Hernán, Susan S Jick, Michael J Olek, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Hepatitis B Vaccine : CK\(30\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Newborn primates receiving mercury-containing hepatitis B vaccines exhibit neurodevelopmental delays.](#) - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(19):1298-313. PMID: [20711932](#)

Article Published Date : Jan 01, 2010

Authors : Laura Hewitson, Lisa A Houser, Carol Stott, Gene Sackett, Jaime L Tomko, David Atwood, Lisa Blue, E Railey White

Study Type : Animal Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccinations is associated with autoimmune hazards.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2005 Feb;4(2):96-100. PMID: [15722255](#)

Article Published Date : Feb 01, 2005

Authors : Marc Girard

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The demyelinating effect of hepatitis B vaccination could be due to the contamination of the vaccine by partial hepatitis B virus polymerase.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2005;65(3):509-20. PMID: [15908138](#)

Article Published Date : Jan 01, 2005

Authors : E Faure

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: Infant Mortality

38,787 adverse events including infant death (highest in 1-3 month olds) after vaccination were reported between 1991-1994. (The authors speciously claim SIDS and not vaccination caused these deaths). - GMI Summary

Pubmed Data : J Pediatr. 1997 Oct;131(4):529-35. PMID: [9386653](#)

Article Published Date : Oct 01, 1997

Authors : M M Braun, S S Ellenberg

Study Type : Meta Analysis

Additional Links

Diseases : [Hearing Loss: Sudden](#) : CK(30) : AC(3), [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Over 600 cases of sudden infant death syndrome following vaccination were reported from 1990-1997. - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2001 Jun-Jul;10(4):279-85. PMID: [11760487](#)

Article Published Date : Jun 01, 2001

Authors : L E Silvers, S S Ellenberg, R P Wise, F E Varricchio, G T Mootrey, M E Salive

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

There is a highly statistically significant correlation between increasing number of vaccine doses and increasing infant mortality rates. - GMI Summary

Pubmed Data : Hum Exp Toxicol. 2011 May 4. Epub 2011 May 4. PMID: [21543527](#)

Article Published Date : May 04, 2011

Authors : Neil Z Miller, Gary S Goldman

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Among female infants, those who receive both BCG and DTP vaccines experience higher mortality than those who receive only one of the two vaccines. - GMI Summary

Pubmed Data : Trop Med Int Health. 2005 Oct;10(10):947-55. PMID: [16185228](#)

Article Published Date : Oct 01, 2005

Authors : Lawrence H Moulton, Lakshmi Rahmathullah, Neal A Halsey, R D Thulasiraj, Joanne Katz, James M Tielsch

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau. - GMI Summary

Pubmed Data : [Vaccine](#). 2013 Dec 7. pii: S0264-410X(13)01663-0. doi: 10.1016/j.vaccine.2013.11.074.

Article Published Date : Dec 06, 2013

Authors : Ane Bærent Fisker, Henrik Ravn, Amabelia Rodrigues, Marie Drivsholm Ostergaard, Carlito Bale, Christine Stabell Benn, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: Combinations : CK\(20\) : AC\(2\)](#)

[Diphtheria-tetanus-peteruss vaccines increase child mortality in rural Guinea-Bissau.](#) - GMI Summary

Pubmed Data : Int J Epidemiol. 2004 Apr;33(2):374-80. PMID: [15082643](#)

Article Published Date : Apr 01, 2004

Authors : Peter Aaby, Henrik Jensen, Joaquim Gomes, Manual Fernandes, Ida Maria Lisse

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau.](#) - GMI Summary

Pubmed Data : [Vaccine.](#) 2007 Jan 26;25(7):1265-9. Epub 2006 Oct 18.

Article Published Date : Jan 25, 2007

Authors : Peter Aaby, Sidu Biai, Jens Erik Veirum, Morten Sodemann, Ida Lisse, May-Lill Garly, Henrik Ravn, Christine Stabell Benn, Amabelia Rodrigues

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Combinations : CK\(20\) : AC\(2\)](#)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects.](#) - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccinaton: Diphtheria : CK\(50\) : AC\(2\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder](#) : CK(134) : AC(12), [Attention Deficit Disorder with Hyperactivity](#) : CK(242) : AC(31), [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Child Mortality](#) : CK(64) : AC(8), [Infant Mortality](#) : CK(249) : AC(25), [Mental Retardation](#) : CK(71) : AC(7), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Thimerosal](#) : CK(3) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: [Whooping Cough](#)

[The risk of adverse events from the pertussis outweighed the risk of pertussis infection during the period of 1970-83 in children living in non-deprived circumstances in Britain.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1985;61:395-405. PMID: [3835080](#)

Article Published Date : Jan 01, 1985

Authors : G T Stewart

Study Type : Meta Analysis

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

["Primary infections with either B. pertussis or Bordetella parapertussis stimulated a vigorous antibody response to ACT. In contrast, patients in whom DTP and DTaP vaccines failed had minimal ACT antibody responses."](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2004 Feb 15 ;38(4):502-7. Epub 2004 Jan 29. PMID: [14765342](#)

Article Published Date : Feb 14, 2004

Authors : James D Cherry, Dorothy X L Xing, Penny Newland, Kashmira Patel, Ulrich Heininger, Michael J Corbel

Study Type : Human Study

Additional Links

Diseases : [Parapertussis](#) : CK(10) : AC(1), [Whooping Cough](#) : CK(66) : AC(7)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis \(Tdap\) vaccine in order to prevent pertussis infection in their offspring, it does not reduce](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14), [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14), [Vaccination: Tetanus](#) : CK(61) : AC(8)

[Pertussis epidemic despite high levels of vaccination coverage with acellular](#)

[pertussis vaccine.](#) - GMI Summary

Article Published Date : Nov 07, 2013

Authors : Maria-Rosa Sala-Farré, César Arias-Varela, Assumpta Recasens-Recasens, Maria Simó-Sanahuja, Carmen Muñoz-Almagro, Josefa Pérez-Jové

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : [CK\(142\)](#) : [AC\(14\)](#), [Whooping Cough](#) : [CK\(66\)](#) : [AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : [CK\(282\)](#) : [AC\(31\)](#)

[Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1994 Jul 7;331(1):16-21. PMID: [8202096](#)

Article Published Date : Jul 07, 1994

Authors : C D Christie, M L Marx, C D Marchant, S F Reising

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : [CK\(142\)](#) : [AC\(14\)](#), [Whooping Cough](#) : [CK\(66\)](#) : [AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : [CK\(282\)](#) : [AC\(31\)](#), [Vaccination: Pertussis](#) : [CK\(116\)](#) : [AC\(14\)](#)

[Vaccinated children and adults may serve as reservoirs for silent pertussis infection and become potential transmitters to unprotected infants.](#) - GMI Summary

Pubmed Data : Emerg Infect Dis. 2000 Sep-Oct;6(5):526-9. PMID: [10998384](#)

Article Published Date : Sep 01, 2000

Authors : I Srugo, D Benilevi, R Madeb, S Shapiro, T Shohat, E Somekh, Y Rimmer, V Gershtein, R Gershtein, E Marva, N Lahat

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : [CK\(142\)](#) : [AC\(14\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#), [Whooping Cough](#) : [CK\(66\)](#) : [AC\(7\)](#)

Additional Keywords : [Whooping Cough](#) : [CK\(66\)](#) : [AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Pertussis](#) : [CK\(116\)](#) : [AC\(14\)](#)

[Lactobacillus bulgaricus contains a substance which may improve immunogenicity and reduce the toxicity of pertussis vaccination \(whooping cough vaccine\).](#) - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 1986 Jan;(1):62-5. PMID: [3705806](#)

Article Published Date : Jan 01, 1986

Authors : I B Shepeleva, N S Zakharova, T N Remova, I G Bazhanova, M V Britsina

Study Type : Animal Study

Additional Links

Substances : [Lactobacillus bulgaricus](#) : [CK\(35\)](#) : [AC\(8\)](#)

Diseases : [Pertussis](#) : [CK\(142\)](#) : [AC\(14\)](#), [Whooping Cough](#) : [CK\(66\)](#) : [AC\(7\)](#)

Additional Keywords : [Vaccine Side Effect Attenuation](#) : [CK\(2\)](#) : [AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis](#) : [CK\(116\)](#) : [AC\(14\)](#)

[Pertussis vaccination and asthma: is there a link?](#) - GMI Summary

Pubmed Data : JAMA. 1994 Aug 24-31;272(8):592-3. PMID: [8057511](#)

Article Published Date : Aug 23, 1994

Authors : M R Odent, E E Culpin, T Kimmel

Study Type : Commentary

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: [Pertussis](#)

[Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis \(Tdap\) vaccine in order to prevent pertussis infection in their offspring, it does not reduce - GMI Summary](#)

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[DPT vaccines have been associated with recurrent seizures. - GMI Summary](#)

Pubmed Data : Am J Dis Child. 1984 Oct;138(10):908-11. PMID: [6206715](#)

Article Published Date : Oct 01, 1984

Authors : J V Murphy, L D Sarff, K M Marquardt

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Seizures : CK\(135\) : AC\(33\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[In Kings County Washington, between 2002-2007, of the 176 confirmed cases of pertussis in infants under age 1 seventy-seven percent were age-appropriately vaccinated. - GMI Summary](#)

Pubmed Data : Arch Pediatr Adolesc Med. 2011 Jul ;165(7):647-52. PMID: [21727277](#)

Article Published Date : Jul 01, 2011

Authors : Matthew P Hanson, Tao S Kwan-Gett, Atar Baer, Krista Rietberg, Mara Ohrt, Jeffrey S Duchin

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pertussis epidemic despite high levels of vaccination coverage with acellular pertussis vaccine. - GMI Summary](#)

Article Published Date : Nov 07, 2013

Authors : Maria-Rosa Sala-Farré, César Arias-Varela, Assumpta Recasens-Recasens, Maria Simó-Sanahuja, Carmen Muñoz-Almagro, Josefa Pérez-Jové

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease. - GMI

Summary

Pubmed Data : N Engl J Med. 1994 Jul 7;331(1):16-21. PMID: [8202096](#)

Article Published Date : Jul 07, 1994

Authors : C D Christie, M L Marx, C D Marchant, S F Reising

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Vaccinated children and adults may serve as reservoirs for silent pertussis infection and become potential transmitters to unprotected infants. - GMI

Summary

Pubmed Data : Emerg Infect Dis. 2000 Sep-Oct;6(5):526-9. PMID: [10998384](#)

Article Published Date : Sep 01, 2000

Authors : I Srugo, D Benilevi, R Madeb, S Shapiro, T Shohat, E Somekh, Y Rimmar, V Gershtein, R Gershtein, E Marva, N Lahat

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Lactobacillus bulgaricus contains a substance which may improve immunogenicity and reduce the toxicity of pertussis vaccination (whooping cough vaccine). - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 1986 Jan;(1):62-5. PMID: [3705806](#)

Article Published Date : Jan 01, 1986

Authors : I B Shepeleva, N S Zakharova, T N Remova, I G Bazhanova, M V Britsina

Study Type : Animal Study

Additional Links

Substances : [Lactobacillus bulgaricus : CK\(35\) : AC\(8\)](#)

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Vaccine Side Effect Attenuation : CK\(2\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Despite high coverage rates for primary immunization in infants and children pertussis incidence rates are increasing. - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2005 May;24(5 Suppl):S10-8. PMID: [15876918](#)

Article Published Date : May 01, 2005

Authors : Tina Tan, Evelinda Trindade, Danuta Skowronski

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Underestimation of central nervous system complications after pertussis immunization appears to be prevalent. - GMI Summary

Pubmed Data : Acta Paediatr Jpn. 1991 Aug;33(4):421-7. PMID: [1792899](#)

Article Published Date : Aug 01, 1991

Authors : W Ehrengut

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: Rubella

"The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate." - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2012 ;2:CD004407. Epub 2012 Feb 15. PMID: [22336803](#)

Article Published Date : Dec 31, 2011

Authors : Vittorio Demicheli, Alessandro Rivetti, Maria Grazia Debalini, Carlo Di Pietrantonj

Study Type : Meta Analysis

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Rubella : CK\(54\) : AC\(4\)](#), [Vaccine Safety : CK\(21\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Congenital malformation is a possible consequence of rubella vaccination during pregnancy. - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population. - GMI Summary

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)

Article Published Date : Dec 31, 2013

Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Brachytherapy : CK\(10\) : AC\(1\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) :](#)

Measles, mumps, and rubella catch up immunisation in a measles epidemic did not appear to confer protection and was associated with a variety of new side effects of the vaccine. - GMI Summary

Pubmed Data : BMJ. 1995 Jun 24 ;310(6995):1629-32. PMID: [7795447](#)

Article Published Date : Jun 23, 1995

Authors : R J Roberts, Q D Sandifer, M R Evans, M Z Nolan-Farrell, P M Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce autoimmune demyelination. - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women. - GMI Summary

Pubmed Data : AmJ Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Autism Spectrum Disorders

Thimerosal-containing vaccines are associated with autism prevalence and measles-containing vaccines are associated with serious neurological disorders. - GMI Summary

Pubmed Data : Med Sci Monit. 2004 Mar;10(3):PI33-9. Epub 2004 Mar 1. PMID: [14976450](#)

Article Published Date : Mar 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Aluminum vaccine adjuvants appear to contribute to the rising prevalence of autism. - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1489-99. Epub 2011 Aug 23. PMID: [22099159](#)

Article Published Date : Nov 01, 2011

Authors : Lucija Tomljenovic, Christopher A Shaw

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#), [Neurotoxic : CK\(1116\) : AC\(188\)](#)

Autistic children have elevated levels of measles antibodies indicating that measles vaccination may be causing autoimmunity in these children. - GMI Summary

Pubmed Data : Pediatr Neurol. 2003 Apr;28(4):292-4. PMID: [12849883](#)

Article Published Date : Apr 01, 2003

Authors : Vijendra K Singh, Ryan L Jensen

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders. - GMI Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein (the protective coating of the nerves) contributing to the pathogenesis of autism. - GMI Summary

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

There is a positive association between autism prevalence and childhood vaccination uptake across the U.S. population. - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2011 Jan ;74(14):903-16. PMID: [21623535](#)

Article Published Date : Jan 01, 2011

Authors : Gayle DeLong

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[There is evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD. - GMI Summary](#)

Pubmed Data : Transl Neurodegener. 2013 ;2(1):25. Epub 2013 Dec 19. PMID: [24354891](#)

Article Published Date : Dec 31, 2012

Authors : David A Geier, Brian S Hooker, Janet K Kern, Paul G King, Lisa K Sykes, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Mercury : CK\(131\) : AC\(17\)](#), [Thimerosal : CK\(367\) : AC\(23\)](#)

[Autism spectrum disorders are associated with vaccination, heavy metal toxicity and excitotoxicity. - GMI Summary](#)

Pubmed Data : Altern Ther Health Med. 2008 Nov-Dec;14(6):46-53. PMID: [19043938](#)

Article Published Date : Nov 01, 2008

Authors : Russell L Blaylock

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Excitotoxicity : CK\(57\) : AC\(34\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Autoimmune autistic disorder, a major subset of autism, is associated with autoantibody formation caused by viral \(wild and vaccine-induced\) infection. - GMI Summary](#)

Pubmed Data : Ann Clin Psychiatry. 2009 Jul-Sep;21(3):148-61. PMID: [19758536](#)

Article Published Date : Jul 01, 2009

Authors : Vijendra K Singh

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Biological assays lend support to the association between measles virus or MMR and autism. - GMI Summary](#)

Pubmed Data : J Neurovirol. 2005 Feb ;11(1):1-10. PMID: [15804954](#)

Article Published Date : Jan 31, 2005

Authors : Jane E Libbey, Thayne L Sweeten, William M McMahon, Robert S Fujinami

Study Type : Review

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Conjugate vaccines may predispose children to autism spectrum disorders. -](#)

GMI Summary

Pubmed Data : Med Hypotheses. 2011 Oct 10. Epub 2011 Oct 10. PMID: [21993250](#)

Article Published Date : Oct 10, 2011

Authors : Brian J Richmand

Study Type : Review

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Conjugate Vaccines : CK\(1\) : AC\(1\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Streptococcus Pneumoniae : CK\(1\) : AC\(1\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-spectrum disorder.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[The epidemic of autism may be linked to both vaccinations and mitochondrial diseases.](#) - GMI Summary

Pubmed Data : Clin Exp Pharmacol Physiol. 2004 Dec;31 Suppl 2:S51-3 PMID: [19043939](#)

Article Published Date : Dec 01, 2004

Authors : Stephanie F Cave

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Mitochondrial Diseases : CK\(157\) : AC\(57\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination may be contributing to autoimmune disease.](#) - GMI Summary

Pubmed Data : J Autoimmun. 2000 Feb;14(1):1-10. PMID: [10648110](#)

Article Published Date : Feb 01, 2000

Authors : Y Shoenfeld, A Aron-Maor

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder : CK\(134\) : AC\(12\)](#), [Attention Deficit Disorder with Hyperactivity : CK\(242\) : AC\(31\)](#), [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Child Mortality : CK\(64\) : AC\(8\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Mental Retardation : CK\(71\) : AC\(7\)](#),

[Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Autism](#)

[Male newborns vaccinated with hepatitis B prior to 1999 had a 3-fold higher risk for parentally reported autism. - GMI Summary](#)

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(24):1665-77. PMID: [21058170](#)

Article Published Date : Jan 01, 2010

Authors : Carolyn M Gallagher, Melody S Goodman

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Thimerosal-containing vaccines are associated with autism prevalence and measles-containing vaccines are associated with serious neurological disorders. - GMI Summary](#)

Pubmed Data : Med Sci Monit. 2004 Mar;10(3):PI33-9. Epub 2004 Mar 1. PMID: [14976450](#)

Article Published Date : Mar 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Aluminum vaccine adjuvants appear to contribute to the rising prevalence of autism. - GMI Summary](#)

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1489-99. Epub 2011 Aug 23. PMID: [22099159](#)

Article Published Date : Nov 01, 2011

Authors : Lucija Tomljenovic, Christopher A Shaw

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#), [Neurotoxic : CK\(1116\) : AC\(188\)](#)

[The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein \(the protective coating of the nerves\) contributing to the pathogenesis of autism. - GMI Summary](#)

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[There is a positive association between autism prevalence and childhood vaccination uptake across the U.S. population. - GMI Summary](#)

Pubmed Data : J Toxicol Environ Health A. 2011 Jan ;74(14):903-16. PMID: [21623535](#)

Article Published Date : Jan 01, 2011

Authors : Gayle DeLong

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[There is evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD. - GMI Summary](#)

Pubmed Data : Transl Neurodegener. 2013 ;2(1):25. Epub 2013 Dec 19. PMID: [24354891](#)

Article Published Date : Dec 31, 2012

Authors : David A Geier, Brian S Hooker, Janet K Kern, Paul G King, Lisa K Sykes, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Mercury : CK\(131\) : AC\(17\)](#), [Thimerosal : CK\(367\) : AC\(23\)](#)

[Autoimmune autistic disorder, a major subset of autism, is associated with autoantibody formation caused by viral \(wild and vaccine-induced\) infection. - GMI Summary](#)

Pubmed Data : Ann Clin Psychiatry. 2009 Jul-Sep;21(3):148-61. PMID: [19758536](#)

Article Published Date : Jul 01, 2009

Authors : Vijendra K Singh

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Conjugate vaccines may predispose children to autism spectrum disorders. - GMI Summary](#)

Pubmed Data : Med Hypotheses. 2011 Oct 10. Epub 2011 Oct 10. PMID: [21993250](#)

Article Published Date : Oct 10, 2011

Authors : Brian J Richmand

Study Type : Review

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Conjugate Vaccines : CK\(1\) : AC\(1\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Streptococcus Pneumoniae : CK\(1\) : AC\(1\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-spectrum disorder. - GMI Summary](#)

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin. - GMI Summary](#)

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children. - GMI Summary](#)

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder : CK\(134\) : AC\(12\)](#), [Attention Deficit Disorder with Hyperactivity : CK\(242\) : AC\(31\)](#), [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Child Mortality : CK\(64\) : AC\(8\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Mental Retardation : CK\(71\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Topic: Guillain-Barre Syndrome](#)

["Chart-confirmed guillain-barre syndrome after 2009 H1N1 influenza vaccination among the Medicare population, 2009-2010." - GMI Summary](#)

Pubmed Data : Am J Epidemiol. 2013 Sep 15 ;178(6):962-73. Epub 2013 May 6. PMID: [23652165](#)

Article Published Date : Sep 14, 2013

Authors : Laura L Polakowski, Sukhminder K Sandhu, David B Martin, Robert Ball, Thomas E Macurdy, Riley L Franks, Jonathan M Gibbs, Garner F Kropp, Armen Avagyan, Jeffrey A Kelman, Christopher M Worrall, Guoying Sun, Rebecca E Kliman, Dale R Burwen

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

["Risk of Guillain-Barré syndrome after 2010-2011 influenza vaccination." - GMI Summary](#)

Pubmed Data : Eur J Epidemiol. 2013 May ;28(5):433-44. Epub 2013 Mar 31. PMID: [23543123](#)

Article Published Date : Apr 30, 2013

Authors : Francesca Galeotti, Marco Massari, Roberto D'Alessandro, Ettore Beghi, Adriano Chiò, Giancarlo Logroscino, Graziella Filippini, Maria Donata Benedetti, Maura Pugliatti, Carmela Santuccio, Roberto Raschetti,

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [H1N1 Infection](#) : CK(468) : AC(88)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis](#) : CK(1493) : AC(221), [Arthritis: Rheumatoid](#) : CK(295) : AC(53), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Glomerulonephritis](#) : CK(41) : AC(9), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Multiple Sclerosis](#) : CK(746) : AC(133), [Myelitis](#) : CK(39) : AC(5), [Optic Neuritis](#) : CK(23) : AC(3), [Pancytopenia](#) : CK(12) : AC(2), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Thrombocytopenia](#) : CK(231) : AC(25)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[In the US the highest number of cases of Guillain-Barre syndrome are associated with influenza and hepatitis B vaccines.](#) - GMI Summary

Pubmed Data : J Clin Neuromuscul Dis. 2009 Sep;11(1):1-6. PMID: [19730016](#)

Article Published Date : Sep 01, 2009

Authors : Nizar Souayah, Abu Nasar, M Fareed K Suri, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy](#) : CK(104) : AC(2), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Influenza](#) : CK(656) : AC(99), [Swine Flu Associated Virus](#) : CK(145) : AC(32), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Influenza Vaccine](#) : CK(10) : AC(1), [Swine Flu Vaccine](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[There were 69 reports of Guillain-Barré Syndrome \(GBS\) after Gardasil vaccination that occurred in the United States between 2006 and 2009.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Sep 23. Epub 2010 Sep 23. PMID: [20869467](#)

Article Published Date : Sep 23, 2010

Authors : Nizar Souayah, P A Michas-Martin, Abu Nasar, Nataliya Krivitskaya, Hussam A Yacoub, Hafiz Khan, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported. - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussières

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections](#) : CK(275) : AC(29), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Influenza](#) : CK(656) : AC(99), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Guillain-Barré syndrome following hepatitis B vaccination has been reported. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2004 Nov-Dec;22(6):767-70. PMID: [15638054](#)

Article Published Date : Nov 01, 2004

Authors : M Khamaisi, Y Shoenfeld, H Orbach

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions. - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis](#) : CK(53) : AC(15), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Hepatitis B](#) : CK(219) : AC(37), [Neuritis: Brachial Plexus](#) : CK(1) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Tetanus](#) : CK(61) : AC(8)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: Thrombocytopenia

Over 1,000 confirmed cases of vaccine-induced thrombocytopenia were reported between 1990-2008. - GMI Summary

Pubmed Data : Vaccine. 2010 Nov 29. Epub 2010 Nov 29. PMID: [21126606](#)

Article Published Date : Nov 29, 2010

Authors : Emily Jane Woo, Robert P Wise, David Menschik, Sean V Shadomy, John Iskander, Judy Beeler, Frederick Varricchio, Robert Ball

Study Type : Meta Analysis

Additional Links

Diseases : [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Measles-mumps-rubella vaccine that is given in the second year of life is associated with an increased risk of immune thrombocytopenia purpura. - GMI Summary

Pubmed Data : Pediatrics. 2008 Mar;121(3):e687-92. PMID: [18310189](#)

Article Published Date : Mar 01, 2008

Authors : Eric K France, Jason Glanz, Stanley Xu, Simon Hambidge, Kristi Yamasaki, Steve B Black, Michael Marcy, John P Mullooly, Lisa A Jackson, James Nordin, Edward A Belongia, K Hohman, Robert T Chen, Robert Davis,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

MMR vaccination is associated with an increased risk for idiopathic thrombocytopenic purpura. - GMI Summary

Pubmed Data : Br J Clin Pharmacol. 2003 Jan;55(1):107-11. PMID: [12534647](#)

Article Published Date : Jan 01, 2003

Authors : Corri Black, James A Kaye, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccination is associated with an increased risk of developing acute immune thrombocytopenia in childhood.](#) - GMI Summary

Pubmed Data : Drug Saf. 2010;33(1):65-72. PMID: [20000868](#)

Article Published Date : Jan 01, 2010

Authors : Federica Bertuola, Carla Morando, Francesca Menniti-Ippolito, Roberto Da Cas, Annalisa Capuano, Giorgio Perilongo, Liviana Da Dalt

Study Type : Human Study

Additional Links

Diseases : [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination is associated with thrombocytopenic purpura in children.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Feb 26;25(10):1838-40. Epub 2006 Nov 9. PMID: [17126957](#)

Article Published Date : Feb 26, 2007

Authors : J Rajantie, B Zeller, I Treutiger, S Rosthøj,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Diabetes Mellitus: Type 1 : CK\(1197\) : AC\(235\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Multiple Sclerosis](#)

["Yellow fever vaccination and increased relapse rate in travelers with multiple sclerosis."](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1267-71. Epub 2011 Jun 13. PMID: [21670384](#)

Article Published Date : Oct 01, 2011

Authors : Mauricio F Farez, Jorge Correale

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

Children vaccinated with MMR before age 10 are at significantly higher risk of multiple sclerosis. - GMI Summary

Pubmed Data : Eur J Epidemiol. 2009;24(9):541-52. Epub 2009 Jul 26. PMID: [19633994](#)

Article Published Date : Jan 01, 2009

Authors : Cecilia Ahlgren, Kjell Torén, Anders Odén, Oluf Andersen

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Hepatitis B vaccination coverage has fallen to beneath 30% in France due to concerns over safety. - GMI Summary

Pubmed Data : J Clin Virol. 2009 Nov;46(3):202-5. Epub 2009 Aug 28. PMID: [19716764](#)

Article Published Date : Nov 01, 2009

Authors : Marta A Balinska

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination is associated with an increased risk of CNS inflammatory demyelination after 3 years of age. - GMI Summary

Pubmed Data : Reprod Toxicol. 2002 May-Jun;16(3):237-43. PMID: [18843097](#)

Article Published Date : May 01, 2002

Authors : Yann Mikaeloff, Guillaume Caridade, Samy Suissa, Marc Tardieu

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Inflammation : CK\(1125\) : AC\(377\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccine is associated with an increased risk of multiple sclerosis. - GMI Summary

Pubmed Data : Neurology. 2004 Sep 14;63(5):838-42. PMID: [15365133](#)

Article Published Date : Sep 14, 2004

Authors : Miguel A Hernán, Susan S Jick, Michael J Olek, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce autoimmune demyelination.](#) - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rubella](#) : CK(54) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Swine flu vaccine adjuvants may cause harm in patients with autoimmune diseases such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2010 Feb 18. Epub 2010 Feb 18. PMID: [20171793](#)

Article Published Date : Feb 18, 2010

Authors : Serefnur Oztürk

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[The demyelinating effect of hepatitis B vaccination could be due to the contamination of the vaccine by partial hepatitis B virus polymerase.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2005;65(3):509-20. PMID: [15908138](#)

Article Published Date : Jan 01, 2005

Authors : E Faure

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Vaccination may be contributing to autoimmune disease.](#) - GMI Summary

Pubmed Data : J Autoimmun. 2000 Feb;14(1):1-10. PMID: [10648110](#)

Article Published Date : Feb 01, 2000

Authors : Y Shoenfeld, A Aron-Maor

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Viruses \(wild-type or recombinant vaccine-type\) can silently prime for and trigger central nervous system autoimmune disease.](#) - GMI Summary

Pubmed Data : J Neurovirol. 2001 Jun;7(3):220-7. PMID: [11517396](#)

Article Published Date : Jun 01, 2001

Authors : D J Theil, I Tsunoda, F Rodriguez, J L Whitton, R S Fujinami

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Multiple Sclerosis](#) : CK(746) : AC(133)

Additional Keywords : [Diseases that are Linked](#) : CK(2142) : AC(272)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Topic: Pregnancy: Vaccination](#)

[Maternal influenza vaccination during pregnancy does not reduce the incidence of acute respiratory illness visits among infants.](#) - GMI Summary

Pubmed Data : Cancer Sci. 2004 Jul;95(7):596-601. PMID: [17146026](#)

Article Published Date : Jul 01, 2004

Authors : Eric K France, Renae Smith-Ray, David McClure, Simon Hambidge, Stanley Xu, Kristi Yamasaki, David Shay, Eric Weintraub, Alicia M Fry, Steve B Black, Henry R Shinefield, John P Mullooly, Lisa A Jackson

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Infections](#) : CK(410) : AC(44), [Pregnancy: Vaccination](#) : CK(92) : AC(16), [Upper Respiratory Infections](#) : CK(824) : AC(90)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Congenital malformation is a possible consequence of rubella vaccination](#)

during pregnancy. - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth. - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women. - GMI Summary

Pubmed Data : AmJ Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Autoimmune Diseases

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination may contribute to autoimmune demyelinating complications due to immunological cross-reactivity between Hepatitis B virus surface antigen and myelin basic protein.](#) - GMI Summary

Pubmed Data : Clin Dev Immunol. 2005 Sep;12(3):217-24. PMID: [16295528](#)

Article Published Date : Sep 01, 2005

Authors : Dimitrios-Petrou Bogdanos, Heather Smith, Yun Ma, Harold Baum, Giorgina Mieli-Vergani, Diego Vergani

Study Type : Human Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Hepatitis B Vaccine : CK\(30\) : AC\(2\)](#), [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein \(the protective coating of the nerves\) contributing to the pathogenesis of autism.](#) - GMI Summary

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Autoimmunity following hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 Feb ;21(2):146-52. PMID: [22235045](#)

Article Published Date : Jan 31, 2012

Authors : Y Zafrir, N Agmon-Levin, Z Paz, T Shilton, Y Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Diabetes Mellitus: Type 1 : CK\(1197\) : AC\(235\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The mercury containing vaccine adjuvant known as thimerosal has immunosuppressive and autoimmune effects in mice.](#) - GMI Summary

Pubmed Data : Toxicol Appl Pharmacol. 2005 Apr 15;204(2):109-21. PMID: [15808517](#)

Article Published Date : Apr 15, 2005

Authors : S Havarinasab, B Häggqvist, E Björn, K M Pollard, P Hultman

Study Type : Animal Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

["Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations."](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):223-30. PMID: [22235057](#)

Article Published Date : Jan 01, 2012

Authors : L Tomljenovic, Ca Shaw

Study Type : Review

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum : CK\(166\) : AC\(43\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

[Adjuvants in vaccines may trigger innate cells response by toll-like receptors,](#)

thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity. - GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Immune Disorders: B-Cell Over-Activity : CK\(2\) : AC\(2\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#)

Autoimmune autistic disorder, a major subset of autism, is associated with autoantibody formation caused by viral (wild and vaccine-induced) infection. - GMI Summary

Pubmed Data : Ann Clin Psychiatry. 2009 Jul-Sep;21(3):148-61. PMID: [19758536](#)

Article Published Date : Jul 01, 2009

Authors : Vijendra K Singh

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Hepatitis B vaccinations is associated with autoimmune hazards. - GMI Summary

Pubmed Data : Autoimmun Rev. 2005 Feb;4(2):96-100. PMID: [15722255](#)

Article Published Date : Feb 01, 2005

Authors : Marc Girard

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility. - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Myasthenia Gravis : CK\(82\) : AC\(14\)](#), [Neuromuscular Diseases : CK\(16\) : AC\(4\)](#), [Neuropathies : CK\(436\) : AC\(72\)](#), [Polyarteritis Nodosa : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Infection and vaccines are triggers for autoimmune disease. - GMI Summary

Pubmed Data : Autoimmunity. 2005 May;38(3):235-45. PMID: [16126512](#)

Article Published Date : May 01, 2005

Authors : Vered Molina, Yehuda Shoenfeld

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-spectrum disorder.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Pertussis vaccination and asthma: is there a link?](#) - GMI Summary

Pubmed Data : JAMA. 1994 Aug 24-31;272(8):592-3. PMID: [8057511](#)

Article Published Date : Aug 23, 1994

Authors : M R Odent, E E Culpin, T Kimmel

Study Type : Commentary

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Swine flu vaccine adjuvants may cause harm in patients with autoimmune diseases such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2010 Feb 18. Epub 2010 Feb 18. PMID: [20171793](#)

Article Published Date : Feb 18, 2010

Authors : Serefnur Oztürk

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[The demyelinating effect of hepatitis B vaccination could be due to the contamination of the vaccine by partial hepatitis B virus polymerase.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2005;65(3):509-20. PMID: [15908138](#)

Article Published Date : Jan 01, 2005

Authors : E Faure

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr](#)

[virus and human myelin. - GMI Summary](#)

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The HPV16 vaccine carries with it significant cross-reactivity risk due to the homologies that exist between the HPV and human proteome. - GMI Summary](#)

Pubmed Data : J Exp Ther Oncol. 2009;8(1):65-76. PMID: [19827272](#)

Article Published Date : Jan 01, 2009

Authors : Darja Kanduc

Study Type : In Vitro Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Vaccination may be contributing to autoimmune disease. - GMI Summary](#)

Pubmed Data : J Autoimmun. 2000 Feb;14(1):1-10. PMID: [10648110](#)

Article Published Date : Feb 01, 2000

Authors : Y Shoenfeld, A Aron-Maor

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary](#)

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Viruses \(wild-type or recombinant vaccine-type\) can silently prime for and trigger central nervous system autoimmune disease. - GMI Summary](#)

Pubmed Data : J Neurovirol. 2001 Jun;7(3):220-7. PMID: [11517396](#)

Article Published Date : Jun 01, 2001

Authors : D J Theil, I Tsunoda, F Rodriguez, J L Whitton, R S Fujinami

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Asthma

[Diphtheria immunisation is weakly associated with an increased risk of asthma by age 7 years.](#) - GMI Summary

Pubmed Data : Thorax. 2007 Mar;62(3):270-5. Epub 2006 Nov 7. PMID: [17090571](#)

Article Published Date : Mar 01, 2007

Authors : Kazunori Nakajima, Shyamali C Dharmage, John B Carlin, Cathryn L Wharton, Mark A Jenkins, Graham G Giles, Michael J Abramson, E Haydn Walters, John L Hopper

Study Type : Meta Analysis

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Atopic Disease : CK\(91\) : AC\(9\)](#), [Hypersensitivity: Immediate : CK\(93\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

[DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents.](#) - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Administration of varicella vaccine before the age of 15 months, and the prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease.](#) - GMI Summary

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Moolooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#), [Corticosteroid-Induced Toxicity : CK\(78\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma.](#) - GMI Summary

Pubmed Data : J Allergy Clin Immunol. 2008 Mar ;121(3):626-31. Epub 2008 Jan 18. PMID: [18207561](#)

Article Published Date : Feb 29, 2008

Authors : Kara L McDonald, Shamima I Huq, Lisa M Lix, Allan B Becker, Anita L Kozyrskyj

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Pertussis vaccination and asthma: is there a link? - GMI Summary](#)

Pubmed Data : JAMA. 1994 Aug 24-31;272(8):592-3. PMID: [8057511](#)

Article Published Date : Aug 23, 1994

Authors : M R Odent, E E Culpin, T Kimmel

Study Type : Commentary

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Topic: Influenza A](#)

[Inactivated flu vaccines have not been proven to be effective or safe in preventing influenza in healthy children under two. - GMI Summary](#)

Pubmed Data : Altern Ther Health Med. 2009 Sep-Oct;15(5):44-6. PMID: [18425905](#)

Article Published Date : Sep 01, 2009

Authors : Tom Jefferson, Alessandro Rivetti, Anthony Harnden, Carlo Di Pietrantonj, Vittorio Demicheli

Study Type : Meta Analysis

Additional Links

Diseases : [Cold and Flu: Infants & Children : CK\(62\) : AC\(6\)](#), [Infection: In Infants & Children : CK\(111\) : AC\(11\)](#), [Influenza A : CK\(292\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is little evidence supporting the belief that vaccines are effective in preventing influenza in healthy adults. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2010(7):CD001269. Epub 2010 Jul 7. PMID: [20614424](#)

Article Published Date : Jan 01, 2010

Authors : Tom Jefferson, Carlo Di Pietrantonj, Alessandro Rivetti, Ghada A Bawazeer, Lubna A Al-Ansary, Eliana Ferroni

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Influenza B : CK\(72\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events. - GMI Summary](#)

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Cardiovascular Diseases : CK\(5342\) : AC\(665\)](#), [Diabetes Mellitus: Type 2 : CK\(3603\) : AC\(359\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Interleukin-6 upregulation : CK\(26\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza-related mortality is not prevented with increasing vaccination coverage. - GMI Summary](#)

Pubmed Data : Vaccine. 2006 Oct 30;24(42-43):6468-75. Epub 2006 Jul 7. PMID: [16876293](#)

Article Published Date : Oct 30, 2006

Authors : Caterina Rizzo, Cécile Viboud, Emanuele Montomoli, Lone Simonsen, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Widening influenza vaccine coverage is not correlated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Topic: Vaccination: Abortion](#)

[Congenital malformation is a possible consequence of rubella vaccination during pregnancy.](#) - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously.](#) - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows.](#) - GMI Summary

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Cheville

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[An animal vaccine was identified as a possible cause of a series of lamb abortions.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Aug 9 ;28(35):5657-63. PMID: [20554095](#)

Article Published Date : Aug 09, 2010

Authors : Nicholas Wheelhouse, Kevin Aitchison, Karine Laroucau, Jill Thomson, David Longbottom

Study Type : Animal Study

Additional Links

Diseases : [Vaccination: Abortion : CK\(40\) : AC\(14\)](#)

[Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%.](#) - GMI Summary

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies.](#) - GMI Summary

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does.](#) - GMI Summary

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly.](#) - GMI Summary

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[There are 76 factors \(cytokines/chemokines/growth factors/others\) that have been identified that are involved in various steps of the establishment of pregnancy and which could become targets/liabilities for vaccine-induced abortion/contraception.](#) - GMI Summary

Pubmed Data : Am J Reprod Immunol. 2011 Jul ;66(1):13-25. Epub 2011 Apr 11. PMID: [21481058](#)

Article Published Date : Jul 01, 2011

Authors : Angela R Lemons, Rajesh K Naz

Study Type : Animal Study

Additional Links

Diseases : [Vaccination: Abortion : CK\(40\) : AC\(14\)](#)

Additional Keywords : [Contraceptive Vaccines : CK\(6\) : AC\(3\)](#)

[There is evidence that a DNA vaccine exhibits anti-fertility properties.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jul 12 ;29(31):4933-9. Epub 2011 May 17. PMID: [21596079](#)

Article Published Date : Jul 12, 2011

Authors : Meng-Fei Yu, Wen-Ning Fang, Gao-Feng Xiong, Ying Yang, Jing-Pian Peng

Study Type : Animal Study

Additional Links

Diseases : [Infertility : CK\(576\) : AC\(109\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Plasmid DNA Vaccines : CK\(3\) : AC\(2\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25.](#) - GMI Summary

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escjadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women.](#) - GMI Summary

Pubmed Data : Am J Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

The number of elective abortions following vaccination during pregnancy may be under-reported and could be substantial. - GMI Summary

Pubmed Data : Vaccine. 2008 May 2;26(19):2428-32. Epub 2008 Mar 17. PMID: [18406499](#)

Article Published Date : May 02, 2008

Authors : Soju Chang, Robert Ball, M Miles Braun

Study Type : Review

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Myelitis

Vaccination is associated with a rare autoimmune neurological condition transverse myelitis. - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1198-204. PMID: [19880568](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, S Kivity, M Szyper-Kravitz, Y Shoenfeld

Study Type : Meta Analysis

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Acute transverse myelitis after influenza vaccination has been reported. - GMI Summary

Pubmed Data : J Neuroimaging. 1996 Oct;6(4):248-50. PMID: [8903080](#)

Article Published Date : Oct 01, 1996

Authors : R Bakshi, J C Mazziotta

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Hepatitis B vaccine may induce myelitis in susceptible individuals. - GMI Summary

Pubmed Data : Eur J Neurol. 2001 Nov;8(6):711-5. PMID: [11784358](#)

Article Published Date : Nov 01, 2001

Authors : F Karaali-Savrun, A Altintaş, S Saip, A Siva

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : [CK\(39\)](#) : [AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

[Immune-mediated myelitis following hepatitis B vaccination has been reported.](#) **- GMI Summary**

Pubmed Data : Autoimmun Rev. 2012 Apr 1. Epub 2012 Apr 1. PMID: [22498789](#)

Article Published Date : Apr 01, 2012

Authors : Joerg-Patrick Stübgen

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : [CK\(39\)](#) : [AC\(5\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

[ransverse myelitis has been reported in association with a nasal attenuated novel influenza A\(H1N1\) vaccine.](#) **- GMI Summary**

Pubmed Data : Arch Neurol. 2010 Aug;67(8):1018-20. PMID: [20697056](#)

Article Published Date : Aug 01, 2010

Authors : Wafa Akkad, Bassel Salem, Jerome W Freeman, Mark K Huntington

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : [CK\(39\)](#) : [AC\(5\)](#), [Swine Flu Associated Virus](#) : [CK\(145\)](#) : [AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Influenza](#) : [CK\(356\)](#) : [AC\(37\)](#), [Vaccination: Nasal](#) : [CK\(3\)](#) : [AC\(1\)](#)

Topic: [Herpes Zoster](#)

[Between 1995 and 2005 25,306 adverse events were reported from varicella vaccine.](#) **- GMI Summary**

Pubmed Data : J Infect Dis. 2008 Mar 1;197 Suppl 2:S170-7. PMID: [18419393](#)

Article Published Date : Mar 01, 2008

Authors : Sandra S Chaves, Penina Haber, Kimp Walton, Robert P Wise, Hector S Izurieta, D Scott Schmid, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster](#) : [CK\(472\)](#) : [AC\(35\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\)](#) : [CK\(174\)](#) : [AC\(21\)](#)

[Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster \(shingles\) cases managed in the same time period.](#) **- GMI Summary**

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox](#) : [CK\(110\)](#) : [AC\(8\)](#), [Herpes Zoster](#) : [CK\(472\)](#) : [AC\(35\)](#), [Shingles](#) : [CK\(472\)](#) : [AC\(35\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection](#) : [CK\(20\)](#) : [AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\)](#) : [CK\(174\)](#) : [AC\(21\)](#)

[Varicella vaccine has been reported to cause herpes zoster skin lesions and meningitis in a previously healthy boy. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2008 Nov 15;198(10):1444-7. PMID: [18826373](#)

Article Published Date : Nov 15, 2008

Authors : Myron J Levin, Roberta L DeBiasi, Vanda Bostik, D Scott Schmid

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Varicella vaccine has been reported to cause chronic, acyclovir-resistant herpes zoster infection in an immunosuppressed child. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2003 Oct 1;188(7):954-9. Epub 2003 Sep 26. PMID: [14513413](#)

Article Published Date : Oct 01, 2003

Authors : Myron J Levin, Karen M Dahl, Adriana Weinberg, Roger Giller, Amita Patel, Philip R Krause

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Acyclovir-Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to viral meningitis in an immunocompetent child. - GMI Summary](#)

Pubmed Data : Ann Emerg Med. 2009 Jun;53(6):792-5. Epub 2008 Nov 22. PMID: [19028409](#)

Article Published Date : Jun 01, 2009

Authors : Sujit Iyer, Manoj K Mittal, Richard L Hodinka

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Undefined : CK\(14\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Reactivation of Herpes Zoster Keratitis in an Adult After Varicella Zoster Vaccination. - GMI Summary](#)

Pubmed Data : Cornea. 2012 Nov 26. Epub 2012 Nov 26. PMID: [23187165](#)

Article Published Date : Nov 25, 2012

Authors : Charles W Hwang, Walter A Steigleman, Erika Saucedo-Sanchez, Sonal S Tuli

Study Type : Human: Case Report

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Herpes Zoster Keratitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella Zoster \(Shingles\) : CK\(3\) : AC\(1\)](#)

Topic: [Varicella](#)

[Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately. - GMI Summary](#)

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures : CK\(83\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Near complete vaccination coverage for varicella does not prevent outbreaks in those treated.](#) - GMI Summary

Pubmed Data : Pediatrics. 2006 Jun;117(6):e1070-7. PMID: [16740809](#)

Article Published Date : Jun 01, 2006

Authors : Adriana S Lopez, Dalya Guris, Laura Zimmerman, Linda Gladden, Tamara Moore, Dirk T Haselow, Vladimir N Loparev, D Scott Schmid, Aisha O Jumaan, Sandra L Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella outbreaks occur in vaccinated populations, even when receiving 2 doses.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Aug;28(8):678-81. PMID: [19593254](#)

Article Published Date : Aug 01, 2009

Authors : Philip L Gould, Jessica Leung, Connie Scott, D Scott Schmid, Helen Deng, Adriana Lopez, Sandra S Chaves, Meredith Reynolds, Linda Gladden, Rafael Harpaz, Sandra Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Topic: Demyelinating Diseases](#)

[Hepatitis B vaccination is associated with an increased risk of CNS inflammatory demyelination after 3 years of age.](#) - GMI Summary

Pubmed Data : Reprod Toxicol. 2002 May-Jun;16(3):237-43. PMID: [18843097](#)

Article Published Date : May 01, 2002

Authors : Yann Mikaeloff, Guillaume Caridade, Samy Suissa, Marc Tardieu

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Inflammation](#) : CK(1125) : AC(377), [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Hepatitis B vaccination may contribute to autoimmune demyelinating complications due to immunological cross-reactivity between Hepatitis B virus surface antigen and myelin basic protein. - GMI Summary

Pubmed Data : Clin Dev Immunol. 2005 Sep;12(3):217-24. PMID: [16295528](#)

Article Published Date : Sep 01, 2005

Authors : Dimitrios-Petrou Bogdanos, Heather Smith, Yun Ma, Harold Baum, Giorgina Mieli-Vergani, Diego Vergani

Study Type : Human Study

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Demyelinating Diseases](#) : CK(1309) : AC(247), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2), [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Hepatitis B vaccine is associated with an increased risk of multiple sclerosis. - GMI Summary

Pubmed Data : Neurology. 2004 Sep 14;63(5):838-42. PMID: [15365133](#)

Article Published Date : Sep 14, 2004

Authors : Miguel A Hernán, Susan S Jick, Michael J Olek, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

HPV vaccination has been linked to demyelination. - GMI Summary

Pubmed Data : J Child Neurol. 2010 Mar;25(3):321-7. PMID: [20189933](#)

Article Published Date : Mar 01, 2010

Authors : Francis J DiMario, Mirna Hajjar, Thomas Ciesielski

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

Human Papilloma Virus (HPV) vaccine is associated with demyelinating events. - GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, II Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [HPV](#) : CK(31) : AC(4), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [HPV Vaccine](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce

[autoimmune demyelination.](#) - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rubella](#) : CK(54) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Acute disseminated encephalomyelitis \(ADEM\) may be caused by vaccination.](#) - GMI Summary

Pubmed Data : J Clin Neurosci. 2008 Dec;15(12):1315-22. Epub 2008 Oct 30. PMID: [18976924](#)

Article Published Date : Dec 01, 2008

Authors : William Huynh, Dennis J Cordato, Elias Kehdi, Lynette T Masters, Chris Dedousis

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Encephalomyelitis](#) : CK(12) : AC(7), [Neuromyelitis Optica](#) : CK(4) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Demyelinating Diseases](#) : CK(1309) : AC(247), [Epstein-Barr Virus Infections](#) : CK(102) : AC(44), [Hepatitis B](#) : CK(219) : AC(37)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Topic: Purpura: Thrombocytopenic](#)

[Measles-mumps-rubella vaccine that is given in the second year of life is associated with an increased risk of immune thrombocytopenia purpura.](#) - GMI Summary

Pubmed Data : Pediatrics. 2008 Mar;121(3):e687-92. PMID: [18310189](#)

Article Published Date : Mar 01, 2008

Authors : Eric K France, Jason Glanz, Stanley Xu, Simon Hambidge, Kristi Yamasaki, Steve B Black, Michael Marcy, John P Mullooly, Lisa A Jackson, James Nordin, Edward A Belongia, K Hohman, Robert T Chen, Robert Davis,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccination is associated with an increased risk for idiopathic thrombocytopenic purpura.](#) - GMI Summary

Pubmed Data : Br J Clin Pharmacol. 2003 Jan;55(1):107-11. PMID: [12534647](#)

Article Published Date : Jan 01, 2003

Authors : Corri Black, James A Kaye, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination is associated with thrombocytopenic purpura in children.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Feb 26;25(10):1838-40. Epub 2006 Nov 9. PMID: [17126957](#)

Article Published Date : Feb 26, 2007

Authors : J Rajantie, B Zeller, I Treutiger, S Rosthøj,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Acute immune thrombocytopenic purpura as adverse reaction to oral polio vaccine \(OPV\).](#) - GMI Summary

Pubmed Data : Hum Vaccin Immunother. 2013 Jun 4 ;9(8). Epub 2013 Jun 4. PMID: [23807364](#)

Article Published Date : Jun 03, 2013

Authors : Cheng-Qiang Jin, Hai-Xin Dong, Zhuo-Xiang Sun, Jian-Wei Zhou, Cui-Yun Dou, Shu-Hua Lu, Rui-Rui Yang

Study Type : Human: Case Report

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked](#)

to a number of serious adverse reactions. - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: Mercury Poisoning

Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem. - GMI Summary

Pubmed Data : Am J Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Infant Chemical Exposures : CK\(165\) : AC\(24\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hair mercury in breast-fed infants exposed to thimerosal-preserved vaccines indicates significant levels of exposure. - GMI Summary

Pubmed Data : Eur J Pediatr. 2007 Sep;166(9):935-41. Epub 2007 Jan 20. PMID: [17237965](#)

Article Published Date : Sep 01, 2007

Authors : Rejane C Marques, José G Dórea, Márlon F Fonseca, Wanderley R Bastos, Olaf Malm

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination is associated with potentially neurotoxic mercury exposure in infants. - GMI Summary

Pubmed Data : Chin Med. 2008 Mar 29;3:4. PMID: [10802503](#)

Article Published Date : Mar 29, 2008

Authors : G V Stajich, G P Lopez, S W Harry, W R Sexson

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

There is evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD. - GMI Summary

Pubmed Data : Transl Neurodegener. 2013 ;2(1):25. Epub 2013 Dec 19. PMID: [24354891](#)

Article Published Date : Dec 31, 2012

Authors : David A Geier, Brian S Hooker, Janet K Kern, Paul G King, Lisa K Sykes, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Mercury Poisoning](#) : CK(172) : AC(45), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Mercury](#) : CK(131) : AC(17), [Thimerosal](#) : CK(367) : AC(23)

[The mercury containing vaccine adjuvant known as thimerosal has immunosuppressive and autoimmune effects in mice.](#) - GMI Summary

Pubmed Data : Toxicol Appl Pharmacol. 2005 Apr 15;204(2):109-21. PMID: [15808517](#)

Article Published Date : Apr 15, 2005

Authors : S Havarinasab, B Häggqvist, E Björn, K M Pollard, P Hultman

Study Type : Animal Study

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Mercury Poisoning](#) : CK(172) : AC(45), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[The vaccine adjuvant thimerosal induces adverse changes in the cerebellum of mice, lending plausibility to the association between autism and low-dose mercury exposure.](#) - GMI Summary

Pubmed Data : Cell Biol Toxicol. 2009 Apr 9. PMID: [19357975](#)

Article Published Date : Apr 09, 2009

Authors : Takeshi Minami, Eriko Miyata, Yamato Sakamoto, Hideo Yamazaki, Seiji Ichida

Study Type : Animal Study

Additional Links

Diseases : [Mercury Poisoning](#) : CK(172) : AC(45), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Thimerosal](#) : CK(3) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[The epidemic of autism may be linked to both vaccinations and mitochondrial diseases.](#) - GMI Summary

Pubmed Data : Clin Exp Pharmacol Physiol. 2004 Dec;31 Suppl 2:S51-3 PMID: [19043939](#)

Article Published Date : Dec 01, 2004

Authors : Stephanie F Cave

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Mercury Poisoning](#) : CK(172) : AC(45), [Mitochondrial Diseases](#) : CK(157) : AC(57), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Diseases that are Linked](#) : CK(2142) : AC(272)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: [Mumps](#)

["The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate."](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2012 ;2:CD004407. Epub 2012 Feb 15. PMID: [22336803](#)

Article Published Date : Dec 31, 2011

Authors : Vittorio Demicheli, Alessandro Rivetti, Maria Grazia Debalini, Carlo Di Pietrantonj

Study Type : Meta Analysis

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Mumps](#) : CK(41) : AC(1), [Rubella](#) : CK(54) : AC(4)

Additional Keywords : [Rubella](#) : CK(54) : AC(4), [Vaccine Safety](#) : CK(21) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population. - GMI Summary

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)

Article Published Date : Dec 31, 2013

Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Brachytherapy : CK\(10\) : AC\(1\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Fifty-one percent of cases of patients in a 1998/1999 mumps outbreak had at least one MMR vaccination, indicating their effectiveness may be overestimated. - GMI Summary

Pubmed Data : Vaccine. 2005 Jul 1 ;23(31):4070-4. PMID: [15950329](#)

Article Published Date : Jun 30, 2005

Authors : Richard Harling, Joanne M White, Mary E Ramsay, Karen F Macsween, Corry van den Bosch

Study Type : Human Study

Additional Links

Diseases : [Mumps : CK\(41\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Measles, mumps, and rubella catch up immunisation in a measles epidemic did not appear to confer protection and was associated with a variety of new side effects of the vaccine. - GMI Summary

Pubmed Data : BMJ. 1995 Jun 24 ;310(6995):1629-32. PMID: [7795447](#)

Article Published Date : Jun 23, 1995

Authors : R J Roberts, Q D Sandifer, M R Evans, M Z Nolan-Farrell, P M Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

"Mumps outbreak among vaccinated university students associated with a large party, the Netherlands, 2010." - GMI Summary

Pubmed Data : Vaccine. 2012 Jun 29 ;30(31):4676-80. Epub 2012 May 8. PMID: [22579874](#)

Article Published Date : Jun 28, 2012

Authors : Katie Greenland, Jane Whelan, Ewout Fanoy, Marjon Borgert, Koen Hulshof, Kioe-Bing Yap, Corien Swaan, Tjibbe Donker, Rob van Binnendijk, Hester de Melker, Susan Hahné

Study Type : Human: Case Report

Additional Links

Diseases : [Mumps : CK\(41\) : AC\(1\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Topic: Infant Infections

Maternal influenza vaccination during pregnancy does not reduce the incidence of acute respiratory illness visits among infants. - GMI Summary

Pubmed Data : Cancer Sci. 2004 Jul;95(7):596-601. PMID: [17146026](#)

Article Published Date : Jul 01, 2004

Authors : Eric K France, Renae Smith-Ray, David McClure, Simon Hambidge, Stanley Xu, Kristi Yamasaki, David Shay, Eric Weintraub, Alicia M Fry, Steve B Black, Henry R Shinefield, John P Mullooly, Lisa A Jackson

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Immunization of mothers with pneumococcal capsular polysaccharide vaccine during pregnancy is ineffective for infants. - GMI Summary](#)

Pubmed Data : Braz J Infect Dis. 2009 Apr;13(2):104-6. PMID: [20140352](#)

Article Published Date : Apr 01, 2009

Authors : Claudia R C Lopes, Eitan N Berezin, Ting Hui Ching, Jaildo de Souza Canuto, Vanilda Oliveira da Costa, Erika Monteiro Klering

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal conjugate vaccination is associated with higher levels of serious adverse respiratory events and nonrespiratory events in infants 6 weeks to 6 months of age. - GMI Summary](#)

Pubmed Data : Pediatr Infect Dis J. 2009 Jun;28(6):455-62. PMID: [19483514](#)

Article Published Date : Jun 01, 2009

Authors : Marilla G Lucero, Hanna Nohynek, Gail Williams, Veronica Tallo, Eric A F Simões, Socorro Lupisan, Diozele Sanvictores, Simon Forsyth, Taneli Puumalainen, Juanita Ugpo, Marites Lechago, Margaret de Campo, Erma Abuzejo-Ladesma, Lydia Sombrero, Antti Nissinen, Anu Soinen, Petri Ruutu, Ian Riley, Helen P Mäkelä

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Respiratory Diseases : CK\(174\) : AC\(29\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Whole cell pertussis vaccines may have been causing serious neurological disorders. - GMI Summary](#)

Pubmed Data : Brain Dev. 2004 Aug;26(5):296-300. PMID: [15165669](#)

Article Published Date : Aug 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Infant Neurological Development : CK\(46\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: Anthrax

[Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy. - GMI Summary](#)

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Birth Defects : CK\(204\) : AC\(39\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Adverse Pharmacological Actions : [Teratogenic : CK\(318\) : AC\(62\)](#)

[Injection site reactions occur in 28% of those who receive the anthrax vaccine, with women having twice the incidence of reaction versus men.](#) - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2007 Mar ;16(3):259-74. PMID: [17245803](#)

Article Published Date : Mar 01, 2007

Authors : Michael M McNeil, I-Shan Chiang, John T Wheeling, Yujia Zhang

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Gender Differences : CK\(63\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The anthrax vaccine is one of the most reactogenic vaccines reported in the Vaccine Adverse Events Reporting System \(VAERS\) database.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2004 May-Jun;51(57):762-7. PMID: [15143911](#)

Article Published Date : May 01, 2004

Authors : Mark R Geier, David A Geier

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The vaccine adjuvant squalene in anthrax vaccines given to soldiers in the Gulf War resulted in the formation of antibodies to squalene which are associated with Gulf War Syndrome.](#) - GMI Summary

Pubmed Data : Neuropharmacology. 2011 Feb-Mar;60(2-3):252-8. Epub 2010 Sep 22. PMID: [12127050](#)

Article Published Date : Feb 01, 2011

Authors : Pamela B Asa, Russell B Wilson, Robert F Garry

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Gulf War Syndrome : CK\(33\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Problem Substances : [Squalene, Adjuvant : CK\(2\) : AC\(1\)](#)

[Anthrax vaccine development suffers from a wide range of potentially insurmountable problems.](#) - GMI Summary

Pubmed Data : Przegl Epidemiol. 2009 ;63(4):505-12. PMID: [20120948](#)

Article Published Date : Jan 01, 2009

Authors : Dorota Zakowska, Janusz Kocik, Michał Bartoszcze

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The development of human vaccines for anthrax has suffered from a number of technical challenges.](#) - GMI Summary

Pubmed Data : Hum Vaccin. 2009 Dec ;5(12):806-16. Epub 2009 Dec 9. PMID: [19786839](#)

Article Published Date : Dec 01, 2009

Authors : Leslie W Baillie

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Topic: [Pneumococcal Infections](#)

[Immunization of mothers with pneumococcal capsular polysaccharide vaccine during pregnancy is ineffective for infants. - GMI Summary](#)

Pubmed Data : Braz J Infect Dis. 2009 Apr;13(2):104-6. PMID: [20140352](#)

Article Published Date : Apr 01, 2009

Authors : Claudia R C Lopes, Eitan N Berezin, Ting Hui Ching, Jaildo de Souza Canuto, Vanilda Oliveira da Costa, Erika Monteiro Klering

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal conjugate vaccine is not effective to prevent ear infections in previously unvaccinated toddlers and children with a history of recurrent ear infections. - GMI Summary](#)

Pubmed Data : Lancet. 2003 Jun 28;361(9376):2189-95. PMID: [12842372](#)

Article Published Date : Jun 28, 2003

Authors : Reinier Veenhoven, Debby Bogaert, Cuno Uiterwaal, Carole Brouwer, Herma Kiezebrink, Jacob Bruin, Ed IJzerman, Peter Hermans, Ronald de Groot, Ben Zegers, Wietse Kuis, Ger Rijkers, Anne Schilder, Elisabeth Sanders

Study Type : Human Study

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines are ineffective in children with a history of recurrent acute ear infections - Article 2. - GMI Summary](#)

Pubmed Data : Int J Pediatr Otorhinolaryngol. 2006 Feb;70(2):275-85. Epub 2005 Sep 2. PMID: [16140397](#)

Article Published Date : Feb 01, 2006

Authors : Muriel J P van Kempen, Judith S Vermeiren, Mario Vaneechoutte, Geert Claeys, Reinier H Veenhoven, Ger T Rijkers, Elisabeth A M Sanders, Ingeborg J Dhooge

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines do not appear to reduce the risk of death from pneumonia in adult populations. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2003(4):CD000422. PMID: [14583920](#)

Article Published Date : Jan 01, 2003

Authors : K Dear, J Holden, R Andrews, D Tatham

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Review: based on currently available research pneumoccal vaccination should not be recommended for large scale use in ear infection prone populations.](#) -

GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2002(2):CD001480. PMID: [12076412](#)

Article Published Date : Jan 01, 2002

Authors : M Straetemans, E A Sanders, R H Veenhoven, A G Schilder, R A Damoiseaux, G A Zielhuis

Study Type : Review

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Topic: [H1N1 Infection](#)

["Risk of Guillain-Barré syndrome after 2010-2011 influenza vaccination."](#) - GMI Summary

Pubmed Data : Eur J Epidemiol. 2013 May ;28(5):433-44. Epub 2013 Mar 31. PMID: [23543123](#)

Article Published Date : Apr 30, 2013

Authors : Francesca Galeotti, Marco Massari, Roberto D'Alessandro, Ettore Beghi, Adriano Chiò, Giancarlo Logroscino, Graziella Filippini, Maria Donata Benedetti, Maura Pugliatti, Carmela Santuccio, Roberto Raschetti,

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Prior receipt of seasonal flu vaccine \(2008-09 \)was associated with increased risk of medically attended pandemic H1N1 illness \(2008-09\).](#) - GMI Summary

Pubmed Data : PLoS Med. 2010;7(4):e1000258. Epub 2010 Apr 6. PMID: [20386731](#)

Article Published Date : Jan 01, 2010

Authors : Danuta M Skowronski, Gaston De Serres, Natasha S Crowcroft, Naveed Z Janjua, Nicole Boulianne, Travis S Hottes, Laura C Rosella, James A Dickinson, Rodica Gilca, Pam Sethi, Najwa Ouhoumane, Donald J Willison, Isabelle Rouleau, Martin Petric, Kevin Fonseca, Steven J Drews, Anuradha Rebbapragada, Hugues Charest, Marie-Eve Hamelin, Guy Boivin, Jennifer L Gardy, Yan Li, Trijntje L Kwindt, David M Patrick, Robert C Brunham,

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Additional Keywords : [Immunosuppressive Flu Vaccines : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Seasonal influenza vaccine \(2008-2009\) is associated with an increased risk of influenza-like illness from pandemic H1N1 infection.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2010 Nov 1;51(9):1017-1027. PMID: [20887210](#)

Article Published Date : Nov 01, 2010

Authors : Naveed Z Janjua, Danuta M Skowronski, Travis S Hottes, William Osei, Evan Adams, Martin Petric, Suzana Sabaiduc, Tracy Chan, Annie Mak, Marcus Lem, Patrick Tang, David M Patrick, Gaston De Serres, David Bowering

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection](#) : CK(468) : AC(88)

Additional Keywords : [Immunosuppressive Flu Vaccines](#) : CK(20) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Widening influenza vaccine coverage is not correleated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection](#) : CK(468) : AC(88), [Influenza](#) : CK(656) : AC(99), [Influenza A](#) : CK(292) : AC(77), [Swine Flu Associated Virus](#) : CK(145) : AC(32)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Vaccination against novel H1N1 may accelerate atherogenesis \(heart disease\).](#) - GMI Summary

Pubmed Data : Med Microbiol Immunol. 2009 Oct 23. PMID: [19851782](#)

Article Published Date : Oct 23, 2009

Authors : Sucharit Bhakdi, Karl Lackner, Hans-Wilhelm Doerr

Study Type : Commentary

Additional Links

Diseases : [H1N1 Infection](#) : CK(468) : AC(88), [Swine Flu Associated Virus](#) : CK(145) : AC(32), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Myopericarditis

[Among US military personnel vaccinated against smallpox, myopericarditis occurred at a rate of 1 per 12,819 primary vaccinees, and 3.6 fold higher in those without previous vaccinia vaccination.](#) - GMI Summary

Pubmed Data : JAMA. 2003 Jun 25;289(24):3283-9. PMID: [12824210](#)

Article Published Date : Jun 25, 2003

Authors : Jeffrey S Halsell, James R Riddle, J Edwin Atwood, Pierce Gardner, Robert Shope, Gregory A Poland, Gregory C Gray, Stephen Ostroff, Robert E Eckart, Duane R Hospenthal, Roger L Gibson, John D Grabenstein, Mark K Arness, David N Tornberg,

Study Type : Human Study

Additional Links

Diseases : [Myopericarditis](#) : CK(40) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Smallpox](#) : CK(71) : AC(8)

[An economic analysis of mass smallpox vaccination reveals that cardiovascular adverse events would be sizeable and costly.](#) - GMI Summary

Pubmed Data : J Rheumatol. 1994 Jul;21(7):1305-9. PMID: [18284356](#)

Article Published Date : Jul 01, 1994

Authors : Ismael R Ortega-Sanchez, Mercedes M Sniadack, Gina T Mootrey

Study Type : Human Study

Additional Links

Diseases : [Myocarditis](#) : CK(54) : AC(8), [Myopericarditis](#) : CK(40) : AC(4), [Pericarditis](#) : CK(35) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Smallpox](#) : CK(71) :

[Myocarditis and pericarditis have been reported following smallpox vaccination in Europe, Australia and the United States.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2008 Mar 15;46 Suppl 3:S242-50. PMID: [18284365](#)

Article Published Date : Mar 15, 2008

Authors : Juliette Morgan, Martha H Roper, Laurence Sperling, Richard A Schieber, James D Heffelfinger, Christine G Casey, Jacqueline W Miller, Scott Santibanez, Barbara Herwaldt, Paige Hightower, Pedro L Moro, Beth F Hibbs, Nancy H Levine, Louisa E Chapman, John Iskander, J Michael Lane, Melinda Wharton, Gina T Mootrey, David L Swerdlow

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Smallpox vaccination has been associated with cardiac complications such as myopericarditis.](#) - GMI Summary

Pubmed Data : South Med J. 2009 May 7. Epub 2009 May 7. PMID: [19434043](#)

Article Published Date : May 07, 2009

Authors : Luis F Mora, Akbar H Khan, Laurence S Sperling

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Topic: Upper Respiratory Infections](#)

[Maternal influenza vaccination during pregnancy does not reduce the incidence of acute respiratory illness visits among infants.](#) - GMI Summary

Pubmed Data : Cancer Sci. 2004 Jul;95(7):596-601. PMID: [17146026](#)

Article Published Date : Jul 01, 2004

Authors : Eric K France, Renae Smith-Ray, David McClure, Simon Hambidge, Stanley Xu, Kristi Yamasaki, David Shay, Eric Weintraub, Alicia M Fry, Steve B Black, Henry R Shinefield, John P Mullooly, Lisa A Jackson

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Immunization of mothers with pneumococcal capsular polysaccharide vaccine during pregnancy is ineffective for infants.](#) - GMI Summary

Pubmed Data : Braz J Infect Dis. 2009 Apr;13(2):104-6. PMID: [20140352](#)

Article Published Date : Apr 01, 2009

Authors : Claudia R C Lopes, Eitan N Berezin, Ting Hui Ching, Jaildo de Souza Canuto, Vanilda Oliveira da Costa, Erika Monteiro Klering

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Increased risk \(4.4 fold\) of noninfluenza respiratory virus infections associated with receipt of inactivated influenza vaccine.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2012 Jun ;54(12):1778-83. Epub 2012 Mar 15. PMID: [22423139](#)

Article Published Date : May 31, 2012

Authors : Benjamin J Cowling, Vicky J Fang, Hiroshi Nishiura, Kwok-Hung Chan, Sophia Ng, Dennis K M Ip, Susan S Chiu, Gabriel M Leung, J S Malik Peiris

Study Type : Human Study

Additional Links

Diseases : [Upper Respiratory Infections](#) : CK(824) : AC(90)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

[Influenza vaccination does not appear to be effective during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants.](#) - GMI Summary

Pubmed Data : Am J Perinatol. 2004 Aug;21(6):333-9. PMID: [15311370](#)

Article Published Date : Aug 01, 2004

Authors : Steven B Black, Henry R Shinefield, Eric K France, Bruce H Fireman, Sharon T Platt, David Shay,

Study Type : Human Study

Additional Links

Diseases : [Pregnancy: Flu](#) : CK(10) : AC(1), [Upper Respiratory Infections](#) : CK(824) : AC(90)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Topic: Poliomyelitis](#)

[At the present time, the only poliovirus-caused poliomyelitis cases reported in Brazil and other countries of the Americas are of vaccine etiology.](#) - GMI Summary

Pubmed Data : Rev Panam Salud Publica. 2000 Apr;7(4):219-24. PMID: [10846924](#)

Article Published Date : Apr 01, 2000

Authors : L H de Oliveira, C J Struchiner

Study Type : Human Study

Additional Links

Diseases : [Poliomyelitis](#) : CK(33) : AC(4)

Additional Keywords : [Iatrogenic Poliomyelitis](#) : CK(20) : AC(2)

Anti Therapeutic Actions : [Vaccination: Polio](#) : CK(94) : AC(15)

[Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\)](#) : CK(12) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Oral Polio Vaccine](#) : CK(10) : AC(1), [Vaccination: Oral Polio Vaccine, Bivalent](#) : CK(10) : AC(1), [Vaccination: Polio](#) : CK(94) : AC(15)

[Vaccine-associated paralytic poliomyelitis \(VAPP\) has emerged as the predominant form of the disease in the United States since 1980.](#) - GMI

Summary

Pubmed Data : Clin Infect Dis. 1992 Feb;14(2):568-79. PMID: [1554844](#)

Article Published Date : Feb 01, 1992

Authors : P M Strebel, R W Sutter, S L Cochi, R J Biellik, E W Brink, O M Kew, M A Pallansch, W A Orenstein, A R Hinman

Study Type : Human Study

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Additional Keywords : [Iatrogenic Poliomyelitis : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

["Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children." - GMI Summary](#)

Pubmed Data : Lancet. 1991 Sep 21 ;338(8769):715-20. PMID: [1679866](#)

Article Published Date : Sep 20, 1991

Authors : R W Sutter, P A Patriarca, S Brogan, P G Malankar, M A Pallansch, O M Kew, A G Bass, S L Cochi, J P Alexander, D B Hall

Study Type : Human: Case Report

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#)

[In 2011, there were an extra 47,500 new cases of non-polio acute flaccid paralysis \(NPAFP\); Clinically indistinguishable from polio paralysis but twice as deadly, the incidence of NPAFP was directly proportional to doses of oral polio received. - GMI Summary](#)

Pubmed Data : Indian J Med Ethics. 2012 Apr-Jun;9(2):114-7. PMID: [22591873](#)

Article Published Date : Apr 01, 2012

Authors : Neetu Vashisht, Jacob Puliyel

Study Type : Review

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Provocation by vaccine injections can increase the risk of paralytic poliomyelitis by up to 25 fold. - GMI Summary](#)

Pubmed Data : Dev Biol Stand. 1986;65:123-6. PMID: [3549394](#)

Article Published Date : Jan 01, 1986

Authors : H V Wyatt

Study Type : Review

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions. - GMI Summary](#)

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura:](#)

[Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: Systemic Lupus Erythematosus

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Systemic lupus erythematosus related to hepatitis B vaccine has been reported. - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1192-7. PMID: [19880567](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, Y Zafrir, Z Paz, T Shilton, G Zandman-Goddard, Y Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Vaccination can precipitate lupus erythematosus. - GMI Summary

Pubmed Data : Semin Arthritis Rheum. 1999 Dec;29(3):131-9. PMID: [10622677](#)

Article Published Date : Dec 01, 1999

Authors : S A Older, D F Battafarano, R J Enzenauer, A M Krieg

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Systemic lupus erythematosus has been triggered by hepatitis B vaccine. - GMI Summary

Pubmed Data : Clin Nephrol. 2010 Aug;74(2):150-3. PMID: [20630136](#)

Article Published Date : Aug 01, 2010

Authors : D Santoro, G Vita, R Vita, A Mallamace, V Savica, G Bellinghieri, S Benvenga, S Gangemi

Study Type : Human: Case Report

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Arthritis](#)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children.](#) - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Hemolytic Anemia](#)

[Vaccination is associated with an increased risk for hemolytic anemia.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7394-7. Epub 2009 Sep 18. PMID: [19766577](#)

Article Published Date : Dec 09, 2009

Authors : Allison L Naleway, Edward A Belongia, James G Donahue, Burney A Kieke, Jason M Glanz,

Study Type : Meta Analysis

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2011 Jan;45(1):e8. Epub 2010 Dec 28. PMID: [21189364](#)

Article Published Date : Jan 01, 2011

Authors : Sabrina Montagnani, Marco Tuccori, Giuseppe Lombardo, Arianna Testi, Stefania Mantarro, Elisa Ruggiero, Corrado Blandizzi

Study Type : Human: Case Report

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Vasculitis](#)

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Influenza vaccines may be causing vasculitis.](#) - GMI Summary

Pubmed Data : J Ethnopharmacol. 2000 Aug;71(3):457-63. PMID: [19734734](#)

Article Published Date : Aug 01, 2000

Authors : Rainer Birck, Isabelle Kaelsch, Peter Schnuelle, Luis Felipe Flores-Suárez, Rainer Nowack

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A case of extensive ulcerating vasculitis following a BCG vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Plast Reconstr Aesthet Surg. 2009 Aug;62(8):e286-9. Epub 2007 Dec 31. PMID: [18166508](#)

Article Published Date : Aug 01, 2009

Authors : A Ghattaura, K A Eley, E Molenaar, G Smith

Study Type : Human: Case Report

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#)

[A case of innfluenza vaccine induced have necrotizing glomerulonephritis in decursu vasculitis has been reported.](#) - GMI Summary

Pubmed Data : Pol Merkur Lekarski. 2005 Jul;19(109):75-7. PMID: [16194032](#)

Article Published Date : Jul 01, 2005

Authors : Lidia Hyla-Klekot, Grazyna Kucharska, Witold Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccines may induce hepatitis-B virus-related vasculitis and severe neuropathy.](#) - GMI Summary

Pubmed Data : J Cardiovasc Pharmacol. 2003 Sep;42(3):329-38. PMID: [18579284](#)

Article Published Date : Sep 01, 2003

Authors : Yuko Wada, Chie Yanagihara, Yo Nishimura, Nobuyuki Oka

Study Type : Commentary

Additional Links

Diseases : [Peripheral Neuropathies : CK\(191\) : AC\(31\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Allergies](#)

[DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents. - GMI Summary](#)

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Allergy to viral and rickettsial vaccines; review of the literature. - GMI Summary](#)

Pubmed Data : Ann Allergy. 1950 Sep-Oct;8(5):699-707. PMID: [14800166](#)

Authors : S UNTRACHT, B RATNER

Study Type : Human: Case Report

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Human Papillomavirus \(HPV\)](#)

[An Italian study found that 61% of women experienced an adverse event after the administration of the first dose of HPV vaccine. - GMI Summary](#)

Pubmed Data : Recenti Prog Med. 2013 Jun ;104(6):262-6. PMID: [23801230](#)

Article Published Date : May 31, 2013

Authors : Stefania Spila-Alegiani, Roberto Da Cas, Cristina Giambi, Roberto Raschetti, Stefania Salmaso

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[HPV vaccination does not have a therapeutic effect in young women with pre-existing human papillomavirus infection. - GMI Summary](#)

Pubmed Data : JAMA. 2007 Aug 15;298(7):743-53. PMID: [17699008](#)

Article Published Date : Aug 15, 2007

Authors : Allan Hildesheim, Rolando Herrero, Sholom Wacholder, Ana C Rodriguez, Diane Solomon, M Concepcion Bratti, John T Schiller, Paula Gonzalez, Gary Dubin, Carolina Porras, Silvia E Jimenez, Douglas R Lowy,

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Human Papilloma Virus (HPV) vaccine is associated with demyelinating events.

- GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, Il Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [HPV](#) : CK(31) : AC(4), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [HPV Vaccine](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

Vaccination may contribute to causing a wide variety of autoimmune disorders.

- GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: Hypersensitivity

DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents.

- GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies](#) : CK(520) : AC(96), [Allergies: Childhood](#) : CK(70) : AC(5), [Asthma](#) : CK(918) : AC(140), [Hypersensitivity](#) : CK(64) : AC(15), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Tetanus](#) : CK(61) : AC(8)

Adjuvants in vaccines may trigger innate cells response by toll-like receptors, thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity.

- GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Hypersensitivity](#) : CK(64) : AC(15), [Immune Disorders: B-Cell Over-Activity](#) : CK(2) : AC(2), [Immune Dysregulation: TH1/TH2 imbalance](#) : CK(148) :

[AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#)

Topic: [Allergies: Childhood](#)

[DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents.](#) - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: [Elderly: Age Specific Diseases](#)

[Influenza vaccination for healthcare workers who work with the elderly has no effect on laboratory-proven influenza, pneumonia or deaths from pneumonia.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD005187. Epub 2010 Feb 17. PMID: [20166073](#)

Article Published Date : Jan 01, 2010

Authors : Roger E Thomas, Tom Jefferson, Toby J Lasserson

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is a lack of evidence for the effectiveness of influenza vaccines in adults aged 65 years or older.](#) - GMI Summary

Pubmed Data : Lancet Infect Dis. 2011 Oct 25. Epub 2011 Oct 25. PMID: [22032844](#)

Article Published Date : Oct 25, 2011

Authors : Michael T Osterholm, Nicholas S Kelley, Alfred Sommer, Edward A Belongia

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Intussusception](#)

[Rates of intussusception associated with rotavirus vaccines may be significantly underestimated.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2009 Nov 1;200 Suppl 1:S264-70. PMID: [19817607](#)

Article Published Date : Nov 01, 2009

Authors : Margaret M Cortese, Mary Allen Staat, Geoffrey A Weinberg, Kathryn Edwards, Marilyn A Rice, Peter G Szilagyi, Caroline B Hall, Daniel C Payne, Umesh D Parashar

Study Type : Human Study

Additional Links

Diseases : [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)
Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[Rotavirus vaccination has been associated with increased risk for gastroenteritis and intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2004 Apr;113(4):e353-9. PMID: [15060267](#)

Article Published Date : Apr 01, 2004

Authors : Penina Haber, Robert T Chen, Lynn R Zanardi, Gina T Mootrey, Roseanne English, M Miles Braun,

Study Type : Human Study

Additional Links

Diseases : [Gastroenteritis : CK\(96\) : AC\(11\)](#), [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[Rotavirus vaccinations have a history of causing adverse effects such as intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2001 Jun;107(6):E97. PMID: [11389295](#)

Article Published Date : Jun 01, 2001

Authors : L R Zanardi, P Haber, G T Mootrey, M T Niu, M Wharton

Study Type : Human Study

Additional Links

Diseases : [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Topic: Myocarditis

[An economic analysis of mass smallpox vaccination reveals that cardiovascular adverse events would be sizeable and costly.](#) - GMI Summary

Pubmed Data : J Rheumatol. 1994 Jul;21(7):1305-9. PMID: [18284356](#)

Article Published Date : Jul 01, 1994

Authors : Ismael R Ortega-Sanchez, Mercedes M Sniadack, Gina T Mootrey

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Myocarditis and pericarditis have been reported following smallpox vaccination in Europe, Australia and the United States.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2008 Mar 15;46 Suppl 3:S242-50. PMID: [18284365](#)

Article Published Date : Mar 15, 2008

Authors : Juliette Morgan, Martha H Roper, Laurence Sperling, Richard A Schieber, James D Heffelfinger, Christine G Casey, Jacqueline W Miller, Scott Santibanez, Barbara Herwaldt, Paige Hightower, Pedro L Moro, Beth F Hibbs, Nancy H Levine, Louisa E Chapman, John Iskander, J Michael Lane, Melinda Wharton, Gina T Mootrey, David L Swerdlow

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Smallpox vaccination has been associated with cardiac complications such as](#)

[myopericarditis.](#) - GMI Summary

Pubmed Data : South Med J. 2009 May 7. Epub 2009 May 7. PMID: [19434043](#)

Article Published Date : May 07, 2009

Authors : Luis F Mora, Akbar H Khan, Laurence S Sperling

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Topic: [Pericarditis](#)

[An economic analysis of mass smallpox vaccination reveals that cardiovascular adverse events would be sizeable and costly.](#) - GMI Summary

Pubmed Data : J Rheumatol. 1994 Jul;21(7):1305-9. PMID: [18284356](#)

Article Published Date : Jul 01, 1994

Authors : Ismael R Ortega-Sanchez, Mercedes M Sniadack, Gina T Mootrey

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Myocarditis and pericarditis have been reported following smallpox vaccination in Europe, Australia and the United States.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2008 Mar 15;46 Suppl 3:S242-50. PMID: [18284365](#)

Article Published Date : Mar 15, 2008

Authors : Juliette Morgan, Martha H Roper, Laurence Sperling, Richard A Schieber, James D Heffelfinger, Christine G Casey, Jacqueline W Miller, Scott Santibanez, Barbara Herwaldt, Paige Hightower, Pedro L Moro, Beth F Hibbs, Nancy H Levine, Louisa E Chapman, John Iskander, J Michael Lane, Melinda Wharton, Gina T Mootrey, David L Swerdlow

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Smallpox vaccination has been associated with cardiac complications such as myopericarditis.](#) - GMI Summary

Pubmed Data : South Med J. 2009 May 7. Epub 2009 May 7. PMID: [19434043](#)

Article Published Date : May 07, 2009

Authors : Luis F Mora, Akbar H Khan, Laurence S Sperling

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Topic: [Swine Flu Associated Virus](#)

[Influenza-related mortality is not prevented with increasing vaccination coverage.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 Oct 30;24(42-43):6468-75. Epub 2006 Jul 7. PMID: [16876293](#)

Article Published Date : Oct 30, 2006

Authors : Caterina Rizzo, Cécile Viboud, Emanuele Montomoli, Lone Simonsen, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Widening influenza vaccine coverage is not correleated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[ransverse myelitis has been reported in association with a nasal attenuated novel influenza A\(H1N1\) vaccine.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2010 Aug;67(8):1018-20. PMID: [20697056](#)

Article Published Date : Aug 01, 2010

Authors : Wafa Akkad, Bassel Salem, Jerome W Freeman, Mark K Huntington

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Nasal : CK\(3\) : AC\(1\)](#)

[Vaccination against novel H1N1 may accelerate atherogenesis \(heart disease\).](#) - GMI Summary

Pubmed Data : Med Microbiol Immunol. 2009 Oct 23. PMID: [19851782](#)

Article Published Date : Oct 23, 2009

Authors : Sucharit Bhakdi, Karl Lackner, Hans-Wilhelm Doerr

Study Type : Commentary

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Immune Dysregulation: TH1/TH2 imbalance

The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects. - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Timing of routine immunisations (earlier = increased) and subsequent hay fever risk. - GMI Summary

Pubmed Data : Arch Dis Child. 2005 Jun ;90(6):567-73. PMID: [15908618](#)

Article Published Date : May 31, 2005

Authors : S A Bremner, I M Carey, S DeWilde, N Richards, W C Maier, S R Hilton, D P Strachan, D G Cook

Study Type : Human Study

Additional Links

Diseases : [Allergic Rhinitis : CK\(340\) : AC\(40\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Adjuvants in vaccines may trigger innate cells response by toll-like receptors, thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity. - GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Immune Disorders: B-Cell Over-Activity : CK\(2\) : AC\(2\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#)

Topic: Birth Defects

Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy. - GMI Summary

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Birth Defects : CK\(204\) : AC\(39\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)
Adverse Pharmacological Actions : [Teratogenic : CK\(318\) : AC\(62\)](#)

[Congenital malformation is a possible consequence of rubella vaccination during pregnancy.](#) - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Erythema

[Erythema multiforme has been reported as a possible side effect of vaccination for human papillomavirus.](#) - GMI Summary

Pubmed Data : Dermatology. 2010;220(1):60-2. Epub 2009 Nov 3. PMID: [19887766](#)

Article Published Date : Jan 01, 2010

Authors : A C Katoulis, A Liakou, E Bozi, M Theodorakis, A Alevizou, A Zafeiraki, M Mistidou, N G Stavrianeas

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Vaccination for DPT, Hepatitis B and influenza has been reported to be associated with the development of erythema multiforme in an infant.](#) - GMI Summary

Pubmed Data : Indian J Dermatol Venereol Leprol. 2008 May-Jun;74(3):251-3. PMID: [18583795](#)

Article Published Date : May 01, 2008

Authors : Sarvjit Kaur, Sanjeev Handa

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: Pneumonia

[Influenza vaccination for healthcare workers who work with the elderly has no effect on laboratory-proven influenza, pneumonia or deaths from pneumonia.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD005187. Epub 2010 Feb 17. PMID: [20166073](#)

Article Published Date : Jan 01, 2010

Authors : Roger E Thomas, Tom Jefferson, Toby J Lasserson

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Pneumococcal vaccines do not appear to reduce the risk of death from pneumonia in adult populations. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2003(4):CD000422. PMID: [14583920](#)

Article Published Date : Jan 01, 2003

Authors : K Dear, J Holden, R Andrews, D Tatham

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. - GMI Summary](#)

Pubmed Data : Am J Clin Nutr. 2004 Jul ;80(1):193-8. PMID: [15213048](#)

Article Published Date : Jun 30, 2004

Authors : Laura E Caulfield, Mercedes de Onis, Monika Blössner, Robert E Black

Study Type : Human Study

Additional Links

Diseases : [Diarrhea : CK\(544\) : AC\(73\)](#), [Malaria : CK\(89\) : AC\(30\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Additional Keywords : [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Childhood Infections](#)

[BCG revaccination may raise mortality in young children. - GMI Summary](#)

Pubmed Data : BMJ. 2010;340:c671. Epub 2010 Mar 15. PMID: [20231251](#)

Article Published Date : Jan 01, 2010

Authors : Adam Edvin Roth, Christine Stabell Benn, Henrik Ravn, Amabelia Rodrigues, Ida Maria Lisse, Maria Yazdanbakhsh, Hilton Whittle, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Tuberculosis : CK\(244\) : AC\(42\)](#)

Anti Therapeutic Actions : [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#)

[Influenza vaccines were not shown to be effective among children 6 to 59 months of age during 2 influenza seasons. - GMI Summary](#)

Pubmed Data : Anticancer Res. 2009 Nov;29(11):4629-32. PMID: [18838647](#)

Article Published Date : Nov 01, 2009

Authors : Peter G Szilagyi, Gerry Fairbrother, Marie R Griffin, Richard W Hornung, Stephanie Donauer, Ardythe Morrow, Mekibib Altaye, Yuwei Zhu, Sandra Ambrose, Kathryn M Edwards, Katherine A Poehling, Geraldine Lofthus, Michol Holloway, Lyn Finelli, Marika Iwane, Mary Allen Staat,

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There has been a five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine. - GMI Summary](#)

Pubmed Data : Pediatr Infect Dis J. 2008 Nov;27(11):1030-2. PMID: [18845981](#)

Article Published Date : Nov 01, 2008

Authors : Debra J Hendrickson, Dean A Blumberg, Jesse P Joad, Sanjay Jhavar, Ruth J McDonald

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Empyema : CK\(10\) : AC\(1\)](#), [Parapneumonic Empyema : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussières

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Optic Neuritis](#)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Optic neuritis following hepatitis B vaccination has been reported.](#) n - GMI Summary

Pubmed Data : J Chin Med Assoc. 2009 Nov;72(11):594-7. PMID: [19948437](#)

Article Published Date : Nov 01, 2009

Authors : Muferet Erguven, Sirin Guven, Umit Akyuz, Olcay Bilgiç, Fuat Laloglu

Study Type : Human: Case Report

Additional Links

Diseases : [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Non-polio acute flaccid paralysis (NPAFP)

Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary. - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#), [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

In 2011, there were an extra 47,500 new cases of non-polio acute flaccid paralysis (NPAFP); Clinically indistinguishable from polio paralysis but twice as deadly, the incidence of NPAFP was directly proportional to doses of oral polio received. - GMI Summary

Pubmed Data : Indian J Med Ethics. 2012 Apr-Jun;9(2):114-7. PMID: [22591873](#)

Article Published Date : Apr 01, 2012

Authors : Neetu Vashisht, Jacob Puliyel

Study Type : Review

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Over 40,000 cases of AFP are reported annually since 2007 regardless of the number of actual polio cases. - GMI Summary

Pubmed Data : BMC Public Health. 2012 ;12:229. Epub 2012 Mar 22. PMID: [22439606](#)

Article Published Date : Jan 01, 2012

Authors : Rie R Yotsu, Katharine Abba, Helen Smith, Abhijit Das

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#), [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Topic: Child Mortality

Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau. - GMI Summary

Article Published Date : Dec 06, 2013

Authors : Ane Bærent Fisker, Henrik Ravn, Amabelia Rodrigues, Marie Drivsholm Ostergaard, Carlito Bale, Christine Stabell Benn, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#)

Additional Keywords : [Child Mortality : CK\(64\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Evidence exists demonstrating that diphtheria-tetanus-pertussis \(DTP\) vaccines increase mortality in children.](#) - GMI Summary

Pubmed Data : Trop Med Int Health. 2007 Jan;12(1):15-24. PMID: [17207144](#)

Article Published Date : Jan 01, 2007

Authors : Peter Aaby, Christine Stabell Benn, Jens Nielsen, Ida Maria Lisse, Amabelia Rodrigues, Henrik Jensen

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[High-titer measles vaccination before 9 months of age has been linked to increased female mortality.](#) - GMI Summary

Pubmed Data : Semin Pediatr Infect Dis. 2003 Jul;14(3):220-32. PMID: [12913835](#)

Article Published Date : Jul 01, 2003

Authors : Peter Aaby, Henrik Jensen, Francois Simondon, Hilton Whittle

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles vaccination in developing countries has resulted in higher infant mortality rates.](#) - GMI Summary

Pubmed Data : BMJ. 1993 Nov 20;307(6915):1294-5. PMID: [8257878](#)

Article Published Date : Nov 20, 1993

Authors : A J Hall, F T Cutts

Study Type : Review

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder : CK\(134\) : AC\(12\)](#), [Attention Deficit Disorder with Hyperactivity : CK\(242\) : AC\(31\)](#), [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Child Mortality : CK\(64\) : AC\(8\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Mental Retardation : CK\(71\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Ear Infection](#)

[Hepatitis B vaccine is positively associated with adverse health outcomes in the](#)

general population of US children. - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Pneumococcal conjugate vaccine is not effective to prevent ear infections in previously unvaccinated toddlers and children with a history of recurrent ear infections. - GMI Summary

Pubmed Data : Lancet. 2003 Jun 28;361(9376):2189-95. PMID: [12842372](#)

Article Published Date : Jun 28, 2003

Authors : Reinier Veenhoven, Debby Bogaert, Cuno Uiterwaal, Carole Brouwer, Herma Kiezebrink, Jacob Bruin, Ed IJzerman, Peter Hermans, Ronald de Groot, Ben Zegers, Wietse Kuis, Ger Rijkers, Anne Schilder, Elisabeth Sanders

Study Type : Human Study

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Review: based on currently available research pneumoccal vaccination should not be recommended for large scale use in ear infection prone populations. - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2002(2):CD001480. PMID: [12076412](#)

Article Published Date : Jan 01, 2002

Authors : M Straetemans, E A Sanders, R H Veenhoven, A G Schilder, R A Damoiseaux, G A Zielhuis

Study Type : Review

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Topic: Arthritis: Juvenile Idiopathic

Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children. - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Thirty-five percent of children with juvenile idiopathic arthritis experienced flare of the disease after vaccination. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2012 Mar 15. Epub 2012 Mar 15. PMID: [22513085](#)

Article Published Date : Mar 15, 2012

Authors : Natasa Toplak, Vesna Subelj, Tanja Kveder, Sasa Cucnik, Katarina Prosenec, Alenka Trampus-Bakija, Ljupco Todorovski, Tadej Avcin

Study Type : Human Study

Additional Links

Diseases : [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Cold and Flu: Infants & Children](#)

[Inactivated flu vaccines have not been proven to be effective or safe in preventing influenza in healthy children under two.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2009 Sep-Oct;15(5):44-6. PMID: [18425905](#)

Article Published Date : Sep 01, 2009

Authors : Tom Jefferson, Alessandro Rivetti, Anthony Harnden, Carlo Di Pietrantonj, Vittorio Demicheli

Study Type : Meta Analysis

Additional Links

Diseases : [Cold and Flu: Infants & Children : CK\(62\) : AC\(6\)](#), [Infection: In Infants & Children : CK\(111\) : AC\(11\)](#), [Influenza A : CK\(292\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Cystic Fibrosis](#)

[There is currently no evidence from randomised studies that influenza vaccine given to people with CF is of benefit to them.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2009 Oct 7;(4):CD001753. PMID: [19821281](#)

Article Published Date : Oct 07, 2009

Authors : Poonam Dharmaraj, Rosalind L Smyth

Study Type : Meta Analysis

Additional Links

Diseases : [Cystic Fibrosis : CK\(523\) : AC\(78\)](#)

Additional Keywords : [Vaccine Research : CK\(20\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Annual influenza vaccination hampers the development of virus-specific CD8\(+\) T cell responses necessary to protect against influenza infection.](#) - GMI Summary

Pubmed Data : J Virol. 2011 Nov ;85(22):11995-2000. Epub 2011 Aug 31. PMID: [21880755](#)

Article Published Date : Nov 01, 2011

Authors : Rogier Bodewes, Pieter L A Fraaij, Martina M Geelhoed-Mieras, Carel A van Baalen, Harm A W M Tiddens, Annemarie M C van Rossum, Fiona R van der Klis, Ron A M Fouchier, Albert D M E Osterhaus, Guus F Rimmelzwaan

Study Type : Human Study

Additional Links

Diseases : [Cystic Fibrosis : CK\(523\) : AC\(78\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Immunosuppressive : CK\(156\) : AC\(26\)](#)

Topic: [Elevated CRP](#)

C-reactive protein (CRP) elevation occur in infants without sepsis after hepatitis B vaccination. - GMI Summary

Pubmed Data : Eur J Pediatr. 2013 Jan 29. Epub 2013 Jan 29. PMID: [23358708](#)

Article Published Date : Jan 28, 2013

Authors : Istemi Han Celik, Gamze Demirel, Fuat Emre Canpolat, Omer Erdeve, Ugur Dilmen

Study Type : Human Study

Additional Links

Diseases : [Elevated CRP : CK\(82\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth. - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: Encephalitis

Pertussis vaccination may activate a genetic predisposition for encephalopathy in susceptible individuals. - GMI Summary

Pubmed Data : Cytotechnology. 2002 Nov;40(1-3):139-49. PMID: [20447868](#)

Article Published Date : Nov 01, 2002

Authors : Anne M McIntosh, Jacinta McMahon, Leanne M Dibbens, Xenia Iona, John C Mulley, Ingrid E Scheffer, Samuel F Berkovic

Study Type : Human Study

Additional Links

Diseases : [Dravet syndrome : CK\(30\) : AC\(3\)](#), [Encephalitis : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Varicella-zoster vaccine has been linked to herpes zoster ophthalmicus and encephalitis as possible, though rare side effects. - GMI Summary

Pubmed Data : Pediatrics. 2010 Apr;125(4):e969-72. Epub 2010 Mar 1. PMID: [20194287](#)

Article Published Date : Apr 01, 2010

Authors : Giorgos Chouliaras, Vana Spoulou, Mark Quinlivan, Judith Breuer, Maria Theodoridou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis : CK\(23\) : AC\(4\)](#), [Herpes: Ocular : CK\(12\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Encephalopathy: Acute Necrotizing

Acute necrotizing encephalopathy secondary to diphtheria, tetanus toxoid and whole-cell pertussis vaccination has been reported. - GMI Summary

Pubmed Data : Pediatr Radiol. 2010 Jul;40(7):1281-4. Epub 2010 Jan 30. PMID: [20119724](#)

Article Published Date : Jul 01, 2010

Authors : Hale Aydin, Esra Ozgul, Ahmet Muhtesem Agildere

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

Serious adverse events associated with whole cell pertussis vaccine, e.g. sudden infant death syndrome and encephalopathy, may have occurred in metabolically vulnerable children. - GMI Summary

Pubmed Data : Pharmazie. 2007 Apr;62(4):299-304. PMID: [19660877](#)

Article Published Date : Apr 01, 2007

Authors : Kumanan Wilson, Beth Potter, Douglas Manuel, Jennifer Keelan, Pranesh Chakraborty

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

Topic: Gulf War Syndrome

Symptomatic Gulf War Syndrome is strongly associated with the presence of autoantibodies to squalene, an adjuvant used in vaccines. - GMI Summary

Pubmed Data : Exp Mol Pathol. 2000 Feb;68(1):55-64. PMID: [10640454](#)

Article Published Date : Feb 01, 2000

Authors : P B Asa, Y Cao, R F Garry

Study Type : Human Study

Additional Links

Diseases : [Gulf War Syndrome](#) : CK(33) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Anthrax](#) : CK(62) : AC(8)

The vaccine adjuvant squalene in anthrax vaccines given to soldiers in the Gulf War resulted in the formation of antibodies to squalene which are associated with Gulf War Syndrome. - GMI Summary

Pubmed Data : Neuropharmacology. 2011 Feb-Mar;60(2-3):252-8. Epub 2010 Sep 22. PMID: [12127050](#)

Article Published Date : Feb 01, 2011

Authors : Pamela B Asa, Russell B Wilson, Robert F Garry

Study Type : Human Study

Additional Links

Diseases : [Anthrax](#) : CK(43) : AC(6), [Gulf War Syndrome](#) : CK(33) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Anthrax](#) : CK(62) : AC(8)

Problem Substances : [Squalene, Adjuvant](#) : CK(2) : AC(1)

Topic: HPV

Human Papilloma Virus (HPV) vaccine is associated with demyelinating events. - GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, Il Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [HPV : CK\(31\) : AC\(4\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [HPV Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardisil\) : CK\(105\) : AC\(13\)](#)

[The way that the effectiveness of HPV vaccines are framed influences whether or not respondents believe they are effective and their acceptance level of vaccine mandate policies.](#) - GMI Summary

Pubmed Data : Patient Educ Couns. 2010 Sep 17. Epub 2010 Sep 17. PMID: [20851560](#)

Article Published Date : Sep 17, 2010

Authors : Cabral A Bigman, Joseph N Cappella, Robert C Hornik

Study Type : Human Study

Additional Links

Diseases : [HPV : CK\(31\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardisil\) : CK\(105\) : AC\(13\)](#)

Topic: Infant Chemical Exposures

[Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem.](#) - GMI Summary

Pubmed Data : Am J Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Infant Chemical Exposures : CK\(165\) : AC\(24\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Infection: In Infants & Children

[Inactivated flu vaccines have not been proven to be effective or safe in preventing influenza in healthy children under two.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2009 Sep-Oct;15(5):44-6. PMID: [18425905](#)

Article Published Date : Sep 01, 2009

Authors : Tom Jefferson, Alessandro Rivetti, Anthony Harnden, Carlo Di Pietrantonj, Vittorio Demicheli

Study Type : Meta Analysis

Additional Links

Diseases : [Cold and Flu: Infants & Children : CK\(62\) : AC\(6\)](#), [Infection: In Infants & Children : CK\(111\) : AC\(11\)](#), [Influenza A : CK\(292\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: Meningitis: Viral

[Varicella vaccine has been reported to cause herpes zoster skin lesions and](#)

[meningitis in a previously healthy boy.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Nov 15;198(10):1444-7. PMID: [18826373](#)

Article Published Date : Nov 15, 2008

Authors : Myron J Levin, Roberta L DeBiasi, Vanda Bostik, D Scott Schmid

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Varicella vaccine has been reported to viral meningitis in an immunocompetent child.](#) - GMI Summary

Pubmed Data : Ann Emerg Med. 2009 Jun;53(6):792-5. Epub 2008 Nov 22. PMID: [19028409](#)

Article Published Date : Jun 01, 2009

Authors : Sujit Iyer, Manoj K Mittal, Richard L Hodinka

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Undefined : CK\(14\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Abortion: Spontaneous

[A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows.](#) - GMI Summary

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Cheville

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%.](#) - GMI Summary

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies.](#) - GMI Summary

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does. - GMI Summary](#)

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly. - GMI Summary](#)

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25. - GMI Summary](#)

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escjadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The number of elective abortions following vaccination during pregnancy may be under-reported and could be substantial. - GMI Summary](#)

Pubmed Data : Vaccine. 2008 May 2;26(19):2428-32. Epub 2008 Mar 17. PMID: [18406499](#)

Article Published Date : May 02, 2008

Authors : Soju Chang, Robert Ball, M Miles Braun

Study Type : Review

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Rheumatoid Arthritis

Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Rabies

Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy. - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Rabies encephalitis in a child: a failure of rabies post exposure prophylaxis? - GMI Summary](#)

Pubmed Data : BMJ Case Rep. 2015 ;2015. Epub 2015 Jan 14. PMID: [25589528](#)

Article Published Date : Dec 31, 2014

Authors : Faten Tinsa, Aida Borgi, Imen Jahouat, Khadija Boussetta

Study Type : Human: Case Report

Additional Links

Diseases : [Rabies : CK\(13\) : AC\(3\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Rabies : CK\(4\) : AC\(3\)](#)

[Rabies vaccine may be ineffective during symptomatic rabies and may contribute to "early death." - GMI Summary](#)

Pubmed Data : Vaccine. 2009 Nov 27;27(51):7173-7. PMID: [19925949](#)

Article Published Date : Nov 27, 2009

Authors : Rodney E Willoughby

Study Type : Animal Study

Additional Links

Diseases : [Rabies : CK\(13\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: Rabies : CK\(4\) : AC\(3\)](#)

Topic: Smallpox

[Adverse events following smallpox vaccination with ACAM2000 in a military population have been reported. - GMI Summary](#)

Pubmed Data : Arch Dermatol. 2010 Jun;146(6):656-61. PMID: [20566929](#)

Article Published Date : Jun 01, 2010

Authors : Thomas M Beachkofsky, Scott C Carrizales, Jeffrey J Bidinger, David E Hrncir, Darren E Whittemore, Chad M Hivnor

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Smallpox vaccine caused iatrogenic vaccinia in children in Russia. - GMI Summary](#)

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr(2):40-5. PMID: [11548257](#)

Article Published Date : Mar 01, 2001

Authors : G G Onishchenko, V I Markov, V N Ustiushin, S V Borisevich, G I Kuznetsova, S Ia Loginova, A M Berezhnoĭ, N T Vasil'ev, V A Maksimov, A A Makhlaĭ

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Review: possible adverse effects that are associated with smallpox vaccination.](#)

- GMI Summary

Pubmed Data : MMWR Recomm Rep. 2003 Feb 21;52(RR-4):1-28. PMID: [12617510](#)

Article Published Date : Feb 21, 2003

Authors : Joanne Cono, Christine G Casey, David M Bell,

Study Type : Review

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Topic: [Acute Autoimmune Neuropathy](#)

[Hepatitis B vaccination has been linked to autoimmune inflammatory polyneuropathy \(PN\).](#) - GMI Summary

Pubmed Data : J Peripher Nerv Syst. 2002 Sep;7(3):163-7. PMID: [12365564](#)

Article Published Date : Sep 01, 2002

Authors : Claude Vital, Anne Vital, Georges Gbikpi-Benissan, Maïté Longy-Boursier, Marie-Thérèse Climas, Yves Castaing, Marie-Hélène Canron, Michel Le Bras, Klaus Petry

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune inflammatory polyneuropathy \(PN\) : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [C-Reactive Protein](#)

[CRP level in infants is elevated in the 48 hours following immunization.](#) - GMI Summary

Pubmed Data : J Pediatr. 2007 Aug ;151(2):167-72. Epub 2007 Jun 22. PMID: [17643770](#)

Article Published Date : Aug 01, 2007

Authors : Massroor Pourcyrus, Sheldon B Korones, Kristopher L Arheart, Henrietta S Bada

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Multiple Vaccines : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza A vaccination containing adjuvant causes cardiac autonomic](#)

dysfunction and inflammation which may transiently increase the risk of cardiovascular events. - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Cardiovascular Diseases : CK\(5342\) : AC\(665\)](#), [Diabetes Mellitus: Type 2 : CK\(3603\) : AC\(359\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Interleukin-6 upregulation : CK\(26\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: Cataract

In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Corticosteroid-Induced Toxicity

Administration of varicella vaccine before the age of 15 months, and the prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease. - GMI Summary

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Mullooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#), [Corticosteroid-Induced Toxicity : CK\(78\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Febrile Seizures

Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately. - GMI Summary

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures : CK\(83\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Lyme Disease](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Neuropathy: Small Fiber](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Premature Birth](#)

[CRP level in infants is elevated in the 48 hours following immunization.](#) - GMI Summary

Pubmed Data : J Pediatr. 2007 Aug ;151(2):167-72. Epub 2007 Jun 22. PMID: [17643770](#)

Article Published Date : Aug 01, 2007

Authors : Massroor Pourcyrus, Sheldon B Korones, Kristopher L Arheart, Henrietta S Bada

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Multiple Vaccines : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Hepatitis B vaccination is associated with potentially neurotoxic mercury exposure in infants.](#) - GMI Summary

Pubmed Data : Chin Med. 2008 Mar 29;3:4. PMID: [10802503](#)

Article Published Date : Mar 29, 2008

Authors : G V Stajich, G P Lopez, S W Harry, W R Sexson

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Vaccinia virus](#)

[Adverse events following smallpox vaccination with ACAM2000 in a military population have been reported.](#) - GMI Summary

Pubmed Data : Arch Dermatol. 2010 Jun;146(6):656-61. PMID: [20566929](#)

Article Published Date : Jun 01, 2010

Authors : Thomas M Beachkofsky, Scott C Carrizales, Jeffrey J Bidinger, David E Hrncir, Darren E Whittemore, Chad M Hivnor

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Smallpox vaccine caused iatrogenic vaccinia in children in Russia.](#) - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr(2):40-5. PMID: [11548257](#)

Article Published Date : Mar 01, 2001

Authors : G G Onishchenko, V I Markov, V N Ustiushin, S V Borisevich, G I Kuznetsova, S Ia Loginova, A M Berezhnoi, N T Vasil'ev, V A Maksimov, A A Makhlaï

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Topic: [Polio](#)

[The oral polio vaccine is unlikely to be able to eradicate polio from India.](#) - GMI Summary

Pubmed Data : Vaccine. 2008 Apr 16 ;26(17):2058-61. Epub 2008 Mar 14. PMID: [18378367](#)

Article Published Date : Apr 16, 2008

Authors : Yash Paul

Study Type : Human Study

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

["Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children."](#) - GMI Summary

Pubmed Data : Lancet. 1991 Sep 21 ;338(8769):715-20. PMID: [1679866](#)

Article Published Date : Sep 20, 1991

Authors : R W Sutter, P A Patriarca, S Brogan, P G Malankar, M A Pallansch, O M Kew, A G Bass, S L Cochi, J P Alexander, D B Hall

Study Type : Human: Case Report

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#)
Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)
Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#)

[Case report: failure to clear persistent vaccine-derived neurovirulent poliovirus infection in an immunodeficient man. - GMI Summary](#)

Pubmed Data : Lancet. 2004 May 8 ;363(9420):1509-13. PMID: [15135598](#)

Article Published Date : May 07, 2004

Authors : Calman MacLennan, Glynis Dunn, Aarnoud P Huissoon, Dinakantha S Kumararatne, Javier Martin, Paula O'Leary, Ronald A Thompson, Husam Osman, Philip Wood, Philip Minor, David J Wood, Deenan Pillay

Study Type : Human: Case Report

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccine-derived poliovirus may become pathogenic in complex viral ecosystems, through frequent recombination events and mutations. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2012 May 1 ;205(9):1363-73. Epub 2012 Mar 29. PMID: [22457288](#)

Article Published Date : May 01, 2012

Authors : Marie-Line Joffret, Sophie Jégouic, Maël Bessaud, Jean Balanant, Coralie Tran, Valerie Caro, Barbara Holmblat, Richter Razafindratsimandresy, Jean-Marc Reynes, Mala Rakoto-Andrianarivelo, Francis Delpeyroux

Study Type : Review

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Topic: Glomerulonephritis](#)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary](#)

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[A case of influenza vaccine induced have necrotizing glomerulonephritis in decursu vasculitis has been reported. - GMI Summary](#)

Pubmed Data : Pol Merkur Lekarski. 2005 Jul;19(109):75-7. PMID: [16194032](#)

Article Published Date : Jul 01, 2005

Authors : Lidia Hyla-Klekot, Grazyna Kucharska, Witold Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) :](#)

Topic: **Lupus Erythematosus: Systemic**

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Possible systemic lupus erythematosus following HPV immunization has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):158-61. PMID: [22235047](#)

Article Published Date : Jan 01, 2012

Authors : Hf Soldevilla, Sfr Briones, Sv Navarra

Study Type : Human: Case Report

Additional Links

Diseases : [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Topic: **Seizures**

[DPT vaccines have been associated with recurrent seizures.](#) - GMI Summary

Pubmed Data : Am J Dis Child. 1984 Oct;138(10):908-11. PMID: [6206715](#)

Article Published Date : Oct 01, 1984

Authors : J V Murphy, L D Sarff, K M Marquardt

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Seizures : CK\(135\) : AC\(33\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[H1N1 vaccination has been linked to possible new-onset seizure.](#) - GMI Summary

Pubmed Data : Pharmacotherapy. 2011 Jan;31(1):113. PMID: [21182364](#)

Article Published Date : Jan 01, 2011

Authors : [No authors listed]

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Seizures : CK\(135\) : AC\(33\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: **Macrophagic myofasciitis**

Aluminum hydroxide-induced macrophagic myofasciitis (MMF) associated with vaccination has been reported. - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1457-63. Epub 2011 Aug 22. PMID: [22099155](#)

Article Published Date : Nov 01, 2011

Authors : Elodie Passeri, Chiara Villa, Maryline Couette, Emmanuel Itti, Pierre Brugieres, Pierre Cesaro, Romain K Gherardi, Anne-Catherine Bachoud-Levi, François-Jérôme Authier

Study Type : Human Study

Additional Links

Diseases : [Macrophagic myofasciitis](#) : CK(15) : AC(3)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2012 Mar 14. Epub 2012 Mar 14. PMID: [22425036](#)

Article Published Date : Mar 14, 2012

Authors : Olivier Guillard, Bernard Fauconneau, Alain Pineau, Annie Marraud, Jean-Pierre Bellocq, Marie-Pierre Chenard

Study Type : Human: Case Report, Review

Additional Links

Diseases : [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Pseudolymphoma](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: Tetanus

Adverse effects of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine in 6- to 7-year-old children. - GMI Summary

Pubmed Data : Pediatr Neonatol. 2011 Feb;52(1):38-41. Epub 2011 Feb 17. PMID: [21385656](#)

Article Published Date : Feb 01, 2011

Authors : Sung-Hsi Wei, Yen-Nan Chao, Song-En Huang, Tsuey-Feng Lee, Luan-Yin Chang

Study Type : Human Study

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)
Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Neonatal tetanus despite protective serum antitoxin concentration.](#) - GMI Summary

Pubmed Data : FEMS Microbiol Immunol. 1991 Jun ;3(3):171-5. PMID: [1878260](#)

Article Published Date : May 31, 1991

Authors : S Y Maselle, R Matre, R Mbise, T Hofstad

Study Type : Human Study

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Severe tetanus has been reported in immunized patients with high anti-tetanus titers.](#) - GMI Summary

Pubmed Data : Neurology. 1992 Apr ;42(4):761-4. PMID: [1565228](#)

Article Published Date : Apr 01, 1992

Authors : N E Crone, A T Reder

Study Type : Human: Case Report

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: [Animal Diseases: Infectious](#)

[A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows.](#) - GMI Summary

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Chevillie

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%.](#) - GMI Summary

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25.](#) - GMI Summary

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escjadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced scrapie has been reported in animals.](#) - GMI Summary

Pubmed Data : J Gen Virol. 2003 Apr;84(Pt 4):1047-52. PMID: [12655108](#)

Article Published Date : Apr 01, 2003

Authors : Gianluigi Zanusso, Cristina Casalone, Pierluigi Acutis, Elena Bozzetta, Alessia Farinazzo, Matteo Gelati, Michele Fiorini, Gianluigi Forloni, Man Sun Sy, Salvatore Monaco, Maria Caramelli

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Animal Diseases: Scrapie : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: Alopecia

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Anemia: Aplastic

[Varicella vaccine may be associated with aplastic anemia in children.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Aug;28(8):746-8. PMID: [19633522](#)

Article Published Date : Aug 01, 2009

Authors : Paola Angelini, Fotini Kavadas, Navneet Sharma, Susan E Richardson, Graham Tipples, Chaim Roifman, Yigal Dror, Yehuda Nofech-Mozes

Study Type : Human Study

Additional Links

Diseases : [Anemia: Aplastic : CK\(30\) : AC\(3\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Arthritis: Juvenile Chronic

[Hepatitis B vaccine is positively associated with adverse health outcomes in the](#)

general population of US children. - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Arthritis: Juvenile Rheumatoid

Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children. - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Arthritis: Rheumatoid

Hepatitis B vaccination is associated with a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Atopic Disease

Diphtheria immunisation is weakly associated with an increased risk of asthma by age 7 years. - GMI Summary

Pubmed Data : Thorax. 2007 Mar;62(3):270-5. Epub 2006 Nov 7. PMID: [17090571](#)

Article Published Date : Mar 01, 2007

Authors : Kazunori Nakajima, Shyamali C Dharmage, John B Carlin, Cathryn L Wharton, Mark A Jenkins, Graham G Giles, Michael J Abramson, E Haydn Walters, John L Hopper

Study Type : Meta Analysis

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Atopic Disease : CK\(91\) : AC\(9\)](#), [Hypersensitivity: Immediate : CK\(93\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Topic: [Autoimmune inflammatory polyneuropathy \(PN\)](#)

[Hepatitis B vaccination has been linked to autoimmune inflammatory polyneuropathy \(PN\).](#) - GMI Summary

Pubmed Data : J Peripher Nerv Syst. 2002 Sep;7(3):163-7. PMID: [12365564](#)

Article Published Date : Sep 01, 2002

Authors : Claude Vital, Anne Vital, Georges Gbikpi-Benissan, Maïté Longy-Boursier, Marie-Thérèse Climas, Yves Castaing, Marie-Hélène Canron, Michel Le Bras, Klaus Petry

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune inflammatory polyneuropathy \(PN\) : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [CRP](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Cardiovascular Diseases](#)

[Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events.](#) - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Cardiovascular Diseases : CK\(5342\) : AC\(665\)](#), [Diabetes Mellitus: Type 2 : CK\(3603\) : AC\(359\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Interleukin-6 upregulation : CK\(26\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: Cervical Cancer

The risk of miscarriage increases following HPV vaccination. - GMI Summary

Pubmed Data : BMJ. 2010;340:c712. Epub 2010 Mar 2. PMID: [20197322](#)

Article Published Date : Jan 01, 2010

Authors : Sholom Wacholder, Bingshu Eric Chen, Allen Wilcox, George Macones, Paula Gonzalez, Brian Befano, Allan Hildesheim, Ana Cecilia Rodríguez, Diane Solomon, Rolando Herrero, Mark Schiffman,

Study Type : Human Study

Additional Links

Diseases : [Cervical Cancer : CK\(222\) : AC\(72\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Topic: Diabetes Mellitus: Type 2

Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events. - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein : CK\(879\) : AC\(84\)](#), [Cardiovascular Diseases : CK\(5342\) : AC\(665\)](#),

[Diabetes Mellitus: Type 2 : CK\(3603\) : AC\(359\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Interleukin-6 upregulation : CK\(26\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: Dravet syndrome

Pertussis vaccination may activate a genetic predisposition for encephalopathy in susceptible individuals. - GMI Summary

Pubmed Data : Cytotechnology. 2002 Nov;40(1-3):139-49. PMID: [20447868](#)

Article Published Date : Nov 01, 2002

Authors : Anne M McIntosh, Jacinta McMahon, Leanne M Dibbens, Xenia Iona, John C Mulley, Ingrid E Scheffer, Samuel F Berkovic

Study Type : Human Study

Additional Links

Diseases : [Dravet syndrome : CK\(30\) : AC\(3\)](#), [Encephalitis : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: Gastroenteritis

Rotavirus vaccination has been associated with increased risk for gastroenteritis and intussusception. - GMI Summary

Pubmed Data : Pediatrics. 2004 Apr;113(4):e353-9. PMID: [15060267](#)

Article Published Date : Apr 01, 2004

Authors : Penina Haber, Robert T Chen, Lynn R Zanardi, Gina T Mootrey, Roseanne English, M Miles

Braun,

Study Type : Human Study

Additional Links

Diseases : [Gastroenteritis : CK\(96\) : AC\(11\)](#), [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Topic: [Gastrointestinal Diseases](#)

[Hepatitis B vaccination was statistically associated with gastrointestinal reactions including: hepatitis, gastrointestinal disease and liver function test abnormalities.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2002 Nov-Dec;49(48):1571-5. PMID: [12397738](#)

Article Published Date : Nov 01, 2002

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Gastrointestinal Diseases : CK\(38\) : AC\(14\)](#), [Hepatitis : CK\(64\) : AC\(24\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Haemophilus influenzae](#)

[A Haemophilus b polysaccharide vaccine resulted in minus 58 percent efficacy in children in Minnesota in August 1985.](#) - GMI Summary

Pubmed Data : JAMA. 1988 Sep 9;260(10):1423-8. PMID: [3261350](#)

Article Published Date : Sep 09, 1988

Authors : M T Osterholm, J H Rambeck, K E White, J L Jacobs, L M Pierson, J D Neaton, C W Hedberg, K L MacDonald, D M Granoff

Study Type : Human Study

Additional Links

Diseases : [Haemophilus influenzae : CK\(54\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#)

Topic: [Hearing Loss: Sudden](#)

[38,787 adverse events including infant death \(highest in 1-3 month olds\) after vaccination were reported between 1991-1994. \(The authors speciously claim SIDS and not vaccination caused these deaths\).](#) - GMI Summary

Pubmed Data : J Pediatr. 1997 Oct;131(4):529-35. PMID: [9386653](#)

Article Published Date : Oct 01, 1997

Authors : M M Braun, S S Ellenberg

Study Type : Meta Analysis

Additional Links

Diseases : [Hearing Loss: Sudden : CK\(30\) : AC\(3\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Hepatitis](#)

Hepatitis B vaccination was statistically associated with gastrointestinal reactions including: hepatitis, gastrointestinal disease and liver function test abnormalities. - GMI Summary

Pubmed Data : Hepatogastroenterology. 2002 Nov-Dec;49(48):1571-5. PMID: [12397738](#)

Article Published Date : Nov 01, 2002

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Gastrointestinal Diseases : CK\(38\) : AC\(14\)](#), [Hepatitis : CK\(64\) : AC\(24\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Herpes: Ocular

Varicella-zoster vaccine has been linked to herpes zoster ophthalmicus and encephalitis as possible, though rare side effects. - GMI Summary

Pubmed Data : Pediatrics. 2010 Apr;125(4):e969-72. Epub 2010 Mar 1. PMID: [20194287](#)

Article Published Date : Apr 01, 2010

Authors : Giorgos Chouliaras, Vana Spoulou, Mark Quinlivan, Judith Breuer, Maria Theodoridou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis : CK\(23\) : AC\(4\)](#), [Herpes: Ocular : CK\(12\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Hypersensitivity: Immediate

Diphtheria immunisation is weakly associated with an increased risk of asthma by age 7 years. - GMI Summary

Pubmed Data : Thorax. 2007 Mar;62(3):270-5. Epub 2006 Nov 7. PMID: [17090571](#)

Article Published Date : Mar 01, 2007

Authors : Kazunori Nakajima, Shyamali C Dharmage, John B Carlin, Cathryn L Wharton, Mark A Jenkins, Graham G Giles, Michael J Abramson, E Haydn Walters, John L Hopper

Study Type : Meta Analysis

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Atopic Disease : CK\(91\) : AC\(9\)](#), [Hypersensitivity: Immediate : CK\(93\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Topic: Iatrogenic Disease

Acute hepatitis B can occur in those who are vaccinated against it and who are exposed through unprotected sexual contact and iatrogenically. - GMI Summary

Pubmed Data : Postgrad Med J. 2006 Mar;82(965):207-10. PMID: [16517803](#)

Article Published Date : Mar 01, 2006

Authors : G Rosner, Y Lurie, L Blendis, Z Halpern, R Oren

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Iatrogenic Disease : CK\(62\) : AC\(7\)](#)

Additional Keywords : [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Infant Neurological Development

Whole cell pertussis vaccines may have been causing serious neurological disorders. - GMI Summary

Pubmed Data : Brain Dev. 2004 Aug;26(5):296-300. PMID: [15165669](#)

Article Published Date : Aug 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Infant Neurological Development : CK\(46\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: Inflammation

Hepatitis B vaccination is associated with an increased risk of CNS inflammatory demyelination after 3 years of age. - GMI Summary

Pubmed Data : Reprod Toxicol. 2002 May-Jun;16(3):237-43. PMID: [18843097](#)

Article Published Date : May 01, 2002

Authors : Yann Mikaeloff, Guillaume Caridade, Samy Suissa, Marc Tardieu

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Inflammation : CK\(1125\) : AC\(377\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Inflammatory Bowel Diseases

Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders. - GMI Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Topic: Influenza B

There is little evidence supporting the belief that vaccines are effective in preventing influenza in healthy adults. - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(7):CD001269. Epub 2010 Jul 7. PMID: [20614424](#)

Article Published Date : Jan 01, 2010

Authors : Tom Jefferson, Carlo Di Pietrantonj, Alessandro Rivetti, Ghada A Bawazeer, Lubna A Al-

Ansary, Eliana Ferroni

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Influenza B : CK\(72\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Joint Diseases](#)

[Anthrax vaccination contributes to joint related adverse reactions.](#) - GMI

Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Mar-Apr;20(2):217-20. PMID: [12051402](#)

Article Published Date : Mar 01, 2002

Authors : D A Geier, M R Geier

Study Type : Human Study

Additional Links

Diseases : [Joint Diseases : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Topic: [Liver Disease](#)

[Hepatitis B vaccine is associated with an increased risk of liver problems in U.S. children less than 6 years old, 1993 and 1994.](#) - GMI Summary

Pubmed Data : Epidemiology. 1999 May;10(3):337-9. PMID: [10230847](#)

Article Published Date : May 01, 1999

Authors : M A Fisher, S A Eklund

Study Type : Human Study

Additional Links

Diseases : [Liver Disease : CK\(112\) : AC\(31\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Pancytopenia](#)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Pharyngeal Diseases](#)

[Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children.](#) - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Pre-Eclampsia](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Pregnancy Complications](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Preterm Birth: Prevention](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Shingles](#)

[Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster \(shingles\) cases managed in the same time period.](#) - GMI Summary

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Shingles : CK\(472\) : AC\(35\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Stroke: Prevention](#)

[Influenza vaccination does not prevent ischemic stroke and it does not reduce the rate of acute previous infections in stroke patients.](#) - GMI Summary

Pubmed Data : Cerebrovasc Dis. 2008;26(4):339-47. Epub 2008 Aug 27. PMID: [18728360](#)

Article Published Date : Jan 01, 2008

Authors : G Piñol-Ripoll, I de la Puerta, S Santos, F Purroy, E Mostacero

Study Type : Human Study

Additional Links

Diseases : [Stroke: Prevention : CK\(163\) : AC\(21\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Syncope](#)

[Postlicensure safety surveillance has revealed a disproportionate reporting of syncope and venous thromboembolic events following quadrivalent HPV vaccination.](#) - GMI Summary

Pubmed Data : JAMA. 2009 Aug 19;302(7):750-7. PMID: [19690307](#)

Article Published Date : Aug 19, 2009

Authors : Barbara A Slade, Laura Leidel, Claudia Vellozzi, Emily Jane Woo, Wei Hua, Andrea Sutherland, Hector S Izurieta, Robert Ball, Nancy Miller, M Miles Braun, Lauri E Markowitz, John Iskander

Study Type : Human Study

Additional Links

Diseases : [Syncope : CK\(10\) : AC\(1\)](#), [Thromboembolism : CK\(205\) : AC\(16\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Topic: Thromboembolism

Postlicensure safety surveillance has revealed a disproportionate reporting of syncope and venous thromboembolic events following quadrivalent HPV vaccination. - GMI Summary

Pubmed Data : JAMA. 2009 Aug 19;302(7):750-7. PMID: [19690307](#)

Article Published Date : Aug 19, 2009

Authors : Barbara A Slade, Laura Leidel, Claudia Vellozzi, Emily Jane Woo, Wei Hua, Andrea Sutherland, Hector S Izurieta, Robert Ball, Nancy Miller, M Miles Braun, Lauri E Markowitz, John Iskander

Study Type : Human Study

Additional Links

Diseases : [Syncope : CK\(10\) : AC\(1\)](#), [Thromboembolism : CK\(205\) : AC\(16\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Topic: Ulcerative Colitis

Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders. - GMI Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Topic: Uveitis

Hepatitis B vaccine may have a possible association with the development of uveitis in some patients. - GMI Summary

Pubmed Data : Cutan Ocul Toxicol. 2010 Mar;29(1):26-9. PMID: [19947819](#)

Article Published Date : Mar 01, 2010

Authors : Frederick W Fraunfelder, Eric B Suhler, Frederick T Fraunfelder

Study Type : Human Study

Additional Links

Diseases : [Uveitis : CK\(73\) : AC\(11\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: Viremia

Varicella vaccine has been associated with viremia and streptococcal toxic shock syndrome. - GMI Summary

Pubmed Data : Med J Aust. 2009 Apr 20;190(8):451-3. PMID: [19374621](#)

Article Published Date : Apr 20, 2009

Authors : Claire M Italiano, Cheryl S Toi, Simon P Chan, Dominic E Dwyer

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Viremia : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Animal Diseases: Porcine Circovirus Type 2 (PCV2)

Experimental in utero inoculation of late-term swine fetuses with porcine circovirus type 2 results in a high rate of reproductive abnormalities, including mummification and stillbirth. - GMI Summary

Pubmed Data : J Vet Diagn Invest. 2002 Nov;14(6):507-12. PMID: [12423036](#)

Article Published Date : Nov 01, 2002

Authors : Charles S Johnson, Han S Joo, Kochakorn Direksin, Kyoung-Jin Yoon, Young K Choi

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Porcine circovirus type 2 (PCV2) vaccination of pregnant pigs may result in vertical transmission of PCV2 to the offspring. - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2009 Jun;16(6):830-4. Epub 2009 Apr 8. PMID: [19357312](#)

Article Published Date : Jun 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

The intranasal inoculation of pregnant sows with porcine circovirus 2 results in abortion and reproductive failure. - GMI Summary

Pubmed Data : J Nutr. 2009 Nov;139(11):2061-6. Epub 2009 Sep 23. PMID: [15737340](#)

Article Published Date : Nov 01, 2009

Authors : J-S Park, J Kim, Y Ha, K Jung, C Choi, J-K Lim, S-H Kim, C Chae

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Vaccine-induced immunity in pregnant pigs is not effective in preventing viremia in offspring. - GMI Summary

Pubmed Data : Theriogenology. 2009 Oct 1;72(6):747-54. Epub 2009 Jun 25. PMID: [19559470](#)

Article Published Date : Oct 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

PCV2 infection is now widespread worldwide, and increasing numbers of disease conditions have been linked to PCV2 infection in pigs. - GMI Summary

Pubmed Data : Virus Res. 2012 Mar ;164(1-2):1-3. Epub 2011 Dec 14. PMID: [22192532](#)

Article Published Date : Mar 01, 2012

Authors : Xiang-Jin Meng

Study Type : Review

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Topic: [Chronic Fatigue Syndrome](#)

[Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24. PMID: [18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications : CK\(32\) : AC\(4\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Silicone Implant Toxicity : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Silicone Implants : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2012 Mar 14. Epub 2012 Mar 14. PMID: [22425036](#)

Article Published Date : Mar 14, 2012

Authors : Olivier Guillard, Bernard Fauconneau, Alain Pineau, Annie Marraud, Jean-Pierre Bellocq, Marie-Pierre Chenard

Study Type : Human: Case Report, Review

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Pseudolymphoma : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[The use of animal cells in the production of vaccines may cause infection by endogenous retroviruses associated with chronic fatigue and prostate cancer.](#) - GMI Summary

Pubmed Data : Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8. PMID: [20378372](#)

Article Published Date : May 01, 2010

Authors : Takayuki Miyazawa

Study Type : Animal Study

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Prostate Cancer : CK\(1024\) : AC\(311\)](#), [Retroviruses : CK\(7\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Aluminium-containing adjuvants in vaccines may be causing autoimmune conditions such as chronic fatigue syndrome and the inflammatory myopathy known as macrophagic myofasciitis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11. PMID: [19004564](#)

Article Published Date : Feb 01, 2009

Authors : Christopher Exley, Louise Swarbrick, Rhomain K Gherardi, Francois-Jérôme Authier

Study Type : Commentary

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#),
[Myopathy: Inflammatory : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Guillain Barre Syndrome: Miller Fisher Variant](#)

[Influenza vaccination may increase the risk of Guillain-Barré Syndrome.](#) - GMI Summary

Pubmed Data : Kidney Int. 2008 Dec;74(11):1461-7. Epub 2008 Sep 24. PMID: [18592444](#)

Article Published Date : Dec 01, 2008

Authors : C I Blanco-Marchite, L Buznego-Suárez, M A Fagúndez-Vargas, M Méndez-Llitas, P Pozo-Martos

Study Type : Human Study

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant : CK\(13\) : AC\(2\)](#), [Influenza : CK\(656\) : AC\(99\)](#),
[Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza vaccination has been reported to cause miller fisher syndrome.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1327-9. PMID: [21987549](#)

Article Published Date : Oct 01, 2011

Authors : Ashkan Shoamanesh, Kristine Chapman, Anthony Traboulsee

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant : CK\(13\) : AC\(2\)](#), [Miller Fisher Syndrome : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Animal Diseases: Smithburn Rift Valley Fever](#)

[Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies.](#) - GMI Summary

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does.](#) - GMI Summary

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: [Inflammatory Myopathy](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#)

- GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Mycoplasma Infections](#)

[High antibody titres against predicted Mycoplasma surface proteins do not prevent sequestration in infected lung tissue in the course of experimental contagious bovine pleuropneumonia.](#)

- GMI Summary

Pubmed Data : Vet Microbiol. 2014 Aug 6 ;172(1-2):285-93. Epub 2014 May 5. PMID: [24880898](#)

Article Published Date : Aug 05, 2014

Authors : Elise Schieck, Anne Liljander, Carl Hamsten, Nimmo Gicheru, Massimo Scacchia, Flavio Sacchini, Martin Heller, Christiane Schnee, Anja Sterner-Kock, Andreas Hlinak, Jan Naessens, Jane Poole, Anja Persson, Joerg Jores

Study Type : Human Study

Additional Links

Diseases : [Mycoplasma Infections : CK\(2\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Mycoplasma testing of cell substrates and biologics is often not performed due to the long turn around.](#)

- GMI Summary

Pubmed Data : Mol Cell Probes. 2011 Apr-Jun;25(2-3):69-77. Epub 2011 Jan 11. PMID: [21232597](#)

Article Published Date : Apr 01, 2011

Authors : Dmitriy V Volokhov, Laurie J Graham, Kurt A Brorson, Vladimir E Chizhikov

Study Type : Review

Additional Links

Diseases : [Mycoplasma Infections : CK\(2\) : AC\(2\)](#)

Additional Keywords : [Mycoplasma Infections : CK\(2\) : AC\(2\)](#), [Vaccine Safety : CK\(21\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Aging

[Pneumococcal vaccines are ineffective in children with a history of recurrent acute ear infections.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2004 Oct 1;39(7):911-9. Epub 2004 Sep 1. PMID: [15472839](#)

Article Published Date : Oct 01, 2004

Authors : Reinier H Veenhoven, Debby Bogaert, Anne G M Schilder, Ger T Rijkers, Cuno S P M Uiterwaal, Herma H Kiezebrink, Muriel J P van Kempen, Inge J Dhooge, Jacob Bruin, Ed P F Ijzerman, Ronald de Groot, Wietse Kuis, Peter W M Hermans, Elisabeth A M Sanders

Study Type : Human Study

Additional Links

Diseases : [Aging](#) : [CK\(1399\)](#) : [AC\(392\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal](#) : [CK\(71\)](#) : [AC\(8\)](#)

Topic: Allergic Rhinitis

[Timing of routine immunisations \(earlier = increased\) and subsequent hay fever risk.](#) - GMI Summary

Pubmed Data : Arch Dis Child. 2005 Jun ;90(6):567-73. PMID: [15908618](#)

Article Published Date : May 31, 2005

Authors : S A Bremner, I M Carey, S DeWilde, N Richards, W C Maier, S R Hilton, D P Strachan, D G Cook

Study Type : Human Study

Additional Links

Diseases : [Allergic Rhinitis](#) : [CK\(340\)](#) : [AC\(40\)](#), [Immune Dysregulation: TH1/TH2 imbalance](#) : [CK\(148\)](#) : [AC\(37\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : [CK\(282\)](#) : [AC\(31\)](#)

Topic: Anaphylaxis

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis](#) : [CK\(53\)](#) : [AC\(15\)](#), [Infant Mortality](#) : [CK\(249\)](#) : [AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\)](#) : [CK\(138\)](#) : [AC\(18\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All](#) : [CK\(4702\)](#) : [AC\(361\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis](#) : [CK\(53\)](#) : [AC\(15\)](#), [Guillain-Barre Syndrome](#) : [CK\(84\)](#) : [AC\(14\)](#), [Hepatitis B](#) : [CK\(219\)](#) : [AC\(37\)](#), [Neuritis: Brachial Plexus](#) : [CK\(1\)](#) : [AC\(1\)](#), [Poliomyelitis](#) : [CK\(33\)](#) : [AC\(4\)](#), [Purpura: Thrombocytopenic](#) : [CK\(231\)](#) : [AC\(25\)](#), [Vaccine-induced Toxicity](#) : [CK\(1242\)](#) : [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : [CK\(282\)](#) : [AC\(31\)](#), [Vaccination: Hepatitis B](#) : [CK\(367\)](#) : [AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : [CK\(228\)](#) : [AC\(26\)](#), [Vaccination: Tetanus](#) : [CK\(61\)](#) : [AC\(8\)](#)

Topic: Breast Augmentation Complications

Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations. - GMI Summary

Pubmed Data : Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24. PMID: [18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications](#) : CK(32) : AC(4), [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Hepatitis B](#) : CK(219) : AC(37), [Silicone Implant Toxicity](#) : CK(10) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Silicone Implants](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Cholera

killed cholera vaccination generates an inferior immune response in comparison to patients with naturally acquired cholera. - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2011 May ;18(5):844-50. Epub 2011 Feb 23. PMID: [21346055](#)

Article Published Date : May 01, 2011

Authors : Mohammad Murshid Alam, M Asrafuzzaman Riyadh, Kaniz Fatema, Mohammad Arif Rahman, Nayeema Akhtar, Tanvir Ahmed, Mohiul Islam Chowdhury, Fahima Chowdhury, Stephen B Calderwood, Jason B Harris, Edward T Ryan, Firdausi Qadri

Study Type : Human Study

Additional Links

Diseases : [Cholera](#) : CK(27) : AC(17)

Additional Keywords : [Cholera](#) : CK(27) : AC(17)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Cholera](#) : CK(20) : AC(2)

Topic: Diarrhea

Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. - GMI Summary

Pubmed Data : Am J Clin Nutr. 2004 Jul ;80(1):193-8. PMID: [15213048](#)

Article Published Date : Jun 30, 2004

Authors : Laura E Caulfield, Mercedes de Onis, Monika Blössner, Robert E Black

Study Type : Human Study

Additional Links

Diseases : [Diarrhea](#) : CK(544) : AC(73), [Malaria](#) : CK(89) : AC(30), [Measles](#) : CK(278) : AC(8), [Pneumonia](#) : CK(330) : AC(40)

Additional Keywords : [Pneumonia](#) : CK(330) : AC(40)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Empyema

There has been a five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine. - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2008 Nov;27(11):1030-2. PMID: [18845981](#)

Article Published Date : Nov 01, 2008

Authors : Debra J Hendrickson, Dean A Blumberg, Jesse P Joad, Sanjay Jhavar, Ruth J McDonald

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Empyema : CK\(10\) : AC\(1\)](#), [Parapneumonic Empyema : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Topic: [Encephalitis: Japanese](#)

[Neutralizing antibodies, elicited by the mouse brain-derived and formalin-inactivated JEV Nakayama vaccine among a limited number of vaccinees, have reduced neutralizing capacity against circulating GI virus.](#) - GMI Summary

Pubmed Data : PLoS Negl Trop Dis. 2012 Sep ;6(9):e1834. Epub 2012 Sep 27. PMID: [23029592](#)

Article Published Date : Aug 31, 2012

Authors : Yi-Chin Fan, Jo-Mei Chen, Hsien-Chung Chiu, Yi-Ying Chen, Jen-Wei Lin, Chen-Chang Shih, Chih-Ming Chen, Chao-Chin Chang, Gwong-Jen J Chang, Shyan-Song Chiou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis: Japanese : CK\(13\) : AC\(4\)](#)

Additional Keywords : [Encephalitis: Japanese : CK\(13\) : AC\(4\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Japanese Encephalitis Virus Vaccine : CK\(10\) : AC\(1\)](#)

Topic: [Fever](#)

[Breastfeeding is associated with a decreased incidence of fever after immunizations.](#) - GMI Summary

Pubmed Data : Pediatrics. 2010 Jun;125(6):e1448-52. Epub 2010 May 17. PMID: [20478932](#)

Article Published Date : Jun 01, 2010

Authors : Alfredo Pisacane, Paola Continisio, Orsola Palma, Stefania Cataldo, Fabiola De Michele, Ugo Vairo

Study Type : Human Study

Additional Links

Substances : [Breast Milk : CK\(428\) : AC\(49\)](#)

Diseases : [Fever : CK\(77\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Hepatitis C](#)

[Hepatitis C prevalence in Southern Italy may be due to iatrogenic transmission through the Salk Polio vaccine 1956-1965.](#) - GMI Summary

Pubmed Data : J Med Virol. 2003 May;70(1):49-50. PMID: [12629643](#)

Article Published Date : May 01, 2003

Authors : Maurizio Montella, Anna Crispo, Maria Grimaldi, Vincenzo Tridente, Mario Fusco

Study Type : Human Study

Additional Links

Diseases : [Hepatitis C : CK\(413\) : AC\(65\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Malaria](#)

[Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles.](#) - GMI Summary

Pubmed Data : Am J Clin Nutr. 2004 Jul ;80(1):193-8. PMID: [15213048](#)

Article Published Date : Jun 30, 2004

Authors : Laura E Caulfield, Mercedes de Onis, Monika Blössner, Robert E Black

Study Type : Human Study

Additional Links

Diseases : [Diarrhea : CK\(544\) : AC\(73\)](#), [Malaria : CK\(89\) : AC\(30\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Additional Keywords : [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Miscarriage](#)

[The use of misoprostol for early pregnancy failure after failed expectant management is less costly than curettage. - GMI Summary](#)

Pubmed Data : Hum Reprod. 2005 Apr;20(4):1067-71. Epub 2004 Dec 23. PMID: [15618248](#)

Article Published Date : Apr 01, 2005

Authors : G C M Graziosi, J W van der Steeg, P H W Reuwer, A P Drogdrop, H W Bruinse, B W J Mol

Study Type : Human Study

Additional Links

Diseases : [Miscarriage : CK\(313\) : AC\(36\)](#), [Miscarriage: Medical Intervention : CK\(125\) : AC\(14\)](#)

Additional Keywords : [Surgical Alternatives : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Obstetric Interventions : CK\(1030\) : AC\(69\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Topic: [Miscarriage: Medical Intervention](#)

[The use of misoprostol for early pregnancy failure after failed expectant management is less costly than curettage. - GMI Summary](#)

Pubmed Data : Hum Reprod. 2005 Apr;20(4):1067-71. Epub 2004 Dec 23. PMID: [15618248](#)

Article Published Date : Apr 01, 2005

Authors : G C M Graziosi, J W van der Steeg, P H W Reuwer, A P Drogdrop, H W Bruinse, B W J Mol

Study Type : Human Study

Additional Links

Diseases : [Miscarriage : CK\(313\) : AC\(36\)](#), [Miscarriage: Medical Intervention : CK\(125\) : AC\(14\)](#)

Additional Keywords : [Surgical Alternatives : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Obstetric Interventions : CK\(1030\) : AC\(69\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Topic: [Narcolepsy](#)

[An association between Pandemrix vaccination and narcolepsy has been observed in Finland and Sweden - GMI Summary](#)

Pubmed Data : Euro Surveill. 2014 ;19(17):15-25. Epub 2014 May 1. PMID: [24821121](#)

Article Published Date : Dec 31, 2013

Authors : D O'Flanagan, A S Barret, M Foley, S Cotter, C Bonner, C Crowe, B Lynch, B Sweeney, H Johnson, B McCoy, E Purcell

Study Type : Human Study

Additional Links

Diseases : [Narcolepsy : CK\(21\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Orchitis](#)

Mumps orchitis occurs vaccinated postpubertal males. - GMI Summary

Pubmed Data : Korean J Urol. 2012 Dec ;53(12):865-9. Epub 2012 Dec 20. PMID: [23301132](#)

Article Published Date : Nov 30, 2012

Authors : Bum Sik Tae, Byeong Kuk Ham, Jae Heon Kim, Jae Young Park, Jae Hyun Bae

Study Type : Human Study

Additional Links

Diseases : [Orchitis](#) : CK(2) : AC(1)

Anti Therapeutic Actions : [Vaccination: Measles](#) : CK(157) : AC(16)

Topic: Parapertussis

"Primary infections with either B. pertussis or Bordetella parapertussis stimulated a vigorous antibody response to ACT. In contrast, patients in whom DTP and DTaP vaccines failed had minimal ACT antibody responses." - GMI Summary

Pubmed Data : Clin Infect Dis. 2004 Feb 15 ;38(4):502-7. Epub 2004 Jan 29. PMID: [14765342](#)

Article Published Date : Feb 14, 2004

Authors : James D Cherry, Dorothy X L Xing, Penny Newland, Kashmira Patel, Ulrich Heininger, Michael J Corbel

Study Type : Human Study

Additional Links

Diseases : [Parapertussis](#) : CK(10) : AC(1), [Whooping Cough](#) : CK(66) : AC(7)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Pertussis](#) : CK(116) : AC(14)

Topic: Parapneumonic Empyema

There has been a five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine. - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2008 Nov;27(11):1030-2. PMID: [18845981](#)

Article Published Date : Nov 01, 2008

Authors : Debra J Hendrickson, Dean A Blumberg, Jesse P Joad, Sanjay Jhavar, Ruth J McDonald

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections](#) : CK(275) : AC(29), [Empyema](#) : CK(10) : AC(1), [Parapneumonic Empyema](#) : CK(10) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Pneumococcal](#) : CK(71) : AC(8)

Topic: Pregnancy: Flu

Influenza vaccination does not appear to be effective during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants. - GMI Summary

Pubmed Data : Am J Perinatol. 2004 Aug;21(6):333-9. PMID: [15311370](#)

Article Published Date : Aug 01, 2004

Authors : Steven B Black, Henry R Shinefield, Eric K France, Bruce H Fireman, Sharon T Platt, David Shay,

Study Type : Human Study

Additional Links

Diseases : [Pregnancy: Flu](#) : CK(10) : AC(1), [Upper Respiratory Infections](#) : CK(824) : AC(90)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Respiratory Diseases

[Pneumococcal conjugate vaccination is associated with higher levels of serious adverse respiratory events and nonrespiratory events in infants 6 weeks to 6 months of age.](#) - GMI Summary

Pubmed Data : [Pediatr Infect Dis J. 2009 Jun;28\(6\):455-62. PMID: 19483514](#)

Article Published Date : Jun 01, 2009

Authors : Marilla G Lucero, Hanna Nohynek, Gail Williams, Veronica Tallo, Eric A F Simões, Socorro Lupisan, Diozele Sanvictores, Simon Forsyth, Taneli Puumalainen, Juanita Ugpo, Marites Lechago, Margaret de Campo, Erma Abuzejo-Ladesma, Lydia Sombrero, Antti Nissinen, Anu Soinen, Petri Ruutu, Ian Riley, Helen P Mäkelä

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Respiratory Diseases : CK\(174\) : AC\(29\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Topic: Rotavirus Infections

["Lack of correlation between serum rotavirus antibody titers and protection following vaccination with reassortant RRV vaccines."](#) - GMI Summary

Pubmed Data : [Vaccine. 1995 Sep ;13\(13\):1226-32. PMID: 8578808](#)

Article Published Date : Aug 31, 1995

Authors : R L Ward, D I Bernstein

Study Type : Human Study

Additional Links

Diseases : [Rotavirus Infections : CK\(75\) : AC\(16\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Topic: Silicone Implant Toxicity

[Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations.](#) - GMI Summary

Pubmed Data : [Autoimmun Rev. 2008 Oct;8\(1\):52-5. Epub 2008 Aug 24. PMID: 18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications : CK\(32\) : AC\(4\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Silicone Implant Toxicity : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Silicone Implants : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Tuberculosis

[BCG revaccination may raise mortality in young children.](#) - GMI Summary

Pubmed Data : [BMJ. 2010;340:c671. Epub 2010 Mar 15. PMID: 20231251](#)

Article Published Date : Jan 01, 2010

Authors : Adam Edvin Roth, Christine Stabell Benn, Henrik Ravn, Amabelia Rodrigues, Ida Maria Lisse, Maria Yazdanbakhsh, Hilton Whittle, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections](#) : CK(275) : AC(29), [Tuberculosis](#) : CK(244) : AC(42)

Anti Therapeutic Actions : [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4)

Topic: [Dermatomyositis](#)

[Hepatitis B vaccine associated with dermatomyositis has been reported.](#) - GMI Summary

Pubmed Data : Rheumatol Int. 2008 Apr;28(6):609-12. Epub 2007 Nov 23. PMID: [18034245](#)

Article Published Date : Apr 01, 2008

Authors : Arie Altman, Martine Szyper-Kravitz, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Dermatomyositis](#) : CK(44) : AC(10), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Dermatomyositis](#) : CK(44) : AC(10), [Myasthenia Gravis](#) : CK(82) : AC(14), [Neuromuscular Diseases](#) : CK(16) : AC(4), [Neuropathies](#) : CK(436) : AC(72), [Polyarteritis Nodosa](#) : CK(1) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: [Acute Inflammatory Demyelinating Polyradiculoneuropathy](#)

[A case of lethal inflammatory polyradiculoneuropathy with spinal cord involvement after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2001 May 1;186(1-2):81-5. PMID: [11412876](#)

Article Published Date : May 01, 2001

Authors : E Sindern, J M Schröder, M Krismann, J P Malin

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Inflammatory Demyelinating Polyradiculoneuropathy](#) : CK(87) : AC(1),

[Polyradiculoneuropathy: Acute Inflammatory](#) : CK(87) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: [Acute Posterior Multifocal Placoid Pigment Epitheliopathy \(APMPPE\)](#)

[Acute posterior multifocal placoid pigment epitheliopathy after hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Arch Ophthalmol. 1995 Mar;113(3):297-300. PMID: [7887843](#)

Article Published Date : Mar 01, 1995

Authors : A P Brézin, P Massin-Korobelnik, M Boudin, A Gaudric, P LeHoang

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Posterior Multifocal Placoid Pigment Epitheliopathy \(APMPPE\) : CK\(3\) : AC\(1\)](#), [Chorioretinitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Aphthosis: Buccal](#)

[Cutaneous lupus erythematosus and buccal aphthosis after hepatitis B vaccination has been reported in a 6-year-old child](#) - GMI Summary

Pubmed Data : Ann Dermatol Venereol. 1996;123(10):657-9. PMID: [9615128](#)

Article Published Date : Jan 01, 1996

Authors : P Grézard, M Chefaï, V Philippot, H Perrot, M Faisant

Study Type : Human: Case Report

Additional Links

Diseases : [Aphthosis: Buccal : CK\(3\) : AC\(1\)](#), [Lupus Erythematosus: Cutaneous : CK\(17\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Bell's Palsy](#)

[Bell's palsy is a possible complication of hepatitis B vaccination in children.](#) - GMI Summary

Pubmed Data : J Health Popul Nutr. 2009 Oct;27(5):707-8. PMID: [19902808](#)

Article Published Date : Oct 01, 2009

Authors : Handan Alp, Hüseyin Tan, Zerrin Orbak

Study Type : Human: Case Report

Additional Links

Diseases : [Bell's Palsy : CK\(13\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Chorioretinitis](#)

[Acute posterior multifocal placoid pigment epitheliopathy after hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Arch Ophthalmol. 1995 Mar;113(3):297-300. PMID: [7887843](#)

Article Published Date : Mar 01, 1995

Authors : A P Brézin, P Massin-Korobelnik, M Boudin, A Gaudric, P LeHoang

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Posterior Multifocal Placoid Pigment Epitheliopathy \(APMPPE\) : CK\(3\) : AC\(1\)](#), [Chorioretinitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Diabetes Mellitus: Type 1](#)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Diabetes Mellitus: Type 1 : CK\(1197\) : AC\(235\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Epilepsy](#)

[A case of lethal status epilepticus and lymphocytic pneumonitis has been reported.](#) - GMI Summary

Pubmed Data : Eur J Intern Med. 2008 Jul;19(5):383-5. Epub 2007 Dec 4. PMID: [18549949](#)

Article Published Date : Jul 01, 2008

Authors : Jozélio Freire de Carvalho, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Epilepsy : CK\(128\) : AC\(29\)](#), [Pneumonitis : CK\(18\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Hydranencephaly](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly.](#) - GMI Summary

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: [Lipoatrophy](#)

[Delayed focal lipoatrophy after AS03-adjuvanted influenza A \(H1N1\) 2009 vaccine has been reported.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Dec 17. Epub 2010 Dec 17. PMID: [21172376](#)

Article Published Date : Dec 17, 2010

Authors : Emilie Javelle, Benjamin Soulier, Christian Brosset, Solène Lorcy, Fabrice Simon

Study Type : Human: Case Report

Additional Links

Diseases : [Lipoatrophy : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Lupus Erythematosus: Cutaneous](#)

[Cutaneous lupus erythematosus and buccal aphthosis after hepatitis B vaccination has been reported in a 6-year-old child](#) - GMI Summary

Pubmed Data : Ann Dermatol Venereol. 1996;123(10):657-9. PMID: [9615128](#)

Article Published Date : Jan 01, 1996

Authors : P Grézard, M Chefaï, V Philippot, H Perrot, M Faisant

Study Type : Human: Case Report

Additional Links

Diseases : [Aphthosis: Buccal](#) : CK(3) : AC(1), [Lupus Erythematosus: Cutaneous](#) : CK(17) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: [Miller Fisher Syndrome](#)

[Influenza vaccination has been reported to cause miller fisher syndrome.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1327-9. PMID: [21987549](#)

Article Published Date : Oct 01, 2011

Authors : Ashkan Shoamanesh, Kristine Chapman, Anthony Traboulsee

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant](#) : CK(13) : AC(2), [Miller Fisher Syndrome](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Topic: [Pneumonitis](#)

[A case of lethal status epilepticus and lymphocytic pneumonitis has been reported.](#) - GMI Summary

Pubmed Data : Eur J Intern Med. 2008 Jul;19(5):383-5. Epub 2007 Dec 4. PMID: [18549949](#)

Article Published Date : Jul 01, 2008

Authors : Jozélio Freire de Carvalho, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Epilepsy](#) : CK(128) : AC(29), [Pneumonitis](#) : CK(18) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: [Polyradiculoneuropathy: Acute Inflammatory](#)

[A case of lethal inflammatory polyradiculoneuropathy with spinal cord involvement after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2001 May 1;186(1-2):81-5. PMID: [11412876](#)

Article Published Date : May 01, 2001

Authors : E Sindern, J M Schröder, M Krismann, J P Malin

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Inflammatory Demyelinating Polyradiculoneuropathy](#) : CK(87) : AC(1),

[Polyradiculoneuropathy: Acute Inflammatory](#) : CK(87) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: [Rhabdomyolysis](#)

[Influenza vaccine has been reported to be a possible trigger of rhabdomyolysis induced acute renal failure in those taking statin drugs.](#) - GMI Summary

Pubmed Data : Nephrol Dial Transplant. 2000 May ;15(5):740-1. PMID: [10809833](#)

Article Published Date : May 01, 2000

Authors : E Plotkin, J Bernheim, S Ben-Chetrit, A Mor, Z Korzets

Study Type : Human: Case Report

Additional Links

Diseases : [Rhabdomyolysis](#) : CK(165) : AC(38), [Statin-Induced Pathologies](#) : CK(1600) : AC(320)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Problem Substances : [Statin Drugs](#) : CK(3971) : AC(475)

Adverse Pharmacological Actions : [Myotoxicity](#) : CK(327) : AC(80)

[Topic: Rift Valley Fever](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does.](#) - GMI Summary

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous](#) : CK(204) : AC(29), [Animal Diseases: Smithburn Rift Valley Fever](#) : CK(4) : AC(2), [Rift Valley Fever](#) : CK(2) : AC(1), [Vaccination: Abortion](#) : CK(40) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Animal Model](#) : CK(41) : AC(17)

[Topic: Statin-Induced Pathologies](#)

[Influenza vaccine has been reported to be a possible trigger of rhabdomyolysis induced acute renal failure in those taking statin drugs.](#) - GMI Summary

Pubmed Data : Nephrol Dial Transplant. 2000 May ;15(5):740-1. PMID: [10809833](#)

Article Published Date : May 01, 2000

Authors : E Plotkin, J Bernheim, S Ben-Chetrit, A Mor, Z Korzets

Study Type : Human: Case Report

Additional Links

Diseases : [Rhabdomyolysis](#) : CK(165) : AC(38), [Statin-Induced Pathologies](#) : CK(1600) : AC(320)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Problem Substances : [Statin Drugs](#) : CK(3971) : AC(475)

Adverse Pharmacological Actions : [Myotoxicity](#) : CK(327) : AC(80)

[Topic: Simian virus 40 \(SV40\)](#)

[Some oral poliovirus vaccines were contaminated with infectious SV40 after 1961.](#) - GMI Summary

Pubmed Data : Cancer Res. 2005 Nov 15 ;65(22):10273-9. PMID: [16288015](#)

Article Published Date : Nov 15, 2005

Authors : Rochelle Cutrone, John Lednicky, Glynis Dunn, Paola Rizzo, Maurizio Bocchetta, Konstantin Chumakov, Philip Minor, Michele Carbone

Study Type : Human In Vitro

Additional Links

Diseases : [Simian virus 40 \(SV40\) : CK\(7\) : AC\(5\)](#)

Additional Keywords : [Vaccine Contamination : CK\(5\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Problem Substances : [Simian virus 40 \(SV40\) : CK\(113\) : AC\(16\)](#)

Topic: [Acute Flaccid Paralysis](#)

[Differential diagnosis of acute flaccid paralysis and its role in poliomyelitis surveillance.](#) - GMI Summary

Pubmed Data : Epidemiol Rev. 2000 ;22(2):298-316. PMID: [11218380](#)

Article Published Date : Jan 01, 2000

Authors : A Marx, J D Glass, R W Sutter

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Over 40,000 cases of AFP are reported annually since 2007 regardless of the number of actual polio cases.](#) - GMI Summary

Pubmed Data : BMC Public Health. 2012 ;12:229. Epub 2012 Mar 22. PMID: [22439606](#)

Article Published Date : Jan 01, 2012

Authors : Rie R Yotsu, Katharine Abba, Helen Smith, Abhijit Das

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#), [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Topic: [Amygdala: Damage/Abnormalities](#)

[Maturational changes in amygdala volume and the binding capacity of an opioid antagonist in the amygdala was significantly altered in infant macaques receiving the vaccine schedule.](#) - GMI Summary

Pubmed Data : Acta Neurobiol Exp (Wars). 2010 ;70(2):147-64. PMID: [20628439](#)

Article Published Date : Dec 31, 2009

Authors : Laura Hewitson, Brian J Lopresti, Carol Stott, N Scott Mason, Jaime Tomko

Study Type : Animal Study

Additional Links

Diseases : [Amygdala: Damage/Abnormalities : CK\(12\) : AC\(1\)](#), [Neurodevelopmental Disorders : CK\(124\) : AC\(13\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Problem Substances : [Thimerosal : CK\(367\) : AC\(23\)](#)

Topic: [Animal Diseases: Scrapie](#)

[Vaccine-induced scrapie has been reported in animals.](#) - GMI Summary

Pubmed Data : J Gen Virol. 2003 Apr;84(Pt 4):1047-52. PMID: [12655108](#)

Article Published Date : Apr 01, 2003

Authors : Gianluigi Zanusso, Cristina Casalone, Pierluigi Acutis, Elena Bozzetta, Alessia Farinazzo, Matteo Gelati, Michele Fiorini, Gianluigi Forloni, Man Sun Sy, Salvatore Monaco, Maria Caramelli

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Animal Diseases: Scrapie : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: [Animal Diseases: Simian Immunodeficiency Virus \(SIV\)](#)

[Vaccine-induced, simian immunodeficiency virus-specific CD8+ T cells reduce virus replication but do not protect from simian immunodeficiency virus disease progression.](#) - GMI Summary

Pubmed Data : J Immunol. 2009 Jul 1;183(1):706-17. PMID: [19542473](#)

Article Published Date : Jul 01, 2009

Authors : Jessica C Engram, Richard M Dunham, George Makedonas, Thomas H Vanderford, Beth Sumpter, Nichole R Klatt, Sarah J Ratcliffe, Seema Garg, Mirko Paiardini, Monica McQuoid, John D Altman, Silvija I Staprans, Michael R Betts, David A Garber, Mark B Feinberg, Guido Silvestri

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Simian Immunodeficiency Virus \(SIV\) : CK\(2\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: [Infertility](#)

[There is evidence that a DNA vaccine exhibits anti-fertility properties.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jul 12 ;29(31):4933-9. Epub 2011 May 17. PMID: [21596079](#)

Article Published Date : Jul 12, 2011

Authors : Meng-Fei Yu, Wen-Ning Fang, Gao-Feng Xiong, Ying Yang, Jing-Pian Peng

Study Type : Animal Study

Additional Links

Diseases : [Infertility : CK\(576\) : AC\(109\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Plasmid DNA Vaccines : CK\(3\) : AC\(2\)](#)

Topic: [Liver Damage](#)

[Hepatitis B vaccine induces cell death in liver cells and mouse liver.](#) - GMI Summary

Pubmed Data : Apoptosis. 2012 Jan 17. Epub 2012 Jan 17. PMID: [22249285](#)

Article Published Date : Jan 17, 2012

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Changchun Li, Mengjin Zhu, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Liver Damage : CK\(648\) : AC\(226\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Hepatotoxic : CK\(301\) : AC\(85\)](#)

Topic: [Neuritis: Brachial Plexus](#)

[The Institute of Medicine determined that routine childhood vaccines are linked](#)

[to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: [Neurodevelopmental Disorders](#)

[Maturational changes in amygdala volume and the binding capacity of an opioid antagonist in the amygdala was significantly altered in infant macaques receiving the vaccine schedule.](#) - GMI Summary

Pubmed Data : Acta Neurobiol Exp (Wars). 2010 ;70(2):147-64. PMID: [20628439](#)

Article Published Date : Dec 31, 2009

Authors : Laura Hewitson, Brian J Lopresti, Carol Stott, N Scott Mason, Jaime Tomko

Study Type : Animal Study

Additional Links

Diseases : [Amygdala: Damage/Abnormalities : CK\(12\) : AC\(1\)](#), [Neurodevelopmental Disorders : CK\(124\) : AC\(13\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Problem Substances : [Thimerosal : CK\(367\) : AC\(23\)](#)

Topic: [Polio: Vaccine-Related](#)

["Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children."](#) - GMI Summary

Pubmed Data : Lancet. 1991 Sep 21 ;338(8769):715-20. PMID: [1679866](#)

Article Published Date : Sep 20, 1991

Authors : R W Sutter, P A Patriarca, S Brogan, P G Malankar, M A Pallansch, O M Kew, A G Bass, S L Cochi, J P Alexander, D B Hall

Study Type : Human: Case Report

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#)

[Vaccine-derived poliovirus may become pathogenic in complex viral ecosystems, through frequent recombination events and mutations.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2012 May 1 ;205(9):1363-73. Epub 2012 Mar 29. PMID: [22457288](#)

Article Published Date : May 01, 2012

Authors : Marie-Line Joffret, Sophie Jégouic, Maël Bessaud, Jean Balanant, Coralie Tran, Valerie Caro, Barbara Holmblat, Richter Razafindratsimandresy, Jean-Marc Reynes, Mala Rakoto-Andrianarivelo, Francis Delpeyroux

Study Type : Review

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Topic: Retroviruses

The use of animal cells in the production of vaccines may cause infection by endogenous retroviruses associated with chronic fatigue and prostate cancer. - GMI Summary

Pubmed Data : Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8. PMID: [20378372](#)

Article Published Date : May 01, 2010

Authors : Takayuki Miyazawa

Study Type : Animal Study

Additional Links

Diseases : [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Prostate Cancer](#) : CK(1024) : AC(311), [Retroviruses](#) : CK(7) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Live attenuated virus Vaccines produced on chicken-derived cells contain low levels of particle-associated reverse transcriptase (RT). - GMI Summary

Pubmed Data : J Virol. 1997 Apr ;71(4):3005-12. PMID: [9060660](#)

Article Published Date : Mar 31, 1997

Authors : R N Weissmahr, J Schüpbach, J Böni

Study Type : Review

Additional Links

Diseases : [Endogenous avian retrovirus \(EAV-0\)](#) : CK(1) : AC(1), [Retroviruses](#) : CK(7) : AC(1)

Additional Keywords : [Cross-Species Infection](#) : CK(4) : AC(3), [Endogenous Retroviruses](#) : CK(53) : AC(12), [Live Attenuated Vaccines](#) : CK(5) : AC(2), [Retroviruses](#) : CK(10) : AC(10)

Anti Therapeutic Actions : [Vaccination: Measles](#) : CK(157) : AC(16)

Problem Substances : [Endogenous avian retrovirus \(EAV-0\)](#) : CK(3) : AC(1)

Vaccines produced in chick embryo cells had significant reverse transcriptase activity. - GMI Summary

Pubmed Data : J Clin Virol. 1998 Jul 24 ;11(1):19-28. PMID: [9784140](#)

Article Published Date : Jul 23, 1998

Authors : T Maudru, K W Peden

Study Type : In Vitro Study

Additional Links

Diseases : [Retroviruses](#) : CK(7) : AC(1)

Additional Keywords : [Endogenous Retroviruses](#) : CK(53) : AC(12), [Live Attenuated Vaccines](#) : CK(5) : AC(2), [Retroviruses](#) : CK(10) : AC(10), [Vaccine Contamination](#) : CK(5) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Glyphosate Toxicity

Measles vaccine and glyphosate-induced parkinsonism has been reported. - GMI Summary

Pubmed Data : Arq Neuropsiquiatr. 2003 Jun ;61(2B):381-6. Epub 2003 Jul 28. PMID: [12894271](#)

Article Published Date : Jun 01, 2003

Authors : Maria do Desterro Leiros da Costa, Lílian Regina Gonçalves, Egberto Reis Barbosa, Luiz Alberto Bacheschi

Study Type : Human: Case Report

Additional Links

Diseases : [Glyphosate Toxicity](#) : CK(29) : AC(14), [Parkinsonian Disorders](#) : CK(15) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Measles](#) : CK(157) : AC(16)

Problem Substances : [Glyphosate](#) : CK(403) : AC(130)

Adverse Pharmacological Actions : [Neurotoxic](#) : CK(1116) : AC(188)

Topic: Hemophilus influenzae

Between May 1985 and September 1987, 228 reports of disease due to Haemophilus influenzae in vaccinated children were submitted to the FDA. - GMI Summary

Pubmed Data : J Infect Dis. 1988 Aug ;158(2):343-8. PMID: [3261314](#)

Article Published Date : Jul 31, 1988

Authors : E E Hiner, C E Frasch

Study Type : Human: Case Report

Additional Links

Diseases : [Hemophilus influenzae : CK\(4\) : AC\(1\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#)

Topic: Herpes Zoster Keratitis

Reactivation of Herpes Zoster Keratitis in an Adult After Varicella Zoster Vaccination. - GMI Summary

Pubmed Data : Cornea. 2012 Nov 26. Epub 2012 Nov 26. PMID: [23187165](#)

Article Published Date : Nov 25, 2012

Authors : Charles W Hwang, Walter A Steigleman, Erika Saucedo-Sanchez, Sonal S Tuli

Study Type : Human: Case Report

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Herpes Zoster Keratitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella Zoster \(Shingles\) : CK\(3\) : AC\(1\)](#)

Topic: Incontinentia Pigmenti

Vaccination as a probable cause of incontinentia pigmenti reactivation has been reported. - GMI Summary

Pubmed Data : Pediatr Dermatol. 2010 Jan-Feb;27(1):62-4. PMID: [20199413](#)

Article Published Date : Jan 01, 2010

Authors : Ali Alikhan, Andrew D Lee, Donald Swing, Christie Carroll, Gil Yosipovitch

Study Type : Human: Case Report

Additional Links

Diseases : [Incontinentia Pigmenti : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: Leukemia Cutis

A case of Leukemia Cutis arising at the site of injection of a Tetanus Booster has been reported. - GMI Summary

Pubmed Data : Actas Dermosifiliogr. 2010 Oct;101(8):727-9. PMID: [20965018](#)

Article Published Date : Oct 01, 2010

Authors : R M Guinovart, J M Carrascosa, C Ferrándiz

Study Type : Human: Case Report

Additional Links

Diseases : [Leukemia Cutis : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: Morphea profunda

[Deep morphea after vaccination in two young children has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Dermatol. 2006 Sep-Oct;23(5):484-7. PMID: [17014648](#)

Article Published Date : Sep 01, 2006

Authors : Antonio Torrelo, José Suárez, Isabel Colmenero, Daniel Azorín, Antonio Perera, Antonio Zambrano

Study Type : Human: Case Report

Additional Links

Diseases : [Morphea profunda](#) : CK(3) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Ovarian Failure

["Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants."](#) - GMI Summary

Pubmed Data : Am J Reprod Immunol. 2013 Oct ;70(4):309-16. Epub 2013 Jul 31. PMID: [23902317](#)

Article Published Date : Sep 30, 2013

Authors : Serena Colafrancesco, Carlo Perricone, Lucija Tomljenovic, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Ovarian Failure](#) : CK(4) : AC(2)

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13)

Topic: Parkinsonian Disorders

[Measles vaccine and glyphosate-induced parkinsonism has been reported.](#) - GMI Summary

Pubmed Data : Arq Neuropsiquiatr. 2003 Jun ;61(2B):381-6. Epub 2003 Jul 28. PMID: [12894271](#)

Article Published Date : Jun 01, 2003

Authors : Maria do Desterro Leiros da Costa, Lílian Regina Gonçalves, Egberto Reis Barbosa, Luiz Alberto Bacheschi

Study Type : Human: Case Report

Additional Links

Diseases : [Glyphosate Toxicity](#) : CK(29) : AC(14), [Parkinsonian Disorders](#) : CK(15) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Measles](#) : CK(157) : AC(16)

Problem Substances : [Glyphosate](#) : CK(403) : AC(130)

Adverse Pharmacological Actions : [Neurotoxic](#) : CK(1116) : AC(188)

Topic: Pseudolymphoma

[The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2012 Mar 14. Epub 2012 Mar 14. PMID: [22425036](#)

Article Published Date : Mar 14, 2012

Authors : Olivier Guillard, Bernard Fauconneau, Alain Pineau, Annie Marraud, Jean-Pierre Bellocq, Marie-Pierre Chenard

Study Type : Human: Case Report, Review

Additional Links

Diseases : [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Pseudolymphoma](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

Topic: [Psychiatric Disorders](#)

[The psychic reactions following injections of bacterial vaccines.](#) - GMI Summary

Pubmed Data : Int Arch Allergy Appl Immunol. 1950 ;1(3):226-43. PMID: [14794265](#)

Authors : J ILAVSKY

Study Type : Human: Case Report

Additional Links

Diseases : [Psychiatric Disorders](#) : CK(71) : AC(10), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: [Shoulder Injuries](#)

[Case report: a shoulder injury related to vaccine administration.](#) - GMI Summary

Pubmed Data : J Am Board Fam Med. 2012 Nov ;25(6):919-22. PMID: [23136333](#)

Article Published Date : Oct 31, 2012

Authors : Matthew G Barnes, Christopher Ledford, Karen Hogan

Study Type : Human: Case Report

Additional Links

Diseases : [Shoulder Injuries](#) : CK(23) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

Topic: [Aluminum Toxicity](#)

["Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations."](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):223-30. PMID: [22235057](#)

Article Published Date : Jan 01, 2012

Authors : L Tomljenovic, Ca Shaw

Study Type : Review

Additional Links

Diseases : [Aluminum Toxicity](#) : CK(108) : AC(40), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum](#) : CK(166) : AC(43), [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

[Aluminium-containing adjuvants in vaccines may be causing autoimmune conditions such as chronic fatigue syndrome and the inflammatory myopathy known as macrophagic myofasciitis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11. PMID: [19004564](#)

Article Published Date : Feb 01, 2009

Authors : Christopher Exley, Louise Swarbrick, Rhomain K Gherardi, Francois-Jérôme Authier

Study Type : Commentary

Additional Links

Diseases : [Aluminum Toxicity](#) : CK(108) : AC(40), [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Myopathy: Inflammatory](#) : CK(1) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Brain Inflammation](#)

["Adverse events associated with 17D-derived yellow fever vaccination--United States, 2001-2002." - GMI Summary](#)

Pubmed Data : MMWR Morb Mortal Wkly Rep. 2002 Nov 8 ;51(44):989-93. PMID: [12455906](#)

Article Published Date : Nov 08, 2002

Study Type : Review

Additional Links

Diseases : [Brain Inflammation : CK\(86\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Topic: [Epstein-Barr Virus Infections](#)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin. - GMI Summary](#)

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Myasthenia Gravis](#)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility. - GMI Summary](#)

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Myasthenia Gravis : CK\(82\) : AC\(14\)](#), [Neuromuscular Diseases : CK\(16\) : AC\(4\)](#), [Neuropathies : CK\(436\) : AC\(72\)](#), [Polyarteritis Nodosa : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Neuromuscular Diseases](#)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility. - GMI Summary](#)

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Myasthenia Gravis : CK\(82\) : AC\(14\)](#), [Neuromuscular Diseases : CK\(16\) : AC\(4\)](#), [Neuropathies : CK\(436\) : AC\(72\)](#), [Polyarteritis Nodosa : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Neuropathies](#)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Myasthenia Gravis : CK\(82\) : AC\(14\)](#), [Neuromuscular Diseases : CK\(16\) : AC\(4\)](#), [Neuropathies : CK\(436\) : AC\(72\)](#), [Polyarteritis Nodosa : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Topic: [Oxidative Stress](#)

[Coriandrum sativum has antioxidant activity.](#) - GMI Summary

Pubmed Data : J Nutr Biochem. 2009 Nov;20(11):901-8. Epub 2008 Nov 6. PMID: [10549163](#)

Article Published Date : Nov 01, 2009

Authors : V Chithra, S Leelamma

Study Type : Animal Study

Additional Links

Substances : [Coriandrum sativum : CK\(51\) : AC\(26\)](#)

Diseases : [Oxidative Stress : CK\(2004\) : AC\(750\)](#)

Pharmacological Actions : [Antioxidants : CK\(3864\) : AC\(1373\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Topic: [Peripheral Neuropathies](#)

[Influenza vaccines may induce hepatitis-B virus-related vasculitis and severe neuropathy.](#) - GMI Summary

Pubmed Data : J Cardiovasc Pharmacol. 2003 Sep;42(3):329-38. PMID: [18579284](#)

Article Published Date : Sep 01, 2003

Authors : Yuko Wada, Chie Yanagihara, Yo Nishimura, Nobuyuki Oka

Study Type : Commentary

Additional Links

Diseases : [Peripheral Neuropathies : CK\(191\) : AC\(31\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Topic: [Polyarteritis Nodosa](#)

Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility. - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Dermatomyositis](#) : CK(44) : AC(10), [Myasthenia Gravis](#) : CK(82) : AC(14), [Neuromuscular Diseases](#) : CK(16) : AC(4), [Neuropathies](#) : CK(436) : AC(72), [Polyarteritis Nodosa](#) : CK(1) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Topic: Prostate Cancer

The use of animal cells in the production of vaccines may cause infection by endogenous retroviruses associated with chronic fatigue and prostate cancer. - GMI Summary

Pubmed Data : Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8. PMID: [20378372](#)

Article Published Date : May 01, 2010

Authors : Takayuki Miyazawa

Study Type : Animal Study

Additional Links

Diseases : [Chronic Fatigue Syndrome](#) : CK(408) : AC(32), [Prostate Cancer](#) : CK(1024) : AC(311), [Retroviruses](#) : CK(7) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Sarcoma

Feline injection site-associated sarcoma is a serious problem associated with malignancy. - GMI Summary

Pubmed Data : Vet Microbiol. 2006 Oct 5;117(1):59-65. PMID: [16769184](#)

Article Published Date : Oct 05, 2006

Authors : Jolle Kirpensteijn

Study Type : Review

Additional Links

Diseases : [Sarcoma](#) : CK(42) : AC(26), [Tumors](#) : CK(199) : AC(116), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Animal Model](#) : CK(41) : AC(17)

Topic: Tumors

Feline injection site-associated sarcoma is a serious problem associated with malignancy. - GMI Summary

Pubmed Data : Vet Microbiol. 2006 Oct 5;117(1):59-65. PMID: [16769184](#)

Article Published Date : Oct 05, 2006

Authors : Jolle Kirpensteijn

Study Type : Review

Additional Links

Diseases : [Sarcoma](#) : CK(42) : AC(26), [Tumors](#) : CK(199) : AC(116), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: [Urinary Tract Infections](#)

[DTP vaccination may contribute to urinary tract disease and sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : [Reprod Biomed Online. 2010 Jul;21\(1\):100-8. Epub 2010 Mar 30. PMID: 15356430](#)

Article Published Date : Jul 01, 2010

Authors : Joseph Prandota

Study Type : Commentary

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Urinary Tract Infections : CK\(338\) : AC\(47\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Topic: [Yellow Fever](#)

[From 1990 to the present, the number of cases \(n = 31\) and deaths \(n = 12\) from the yellow fever vaccine in travelers has exceeded the reports of YF \(n = 6\) acquired by natural infection.](#) - GMI Summary

Pubmed Data : [Expert Rev Vaccines. 2012 Apr ;11\(4\):427-48. PMID: 22551029](#)

Article Published Date : Apr 01, 2012

Authors : Thomas P Monath

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Yellow Fever : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Topic: [Attention Deficit Disorder](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : [J Pediatr. 2009 Apr;154\(4\):514-520.e4. Epub 2008 Dec 3. PMID: 19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder : CK\(134\) : AC\(12\)](#), [Attention Deficit Disorder with Hyperactivity : CK\(242\) : AC\(31\)](#), [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Child Mortality : CK\(64\) : AC\(8\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Mental Retardation : CK\(71\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Attention Deficit Disorder with Hyperactivity](#)

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : [J Pediatr. 2009 Apr;154\(4\):514-520.e4. Epub 2008 Dec 3. PMID: 19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder : CK\(134\) : AC\(12\)](#), [Attention Deficit Disorder with Hyperactivity : CK\(242\) : AC\(31\)](#), [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Child Mortality : CK\(64\) : AC\(8\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Mental Retardation : CK\(71\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Encephalomyelitis](#)

[Acute disseminated encephalomyelitis \(ADEM\) may be caused by vaccination.](#) - GMI Summary

Pubmed Data : J Clin Neurosci. 2008 Dec;15(12):1315-22. Epub 2008 Oct 30. PMID: [18976924](#)

Article Published Date : Dec 01, 2008

Authors : William Huynh, Dennis J Cordato, Elias Kehdi, Lynette T Masters, Chris Dedousis

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Encephalomyelitis : CK\(12\) : AC\(7\)](#), [Neuromyelitis Optica : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Encephalopathies](#)

[The use of post-mortem tissues in the production of biologicals, vaccines and feedstuffs may be contributing to transmissible encephalopathies.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1996;88:237-41. PMID: [9119144](#)

Article Published Date : Jan 01, 1996

Authors : M M Robinson

Study Type : Review

Additional Links

Diseases : [Encephalopathies : CK\(11\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Endogenous avian retrovirus \(EAV-0\)](#)

[Live attenuated virus Vaccines produced on chicken-derived cells contain low levels of particle-associated reverse transcriptase \(RT\).](#) - GMI Summary

Pubmed Data : J Virol. 1997 Apr ;71(4):3005-12. PMID: [9060660](#)

Article Published Date : Mar 31, 1997

Authors : R N Weissmahr, J Schüpbach, J Böni

Study Type : Review

Additional Links

Diseases : [Endogenous avian retrovirus \(EAV-0\) : CK\(1\) : AC\(1\)](#), [Retroviruses : CK\(7\) : AC\(1\)](#)

Additional Keywords : [Cross-Species Infection : CK\(4\) : AC\(3\)](#), [Endogenous Retroviruses : CK\(53\) : AC\(12\)](#), [Live Attenuated Vaccines : CK\(5\) : AC\(2\)](#), [Retroviruses : CK\(10\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

Problem Substances : [Endogenous avian retrovirus \(EAV-0\) : CK\(3\) : AC\(1\)](#)

Topic: [Excitotoxicity](#)

[Autism spectrum disorders are associated with vaccination, heavy metal toxicity and excitotoxicity.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2008 Nov-Dec;14(6):46-53. PMID: [19043938](#)

Article Published Date : Nov 01, 2008

Authors : Russell L Blaylock

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Excitotoxicity](#) : CK(57) : AC(34), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Topic: Immune Disorders: B-Cell Over-Activity

[Adjuvants in vaccines may trigger innate cells response by toll-like receptors, thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity.](#) - GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Hypersensitivity](#) : CK(64) : AC(15), [Immune Disorders: B-Cell Over-Activity](#) : CK(2) : AC(2), [Immune Dysregulation: TH1/TH2 imbalance](#) : CK(148) : AC(37), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Adjuvant](#) : CK(18) : AC(6)

Topic: Infertility: Female

[Tetanus vaccine given to Phillipino women of reproductive age may have been designed to induce an anti-fertility action.](#) - GMI Summary

Pubmed Data : Vaccine Wkly. 1995 May 29 - Jun 5:9-10. PMID: [12346214](#)

Article Published Date : May 29, 1995

Authors : [No authors listed]

Study Type : Commentary

Additional Links

Diseases : [Infertility: Female](#) : CK(238) : AC(40)

Additional Keywords : [Population Control](#) : CK(1) : AC(1)

Anti Therapeutic Actions : [Vaccination: Tetanus](#) : CK(61) : AC(8)

Topic: Mental Retardation

[Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children.](#) - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder](#) : CK(134) : AC(12), [Attention Deficit Disorder with Hyperactivity](#) : CK(242) : AC(31), [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Child Mortality](#) : CK(64) : AC(8), [Infant Mortality](#) : CK(249) : AC(25), [Mental Retardation](#) : CK(71) : AC(7), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)
Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Mitochondrial Diseases](#)

[The epidemic of autism may be linked to both vaccinations and mitochondrial diseases.](#) - GMI Summary

Pubmed Data : Clin Exp Pharmacol Physiol. 2004 Dec;31 Suppl 2:S51-3 PMID: [19043939](#)

Article Published Date : Dec 01, 2004

Authors : Stephanie F Cave

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Mitochondrial Diseases : CK\(157\) : AC\(57\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Myopathy: Inflammatory](#)

[Aluminium-containing adjuvants in vaccines may be causing autoimmune conditions such as chronic fatigue syndrome and the inflammatory myopathy known as macrophagic myofasciitis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11. PMID: [19004564](#)

Article Published Date : Feb 01, 2009

Authors : Christopher Exley, Louise Swarbrick, Rhomain K Gherardi, Francois-Jérôme Authier

Study Type : Commentary

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Myopathy: Inflammatory : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Neuromyelitis Optica](#)

[Acute disseminated encephalomyelitis \(ADEM\) may be caused by vaccination.](#) - GMI Summary

Pubmed Data : J Clin Neurosci. 2008 Dec;15(12):1315-22. Epub 2008 Oct 30. PMID: [18976924](#)

Article Published Date : Dec 01, 2008

Authors : William Huynh, Dennis J Cordato, Elias Kehdi, Lynette T Masters, Chris Dedousis

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Encephalomyelitis : CK\(12\) : AC\(7\)](#), [Neuromyelitis Optica : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Spongiform Encephalopathies: Transmissible](#)

[Transmissible spongiform encephalopathies may be passed iatrogenically through vaccines.](#) - GMI Summary

Pubmed Data : Dev Biol (Basel). 2001;106:455-9; discussion 460-1, 465-75. PMID: [11761262](#)

Article Published Date : Jan 01, 2001

Authors : N R Cashman

Study Type : Commentary

Additional Links

Diseases : [Spongiform Encephalopathies: Transmissible](#) : CK(2) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Category: Adverse Pharmacological Actions

Topic: [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP](#) : CK(30) : AC(3), [Elevated CRP](#) : CK(82) : AC(8), [Pre-Eclampsia](#) : CK(299) : AC(33), [Pregnancy: Vaccination](#) : CK(92) : AC(16), [Pregnancy Complications](#) : CK(168) : AC(20), [Preterm Birth: Prevention](#) : CK(111) : AC(9), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation](#) : CK(14) : AC(3), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#) : CK(42) : AC(4)

[Thirty-five percent of children with juvenile idiopathic arthritis experienced flare of the disease after vaccination.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2012 Mar 15. Epub 2012 Mar 15. PMID: [22513085](#)

Article Published Date : Mar 15, 2012

Authors : Natasa Toplak, Vesna Subelj, Tanja Kveder, Sasa Cucnik, Katarina Prosenec, Alenka Trampus-Bakija, Ljupco Todorovski, Tadej Avcin

Study Type : Human Study

Additional Links

Diseases : [Arthritis: Juvenile Idiopathic](#) : CK(20) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#) : CK(42) : AC(4)

Topic: [Immunotoxic](#)

["Yellow fever vaccination and increased relapse rate in travelers with multiple sclerosis."](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1267-71. Epub 2011 Jun 13. PMID: [21670384](#)

Article Published Date : Oct 01, 2011

Authors : Mauricio F Farez, Jorge Correale

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: Yellow Fever](#) : CK(13) : AC(2)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

[Aluminum vaccine adjuvants appear to contribute to the rising prevalence of autism.](#) - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1489-99. Epub 2011 Aug 23. PMID: [22099159](#)

Article Published Date : Nov 01, 2011

Authors : Lucija Tomljenovic, Christopher A Shaw

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#), [Neurotoxic : CK\(1116\) : AC\(188\)](#)

[Increased risk \(4.4 fold\) of noninfluenza respiratory virus infections associated with receipt of inactivated influenza vaccine. - GMI Summary](#)

Pubmed Data : Clin Infect Dis. 2012 Jun ;54(12):1778-83. Epub 2012 Mar 15. PMID: [22423139](#)

Article Published Date : May 31, 2012

Authors : Benjamin J Cowling, Vicky J Fang, Hiroshi Nishiura, Kwok-Hung Chan, Sophia Ng, Dennis K M Ip, Susan S Chiu, Gabriel M Leung, J S Malik Peiris

Study Type : Human Study

Additional Links

Diseases : [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[Autoimmunity following hepatitis B vaccine has been reported. - GMI Summary](#)

Pubmed Data : Lupus. 2012 Feb ;21(2):146-52. PMID: [22235045](#)

Article Published Date : Jan 31, 2012

Authors : Y Zafrir, N Agmon-Levin, Z Paz, T Shilton, Y Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. - GMI Summary](#)

Pubmed Data : J Trace Elem Med Biol. 2012 Mar 14. Epub 2012 Mar 14. PMID: [22425036](#)

Article Published Date : Mar 14, 2012

Authors : Olivier Guillard, Bernard Fauconneau, Alain Pineau, Annie Marraud, Jean-Pierre Bellocq, Marie-Pierre Chenard

Study Type : Human: Case Report, Review

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Pseudolymphoma : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[Topic: Immunosuppressive](#)

[Annual influenza vaccination hampers the development of virus-specific CD8\(+\) T cell responses necessary to protect against influenza infection. - GMI Summary](#)

Pubmed Data : J Virol. 2011 Nov ;85(22):11995-2000. Epub 2011 Aug 31. PMID: [21880755](#)

Article Published Date : Nov 01, 2011

Authors : Rogier Bodewes, Pieter L A Fraaij, Martina M Geelhoed-Mieras, Carel A van Baalen, Harm A W M Tiddens, Annemarie M C van Rossum, Fiona R van der Klis, Ron A M Fouchier, Albert D M E Osterhaus, Guus F Rimmelzwaan

Study Type : Human Study

Additional Links

Diseases : [Cystic Fibrosis : CK\(523\) : AC\(78\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Immunosuppressive : CK\(156\) : AC\(26\)](#)

Topic: [Interleukin-6 up-regulation](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

Topic: [Teratogenic](#)

[Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Birth Defects : CK\(204\) : AC\(39\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Adverse Pharmacological Actions : [Teratogenic : CK\(318\) : AC\(62\)](#)

Topic: [Neurotoxic](#)

[Aluminum vaccine adjuvants appear to contribute to the rising prevalence of autism.](#) - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1489-99. Epub 2011 Aug 23. PMID: [22099159](#)

Article Published Date : Nov 01, 2011

Authors : Lucija Tomljenovic, Christopher A Shaw

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#), [Neurotoxic : CK\(1116\) : AC\(188\)](#)

[Measles vaccine and glyphosate-induced parkinsonism has been reported.](#) - GMI Summary

Pubmed Data : Arq Neuropsiquiatr. 2003 Jun ;61(2B):381-6. Epub 2003 Jul 28. PMID: [12894271](#)

Article Published Date : Jun 01, 2003

Authors : Maria do Desterro Leiros da Costa, Lílian Regina Gonçalves, Egberto Reis Barbosa, Luiz Alberto Bacheschi

Study Type : Human: Case Report

Additional Links

Diseases : [Glyphosate Toxicity : CK\(29\) : AC\(14\)](#), [Parkinsonian Disorders : CK\(15\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

Problem Substances : [Glyphosate : CK\(403\) : AC\(130\)](#)

Adverse Pharmacological Actions : [Neurotoxic : CK\(1116\) : AC\(188\)](#)

Topic: Myotoxicity

[Influenza vaccine has been reported to be a possible trigger of rhabdomyolysis induced acute renal failure in those taking statin drugs.](#) - GMI Summary

Pubmed Data : Nephrol Dial Transplant. 2000 May ;15(5):740-1. PMID: [10809833](#)

Article Published Date : May 01, 2000

Authors : E Plotkin, J Bernheim, S Ben-Chetrit, A Mor, Z Korzets

Study Type : Human: Case Report

Additional Links

Diseases : [Rhabdomyolysis : CK\(165\) : AC\(38\)](#), [Statin-Induced Pathologies : CK\(1600\) : AC\(320\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Problem Substances : [Statin Drugs : CK\(3971\) : AC\(475\)](#)

Adverse Pharmacological Actions : [Myotoxicity : CK\(327\) : AC\(80\)](#)

Topic: Hepatotoxic

[Hepatitis B vaccine induces cell death in liver cells and mouse liver.](#) - GMI Summary

Pubmed Data : Apoptosis. 2012 Jan 17. Epub 2012 Jan 17. PMID: [22249285](#)

Article Published Date : Jan 17, 2012

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Changchun Li, Mengjin Zhu, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Liver Damage : CK\(648\) : AC\(226\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Hepatotoxic : CK\(301\) : AC\(85\)](#)

Category: Anti-Therapeutic Actions

Topic: Vaccination: All

["The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate."](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2012 ;2:CD004407. Epub 2012 Feb 15. PMID: [22336803](#)

Article Published Date : Dec 31, 2011

Authors : Vittorio Demicheli, Alessandro Rivetti, Maria Grazia Debalini, Carlo Di Pietrantonj

Study Type : Meta Analysis

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Rubella : CK\(54\) : AC\(4\)](#), [Vaccine Safety : CK\(21\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[38,787 adverse events including infant death \(highest in 1-3 month olds\) after vaccination were reported between 1991-1994. \(The authors speciously claim SIDS and not vaccination caused these deaths\).](#) - GMI Summary

Pubmed Data : J Pediatr. 1997 Oct;131(4):529-35. PMID: [9386653](#)

Article Published Date : Oct 01, 1997

Authors : M M Braun, S S Ellenberg

Study Type : Meta Analysis

Additional Links

Diseases : [Hearing Loss: Sudden : CK\(30\) : AC\(3\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Diphtheria immunisation is weakly associated with an increased risk of asthma by age 7 years.](#) - GMI Summary

Pubmed Data : Thorax. 2007 Mar;62(3):270-5. Epub 2006 Nov 7. PMID: [17090571](#)

Article Published Date : Mar 01, 2007

Authors : Kazunori Nakajima, Shyamali C Dharmage, John B Carlin, Cathryn L Wharton, Mark A Jenkins, Graham G Giles, Michael J Abramson, E Haydn Walters, John L Hopper

Study Type : Meta Analysis

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Atopic Disease : CK\(91\) : AC\(9\)](#), [Hypersensitivity: Immediate : CK\(93\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

[DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents.](#) - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Inactivated flu vaccines have not been proven to be effective or safe in preventing influenza in healthy children under two.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2009 Sep-Oct;15(5):44-6. PMID: [18425905](#)

Article Published Date : Sep 01, 2009

Authors : Tom Jefferson, Alessandro Rivetti, Anthony Harnden, Carlo Di Pietrantonj, Vittorio Demicheli

Study Type : Meta Analysis

Additional Links

Diseases : [Cold and Flu: Infants & Children : CK\(62\) : AC\(6\)](#), [Infection: In Infants & Children : CK\(111\) : AC\(11\)](#), [Influenza A : CK\(292\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Male newborns vaccinated with hepatitis B prior to 1999 had a 3-fold higher risk for parentally reported autism. - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(24):1665-77. PMID: [21058170](#)

Article Published Date : Jan 01, 2010

Authors : Carolyn M Gallagher, Melody S Goodman

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Maternal influenza vaccination during pregnancy does not reduce the incidence of acute respiratory illness visits among infants. - GMI Summary

Pubmed Data : Cancer Sci. 2004 Jul;95(7):596-601. PMID: [17146026](#)

Article Published Date : Jul 01, 2004

Authors : Eric K France, Renae Smith-Ray, David McClure, Simon Hambidge, Stanley Xu, Kristi Yamasaki, David Shay, Eric Weintraub, Alicia M Fry, Steve B Black, Henry R Shinefield, John P Mullooly, Lisa A Jackson

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem. - GMI Summary

Pubmed Data : Am J Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Infant Chemical Exposures : CK\(165\) : AC\(24\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Over 1,000 confirmed cases of vaccine-induced thrombocytopenia were reported between 1990-2008. - GMI Summary

Pubmed Data : Vaccine. 2010 Nov 29. Epub 2010 Nov 29. PMID: [21126606](#)

Article Published Date : Nov 29, 2010

Authors : Emily Jane Woo, Robert P Wise, David Menschik, Sean V Shadomy, John Iskander, Judy Beeler, Frederick Varricchio, Robert Ball

Study Type : Meta Analysis

Additional Links

Diseases : [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Over 600 cases of sudden infant death syndrome following vaccination were reported from 1990-1997. - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2001 Jun-Jul;10(4):279-85. PMID: [11760487](#)

Article Published Date : Jun 01, 2001

Authors : L E Silvers, S S Ellenberg, R P Wise, F E Varricchio, G T Mootrey, M E Salive

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The risk of adverse events from the pertussis outweighed the risk of pertussis infection during the period of 1970-83 in children living in non-deprived circumstances in Britain. - GMI Summary](#)

Pubmed Data : Dev Biol Stand. 1985;61:395-405. PMID: [3835080](#)

Article Published Date : Jan 01, 1985

Authors : G T Stewart

Study Type : Meta Analysis

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[There are no randomized controlled trials that assessed the effects of hepatitis B vaccine during pregnancy for preventing infant infection. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2011(3):CD007879. Epub 2011 Mar 16. PMID: [21412913](#)

Article Published Date : Jan 01, 2011

Authors : Ussanee S Sangkomkamhang, Pisake Lumbiganon, Malinee Laopaiboon

Study Type : Meta Analysis

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[There is a highly statistically significant correlation between increasing number of vaccine doses and increasing infant mortality rates. - GMI Summary](#)

Pubmed Data : Hum Exp Toxicol. 2011 May 4. Epub 2011 May 4. PMID: [21543527](#)

Article Published Date : May 04, 2011

Authors : Neil Z Miller, Gary S Goldman

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[There is a lack of evidence for the effectiveness of influenza vaccines in adults aged 65 years or older. - GMI Summary](#)

Pubmed Data : Lancet Infect Dis. 2011 Oct 25. Epub 2011 Oct 25. PMID: [22032844](#)

Article Published Date : Oct 25, 2011

Authors : Michael T Osterholm, Nicholas S Kelley, Alfred Sommer, Edward A Belongia

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Thimerosal-containing vaccines are associated with autism prevalence and measles-containing vaccines are associated with serious neurological disorders. - GMI Summary](#)

Pubmed Data : Med Sci Monit. 2004 Mar;10(3):PI33-9. Epub 2004 Mar 1. PMID: [14976450](#)

Article Published Date : Mar 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination in infants less than 3 months is associated with an increased risk of sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : Fundam Clin Pharmacol. 1995;9(3):263-70. PMID: [7557822](#)

Article Published Date : Jan 01, 1995

Authors : A P Jonville-Bera, E Autret, J Laugier

Study Type : Meta Analysis

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccination is associated with an increased risk for hemolytic anemia.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7394-7. Epub 2009 Sep 18. PMID: [19766577](#)

Article Published Date : Dec 09, 2009

Authors : Allison L Naleway, Edward A Belongia, James G Donahue, Burney A Kieke, Jason M Glanz,

Study Type : Meta Analysis

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[We concluded that there is no credible evidence that vaccination of healthy people under the age of 60, who are healthcare workers caring for the elderly, affects influenza complications in those cared for.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2006 ;3:CD005187. Epub 2006 Jul 19. PMID: [16856082](#)

Article Published Date : Jan 01, 2006

Authors : R E Thomas, T Jefferson, V Demicheli, D Rivetti

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#)

Additional Keywords : [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[When polled 5% of nonpediatricians would not use Haemophilus influenzae type b vaccine if they had a child born in 2004.](#) - GMI Summary

Pubmed Data : Pediatrics. 2005 Nov;116(5):e623-33. PMID: [16263976](#)

Article Published Date : Nov 01, 2005

Authors : Klara M Posfay-Barbe, Ulrich Heininger, Christoph Aebi, Daniel Desgrandchamps, Bernard Vaudaux, Claire-Anne Siegrist

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

["A history of prior vaccination is not always associated with immunity nor with the presence of specific antibodies."](#) - GMI Summary

Pubmed Data : Clin Invest Med. 1988 Aug ;11(4):304-9. PMID: [3168353](#)

Article Published Date : Jul 31, 1988

Authors : L Sekla, W Stackiw, G Eibisch, I Johnson

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[20.7% \(6 of 29\) of persons known to have received measles vaccine had non-protective titers. - GMI Summary](#)

Pubmed Data : Am J Trop Med Hyg. 2008 Nov;79(5):787-92. PMID: [18981523](#)

Article Published Date : Nov 01, 2008

Authors : Inácio M Mandomando, Denise Naniche, Marcela F Pasetti, Xavier Vallès, Lilian Cuberos, Ariel Nhacolo, Karen L Kotloff, Helder Martins, Myron M Levine, Pedro Alonso

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A 1993 outbreak of measles in a highly immunised Australian population. - GMI Summary](#)

Pubmed Data : Aust J Public Health. 1994 Sep ;18(3):249-52. PMID: [7841251](#)

Article Published Date : Aug 31, 1994

Authors : A Herceg, I Passaris, C Mead

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A Haemophilus b polysaccharide vaccine resulted in minus 58 percent efficacy in children in Minnesota in August 1985. - GMI Summary](#)

Pubmed Data : JAMA. 1988 Sep 9;260(10):1423-8. PMID: [3261350](#)

Article Published Date : Sep 09, 1988

Authors : M T Osterholm, J H Rambeck, K E White, J L Jacobs, L M Pierson, J D Neaton, C W Hedberg, K L MacDonald, D M Granoff

Study Type : Human Study

Additional Links

Diseases : [Haemophilus influenzae : CK\(54\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#)

[A major measles epidemic occurred in 1989 in the region of Quebec despite a 99% vaccine coverage. - GMI Summary](#)

Pubmed Data : Can J Public Health. 1991 May-Jun;82(3):189-90. PMID: [1884314](#)

Article Published Date : Apr 30, 1991

Authors : N Boulianne, G De Serres, B Duval, J R Joly, F Meyer, P Déry, M Alary, D Le Hénaff, N Thériault

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak at a college with a prematriculation immunization requirement.](#) - GMI Summary

Pubmed Data : Am J Public Health. 1991 Mar ;81(3):360-4. PMID: [1994745](#)

Article Published Date : Feb 28, 1991

Authors : B S Hersh, L E Markowitz, R E Hoffman, D R Hoff, M J Doran, J C Fleishman, S R Preblud, W A Orenstein

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak in Montana in 1985 indicates vaccine failure.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 1987 Sep ;126(3):438-49. PMID: [3618578](#)

Article Published Date : Aug 31, 1987

Authors : R M Davis, E D Whitman, W A Orenstein, S R Preblud, L E Markowitz, A R Hinman

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A modified self-controlled case series method links multidose vaccinations to sudden unexpected death.](#) - GMI Summary

Pubmed Data : Stat Med. 2011 Mar 15;30(6):666-77. Epub 2010 Nov 30. PMID: [21337361](#)

Article Published Date : Mar 15, 2011

Authors : Ronny Kuhnert, Hartmut Hecker, Christina Poethko-Müller, Martin Schlaud, Mechtild Vennemann, Heather J Whitaker, C Paddy Farrington

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Acute hepatitis B can occur in those who are vaccinated against it and who are exposed through unprotected sexual contact and iatrogenically.](#) - GMI Summary

Pubmed Data : Postgrad Med J. 2006 Mar;82(965):207-10. PMID: [16517803](#)

Article Published Date : Mar 01, 2006

Authors : G Rosner, Y Lurie, L Blendis, Z Halpern, R Oren

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Iatrogenic Disease : CK\(62\) : AC\(7\)](#)

Additional Keywords : [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Acute necrotizing encephalopathy secondary to diphtheria, tetanus toxoid and whole-cell pertussis vaccination has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Radiol. 2010 Jul;40(7):1281-4. Epub 2010 Jan 30. PMID: [20119724](#)

Article Published Date : Jul 01, 2010

Authors : Hale Aydin, Esra Ozgul, Ahmet Muhtesem Agildere

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Administration of varicella vaccine before the age of 15 months, and the prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease.](#) - GMI Summary

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Mullooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma](#) : CK(918) : AC(140), [Chickenpox](#) : CK(110) : AC(8), [Corticosteroid-Induced Toxicity](#) : CK(78) : AC(17)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Aluminum hydroxide-induced macrophagic myofasciitis \(MMF\) associated with vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1457-63. Epub 2011 Aug 22. PMID: [22099155](#)

Article Published Date : Nov 01, 2011

Authors : Elodie Passeri, Chiara Villa, Maryline Couette, Emmanuel Itti, Pierre Brugieres, Pierre Cesaro, Romain K Gherardi, Anne-Catherine Bachoud-Levi, François-Jérôme Authier

Study Type : Human Study

Additional Links

Diseases : [Macrophagic myofasciitis](#) : CK(15) : AC(3)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

[Aluminum vaccine adjuvants appear to contribute to the rising prevalence of autism.](#) - GMI Summary

Pubmed Data : J Inorg Biochem. 2011 Nov ;105(11):1489-99. Epub 2011 Aug 23. PMID: [22099159](#)

Article Published Date : Nov 01, 2011

Authors : Lucija Tomljenovic, Christopher A Shaw

Study Type : Human Study

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Problem Substances : [Aluminum Hydroxide](#) : CK(56) : AC(14)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48), [Neurotoxic](#) : CK(1116) : AC(188)

[Among female infants, those who receive both BCG and DTP vaccines experience higher mortality than those who receive only one of the two vaccines.](#) - GMI Summary

Pubmed Data : Trop Med Int Health. 2005 Oct;10(10):947-55. PMID: [16185228](#)

Article Published Date : Oct 01, 2005

Authors : Lawrence H Moulton, Lakshmi Rahmathullah, Neal A Halsey, R D Thulasiraj, Joanne Katz, James M Tielsch

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Among US military personnel vaccinated against smallpox, myopericarditis occurred at a rate of 1 per 12,819 primary vaccinees, and 3.6 fold higher in those without previous vaccinia vaccination. - GMI Summary](#)

Pubmed Data : JAMA. 2003 Jun 25;289(24):3283-9. PMID: [12824210](#)

Article Published Date : Jun 25, 2003

Authors : Jeffrey S Halsell, James R Riddle, J Edwin Atwood, Pierce Gardner, Robert Shope, Gregory A Poland, Gregory C Gray, Stephen Ostroff, Robert E Eckart, Duane R Hospenenthal, Roger L Gibson, John D Grabenstein, Mark K Arness, David N Tornberg,

Study Type : Human Study

Additional Links

Diseases : [Myopericarditis : CK\(40\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[An economic analysis of mass smallpox vaccination reveals that cardiovascular adverse events would be sizeable and costly. - GMI Summary](#)

Pubmed Data : J Rheumatol. 1994 Jul;21(7):1305-9. PMID: [18284356](#)

Article Published Date : Jul 01, 1994

Authors : Ismael R Ortega-Sanchez, Mercedes M Sniadack, Gina T Mootrey

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Annual influenza vaccination hampers the development of virus-specific CD8\(+\) T cell responses necessary to protect against influenza infection. - GMI Summary](#)

Pubmed Data : J Virol. 2011 Nov ;85(22):11995-2000. Epub 2011 Aug 31. PMID: [21880755](#)

Article Published Date : Nov 01, 2011

Authors : Rogier Bodewes, Pieter L A Fraaij, Martina M Geelhoed-Mieras, Carel A van Baalen, Harm A W M Tiddens, Annemarie M C van Rossum, Fiona R van der Klis, Ron A M Fouchier, Albert D M E Osterhaus, Guus F Rimmelzwaan

Study Type : Human Study

Additional Links

Diseases : [Cystic Fibrosis : CK\(523\) : AC\(78\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Immunosuppressive : CK\(156\) : AC\(26\)](#)

[Anthrax vaccination contributes to joint related adverse reactions. - GMI Summary](#)

Pubmed Data : Clin Exp Rheumatol. 2002 Mar-Apr;20(2):217-20. PMID: [12051402](#)

Article Published Date : Mar 01, 2002

Authors : D A Geier, M R Geier

Study Type : Human Study

Additional Links

Diseases : [Joint Diseases : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[Autistic children have elevated levels of measles antibodies indicating that measles vaccination may be causing autoimmunity in these children. - GMI Summary](#)

Pubmed Data : Pediatr Neurol. 2003 Apr;28(4):292-4. PMID: [12849883](#)

Article Published Date : Apr 01, 2003

Authors : Vijendra K Singh, Ryan L Jensen

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Between 1995 and 2005 25,306 adverse events were reported from varicella vaccine. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2008 Mar 1;197 Suppl 2:S170-7. PMID: [18419393](#)

Article Published Date : Mar 01, 2008

Authors : Sandra S Chaves, Penina Haber, Kimp Walton, Robert P Wise, Hector S Izurieta, D Scott Schmid, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy. - GMI Summary](#)

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Birth Defects : CK\(204\) : AC\(39\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Adverse Pharmacological Actions : [Teratogenic : CK\(318\) : AC\(62\)](#)

[Breastfeeding attenuates reductions in energy intake induced by a mild immunologic stimulus represented by DPTH immunization. - GMI Summary](#)

Pubmed Data : J Nutr. 2002 Jun;132(6):1293-8. PMID: [12042449](#)

Article Published Date : Jun 01, 2002

Authors : Mardya López-Alarcón, Cutberto Garza, Jean-Pierre Habicht, Lourdes Martínez, Virginia Pegueros, Salvador Villalpando

Study Type : Human Study

Additional Links

Substances : [Breast Milk : CK\(428\) : AC\(49\)](#)

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Breastfeeding is associated with a decreased incidence of fever after immunizations. - GMI Summary](#)

Pubmed Data : Pediatrics. 2010 Jun;125(6):e1448-52. Epub 2010 May 17. PMID: [20478932](#)

Article Published Date : Jun 01, 2010

Authors : Alfredo Pisacane, Paola Continisio, Orsola Palma, Stefania Cataldo, Fabiola De Michele, Ugo Vairo

Study Type : Human Study

Additional Links

Substances : [Breast Milk : CK\(428\) : AC\(49\)](#)

Diseases : [Fever : CK\(77\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[C-reactive protein \(CRP\) elevation occur in infants without sepsis after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : Eur J Pediatr. 2013 Jan 29. Epub 2013 Jan 29. PMID: [23358708](#)

Article Published Date : Jan 28, 2013

Authors : Istemi Han Celik, Gamze Demirel, Fuat Emre Canpolat, Omer Erdeve, Ugur Dilmen

Study Type : Human Study

Additional Links

Diseases : [Elevated CRP : CK\(82\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Children vaccinated with MMR before age 10 are at significantly higher risk of multiple sclerosis.](#) - GMI Summary

Pubmed Data : Eur J Epidemiol. 2009;24(9):541-52. Epub 2009 Jul 26. PMID: [19633994](#)

Article Published Date : Jan 01, 2009

Authors : Cecilia Ahlgren, Kjell Torén, Anders Odén, Oluf Andersen

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Chronic fatigue syndrome may be associated with silicone implants and/or vaccinations.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24. PMID: [18725327](#)

Article Published Date : Oct 01, 2008

Authors : Agmon-Levin Nancy, Yehuda Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Breast Augmentation Complications : CK\(32\) : AC\(4\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Silicone Implant Toxicity : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Silicone Implants : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau.](#) - GMI Summary

Article Published Date : Dec 06, 2013

Authors : Ane Bærent Fisker, Henrik Ravn, Amabelia Rodrigues, Marie Drivsholm Ostergaard, Carlito Bale, Christine Stabell Benn, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#)

Additional Keywords : [Child Mortality : CK\(64\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures](#) : CK(83) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Varicella](#) : CK(50) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Congenital malformation is a possible consequence of rubella vaccination during pregnancy.](#) - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects](#) : CK(204) : AC(39), [Pregnancy: Vaccination](#) : CK(92) : AC(16), [Rubella](#) : CK(54) : AC(4), [Vaccination: Abortion](#) : CK(40) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Adult Rubella](#) : CK(24) : AC(5), [Vaccination: All](#) : CK(4702) : AC(361)

[CRP level in infants is elevated in the 48 hours following immunization.](#) - GMI Summary

Pubmed Data : J Pediatr. 2007 Aug ;151(2):167-72. Epub 2007 Jun 22. PMID: [17643770](#)

Article Published Date : Aug 01, 2007

Authors : Massroor Pourcyrus, Sheldon B Korones, Kristopher L Arheart, Henrietta S Bada

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein](#) : CK(879) : AC(84), [Premature Birth](#) : CK(414) : AC(44), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Multiple Vaccines](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Despite a high coverage with measles vaccines in parts of west Africa, epidemics of measles occur with reduced severity in an increasing proportion of older children who have been vaccinated.](#) - GMI Summary

Pubmed Data : Lancet. 1999 Jan 9 ;353(9147):98-102. PMID: [10023894](#)

Article Published Date : Jan 08, 1999

Authors : H C Whittle, P Aaby, B Samb, H Jensen, J Bennett, F Simondon

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Measles](#) : CK(157) : AC(16)

[Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis \(Tdap\) vaccine in order to prevent pertussis infection in their offspring, it does not reduce](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14), [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14), [Vaccination: Tetanus](#) : CK(61) :

[Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18. PMID: [21093496](#)

Article Published Date : Jan 10, 2011

Authors : J Agergaard, E Nante, G Poulstrup, J Nielsen, K L Flanagan, L Østergaard, C S Benn, P Aaby

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Diphtheria-tetanus-peteruss vaccines increase child mortality in rural Guinea-Bissau.](#) - GMI Summary

Pubmed Data : Int J Epidemiol. 2004 Apr;33(2):374-80. PMID: [15082643](#)

Article Published Date : Apr 01, 2004

Authors : Peter Aaby, Henrik Jensen, Joaquim Gomes, Manual Fernandes, Ida Maria Lisse

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[DPT vaccines have been associated with recurrent seizures.](#) - GMI Summary

Pubmed Data : Am J Dis Child. 1984 Oct;138(10):908-11. PMID: [6206715](#)

Article Published Date : Oct 01, 1984

Authors : J V Murphy, L D Sarff, K M Marquardt

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Seizures : CK\(135\) : AC\(33\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Erythema multiforme has been reported as a possible side effect of vaccination for human papillomavirus.](#) - GMI Summary

Pubmed Data : Dermatology. 2010;220(1):60-2. Epub 2009 Nov 3. PMID: [19887766](#)

Article Published Date : Jan 01, 2010

Authors : A C Katoulis, A Liakou, E Bozi, M Theodorakis, A Alevizou, A Zafeiraki, M Mistidou, N G Stavrianeas

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardisil\) : CK\(105\) : AC\(13\)](#)

[Even though 95% of the children had measles antibodies after vaccination, vaccine efficacy was not more than 68%.](#) - GMI Summary

Pubmed Data : J Infect Dis. 1990 Nov ;162(5):1043-8. PMID: [2230232](#)

Article Published Date : Oct 31, 1990

Authors : P Aaby, K Knudsen, T G Jensen, J Thårup, A Poulsen, M Sodemann, M C da Silva, H Whittle

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)
Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)
Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Evidence exists demonstrating that diphtheria-tetanus-pertussis \(DTP\) vaccines increase mortality in children.](#) - GMI Summary

Pubmed Data : Trop Med Int Health. 2007 Jan;12(1):15-24. PMID: [17207144](#)

Article Published Date : Jan 01, 2007

Authors : Peter Aaby, Christine Stabell Benn, Jens Nielsen, Ida Maria Lisse, Amabelia Rodrigues, Henrik Jensen

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Extra-immunization is associated with receiving immunizations from multiple providers and multiple facility types.](#) - GMI Summary

Pubmed Data : Public Health Rep. 2011 Jul-Aug;126 Suppl 2:48-59. PMID: [21812169](#)

Article Published Date : Jul 01, 2011

Authors : Paul M Darden, Kristina K Gustafson, Paul J Nietert, Robert M Jacobson

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP : CK\(30\) : AC\(3\)](#), [Elevated CRP : CK\(82\) : AC\(8\)](#), [Pre-Eclampsia : CK\(299\) : AC\(33\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Pregnancy Complications : CK\(168\) : AC\(20\)](#), [Preterm Birth: Prevention : CK\(111\) : AC\(9\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation : CK\(14\) : AC\(3\)](#), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

[Food/medicine vouchers have been used as an incentive to mothers of infants visiting Expanded Program on Immunization \(EPI\) centers in a low socio-economic area to increase vaccine rates.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Apr 26;28(19):3473-8. Epub 2010 Mar 1. PMID: [20199756](#)

Article Published Date : Apr 26, 2010

Authors : S Chandir, A J Khan, H Hussain, H R Usman, S Khowaja, N A Halsey, S B Omer

Study Type : Human Study

Additional Links

Additional Keywords : [Bribing : CK\(20\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Hepatitis B vaccination coverage has fallen to beneath 30% in France due to concerns over safety.](#) - GMI Summary

Pubmed Data : J Clin Virol. 2009 Nov;46(3):202-5. Epub 2009 Aug 28. PMID: [19716764](#)

Article Published Date : Nov 01, 2009

Authors : Marta A Balinska

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination has been linked to autoimmune inflammatory polyneuropathy \(PN\).](#) - GMI Summary

Pubmed Data : J Peripher Nerv Syst. 2002 Sep;7(3):163-7. PMID: [12365564](#)

Article Published Date : Sep 01, 2002

Authors : Claude Vital, Anne Vital, Georges Gbikpi-Benissan, Maïté Longy-Boursier, Marie-Thérèse Climas, Yves Castaing, Marie-Hélène Canron, Michel Le Bras, Klaus Petry

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy](#) : CK(104) : AC(2), [Autoimmune inflammatory polyneuropathy \(PN\)](#) : CK(10) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination is associated with a wide range of autoimmune diseases.](#) - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis](#) : CK(1493) : AC(221), [Arthritis: Rheumatoid](#) : CK(295) : AC(53), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Glomerulonephritis](#) : CK(41) : AC(9), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Multiple Sclerosis](#) : CK(746) : AC(133), [Myelitis](#) : CK(39) : AC(5), [Optic Neuritis](#) : CK(23) : AC(3), [Pancytopenia](#) : CK(12) : AC(2), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Thrombocytopenia](#) : CK(231) : AC(25)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination is associated with an increased risk of CNS inflammatory demyelination after 3 years of age.](#) - GMI Summary

Pubmed Data : Reprod Toxicol. 2002 May-Jun;16(3):237-43. PMID: [18843097](#)

Article Published Date : May 01, 2002

Authors : Yann Mikaeloff, Guillaume Caridade, Samy Suissa, Marc Tardieu

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Inflammation](#) : CK(1125) : AC(377), [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination is associated with potentially neurotoxic mercury exposure in infants.](#) - GMI Summary

Pubmed Data : Chin Med. 2008 Mar 29;3:4. PMID: [10802503](#)

Article Published Date : Mar 29, 2008

Authors : G V Stajich, G P Lopez, S W Harry, W R Sexson

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning](#) : CK(172) : AC(45), [Premature Birth](#) : CK(414) : AC(44)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) :

[Hepatitis B vaccination may contribute to autoimmune demyelinating complications due to immunological cross-reactivity between Hepatitis B virus surface antigen and myelin basic protein. - GMI Summary](#)

Pubmed Data : Clin Dev Immunol. 2005 Sep;12(3):217-24. PMID: [16295528](#)

Article Published Date : Sep 01, 2005

Authors : Dimitrios-Petrou Bogdanos, Heather Smith, Yun Ma, Harold Baum, Giorgina Mieli-Vergani, Diego Vergani

Study Type : Human Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Hepatitis B Vaccine : CK\(30\) : AC\(2\)](#), [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases. - GMI Summary](#)

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination was statistically associated with gastrointestinal reactions including: hepatitis, gastrointestinal disease and liver function test abnormalities. - GMI Summary](#)

Pubmed Data : Hepatogastroenterology. 2002 Nov-Dec;49(48):1571-5. PMID: [12397738](#)

Article Published Date : Nov 01, 2002

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Gastrointestinal Diseases : CK\(38\) : AC\(14\)](#), [Hepatitis : CK\(64\) : AC\(24\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine is associated with an increased risk of liver problems in U.S. children less than 6 years old, 1993 and 1994. - GMI Summary](#)

Pubmed Data : Epidemiology. 1999 May;10(3):337-9. PMID: [10230847](#)

Article Published Date : May 01, 1999

Authors : M A Fisher, S A Eklund

Study Type : Human Study

Additional Links

Diseases : [Liver Disease : CK\(112\) : AC\(31\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine is associated with an increased risk of multiple sclerosis. - GMI Summary](#)

Pubmed Data : Neurology. 2004 Sep 14;63(5):838-42. PMID: [15365133](#)

Article Published Date : Sep 14, 2004

Authors : Miguel A Hernán, Susan S Jick, Michael J Olek, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Hepatitis B Vaccine](#) : CK(30) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children.](#) - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis](#) : CK(1493) : AC(221), [Arthritis: Juvenile Chronic](#) : CK(20) : AC(1), [Arthritis: Juvenile Idiopathic](#) : CK(20) : AC(1), [Arthritis: Juvenile Rheumatoid](#) : CK(10) : AC(1), [Ear Infection](#) : CK(259) : AC(32), [Pharyngeal Diseases](#) : CK(20) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine may have a possible association with the development of uveitis in some patients.](#) - GMI Summary

Pubmed Data : Cutan Ocul Toxicol. 2010 Mar;29(1):26-9. PMID: [19947819](#)

Article Published Date : Mar 01, 2010

Authors : Frederick W Fraunfelder, Eric B Suhler, Frederick T Fraunfelder

Study Type : Human Study

Additional Links

Diseases : [Uveitis](#) : CK(73) : AC(11), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis C prevalence in Southern Italy may be due to iatrogenic transmission through the Salk Polio vaccine 1956-1965.](#) - GMI Summary

Pubmed Data : J Med Virol. 2003 May;70(1):49-50. PMID: [12629643](#)

Article Published Date : May 01, 2003

Authors : Maurizio Montella, Anna Crispo, Maria Grimaldi, Vincenzo Tridente, Mario Fusco

Study Type : Human Study

Additional Links

Diseases : [Hepatitis C](#) : CK(413) : AC(65), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[High antibody titres against predicted Mycoplasma surface proteins do not prevent sequestration in infected lung tissue in the course of experimental contagious bovine pleuropneumonia.](#) - GMI Summary

Pubmed Data : Vet Microbiol. 2014 Aug 6 ;172(1-2):285-93. Epub 2014 May 5. PMID: [24880898](#)

Article Published Date : Aug 05, 2014

Authors : Elise Schieck, Anne Liljander, Carl Hamsten, Nimmo Gicheru, Massimo Scacchia, Flavio Sacchini, Martin Heller, Christiane Schnee, Anja Sterner-Kock, Andreas Hlinak, Jan Naessens, Jane Poole, Anja Persson, Joerg Jores

Study Type : Human Study

Additional Links

Diseases : [Mycoplasma Infections](#) : CK(2) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Antibody Theory Of Vaccinology](#) : CK(75) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

High titre measles vaccination increases female mortality in those receiving immunization in West Africa. - GMI Summary

Pubmed Data : Int J Epidemiol. 1996 Jun;25(3):665-73. PMID: [8671571](#)

Article Published Date : Jun 01, 1996

Authors : K M Knudsen, P Aaby, H Whittle, M Rowe, B Samb, F Simondon, J Sterne, P Fine

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

High-titer measles vaccination before 9 months of age has been linked to increased female mortality. - GMI Summary

Pubmed Data : Semin Pediatr Infect Dis. 2003 Jul;14(3):220-32. PMID: [12913835](#)

Article Published Date : Jul 01, 2003

Authors : Peter Aaby, Henrik Jensen, Francois Simondon, Hilton Whittle

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

HPV vaccination does not have a therapeutic effect in young women with pre-existing human papillomavirus infection. - GMI Summary

Pubmed Data : JAMA. 2007 Aug 15;298(7):743-53. PMID: [17699008](#)

Article Published Date : Aug 15, 2007

Authors : Allan Hildesheim, Rolando Herrero, Sholom Wacholder, Ana C Rodriguez, Diane Solomon, M Concepcion Bratti, John T Schiller, Paula Gonzalez, Gary Dubin, Carolina Porras, Silvia E Jimenez, Douglas R Lowy,

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

HPV vaccination has been linked to demyelination. - GMI Summary

Pubmed Data : J Child Neurol. 2010 Mar;25(3):321-7. PMID: [20189933](#)

Article Published Date : Mar 01, 2010

Authors : Francis J DiMario, Mirna Hajjar, Thomas Ciesielski

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Human Papilloma Virus (HPV) vaccine is associated with demyelinating events. - GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, Il Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [HPV : CK\(31\) : AC\(4\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [HPV Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Immunization of mothers with pneumococcal capsular polysaccharide vaccine during pregnancy is ineffective for infants. - GMI Summary](#)

Pubmed Data : Braz J Infect Dis. 2009 Apr;13(2):104-6. PMID: [20140352](#)

Article Published Date : Apr 01, 2009

Authors : Claudia R C Lopes, Eitan N Berezin, Ting Hui Ching, Jaildo de Souza Canuto, Vanilda Oliveira da Costa, Erika Monteiro Klering

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[In a measles outbreak from March 1991 to April 1992 in Rio de Janeiro 76.4% of those suspected to be infected had received measles vaccine before their first birthday. - GMI Summary](#)

Pubmed Data : Rev Soc Bras Med Trop. 1995 Oct-Dec;28(4):339-43. PMID: [8668833](#)

Article Published Date : Sep 30, 1995

Authors : S A de Oliveira, W N Soares, M O Dalston, M T de Almeida, A J Costa

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[In Kings County Washington, between 2002-2007, of the 176 confirmed cases of pertussis in infants under age 1 seventy-seven percent were age-appropriately vaccinated. - GMI Summary](#)

Pubmed Data : Arch Pediatr Adolesc Med. 2011 Jul ;165(7):647-52. PMID: [21727277](#)

Article Published Date : Jul 01, 2011

Authors : Matthew P Hanson, Tao S Kwan-Gett, Atar Baer, Krista Rietberg, Mara Ohrt, Jeffrey S Duchin

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary](#)

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[In the US the highest number of cases of Guillain-Barre syndrome are associated with influenza and hepatitis B vaccines. - GMI Summary](#)

Pubmed Data : J Clin Neuromuscul Dis. 2009 Sep;11(1):1-6. PMID: [19730016](#)

Article Published Date : Sep 01, 2009

Authors : Nizar Souayah, Abu Nasar, M Fareed K Suri, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Incidence of adverse reactions to vaccines in pediatric populations are under-reported and may be as high as 43.4% for certain vaccine combinations.](#) - GMI Summary

Pubmed Data : Clin Drug Investig. 2004;24(8):457-63. PMID: [17523706](#)

Article Published Date : Jan 01, 2004

Authors : Pilar Carrasco-Garrido, Carmen Gallardo-Pino, Rodrigo Jiménez-García, Miguel A Tapias, Angel Gil de Miguel

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster \(shingles\) cases managed in the same time period.](#) - GMI Summary

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox](#) : CK(110) : AC(8), [Herpes Zoster](#) : CK(472) : AC(35), [Shingles](#) : CK(472) : AC(35), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection](#) : CK(20) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events.](#) - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein](#) : CK(879) : AC(84), [Cardiovascular Diseases](#) : CK(5342) : AC(665), [Diabetes Mellitus: Type 2](#) : CK(3603) : AC(359), [Influenza A](#) : CK(292) : AC(77), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Pharmacological Actions : [Interleukin-6 upregulation](#) : CK(26) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Influenza vaccination does not appear to be effective during pregnancy in preventing hospitalizations and outpatient visits for respiratory illness in pregnant women and their infants.](#) - GMI Summary

Pubmed Data : Am J Perinatol. 2004 Aug;21(6):333-9. PMID: [15311370](#)

Article Published Date : Aug 01, 2004

Authors : Steven B Black, Henry R Shinefield, Eric K France, Bruce H Fireman, Sharon T Platt, David Shay,

Study Type : Human Study

Additional Links

Diseases : [Pregnancy: Flu : CK\(10\) : AC\(1\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza vaccination does not prevent ischemic stroke and it does not reduce the rate of acute previous infections in stroke patients.](#) - GMI Summary

Pubmed Data : Cerebrovasc Dis. 2008;26(4):339-47. Epub 2008 Aug 27. PMID: [18728360](#)

Article Published Date : Jan 01, 2008

Authors : G Piñol-Ripoll, I de la Puerta, S Santos, F Purroy, E Mostacero

Study Type : Human Study

Additional Links

Diseases : [Stroke: Prevention : CK\(163\) : AC\(21\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination may increase the risk of Guillain-Barré Syndrome.](#) - GMI Summary

Pubmed Data : Kidney Int. 2008 Dec;74(11):1461-7. Epub 2008 Sep 24. PMID: [18592444](#)

Article Published Date : Dec 01, 2008

Authors : C I Blanco-Marchite, L Buznego-Suárez, M A Fagúndez-Vargas, M Méndez-Llatas, P Pozo-Martos

Study Type : Human Study

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant : CK\(13\) : AC\(2\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza vaccines may be causing vasculitis.](#) - GMI Summary

Pubmed Data : J Ethnopharmacol. 2000 Aug;71(3):457-63. PMID: [19734734](#)

Article Published Date : Aug 01, 2000

Authors : Rainer Birck, Isabelle Kaelsch, Peter Schnuelle, Luis Felipe Flores-Suárez, Rainer Nowack

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccines were not shown to be effective among children 6 to 59 months of age during 2 influenza seasons.](#) - GMI Summary

Pubmed Data : Anticancer Res. 2009 Nov;29(11):4629-32. PMID: [18838647](#)

Article Published Date : Nov 01, 2009

Authors : Peter G Szilagyi, Gerry Fairbrother, Marie R Griffin, Richard W Hornung, Stephanie Donauer, Ardythe Morrow, Mekibib Altaye, Yuwei Zhu, Sandra Ambrose, Kathryn M Edwards, Katherine A Poehling, Geraldine Lofthus, Michol Holloway, Lyn Finelli, Marika Iwane, Mary Allen Staat,

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza-related mortality is not prevented with increasing vaccination coverage.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 Oct 30;24(42-43):6468-75. Epub 2006 Jul 7. PMID: [16876293](#)

Article Published Date : Oct 30, 2006

Authors : Caterina Rizzo, Cécile Viboud, Emanuele Montomoli, Lone Simonsen, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Injection site reactions occur in 28% of those who receive the anthrax vaccine, with women having twice the incidence of reaction versus men.](#) - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2007 Mar ;16(3):259-74. PMID: [17245803](#)

Article Published Date : Mar 01, 2007

Authors : Michael M McNeil, I-Shan Chiang, John T Wheeling, Yujia Zhang

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Gender Differences : CK\(63\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[killed cholera vaccination generates an inferior immune response in comparison to patients with naturally acquired cholera.](#) - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2011 May ;18(5):844-50. Epub 2011 Feb 23. PMID: [21346055](#)

Article Published Date : May 01, 2011

Authors : Mohammad Murshid Alam, M Asrafuzzaman Riyadh, Kaniz Fatema, Mohammad Arif Rahman, Nayeema Akhtar, Tanvir Ahmed, Mohiul Islam Chowdhury, Fahima Chowdhury, Stephen B Calderwood, Jason B Harris, Edward T Ryan, Firdausi Qadri

Study Type : Human Study

Additional Links

Diseases : [Cholera : CK\(27\) : AC\(17\)](#)

Additional Keywords : [Cholera : CK\(27\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Cholera : CK\(20\) : AC\(2\)](#)

[Measles outbreak in a fully immunized secondary-school population with up to 99 percent vaccination.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1987 Mar 26 ;316(13):771-4. PMID: [3821823](#)

Article Published Date : Mar 25, 1987

Authors : T L Gustafson, A W Lievens, P A Brunell, R G Moellenberg, C M Buttery, L M Sehulster

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders.](#) - GMI Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Measles, mumps, and rubella catch up immunisation in a measles epidemic did not appear to confer protection and was associated with a variety of new side effects of the vaccine.](#) - GMI Summary

Pubmed Data : BMJ. 1995 Jun 24 ;310(6995):1629-32. PMID: [7795447](#)

Article Published Date : Jun 23, 1995

Authors : R J Roberts, Q D Sandifer, M R Evans, M Z Nolan-Farrell, P M Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Measles-mumps-rubella vaccine that is given in the second year of life is associated with an increased risk of immune thrombocytopenia purpura.](#) - GMI Summary

Pubmed Data : Pediatrics. 2008 Mar;121(3):e687-92. PMID: [18310189](#)

Article Published Date : Mar 01, 2008

Authors : Eric K France, Jason Glanz, Stanley Xu, Simon Hambidge, Kristi Yamasaki, Steve B Black, Michael Marcy, John P Mullooly, Lisa A Jackson, James Nordin, Edward A Belongia, K Hohman, Robert T Chen, Robert Davis,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccination is associated with an increased risk for idiopathic thrombocytopaenic purpura.](#) - GMI Summary

Pubmed Data : Br J Clin Pharmacol. 2003 Jan;55(1):107-11. PMID: [12534647](#)

Article Published Date : Jan 01, 2003

Authors : Corri Black, James A Kaye, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Myocarditis and pericarditis have been reported following smallpox vaccination in Europe, Australia and the United States.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2008 Mar 15;46 Suppl 3:S242-50. PMID: [18284365](#)

Article Published Date : Mar 15, 2008

Authors : Juliette Morgan, Martha H Roper, Laurence Sperling, Richard A Schieber, James D Heffelfinger, Christine G Casey, Jacqueline W Miller, Scott Santibanez, Barbara Herwaldt, Paige Hightower, Pedro L Moro, Beth F Hibbs, Nancy H Levine, Louisa E Chapman, John Iskander, J Michael Lane, Melinda Wharton, Gina T Mootrey, David L Swerdlow

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Near complete vaccination coverage for varicella does not prevent outbreaks in](#)

those treated. - GMI Summary

Pubmed Data : Pediatrics. 2006 Jun;117(6):e1070-7. PMID: [16740809](#)

Article Published Date : Jun 01, 2006

Authors : Adriana S Lopez, Dalya Guris, Laura Zimmerman, Linda Gladden, Tamara Moore, Dirk T Haselow, Vladimir N Loparev, D Scott Schmid, Aisha O Jumaan, Sandra L Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Noticeable adverse reactions to the HPV vaccine occurred in 22% of those polled. - GMI Summary

Pubmed Data : Aten Primaria. 2010 Dec 14. Epub 2010 Dec 14. PMID: [21163554](#)

Article Published Date : Dec 14, 2010

Authors : M Amparo Torrecilla Rojas, Miguel Pedregal González, Fermín García Rodríguez, Josefa Ruiz Fernández

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary. - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#), [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Pertussis vaccination may activate a genetic predisposition for encephalopathy in susceptible individuals. - GMI Summary

Pubmed Data : Cytotechnology. 2002 Nov;40(1-3):139-49. PMID: [20447868](#)

Article Published Date : Nov 01, 2002

Authors : Anne M McIntosh, Jacinta McMahon, Leanne M Dibbens, Xenia Iona, John C Mulley, Ingrid E Scheffer, Samuel F Berkovic

Study Type : Human Study

Additional Links

Diseases : [Dravet syndrome : CK\(30\) : AC\(3\)](#), [Encephalitis : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Pertussis vaccine has been linked to hypotonic-hyporesponsive episodes (HHE) in infants and children. - GMI Summary

Pubmed Data : Drug Saf. 2002;25(2):85-90. PMID: [11888351](#)

Article Published Date : Jan 01, 2002

Authors : Michael S Gold

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pneumococcal conjugate vaccine is not effective to prevent ear infections in previously unvaccinated toddlers and children with a history of recurrent ear infections.](#) - GMI Summary

Pubmed Data : Lancet. 2003 Jun 28;361(9376):2189-95. PMID: [12842372](#)

Article Published Date : Jun 28, 2003

Authors : Reinier Veenhoven, Debby Bogaert, Cuno Uiterwaal, Carole Brouwer, Herma Kiezebrink, Jacob Bruin, Ed IJzerman, Peter Hermans, Ronald de Groot, Ben Zegers, Wietse Kuis, Ger Rijkers, Anne Schilder, Elisabeth Sanders

Study Type : Human Study

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines are ineffective in children with a history of recurrent acute ear infections - Article 2.](#) - GMI Summary

Pubmed Data : Int J Pediatr Otorhinolaryngol. 2006 Feb;70(2):275-85. Epub 2005 Sep 2. PMID: [16140397](#)

Article Published Date : Feb 01, 2006

Authors : Muriel J P van Kempen, Judith S Vermeiren, Mario Vaneechoutte, Geert Claeys, Reinier H Veenhoven, Ger T Rijkers, Elisabeth A M Sanders, Ingeborg J Dhooge

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines do not appear to reduce the risk of death from pneumonia in adult populations.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2003(4):CD000422. PMID: [14583920](#)

Article Published Date : Jan 01, 2003

Authors : K Dear, J Holden, R Andrews, D Tatham

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Postlicensure safety surveillance has revealed a disproportionate reporting of syncope and venous thromboembolic events following quadrivalent HPV vaccination.](#) - GMI Summary

Pubmed Data : JAMA. 2009 Aug 19;302(7):750-7. PMID: [19690307](#)

Article Published Date : Aug 19, 2009

Authors : Barbara A Slade, Laura Leidel, Claudia Vellozzi, Emily Jane Woo, Wei Hua, Andrea Sutherland, Hector S Izurieta, Robert Ball, Nancy Miller, M Miles Braun, Lauri E Markowitz, John Iskander

Study Type : Human Study

Additional Links

Diseases : [Syncope : CK\(10\) : AC\(1\)](#), [Thromboembolism : CK\(205\) : AC\(16\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Primary and secondary vaccine failure may explain the 1992 measles epidemic in Cape Town. - GMI Summary

Pubmed Data : S Afr Med J. 1994 Mar ;84(3):145-9. PMID: [7740350](#)

Article Published Date : Feb 28, 1994

Authors : N Coetzee, G D Hussey, G Visser, P Barron, A Keen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

Prior receipt of seasonal flu vaccine (2008-09)was associated with increased risk of medically attended pandemic H1N1 illness (2008-09). - GMI Summary

Pubmed Data : PLoS Med. 2010;7(4):e1000258. Epub 2010 Apr 6. PMID: [20386731](#)

Article Published Date : Jan 01, 2010

Authors : Danuta M Skowronski, Gaston De Serres, Natasha S Crowcroft, Naveed Z Janjua, Nicole Boulianne, Travis S Hottes, Laura C Rosella, James A Dickinson, Rodica Gilca, Pam Sethi, Najwa Ouhoumane, Donald J Willison, Isabelle Rouleau, Martin Petric, Kevin Fonseca, Steven J Drews, Anuradha Rebbapragada, Hugues Charest, Marie-Eve Hamelin, Guy Boivin, Jennifer L Gardy, Yan Li, Trijntje L Kwindt, David M Patrick, Robert C Brunham,

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Additional Keywords : [Immunosuppressive Flu Vaccines : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Rates of intussusception associated with rotavirus vaccines may be significantly underestimated. - GMI Summary

Pubmed Data : J Infect Dis. 2009 Nov 1;200 Suppl 1:S264-70. PMID: [19817607](#)

Article Published Date : Nov 01, 2009

Authors : Margaret M Cortese, Mary Allen Staat, Geoffrey A Weinberg, Kathryn Edwards, Marilyn A Rice, Peter G Szilagyi, Caroline B Hall, Daniel C Payne, Umesh D Parashar

Study Type : Human Study

Additional Links

Diseases : [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Rotavirus vaccination has been associated with increased risk for gastroenteritis and intussusception. - GMI Summary

Pubmed Data : Pediatrics. 2004 Apr;113(4):e353-9. PMID: [15060267](#)

Article Published Date : Apr 01, 2004

Authors : Penina Haber, Robert T Chen, Lynn R Zanardi, Gina T Mootrey, Roseanne English, M Miles Braun,

Study Type : Human Study

Additional Links

Diseases : [Gastroenteritis : CK\(96\) : AC\(11\)](#), [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Rotavirus vaccinations have a history of causing adverse effects such as intussusception. - GMI Summary

Pubmed Data : Pediatrics. 2001 Jun;107(6):E97. PMID: [11389295](#)

Article Published Date : Jun 01, 2001

Authors : L R Zanardi, P Haber, G T Mootrey, M T Niu, M Wharton

Study Type : Human Study

Additional Links

Diseases : [Intussusception](#) : CK(30) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Rotavirus](#) : CK(33) : AC(6)

[Seasonal influenza vaccine \(2008-2009\) is associated with an increased risk of influenza-like illness from pandemic H1N1 infection.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2010 Nov 1;51(9):1017-1027. PMID: [20887210](#)

Article Published Date : Nov 01, 2010

Authors : Naveed Z Janjua, Danuta M Skowronski, Travis S Hottes, William Osei, Evan Adams, Martin Petric, Suzana Sabaiduc, Tracy Chan, Annie Mak, Marcus Lem, Patrick Tang, David M Patrick, Gaston De Serres, David Bowering

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection](#) : CK(468) : AC(88)

Additional Keywords : [Immunosuppressive Flu Vaccines](#) : CK(20) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Serious adverse events associated with whole cell pertussis vaccine, e.g. sudden infant death syndrome and encephalopathy, may have occurred in metabolically vulnerable children.](#) - GMI Summary

Pubmed Data : Pharmazie. 2007 Apr;62(4):299-304. PMID: [19660877](#)

Article Published Date : Apr 01, 2007

Authors : Kumanan Wilson, Beth Potter, Douglas Manuel, Jennifer Keelan, Pranesh Chakraborty

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1994 Jul 7;331(1):16-21. PMID: [8202096](#)

Article Published Date : Jul 07, 1994

Authors : C D Christie, M L Marx, C D Marchant, S F Reising

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14), [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Smallpox vaccination has been associated with cardiac complications such as myopericarditis.](#) - GMI Summary

Pubmed Data : South Med J. 2009 May 7. Epub 2009 May 7. PMID: [19434043](#)

Article Published Date : May 07, 2009

Authors : Luis F Mora, Akbar H Khan, Laurence S Sperling

Study Type : Human Study

Additional Links

Diseases : [Myocarditis](#) : CK(54) : AC(8), [Myopericarditis](#) : CK(40) : AC(4), [Pericarditis](#) : CK(35) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Smallpox](#) : CK(71) :

[Smallpox vaccine caused iatrogenic vaccinia in children in Russia. - GMI](#)

Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr(2):40-5. PMID: [11548257](#)

Article Published Date : Mar 01, 2001

Authors : G G Onishchenko, V I Markov, V N Ustiushin, S V Borisevich, G I Kuznetsova, S Ia Loginova, A M Berezhnoi, N T Vasil'ev, V A Maksimov, A A Makhlaï

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Sudden infant death syndrome and DTP vaccine timing may be linked. - GMI](#)

Summary

Pubmed Data : Otol Neurotol. 2002 Jul;23(4):447-51. PMID: [6835859](#)

Article Published Date : Jul 01, 2002

Authors : L J Baraff, W J Ablon, R C Weiss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Sudden Infant Death syndrome mortality rate in the period zero to three days following DTP was found to be 7.3 times higher than in the period 30 days after immunization. - GMI Summary](#)

Pubmed Data : Am J Public Health. 1987 Aug;77(8):945-51. PMID: [3496805](#)

Article Published Date : Aug 01, 1987

Authors : A M Walker, H Jick, D R Perera, R S Thompson, T A Knauss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Swine and influenza vaccines induce anti-ganglioside antibodies associated with autoimmune neuropathies such as Guillain-Barre syndrome. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2008 Jul 15;198(2):226-33. PMID: [18522505](#)

Article Published Date : Jul 15, 2008

Authors : Irving Nachamkin, Sean V Shadomy, Anthony P Moran, Nancy Cox, Collette Fitzgerald, Huong Ung, Adrian T Corcoran, John K Iskander, Lawrence B Schonberger, Robert T Chen

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Influenza Vaccine : CK\(10\) : AC\(1\)](#), [Swine Flu Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Symptomatic Gulf War Syndrome is strongly associated with the presence of autoantibodies to squalene, an adjuvant used in vaccines. - GMI Summary](#)

Pubmed Data : Exp Mol Pathol. 2000 Feb;68(1):55-64. PMID: [10640454](#)

Article Published Date : Feb 01, 2000

Authors : P B Asa, Y Cao, R F Garry

Study Type : Human Study

Additional Links

Diseases : [Gulf War Syndrome](#) : CK(33) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Anthrax](#) : CK(62) : AC(8)

[Systemic lupus erythematosus related to hepatitis B vaccine has been reported.](#) **- GMI Summary**

Pubmed Data : Lupus. 2009 Nov;18(13):1192-7. PMID: [19880567](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, Y Zafrir, Z Paz, T Shilton, G Zandman-Goddard, Y Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus](#) : CK(381) : AC(52)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[The anthrax vaccine is one of the most reactogenic vaccines reported in the Vaccine Adverse Events Reporting System \(VAERS\) database.](#) **- GMI Summary**

Pubmed Data : Hepatogastroenterology. 2004 May-Jun;51(57):762-7. PMID: [15143911](#)

Article Published Date : May 01, 2004

Authors : Mark R Geier, David A Geier

Study Type : Human Study

Additional Links

Diseases : [Anthrax](#) : CK(43) : AC(6), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Anthrax](#) : CK(62) : AC(8)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects.](#) **- GMI Summary**

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance](#) : CK(148) : AC(37), [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Diphtheria](#) : CK(50) : AC(2)

Problem Substances : [Adjuvant](#) : CK(18) : AC(6), [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) **- GMI Summary**

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Combinations](#) : CK(20) : AC(2), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Polio](#) : CK(94) : AC(15)

[The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein \(the protective coating of the nerves\) contributing](#)

[to the pathogenesis of autism.](#) - GMI Summary

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[The occurrence of secondary vaccine failure and vaccine-modified measles in the United States may lead to underreporting of measles cases and result in overestimation of vaccine efficacy in h](#) - GMI Summary

Pubmed Data : JAMA. 1990 May 9 ;263(18):2467-71. PMID: [2278542](#)

Article Published Date : May 08, 1990

Authors : M B Edmonson, D G Addiss, J T McPherson, J L Berg, S R Circo, J P Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[The oral polio vaccine is unlikely to be able to eradicate polio from India.](#) - GMI Summary

Pubmed Data : Vaccine. 2008 Apr 16 ;26(17):2058-61. Epub 2008 Mar 14. PMID: [18378367](#)

Article Published Date : Apr 16, 2008

Authors : Yash Paul

Study Type : Human Study

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The risk of miscarriage increases following HPV vaccination.](#) - GMI Summary

Pubmed Data : BMJ. 2010;340:c712. Epub 2010 Mar 2. PMID: [20197322](#)

Article Published Date : Jan 01, 2010

Authors : Sholom Wacholder, Bingshu Eric Chen, Allen Wilcox, George Macones, Paula Gonzalez, Brian Befano, Allan Hildesheim, Ana Cecilia Rodríguez, Diane Solomon, Rolando Herrero, Mark Schiffman,

Study Type : Human Study

Additional Links

Diseases : [Cervical Cancer : CK\(222\) : AC\(72\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[The vaccine adjuvant squalene in anthrax vaccines given to soldiers in the Gulf War resulted in the formation of antibodies to squalene which are associated with Gulf War Syndrome.](#) - GMI Summary

Pubmed Data : Neuropharmacology. 2011 Feb-Mar;60(2-3):252-8. Epub 2010 Sep 22. PMID: [12127050](#)

Article Published Date : Feb 01, 2011

Authors : Pamela B Asa, Russell B Wilson, Robert F Garry

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Gulf War Syndrome : CK\(33\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Problem Substances : [Squalene, Adjuvant : CK\(2\) : AC\(1\)](#)

The way that the effectiveness of HPV vaccines are framed influences whether or not respondents believe they are effective and their acceptance level of vaccine mandate policies. - GMI Summary

Pubmed Data : Patient Educ Couns. 2010 Sep 17. Epub 2010 Sep 17. PMID: [20851560](#)

Article Published Date : Sep 17, 2010

Authors : Cabral A Bigman, Joseph N Cappella, Robert C Hornik

Study Type : Human Study

Additional Links

Diseases : [HPV : CK\(31\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

There is a positive association between autism prevalence and childhood vaccination uptake across the U.S. population. - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2011 Jan ;74(14):903-16. PMID: [21623535](#)

Article Published Date : Jan 01, 2011

Authors : Gayle DeLong

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

There is evidence supporting an association between increasing organic-Hg exposure from Thimerosal-containing childhood vaccines and the subsequent risk of an ASD. - GMI Summary

Pubmed Data : Transl Neurodegener. 2013 ;2(1):25. Epub 2013 Dec 19. PMID: [24354891](#)

Article Published Date : Dec 31, 2012

Authors : David A Geier, Brian S Hooker, Janet K Kern, Paul G King, Lisa K Sykes, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Mercury : CK\(131\) : AC\(17\)](#), [Thimerosal : CK\(367\) : AC\(23\)](#)

There were 69 reports of Guillain-Barré Syndrome (GBS) after Gardasil vaccination that occurred in the United States between 2006 and 2009. - GMI Summary

Pubmed Data : Vaccine. 2010 Sep 23. Epub 2010 Sep 23. PMID: [20869467](#)

Article Published Date : Sep 23, 2010

Authors : Nizar Souayah, P A Michas-Martin, Abu Nasar, Nataliya Krivitskaya, Hussam A Yacoub, Hafiz Khan, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Thirty-five percent of children with juvenile idiopathic arthritis experienced flare of the disease after vaccination. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2012 Mar 15. Epub 2012 Mar 15. PMID: [22513085](#)

Article Published Date : Mar 15, 2012

Authors : Natasa Toplak, Vesna Subelj, Tanja Kveder, Sasa Cucnik, Katarina Prosenc, Alenka Trampus-

Bakija, Ljupco Todorovski, Tadej Avcin

Study Type : Human Study

Additional Links

Diseases : [Arthritis: Juvenile Idiopathic](#) : CK(20) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#) : CK(42) : AC(4)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles.](#) - GMI Summary

Pubmed Data : Am J Clin Nutr. 2004 Jul ;80(1):193-8. PMID: [15213048](#)

Article Published Date : Jun 30, 2004

Authors : Laura E Caulfield, Mercedes de Onis, Monika Blössner, Robert E Black

Study Type : Human Study

Additional Links

Diseases : [Diarrhea](#) : CK(544) : AC(73), [Malaria](#) : CK(89) : AC(30), [Measles](#) : CK(278) : AC(8), [Pneumonia](#) : CK(330) : AC(40)

Additional Keywords : [Pneumonia](#) : CK(330) : AC(40)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Unvaccinated children tended to be white, to have a mother who was married and had a college degree, to live in a household with an annual income exceeding 75,000 dollars, and to have parents who expressed concerns regarding the safety of vaccines.](#) - GMI Summary

Pubmed Data : Pediatrics. 2004 Jul;114(1):187-95. PMID: [15231927](#)

Article Published Date : Jul 01, 2004

Authors : Philip J Smith, Susan Y Chu, Lawrence E Barker

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Vaccination for DPT, Hepatitis B and influenza has been reported to be associated with the development of erythema multiforme in an infant.](#) - GMI Summary

Pubmed Data : Indian J Dermatol Venereol Leprol. 2008 May-Jun;74(3):251-3. PMID: [18583795](#)

Article Published Date : May 01, 2008

Authors : Sarvjit Kaur, Sanjeev Handa

Study Type : Human Study

Additional Links

Diseases : [Erythema](#) : CK(44) : AC(6), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Vaccinated children and adults may serve as reservoirs for silent pertussis](#)

[infection and become potential transmitters to unprotected infants.](#) - GMI Summary

Pubmed Data : Emerg Infect Dis. 2000 Sep-Oct;6(5):526-9. PMID: [10998384](#)

Article Published Date : Sep 01, 2000

Authors : I Srugo, D Benilevi, R Madeb, S Shapiro, T Shohat, E Somekh, Y Rimmar, V Gershtein, R Gershtein, E Marva, N Lahat

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Vaccination can precipitate lupus erythematosus.](#) - GMI Summary

Pubmed Data : Semin Arthritis Rheum. 1999 Dec;29(3):131-9. PMID: [10622677](#)

Article Published Date : Dec 01, 1999

Authors : S A Older, D F Battafarano, R J Enzenauer, A M Krieg

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Vaccination is associated with thrombocytopenic purpura in children.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Feb 26;25(10):1838-40. Epub 2006 Nov 9. PMID: [17126957](#)

Article Published Date : Feb 26, 2007

Authors : J Rajantie, B Zeller, I Treutiger, S Rosthøj,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination timing and co-administration may be associated with increased mortality, especially in females.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 May 29;24(22):4701-8. Epub 2006 Mar 31. PMID: [16621182](#)

Article Published Date : May 29, 2006

Authors : Peter Aaby, Henrik Jensen, Gijs Walraven

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) :](#)

[Vaccination with measles after DTP and polio vaccine is associated with 2-fold increase in female mortality.](#) - GMI Summary

Pubmed Data : [Pediatr Infect Dis J. 2007 Mar;26\(3\):247-52. PMID: 17484223](#)

Article Published Date : Mar 01, 2007

Authors : Peter Aaby, May-Lill Garly, Jens Nielsen, Henrik Ravn, Cesario Martins, Carlitos Balé, Amabelia Rodrigues, Christine Stabell Benn, Ida Maria Lisse

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccination-associated adverse events occur in approximately 1 of every 6 toddlers receiving measles-mumps-rubella vaccine dose 1, with high fever occurring in 1 of 20](#) - GMI Summary

Pubmed Data : [Pediatrics. 2006 Oct;118\(4\):1422-30. PMID: 17015532](#)

Article Published Date : Oct 01, 2006

Authors : Charles W LeBaron, Daoling Bi, Bradley J Sullivan, Carol Beck, Paul Gargiullo

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Varicella vaccine has been reported to cause herpes zoster skin lesions and meningitis in a previously healthy boy.](#) - GMI Summary

Pubmed Data : [J Infect Dis. 2008 Nov 15;198\(10\):1444-7. PMID: 18826373](#)

Article Published Date : Nov 15, 2008

Authors : Myron J Levin, Roberta L DeBiasi, Vanda Bostik, D Scott Schmid

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Varicella outbreaks occur in vaccinated populations, even when receiving 2 doses.](#) - GMI Summary

Pubmed Data : [Pediatr Infect Dis J. 2009 Aug;28\(8\):678-81. PMID: 19593254](#)

Article Published Date : Aug 01, 2009

Authors : Philip L Gould, Jessica Leung, Connie Scott, D Scott Schmid, Helen Deng, Adriana Lopez, Sandra S Chaves, Meredith Reynolds, Linda Gladden, Rafael Harpaz, Sandra Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been associated with viremia and streptococcal toxic shock syndrome.](#) - GMI Summary

Pubmed Data : [Med J Aust. 2009 Apr 20;190\(8\):451-3. PMID: 19374621](#)

Article Published Date : Apr 20, 2009

Authors : Claire M Italiano, Cheryl S Toi, Simon P Chan, Dominic E Dwyer

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Viremia : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to cause chronic, acyclovir-resistant herpes zoster infection in an immunosuppressed child.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2003 Oct 1;188(7):954-9. Epub 2003 Sep 26. PMID: [14513413](#)

Article Published Date : Oct 01, 2003

Authors : Myron J Levin, Karen M Dahl, Adriana Weinberg, Roger Giller, Amita Patel, Philip R Krause

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Acyclovir-Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to viral meningitis in an immunocompetent child.](#) - GMI Summary

Pubmed Data : Ann Emerg Med. 2009 Jun;53(6):792-5. Epub 2008 Nov 22. PMID: [19028409](#)

Article Published Date : Jun 01, 2009

Authors : Sujit Iyer, Manoj K Mittal, Richard L Hodinka

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Undefined : CK\(14\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine may be associated with aplastic anemia in children.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Aug;28(8):746-8. PMID: [19633522](#)

Article Published Date : Aug 01, 2009

Authors : Paola Angelini, Fotini Kavadas, Navneet Sharma, Susan E Richardson, Graham Tipples, Chaim Roifman, Yigal Dror, Yehuda Nofech-Mozes

Study Type : Human Study

Additional Links

Diseases : [Anemia: Aplastic : CK\(30\) : AC\(3\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others - Article 2.](#) - GMI Summary

Pubmed Data : J Infect Dis. 1997 Oct;176(4):1072-5. PMID: [9333170](#)

Article Published Date : Oct 01, 1997

Authors : P LaRussa, S Steinberg, F Meurice, A Gershon

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others.](#) - GMI Summary

Pubmed Data : Homeopathy. 2009 Apr;98(2):77-82. PMID: [9255208](#)

Article Published Date : Apr 01, 2009

Authors : M B Salzman, R G Sharrar, S Steinberg, P LaRussa

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella-zoster vaccine has been linked to herpes zoster ophthalmicus and encephalitis as possible, though rare side effects.](#) - GMI Summary

Pubmed Data : Pediatrics. 2010 Apr;125(4):e969-72. Epub 2010 Mar 1. PMID: [20194287](#)

Article Published Date : Apr 01, 2010

Authors : Giorgos Chouliaras, Vana Spoulou, Mark Quinlivan, Judith Breuer, Maria Theodoridou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis : CK\(23\) : AC\(4\)](#), [Herpes: Ocular : CK\(12\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Whole cell pertussis vaccines may have been causing serious neurological disorders.](#) - GMI Summary

Pubmed Data : Brain Dev. 2004 Aug;26(5):296-300. PMID: [15165669](#)

Article Published Date : Aug 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Infant Neurological Development : CK\(46\) : AC\(7\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Widening influenza vaccine coverage is not correlated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Zinc supplementation has a beneficial effect on malaise, one of the influenza vaccine associated adverse events, and decrease serum TNF- \$\alpha\$ levels.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2011 Apr 21. Epub 2011 Apr 21. PMID: [21514808](#)

Article Published Date : Apr 21, 2011

Authors : S Songül Yalçın, Defne Engür-Karasımaç, Dursun Alehan, Kadriye Yurdakök, Süheyla Ozkutlu, Turgay Coşkun

Study Type : Human Study

Additional Links

Substances : [Zinc : CK\(880\) : AC\(128\)](#)

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)
Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A case of extensive ulcerating vasculitis following a BCG vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Plast Reconstr Aesthet Surg. 2009 Aug;62(8):e286-9. Epub 2007 Dec 31. PMID: [18166508](#)

Article Published Date : Aug 01, 2009

Authors : A Ghattaura, K A Eley, E Molenaar, G Smith

Study Type : Human: Case Report

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#)

[A case of influenza vaccine induced have necrotizing glomerulonephritis in decursu vasculitis has been reported.](#) - GMI Summary

Pubmed Data : Pol Merkur Lekarski. 2005 Jul;19(109):75-7. PMID: [16194032](#)

Article Published Date : Jul 01, 2005

Authors : Lidia Hyla-Klekot, Grazyna Kucharska, Witold Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A case of lethal inflammatory polyradiculoneuropathy with spinal cord involvement after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2001 May 1;186(1-2):81-5. PMID: [11412876](#)

Article Published Date : May 01, 2001

Authors : E Sindern, J M Schröder, M Krismann, J P Malin

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Inflammatory Demyelinating Polyradiculoneuropathy : CK\(87\) : AC\(1\)](#),

[Polyradiculoneuropathy: Acute Inflammatory : CK\(87\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[A case of lethal status epilepticus and lymphocytic pneumonitis has been reported.](#) - GMI Summary

Pubmed Data : Eur J Intern Med. 2008 Jul;19(5):383-5. Epub 2007 Dec 4. PMID: [18549949](#)

Article Published Date : Jul 01, 2008

Authors : Jozélio Freire de Carvalho, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Epilepsy : CK\(128\) : AC\(29\)](#), [Pneumonitis : CK\(18\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[A case of sudden infant death associated with hexavalent immunization has been reported.](#) - GMI Summary

Pubmed Data : Forensic Sci Int. 2008 Aug 6;179(2-3):e25-9. Epub 2008 Jun 6. PMID: [18538957](#)

Article Published Date : Aug 06, 2008

Authors : Stefano D'Errico, Margherita Neri, Irene Riezzo, Giuseppina Rossi, Cristoforo Pomara, Emanuela Turillazzi, Vittorio Fineschi

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

[Acute posterior multifocal placoid pigment epitheliopathy after hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Arch Ophthalmol. 1995 Mar;113(3):297-300. PMID: [7887843](#)

Article Published Date : Mar 01, 1995

Authors : A P Brézin, P Massin-Korobelnik, M Boudin, A Gaudric, P LeHoang

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Posterior Multifocal Placoid Pigment Epitheliopathy \(APMPPE\) : CK\(3\) : AC\(1\)](#), [Chorioretinitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Acute transverse myelitis after influenza vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Neuroimaging. 1996 Oct;6(4):248-50. PMID: [8903080](#)

Article Published Date : Oct 01, 1996

Authors : R Bakshi, J C Mazziotta

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Allergy to viral and rickettsial vaccines; review of the literature.](#) - GMI Summary

Pubmed Data : Ann Allergy. 1950 Sep-Oct;8(5):699-707. PMID: [14800166](#)

Authors : S UNTRACHT, B RATNER

Study Type : Human: Case Report

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2011 Jan;45(1):e8. Epub 2010 Dec 28. PMID: [21189364](#)

Article Published Date : Jan 01, 2011

Authors : Sabrina Montagnani, Marco Tuccori, Giuseppe Lombardo, Arianna Testi, Stefania Mantarro, Elisa Ruggiero, Corrado Blandizzi

Study Type : Human: Case Report

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Bell's palsy is a possible complication of hepatitis B vaccination in children.](#) - GMI Summary

Pubmed Data : J Health Popul Nutr. 2009 Oct;27(5):707-8. PMID: [19902808](#)

Article Published Date : Oct 01, 2009

Authors : Handan Alp, Hüseyin Tan, Zerrin Orbak

Study Type : Human: Case Report

Additional Links

Diseases : [Bell's Palsy](#) : CK(13) : AC(3)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Cutaneous lupus erythematosus and buccal aphthosis after hepatitis B vaccination has been reported in a 6-year-old child](#) - GMI Summary

Pubmed Data : Ann Dermatol Venereol. 1996;123(10):657-9. PMID: [9615128](#)

Article Published Date : Jan 01, 1996

Authors : P Grézard, M Chefaï, V Philippot, H Perrot, M Faisant

Study Type : Human: Case Report

Additional Links

Diseases : [Aphthosis: Buccal](#) : CK(3) : AC(1), [Lupus Erythematosus: Cutaneous](#) : CK(17) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Deep morphea after vaccination in two young children has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Dermatol. 2006 Sep-Oct;23(5):484-7. PMID: [17014648](#)

Article Published Date : Sep 01, 2006

Authors : Antonio Torrelo, José Suárez, Isabel Colmenero, Daniel Azorín, Antonio Perera, Antonio Zambrano

Study Type : Human: Case Report

Additional Links

Diseases : [Morphea profunda](#) : CK(3) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Delayed focal lipoatrophy after AS03-adjuvanted influenza A \(H1N1\) 2009 vaccine has been reported.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Dec 17. Epub 2010 Dec 17. PMID: [21172376](#)

Article Published Date : Dec 17, 2010

Authors : Emilie Javelle, Benjamin Soulier, Christian Brosset, Solène Lorcy, Fabrice Simon

Study Type : Human: Case Report

Additional Links

Diseases : [Lipoatrophy](#) : CK(3) : AC(1), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Diabetes Mellitus: Type 1](#) : CK(1197) : AC(235), [Thrombocytopenia](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussières

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Guillain-Barré syndrome following hepatitis B vaccination has been reported.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2004 Nov-Dec;22(6):767-70. PMID: [15638054](#)

Article Published Date : Nov 01, 2004

Authors : M Khamaisi, Y Shoenfeld, H Orbach

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[H1N1 vaccination has been linked to possible new-onset seizure.](#) - GMI Summary

Pubmed Data : Pharmacotherapy. 2011 Jan;31(1):113. PMID: [21182364](#)

Article Published Date : Jan 01, 2011

Authors : [No authors listed]

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Seizures : CK\(135\) : AC\(33\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine associated with dermatomyositis has been reported.](#) - GMI Summary

Pubmed Data : Rheumatol Int. 2008 Apr;28(6):609-12. Epub 2007 Nov 23. PMID: [18034245](#)

Article Published Date : Apr 01, 2008

Authors : Arie Altman, Martine Szyper-Kravitz, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine may induce myelitis in susceptible individuals.](#) - GMI Summary

Pubmed Data : Eur J Neurol. 2001 Nov;8(6):711-5. PMID: [11784358](#)

Article Published Date : Nov 01, 2001

Authors : F Karaali-Savrun, A Altıntaş, S Saip, A Siva

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : CK(39) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Immune-mediated myelitis following hepatitis B vaccination has been reported.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2012 Apr 1. Epub 2012 Apr 1. PMID: [22498789](#)

Article Published Date : Apr 01, 2012

Authors : Joerg-Patrick Stübgen

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis](#) : CK(39) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[In 1985 twin boys simultaneously succumbed to sudden unexpected deaths two to three hours after vaccination with diphtheria, tetanus, and pertussis vaccine \(DTP\).](#) - GMI Summary

Pubmed Data : Arch Dis Child. 1987 Jul;62(7):754-9. PMID: [3498443](#)

Article Published Date : Jul 01, 1987

Authors : S C Roberts

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Influenza vaccination has been reported to cause miller fisher syndrome.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1327-9. PMID: [21987549](#)

Article Published Date : Oct 01, 2011

Authors : Ashkan Shoamanesh, Kristine Chapman, Anthony Traboulsee

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant](#) : CK(13) : AC(2), [Miller Fisher Syndrome](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Influenza vaccine has been reported to be a possible trigger of rhabdomyolysis induced acute renal failure in those taking statin drugs.](#) - GMI Summary

Pubmed Data : Nephrol Dial Transplant. 2000 May ;15(5):740-1. PMID: [10809833](#)

Article Published Date : May 01, 2000

Authors : E Plotkin, J Bernheim, S Ben-Chetrit, A Mor, Z Korzets

Study Type : Human: Case Report

Additional Links

Diseases : [Rhabdomyolysis](#) : CK(165) : AC(38), [Statin-Induced Pathologies](#) : CK(1600) : AC(320)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Problem Substances : [Statin Drugs](#) : CK(3971) : AC(475)

Adverse Pharmacological Actions : [Myotoxicity](#) : CK(327) : AC(80)

[Optic neuritis following hepatitis B vaccination has been reported.](#) n - GMI Summary

Pubmed Data : J Chin Med Assoc. 2009 Nov;72(11):594-7. PMID: [19948437](#)

Article Published Date : Nov 01, 2009

Authors : Muferet Erguven, Sirin Guven, Umit Akyuz, Olcay Bilgiç, Fuat Laloglu

Study Type : Human: Case Report

Additional Links

Diseases : [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Possible systemic lupus erythematosus following HPV immunization has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):158-61. PMID: [22235047](#)

Article Published Date : Jan 01, 2012

Authors : Hf Soldevilla, Sfr Briones, Sv Navarra

Study Type : Human: Case Report

Additional Links

Diseases : [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[ransverse myelitis has been reported in association with a nasal attenuated novel influenza A\(H1N1\) vaccine.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2010 Aug;67(8):1018-20. PMID: [20697056](#)

Article Published Date : Aug 01, 2010

Authors : Wafa Akkad, Bassel Salem, Jerome W Freeman, Mark K Huntington

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Nasal : CK\(3\) : AC\(1\)](#)

[Simultaneous sudden infant death syndrome has been reported in twins two days after receiving mutiple vaccinations.](#) - GMI Summary

Pubmed Data : J Forensic Leg Med. 2007 Feb;14(2):87-91. PMID: [17654772](#)

Article Published Date : Feb 01, 2007

Authors : Yasemin Balci, Mehmet Tok, B Kenan Kocaturk, Cinar Yenilmez, Coşkun Yirulmaz

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Sudden infant death syndrome \(SIDS\) shortly after hexavalent vaccination has been reported.](#) - GMI Summary

Pubmed Data : Virchows Arch. 2006 Jan;448(1):100-4. Epub 2005 Oct 18. PMID: [16231176](#)

Article Published Date : Jan 01, 2006

Authors : Giulia Ottaviani, Anna Maria Lavezzi, Luigi Maturri

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

[Systemic lupus erythematosus has been triggered by hepatitis B vaccine.](#) - GMI

Summary

Pubmed Data : Clin Nephrol. 2010 Aug;74(2):150-3. PMID: [20630136](#)

Article Published Date : Aug 01, 2010

Authors : D Santoro, G Vita, R Vita, A Mallamace, V Savica, G Bellinghieri, S Benvenga, S Gangemi

Study Type : Human: Case Report

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2012 Mar 14. Epub 2012 Mar 14. PMID: [22425036](#)

Article Published Date : Mar 14, 2012

Authors : Olivier Guillard, Bernard Fauconneau, Alain Pineau, Annie Marraud, Jean-Pierre Bellocq, Marie-Pierre Chenard

Study Type : Human: Case Report, Review

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Pseudolymphoma : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

[The psychic reactions following injections of bacterial vaccines.](#) - GMI Summary

Pubmed Data : Int Arch Allergy Appl Immunol. 1950 ;1(3):226-43. PMID: [14794265](#)

Authors : J ILAVSKY

Study Type : Human: Case Report

Additional Links

Diseases : [Psychiatric Disorders : CK\(71\) : AC\(10\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination as a probable cause of incontinentia pigmenti reactivation has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Dermatol. 2010 Jan-Feb;27(1):62-4. PMID: [20199413](#)

Article Published Date : Jan 01, 2010

Authors : Ali Ali Khan, Andrew D Lee, Donald Swing, Christie Carroll, Gil Yosipovitch

Study Type : Human: Case Report

Additional Links

Diseases : [Incontinentia Pigmenti : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows.](#) - GMI Summary

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Cheville

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#),

[Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce autoimmune demyelination. - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Contraceptive vaccines are being developed. - GMI Summary

Pubmed Data : Mol Reprod Dev. 2012 Feb ;79(2):97-106. Epub 2011 Dec 2. PMID: [22139866](#)

Article Published Date : Feb 01, 2012

Authors : Angela R Lemons, Rajesh K Naz

Study Type : Animal Study

Additional Links

Additional Keywords : [Contraceptive Vaccines : CK\(6\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Experimental in utero inoculation of late-term swine fetuses with porcine circovirus type 2 results in a high rate of reproductive abnormalities, including mummification and stillbirth. - GMI Summary

Pubmed Data : J Vet Diagn Invest. 2002 Nov;14(6):507-12. PMID: [12423036](#)

Article Published Date : Nov 01, 2002

Authors : Charles S Johnson, Han S Joo, Kochakorn Direksin, Kyoung-Jin Yoon, Young K Choi

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Fatal adverse pulmonary reaction in calves after inadvertent intravenous vaccination has been reported. - GMI Summary

Pubmed Data : Vet Pathol. 2005 Jul;42(4):492-5. PMID: [16006609](#)

Article Published Date : Jul 01, 2005

Authors : J D Ramsay, C L Williams, E Simko

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Hepatitis B vaccine alters the expression of 144 genes in the mouse liver within 1 day of vaccination, 7 of which are related to inflammation and metabolism.](#) - GMI Summary

Pubmed Data : Mol Biol Rep. 2011 Jun 21. Epub 2011 Jun 21. PMID: [21691704](#)

Article Published Date : Jun 21, 2011

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine induces cell death in liver cells and mouse liver.](#) - GMI Summary

Pubmed Data : Apoptosis. 2012 Jan 17. Epub 2012 Jan 17. PMID: [22249285](#)

Article Published Date : Jan 17, 2012

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Changchun Li, Mengjin Zhu, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Liver Damage : CK\(648\) : AC\(226\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Hepatotoxic : CK\(301\) : AC\(85\)](#)

[Maturation changes in amygdala volume and the binding capacity of an opioid antagonist in the amygdala was significantly altered in infant macaques receiving the vaccine schedule.](#) - GMI Summary

Pubmed Data : Acta Neurobiol Exp (Wars). 2010 ;70(2):147-64. PMID: [20628439](#)

Article Published Date : Dec 31, 2009

Authors : Laura Hewitson, Brian J Lopresti, Carol Stott, N Scott Mason, Jaime Tomko

Study Type : Animal Study

Additional Links

Diseases : [Amygdala: Damage/Abnormalities : CK\(12\) : AC\(1\)](#), [Neurodevelopmental Disorders : CK\(124\) : AC\(13\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Problem Substances : [Thimerosal : CK\(367\) : AC\(23\)](#)

[Mice exhibit lung pathology after vaccination with pertussis vaccines.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Mar 8;25(12):2346-60. Epub 2006 Dec 12. PMID: [17224216](#)

Article Published Date : Mar 08, 2007

Authors : Rob J Vandebriel, Eric R Gremmer, Jolanda P Vermeulen, Sandra M M Hellwig, Jan A M A Dormans, Paul J M Roholl, Frits R Mooi

Study Type : Animal Study

Additional Links

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Newborn primates receiving mercury-containing hepatitis B vaccines exhibit neurodevelopmental delays.](#) - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(19):1298-313. PMID: [20711932](#)

Article Published Date : Jan 01, 2010

Authors : Laura Hewitson, Lisa A Houser, Carol Stott, Gene Sackett, Jaime L Tomko, David Atwood, Lisa Blue, E Railey White

Study Type : Animal Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Porcine circovirus type 2 \(PCV2\) vaccination of pregnant pigs may result in vertical transmission of PCV2 to the offspring.](#) - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2009 Jun;16(6):830-4. Epub 2009 Apr 8. PMID: [19357312](#)

Article Published Date : Jun 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Post-infection rabies vaccination increases mortality in mice.](#) - GMI Summary

Pubmed Data : Comp Immunol Microbiol Infect Dis. 1988;11(2):139-42. PMID: [2972508](#)

Article Published Date : Jan 01, 1988

Authors : J Blancou, D Sitte

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%.](#) - GMI Summary

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#),

[Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies.](#) - GMI Summary

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever :](#)

[CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does.](#) - GMI Summary

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The intranasal inoculation of pregnant sows with porcine circovirus 2 results in abortion and reproductive failure.](#) - GMI Summary

Pubmed Data : J Nutr. 2009 Nov;139(11):2061-6. Epub 2009 Sep 23. PMID: [15737340](#)

Article Published Date : Nov 01, 2009

Authors : J-S Park, J Kim, Y Ha, K Jung, C Choi, J-K Lim, S-H Kim, C Chae

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The mercury containing vaccine adjuvant known as thimerosal has immunosuppressive and autoimmune effects in mice.](#) - GMI Summary

Pubmed Data : Toxicol Appl Pharmacol. 2005 Apr 15;204(2):109-21. PMID: [15808517](#)

Article Published Date : Apr 15, 2005

Authors : S Havarinasab, B Häggqvist, E Björn, K M Pollard, P Hultman

Study Type : Animal Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The use of animal cells in the production of vaccines may cause infection by endogenous retroviruses associated with chronic fatigue and prostate cancer.](#) - GMI Summary

Pubmed Data : Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8. PMID: [20378372](#)

Article Published Date : May 01, 2010

Authors : Takayuki Miyazawa

Study Type : Animal Study

Additional Links

Diseases : [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Prostate Cancer : CK\(1024\) : AC\(311\)](#), [Retroviruses : CK\(7\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly.](#) - GMI Summary

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The vaccine adjuvant thimerosal induces adverse changes in the cerebellum of mice, lending plausibility to the association between autism and low-dose mercury exposure. - GMI Summary](#)

Pubmed Data : Cell Biol Toxicol. 2009 Apr 9. PMID: [19357975](#)

Article Published Date : Apr 09, 2009

Authors : Takeshi Minami, Eriko Miyata, Yamato Sakamoto, Hideo Yamazaki, Seiji Ichida

Study Type : Animal Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Thimerosal : CK\(3\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25. - GMI Summary](#)

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escjadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced immunity in pregnant pigs is not effective in preventing viremia in offspring. - GMI Summary](#)

Pubmed Data : Theriogenology. 2009 Oct 1;72(6):747-54. Epub 2009 Jun 25. PMID: [19559470](#)

Article Published Date : Oct 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced scrapie has been reported in animals. - GMI Summary](#)

Pubmed Data : J Gen Virol. 2003 Apr;84(Pt 4):1047-52. PMID: [12655108](#)

Article Published Date : Apr 01, 2003

Authors : Gianluigi Zanusso, Cristina Casalone, Pierluigi Acutis, Elena Bozzetta, Alessia Farinazzo, Matteo Gelati, Michele Fiorini, Gianluigi Forloni, Man Sun Sy, Salvatore Monaco, Maria Caramelli

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Animal Diseases: Scrapie : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced, simian immunodeficiency virus-specific CD8+ T cells reduce virus replication but do not protect from simian immunodeficiency virus disease progression. - GMI Summary](#)

Pubmed Data : J Immunol. 2009 Jul 1;183(1):706-17. PMID: [19542473](#)

Article Published Date : Jul 01, 2009

Authors : Jessica C Engram, Richard M Dunham, George Makedonas, Thomas H Vanderford, Beth Sumpter, Nichole R Klatt, Sarah J Ratcliffe, Seema Garg, Mirko Paiardini, Monica McQuoid, John D Altman, Silvija I Staprans, Michael R Betts, David A Garber, Mark B Feinberg, Guido Silvestri

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Simian Immunodeficiency Virus \(SIV\) : CK\(2\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

"Adverse events associated with 17D-derived yellow fever vaccination--United States, 2001-2002." - GMI Summary

Pubmed Data : MMWR Morb Mortal Wkly Rep. 2002 Nov 8 ;51(44):989-93. PMID: [12455906](#)

Article Published Date : Nov 08, 2002

Study Type : Review

Additional Links

Diseases : [Brain Inflammation : CK\(86\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

"Hypothesis: is Alzheimer's disease a metal-induced immune disorder?" - GMI Summary

Pubmed Data : Neurodegeneration. 1995 Mar ;4(1):107-11. PMID: [7600179](#)

Article Published Date : Feb 28, 1995

Authors : R A Armstrong, S J Winsper, J A Blair

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum : CK\(166\) : AC\(43\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

"Mechanisms of aluminum adjuvant toxicity and autoimmunity in pediatric populations." - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):223-30. PMID: [22235057](#)

Article Published Date : Jan 01, 2012

Authors : L Tomljenovic, Ca Shaw

Study Type : Review

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Aluminum : CK\(166\) : AC\(43\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

"New strategies for the elimination of polio from India." - GMI Summary

Pubmed Data : Science. 2006 Nov 17 ;314(5802):1150-3. PMID: [17110580](#)

Article Published Date : Nov 17, 2006

Authors : Nicholas C Grassly, Christophe Fraser, Jay Wenger, Jagadish M Deshpande, Roland W Sutter, David L Heymann, R Bruce Aylward

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

"Viral nucleic acids in live-attenuated vaccines: detection of minority variants and an adventitious virus." - GMI Summary

Pubmed Data : J Virol. 2010 Jun ;84(12):6033-40. Epub 2010 Apr 7. PMID: [20375174](#)

Article Published Date : May 31, 2010

Authors : Joseph G Victoria, Chunlin Wang, Morris S Jones, Crystal Jaing, Kevin McLoughlin, Shea

Gardner, Eric L Delwart

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Adventitious Viruses : CK\(18\) : AC\(9\)](#), [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[Acute disseminated encephalomyelitis \(ADEM\) may be caused by vaccination.](#) - GMI Summary

Pubmed Data : J Clin Neurosci. 2008 Dec;15(12):1315-22. Epub 2008 Oct 30. PMID: [18976924](#)

Article Published Date : Dec 01, 2008

Authors : William Huynh, Dennis J Cordato, Elias Kehdi, Lynette T Masters, Chris Dedousis

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Encephalomyelitis : CK\(12\) : AC\(7\)](#),

[Neuromyelitis Optica : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Adjuvants in vaccines may trigger innate cells response by toll-like receptors, thus eliciting a possible non-IgE mediated allergy phenomenon or causing B-cell activation and autoimmunity.](#) - GMI Summary

Pubmed Data : Hum Vaccin. 2011 Aug 1 ;7(8). Epub 2011 Aug 1. PMID: [21785282](#)

Article Published Date : Aug 01, 2011

Authors : Salvatore Chirumbolo

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Immune Disorders: B-Cell Over-Activity : CK\(2\) : AC\(2\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#)

[Aluminium-containing adjuvants in vaccines may be causing autoimmune conditions such as chronic fatigue syndrome and the inflammatory myopathy known as macrophagic myofasciitis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11. PMID: [19004564](#)

Article Published Date : Feb 01, 2009

Authors : Christopher Exley, Louise Swarbrick, Rhomain K Gherardi, Francois-Jérôme Authier

Study Type : Commentary

Additional Links

Diseases : [Aluminum Toxicity : CK\(108\) : AC\(40\)](#), [Chronic Fatigue Syndrome : CK\(408\) : AC\(32\)](#), [Myopathy: Inflammatory : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Anthrax vaccine development suffers from a wide range of potentially insurmountable problems.](#) - GMI Summary

Pubmed Data : Przegl Epidemiol. 2009 ;63(4):505-12. PMID: [20120948](#)

Article Published Date : Jan 01, 2009

Authors : Dorota Zakowska, Janusz Kocik, Michał Bartoszcze

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[Autism spectrum disorders are associated with vaccination, heavy metal](#)

[toxicity and excitotoxicity.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2008 Nov-Dec;14(6):46-53. PMID: [19043938](#)

Article Published Date : Nov 01, 2008

Authors : Russell L Blaylock

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Excitotoxicity](#) : CK(57) : AC(34), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[Autoimmune autistic disorder, a major subset of autism, is associated with autoantibody formation caused by viral \(wild and vaccine-induced\) infection.](#) - GMI Summary

Pubmed Data : Ann Clin Psychiatry. 2009 Jul-Sep;21(3):148-61. PMID: [19758536](#)

Article Published Date : Jul 01, 2009

Authors : Vijendra K Singh

Study Type : Commentary

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Autoimmune Diseases](#) : CK(5523) : AC(880)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Despite high coverage rates for primary immunization in infants and children pertussis incidence rates are increasing.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2005 May;24(5 Suppl):S10-8. PMID: [15876918](#)

Article Published Date : May 01, 2005

Authors : Tina Tan, Evelinda Trindade, Danuta Skowronski

Study Type : Review

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14)

Additional Keywords : [Vaccine Resistance](#) : CK(11) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Differential diagnosis of acute flaccid paralysis and its role in poliomyelitis surveillance.](#) - GMI Summary

Pubmed Data : Epidemiol Rev. 2000 ;22(2):298-316. PMID: [11218380](#)

Article Published Date : Jan 01, 2000

Authors : A Marx, J D Glass, R W Sutter

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Polio](#) : CK(94) : AC(15)

[DNA plasmid vaccines may carry under reported risks associated with structural instability.](#) - GMI Summary

Pubmed Data : Appl Microbiol Biotechnol. 2010 Aug;87(6):2157-67. Epub 2010 May 23. PMID: [20496146](#)

Article Published Date : Aug 01, 2010

Authors : Pedro H Oliveira, Kristala Jones Prather, Duarte M F Prazeres, Gabriel A Monteiro

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Plasmid DNA Vaccines](#) : CK(3) : AC(2)

DTP vaccination may contribute to urinary tract disease and sudden infant death syndrome. - GMI Summary

Pubmed Data : Reprod Biomed Online. 2010 Jul;21(1):100-8. Epub 2010 Mar 30. PMID: [15356430](#)

Article Published Date : Jul 01, 2010

Authors : Joseph Prandota

Study Type : Commentary

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Urinary Tract Infections : CK\(338\) : AC\(47\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women. - GMI Summary

Pubmed Data : Am J Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Feline injection site-associated sarcoma is a serious problem associated with malignancy. - GMI Summary

Pubmed Data : Vet Microbiol. 2006 Oct 5;117(1):59-65. PMID: [16769184](#)

Article Published Date : Oct 05, 2006

Authors : Jolle Kirpensteijn

Study Type : Review

Additional Links

Diseases : [Sarcoma : CK\(42\) : AC\(26\)](#), [Tumors : CK\(199\) : AC\(116\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

From 1990 to the present, the number of cases (n = 31) and deaths (n = 12) from the yellow fever vaccine in travelers has exceeded the reports of YF (n = 6) acquired by natural infection. - GMI Summary

Pubmed Data : Expert Rev Vaccines. 2012 Apr ;11(4):427-48. PMID: [22551029](#)

Article Published Date : Apr 01, 2012

Authors : Thomas P Monath

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Yellow Fever : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis. - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases](#) : CK(1309) : AC(247), [Hepatitis B](#) : CK(219) : AC(37), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccinations is associated with autoimmune hazards.](#) - GMI Summary

Pubmed Data : Autoimmun Rev. 2005 Feb;4(2):96-100. PMID: [15722255](#)

Article Published Date : Feb 01, 2005

Authors : Marc Girard

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Hepatitis B](#) : CK(219) : AC(37), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Molecular Mimicry](#) : CK(47) : AC(10)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Dermatomyositis](#) : CK(44) : AC(10), [Myasthenia Gravis](#) : CK(82) : AC(14), [Neuromuscular Diseases](#) : CK(16) : AC(4), [Neuropathies](#) : CK(436) : AC(72), [Polyarteritis Nodosa](#) : CK(1) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[HIV-1/AIDS may have been caused by contaminated polio vaccines grown in SIV infected chimpanzee kidney cells during the late 1950's.](#) - GMI Summary

Pubmed Data : Mol Nutr Food Res. 2010 Jan 28. Epub 2010 Jan 28. PMID: [11405924](#)

Article Published Date : Jan 28, 2010

Authors : E Hooper

Study Type : Commentary

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

[In 2011, there were an extra 47,500 new cases of non-polio acute flaccid paralysis \(NPAFP\); Clinically indistinguishable from polio paralysis but twice as deadly, the incidence of NPAFP was directly proportional to doses of oral polio received.](#) - GMI Summary

Pubmed Data : Indian J Med Ethics. 2012 Apr-Jun;9(2):114-7. PMID: [22591873](#)

Article Published Date : Apr 01, 2012

Authors : Neetu Vashisht, Jacob Puliyel

Study Type : Review

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\)](#) : CK(12) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Polio](#) : CK(94) : AC(15)

[Infection and vaccines are triggers for autoimmune disease.](#) - GMI Summary

Pubmed Data : Autoimmunity. 2005 May;38(3):235-45. PMID: [16126512](#)

Article Published Date : May 01, 2005

Authors : Vered Molina, Yehuda Shoenfeld

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Influenza vaccines may induce hepatitis-B virus-related vasculitis and severe neuropathy.](#) - GMI Summary

Pubmed Data : J Cardiovasc Pharmacol. 2003 Sep;42(3):329-38. PMID: [18579284](#)

Article Published Date : Sep 01, 2003

Authors : Yuko Wada, Chie Yanagihara, Yo Nishimura, Nobuyuki Oka

Study Type : Commentary

Additional Links

Diseases : [Peripheral Neuropathies : CK\(191\) : AC\(31\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Measles vaccination in developing countries has resulted in higher infant mortality rates.](#) - GMI Summary

Pubmed Data : BMJ. 1993 Nov 20;307(6915):1294-5. PMID: [8257878](#)

Article Published Date : Nov 20, 1993

Authors : A J Hall, F T Cutts

Study Type : Review

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-spectrum disorder.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Mosquitos are being engineered so that they can be used as flying syringes, capable of injecting malarial proteins into human subjects as an immunization strategy.](#) - GMI Summary

Pubmed Data : Acta Med Okayama. 2010 Aug;64(4):233-41. PMID: [20802540](#)

Article Published Date : Aug 01, 2010

Authors : Hiroyuki Matsuoka, Tsunetaka Ikezawa, Makoto Hirai

Study Type : Commentary

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Mycoplasma testing of cell substrates and biologics is often not performed due to the long turn around. - GMI Summary](#)

Pubmed Data : Mol Cell Probes. 2011 Apr-Jun;25(2-3):69-77. Epub 2011 Jan 11. PMID: [21232597](#)

Article Published Date : Apr 01, 2011

Authors : Dmitriy V Volokhov, Laurie J Graham, Kurt A Brorson, Vladimir E Chizhikov

Study Type : Review

Additional Links

Diseases : [Mycoplasma Infections : CK\(2\) : AC\(2\)](#)

Additional Keywords : [Mycoplasma Infections : CK\(2\) : AC\(2\)](#), [Vaccine Safety : CK\(21\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Over 40,000 cases of AFP are reported annually since 2007 regardless of the number of actual polio cases. - GMI Summary](#)

Pubmed Data : BMC Public Health. 2012 ;12:229. Epub 2012 Mar 22. PMID: [22439606](#)

Article Published Date : Jan 01, 2012

Authors : Rie R Yotsu, Katharine Abba, Helen Smith, Abhijit Das

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#), [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Provocation by vaccine injections can increase the risk of paralytic poliomyelitis by up to 25 fold. - GMI Summary](#)

Pubmed Data : Dev Biol Stand. 1986;65:123-6. PMID: [3549394](#)

Article Published Date : Jan 01, 1986

Authors : H V Wyatt

Study Type : Review

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Review: based on currently available research pneumococcal vaccination should not be recommended for large scale use in ear infection prone populations. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2002(2):CD001480. PMID: [12076412](#)

Article Published Date : Jan 01, 2002

Authors : M Straetemans, E A Sanders, R H Veenhoven, A G Schilder, R A Damoiseaux, G A Zielhuis

Study Type : Review

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Review: Biological safety concepts of genetically modified live bacterial vaccines. - GMI Summary](#)

Pubmed Data : Vaccine. 2007 Jul 26 ;25(30):5598-605. Epub 2006 Dec 5. PMID: [17239999](#)

Article Published Date : Jul 26, 2007

Authors : Joachim Frey

Study Type : Review

Additional Links

Additional Keywords : [GMO Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Genetically Modified Organisms : CK\(83\) : AC\(58\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: GMO Vaccines : CK\(1\) : AC\(1\)](#)

Review: Plant-made Pharmaceuticals & Vaccines - GMI Summary

Pubmed Data : Int J Mol Sci. 2011;12(5):3220-36. Epub 2011 May 17. PMID: [21686181](#)

Article Published Date : Jan 01, 2011

Authors : David R Thomas, Claire A Penney, Amrita Majumder, Amanda M Walmsley

Study Type : Review

Additional Links

Additional Keywords : [Edible Vaccines : CK\(14\) : AC\(12\)](#), [Plant Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Review: possible adverse effects that are associated with smallpox vaccination. - GMI Summary

Pubmed Data : MMWR Recomm Rep. 2003 Feb 21;52(RR-4):1-28. PMID: [12617510](#)

Article Published Date : Feb 21, 2003

Authors : Joanne Cono, Christine G Casey, David M Bell,

Study Type : Review

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Swine flu vaccine adjuvants may cause harm in patients with autoimmune diseases such as multiple sclerosis. - GMI Summary

Pubmed Data : Med Hypotheses. 2010 Feb 18. Epub 2010 Feb 18. PMID: [20171793](#)

Article Published Date : Feb 18, 2010

Authors : Serefnur Oztürk

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

The clinical development of a vaccines does not focus on effectiveness (whether a vaccine actually helps people) but efficacy (the successful elevation of antibody titers). - GMI Summary

Pubmed Data : Dev Biol Stand. 1998;95:195-201. PMID: [9855432](#)

Article Published Date : Jan 01, 1998

Authors : D S Fedson

Study Type : Commentary

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

The demyelinating effect of hepatitis B vaccination could be due to the contamination of the vaccine by partial hepatitis B virus polymerase. - GMI Summary

Pubmed Data : Med Hypotheses. 2005;65(3):509-20. PMID: [15908138](#)

Article Published Date : Jan 01, 2005

Authors : E Faure

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

The development of human vaccines for anthrax has suffered from a number of technical challenges. - GMI Summary

Pubmed Data : Hum Vaccin. 2009 Dec ;5(12):806-16. Epub 2009 Dec 9. PMID: [19786839](#)

Article Published Date : Dec 01, 2009

Authors : Leslie W Baillie

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

The epidemic of autism may be linked to both vaccinations and mitochondrial diseases. - GMI Summary

Pubmed Data : Clin Exp Pharmacol Physiol. 2004 Dec;31 Suppl 2:S51-3 PMID: [19043939](#)

Article Published Date : Dec 01, 2004

Authors : Stephanie F Cave

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Mitochondrial Diseases : CK\(157\) : AC\(57\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin. - GMI Summary

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

The HPV16 vaccine carries with it significant cross-reactivity risk due to the homologies that exist between the HPV and human proteome. - GMI Summary

Pubmed Data : J Exp Ther Oncol. 2009;8(1):65-76. PMID: [19827272](#)

Article Published Date : Jan 01, 2009

Authors : Darja Kanduc

Study Type : In Vitro Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

The number of elective abortions following vaccination during pregnancy may be under-reported and could be substantial. - GMI Summary

Pubmed Data : Vaccine. 2008 May 2;26(19):2428-32. Epub 2008 Mar 17. PMID: [18406499](#)

Article Published Date : May 02, 2008

Authors : Soju Chang, Robert Ball, M Miles Braun

Study Type : Review

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[The use of post-mortem tissues in the production of biologicals, vaccines and feedstuffs may be contributing to transmissible encephalopathies.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1996;88:237-41. PMID: [9119144](#)

Article Published Date : Jan 01, 1996

Authors : M M Robinson

Study Type : Review

Additional Links

Diseases : [Encephalopathies : CK\(11\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Transmissible spongiform encephalopathies may be passed iatrogenically through vaccines.](#) - GMI Summary

Pubmed Data : Dev Biol (Basel). 2001;106:455-9; discussion 460-1, 465-75. PMID: [11761262](#)

Article Published Date : Jan 01, 2001

Authors : N R Cashman

Study Type : Commentary

Additional Links

Diseases : [Spongiform Encephalopathies: Transmissible : CK\(2\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Underestimation of central nervous system complications after pertussis immunization appears to be prevalent.](#) - GMI Summary

Pubmed Data : Acta Paediatr Jpn. 1991 Aug;33(4):421-7. PMID: [1792899](#)

Article Published Date : Aug 01, 1991

Authors : W Ehrengut

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Vaccination against novel H1N1 may accelerate atherogenesis \(heart disease\).](#) - GMI Summary

Pubmed Data : Med Microbiol Immunol. 2009 Oct 23. PMID: [19851782](#)

Article Published Date : Oct 23, 2009

Authors : Sucharit Bhakdi, Karl Lackner, Hans-Wilhelm Doerr

Study Type : Commentary

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

[Vaccination for contraception.](#) - GMI Summary

Pubmed Data : Aust N Z J Obstet Gynaecol. 1994 Jun;34(3):320-9. PMID: [7848209](#)

Article Published Date : Jun 01, 1994

Authors : W R Jones

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anti-Fertility : CK\(1\) : AC\(1\)](#)

Vaccination may be contributing to autoimmune disease. - GMI Summary

Pubmed Data : J Autoimmun. 2000 Feb;14(1):1-10. PMID: [10648110](#)

Article Published Date : Feb 01, 2000

Authors : Y Shoenfeld, A Aron-Maor

Study Type : Commentary

Additional Links

Diseases : [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Vaccination proponents have suggested that breastfeeding should be delayed in order to prevent immune factors within breast milk from inactivating vaccine-associated antibody titer elevations and vaccine potency. - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2010 Oct;29(10):919-923. PMID: [20442687](#)

Article Published Date : Oct 01, 2010

Authors : Sung-Sil Moon, Yuhuan Wang, Andi L Shane, Trang Nguyen, Pratima Ray, Penelope Dennehy, Luck Ju Baek, Umesh Parashar, Roger I Glass, Baoming Jiang

Study Type : Commentary

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Therapeutic Actions : [Breastfeeding](#) : CK(739) : AC(77)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Vaccines and flu shots containing mercury may contribute to severe neurological diseases and/or death in children. - GMI Summary

Pubmed Data : J Pediatr. 2009 Apr;154(4):514-520.e4. Epub 2008 Dec 3. PMID: [19205900](#)

Article Published Date : Apr 01, 2009

Authors : Donald A Drum

Study Type : Commentary

Additional Links

Diseases : [Attention Deficit Disorder](#) : CK(134) : AC(12), [Attention Deficit Disorder with Hyperactivity](#) : CK(242) : AC(31), [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Child Mortality](#) : CK(64) : AC(8), [Infant Mortality](#) : CK(249) : AC(25), [Mental Retardation](#) : CK(71) : AC(7), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Additional Keywords : [Thimerosal](#) : CK(3) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361)

Vaccines produced in chick embryo cells had significant reverse transcriptase

activity. - GMI Summary

Pubmed Data : J Clin Virol. 1998 Jul 24 ;11(1):19-28. PMID: [9784140](#)

Article Published Date : Jul 23, 1998

Authors : T Maudru, K W Peden

Study Type : In Vitro Study

Additional Links

Diseases : [Retroviruses : CK\(7\) : AC\(1\)](#)

Additional Keywords : [Endogenous Retroviruses : CK\(53\) : AC\(12\)](#), [Live Attenuated Vaccines : CK\(5\) : AC\(2\)](#), [Retroviruses : CK\(10\) : AC\(10\)](#), [Vaccine Contamination : CK\(5\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Viruses (wild-type or recombinant vaccine-type) can silently prime for and trigger central nervous system autoimmune disease. - GMI Summary

Pubmed Data : J Neurovirol. 2001 Jun;7(3):220-7. PMID: [11517396](#)

Article Published Date : Jun 01, 2001

Authors : D J Theil, I Tsunoda, F Rodriguez, J L Whitton, R S Fujinami

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Vaccination: Diphtheria-Pertussis-Tetanus

DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents. - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Vaccination in infants less than 3 months is associated with an increased risk of sudden infant death syndrome. - GMI Summary

Pubmed Data : Fundam Clin Pharmacol. 1995;9(3):263-70. PMID: [7557822](#)

Article Published Date : Jan 01, 1995

Authors : A P Jonville-Bera, E Autret, J Laugier

Study Type : Meta Analysis

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Vaccination is associated with a rare autoimmune neurological condition transverse myelitis. - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1198-204. PMID: [19880568](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, S Kivity, M Szyper-Kravitz, Y Shoenfeld

Study Type : Meta Analysis

Additional Links

Diseases : [Myelitis](#) : CK(39) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Vaccination is associated with an increased risk for hemolytic anemia.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7394-7. Epub 2009 Sep 18. PMID: [19766577](#)

Article Published Date : Dec 09, 2009

Authors : Allison L Naleway, Edward A Belongia, James G Donahue, Burney A Kieke, Jason M Glanz,

Study Type : Meta Analysis

Additional Links

Diseases : [Hemolytic Anemia](#) : CK(75) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Acute necrotizing encephalopathy secondary to diphtheria, tetanus toxoid and whole-cell pertussis vaccination has been reported.](#) - GMI Summary

Pubmed Data : Pediatr Radiol. 2010 Jul;40(7):1281-4. Epub 2010 Jan 30. PMID: [20119724](#)

Article Published Date : Jul 01, 2010

Authors : Hale Aydin, Esra Ozgul, Ahmet Muhtesem Agildere

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Adverse effects of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine in 6- to 7-year-old children.](#) - GMI Summary

Pubmed Data : Pediatr Neonatol. 2011 Feb;52(1):38-41. Epub 2011 Feb 17. PMID: [21385656](#)

Article Published Date : Feb 01, 2011

Authors : Sung-Hsi Wei, Yen-Nan Chao, Song-En Huang, Tsuey-Feng Lee, Luan-Yin Chang

Study Type : Human Study

Additional Links

Diseases : [Tetanus](#) : CK(47) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Among female infants, those who receive both BCG and DTP vaccines experience higher mortality than those who receive only one of the two vaccines.](#) - GMI Summary

Pubmed Data : Trop Med Int Health. 2005 Oct;10(10):947-55. PMID: [16185228](#)

Article Published Date : Oct 01, 2005

Authors : Lawrence H Moulton, Lakshmi Rahmathullah, Neal A Halsey, R D Thulasiraj, Joanne Katz, James M Tielsch

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[Breastfeeding attenuates reductions in energy intake induced by a mild immunologic stimulus represented by DPTH immunization.](#) - GMI Summary

Pubmed Data : J Nutr. 2002 Jun;132(6):1293-8. PMID: [12042449](#)

Article Published Date : Jun 01, 2002

Authors : Mardya López-Alarcón, Cutberto Garza, Jean-Pierre Habicht, Lourdes Martínez, Virginia Pegueros, Salvador Villalpando

Study Type : Human Study

Additional Links

Substances : [Breast Milk : CK\(428\) : AC\(49\)](#)

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma. - GMI Summary](#)

Pubmed Data : J Allergy Clin Immunol. 2008 Mar ;121(3):626-31. Epub 2008 Jan 18. PMID: [18207561](#)

Article Published Date : Feb 29, 2008

Authors : Kara L McDonald, Shamima I Huq, Lisa M Lix, Allan B Becker, Anita L Kozyrskyj

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis \(Tdap\) vaccine in order to prevent pertussis infection in their offspring, it does not reduce - GMI Summary](#)

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. - GMI Summary](#)

Pubmed Data : Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18. PMID: [21093496](#)

Article Published Date : Jan 10, 2011

Authors : J Agergaard, E Nante, G Poustrup, J Nielsen, K L Flanagan, L Østergaard, C S Benn, P Aaby

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[DPT vaccines have been associated with recurrent seizures. - GMI Summary](#)

Pubmed Data : Am J Dis Child. 1984 Oct;138(10):908-11. PMID: [6206715](#)

Article Published Date : Oct 01, 1984

Authors : J V Murphy, L D Sarff, K M Marquardt

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Seizures : CK\(135\) : AC\(33\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Hair mercury in breast-fed infants exposed to thimerosal-preserved vaccines indicates significant levels of exposure.](#) - GMI Summary

Pubmed Data : Eur J Pediatr. 2007 Sep;166(9):935-41. Epub 2007 Jan 20. PMID: [17237965](#)

Article Published Date : Sep 01, 2007

Authors : Rejane C Marques, José G Dórea, Márlon F Fonseca, Wanderley R Bastos, Olaf Malm

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Incidence of adverse reactions to vaccines in pediatric populations are under-reported and may be as high as 43.4% for certain vaccine combinations.](#) - GMI Summary

Pubmed Data : Clin Drug Investig. 2004;24(8):457-63. PMID: [17523706](#)

Article Published Date : Jan 01, 2004

Authors : Pilar Carrasco-Garrido, Carmen Gallardo-Pino, Rodrigo Jiménez-García, Miguel A Tapias, Angel Gil de Miguel

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Pertussis epidemic despite high levels of vaccination coverage with acellular pertussis vaccine.](#) - GMI Summary

Article Published Date : Nov 07, 2013

Authors : Maria-Rosa Sala-Farré, César Arias-Varela, Assumpta Recasens-Recasens, Maria Simó-Sanahuja, Carmen Muñoz-Almagro, Josefa Pérez-Jové

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1994 Jul 7;331(1):16-21. PMID: [8202096](#)

Article Published Date : Jul 07, 1994

Authors : C D Christie, M L Marx, C D Marchant, S F Reising

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Sudden infant death syndrome and DTP vaccine timing may be linked.](#) - GMI Summary

Pubmed Data : Otol Neurotol. 2002 Jul;23(4):447-51. PMID: [6835859](#)

Article Published Date : Jul 01, 2002

Authors : L J Baraff, W J Ablon, R C Weiss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Sudden Infant Death syndrome mortality rate in the period zero to three days following DTP was found to be 7.3 times higher than in the period 30 days after immunization.](#) - GMI Summary

Pubmed Data : AmJ Public Health. 1987 Aug;77(8):945-51. PMID: [3496805](#)

Article Published Date : Aug 01, 1987

Authors : A M Walker, H Jick, D R Perera, R S Thompson, T A Knauss

Study Type : Human Study

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects.](#) - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) - GMI Summary

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The use of misoprostol for early pregnancy failure after failed expectant management is less costly than curettage.](#) - GMI Summary

Pubmed Data : Hum Reprod. 2005 Apr;20(4):1067-71. Epub 2004 Dec 23. PMID: [15618248](#)

Article Published Date : Apr 01, 2005

Authors : G C M Graziosi, J W van der Steeg, P H W Reuwer, A P Drogtop, H W Bruinse, B W J Mol

Study Type : Human Study

Additional Links

Diseases : [Miscarriage : CK\(313\) : AC\(36\)](#), [Miscarriage: Medical Intervention : CK\(125\) : AC\(14\)](#)

Additional Keywords : [Surgical Alternatives : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Obstetric Interventions : CK\(1030\) : AC\(69\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Timing of routine immunisations \(earlier = increased\) and subsequent hay fever risk.](#) - GMI Summary

Pubmed Data : Arch Dis Child. 2005 Jun ;90(6):567-73. PMID: [15908618](#)

Article Published Date : May 31, 2005

Authors : S A Bremner, I M Carey, S DeWilde, N Richards, W C Maier, S R Hilton, D P Strachan, D G Cook

Study Type : Human Study

Additional Links

Diseases : [Allergic Rhinitis : CK\(340\) : AC\(40\)](#), [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Vaccination timing and co-administration may be associated with increased mortality, especially in females.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 May 29;24(22):4701-8. Epub 2006 Mar 31. PMID: [16621182](#)

Article Published Date : May 29, 2006

Authors : Peter Aaby, Henrik Jensen, Gijs Walraven

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination with measles after DTP and polio vaccine is associated with 2-fold increase in female mortality.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2007 Mar;26(3):247-52. PMID: [17484223](#)

Article Published Date : Mar 01, 2007

Authors : Peter Aaby, May-Lill Garly, Jens Nielsen, Henrik Ravn, Cesario Martins, Carlitos Balé, Amabelia Rodrigues, Christine Stabell Benn, Ida Maria Lisse

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[In 1985 twin boys simultaneously succumbed to sudden unexpected deaths two to three hours after vaccination with diphtheria, tetanus, and pertussis vaccine \(DTP\).](#) - GMI Summary

Pubmed Data : Arch Dis Child. 1987 Jul;62(7):754-9. PMID: [3498443](#)

Article Published Date : Jul 01, 1987

Authors : S C Roberts

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\)](#)

: [AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Simultaneous sudden infant death syndrome has been reported in twins two days after receiving mutple vaccinations.](#) - GMI Summary

Pubmed Data : J Forensic Leg Med. 2007 Feb;14(2):87-91. PMID: [17654772](#)

Article Published Date : Feb 01, 2007

Authors : Yasemin Balci, Mehmet Tok, B Kenan Kocaturk, Cinar Yenilmez, Coşkun Yirulmaz

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Despite high coverage rates for primary immunization in infants and children pertussis incidence rates are increasing.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2005 May;24(5 Suppl):S10-8. PMID: [15876918](#)

Article Published Date : May 01, 2005

Authors : Tina Tan, Evelinda Trindade, Danuta Skowronski

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[DTP vaccination may contribute to urinary tract disease and sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : Reprod Biomed Online. 2010 Jul;21(1):100-8. Epub 2010 Mar 30. PMID: [15356430](#)

Article Published Date : Jul 01, 2010

Authors : Joseph Prandota

Study Type : Commentary

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Urinary Tract Infections : CK\(338\) : AC\(47\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

[Provocation by vaccine injections can increase the risk of paralytic poliomyelitis by up to 25 fold.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1986;65:123-6. PMID: [3549394](#)

Article Published Date : Jan 01, 1986

Authors : H V Wyatt

Study Type : Review

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis](#) : CK(53) : AC(15), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Hepatitis B](#) : CK(219) : AC(37), [Neuritis: Brachial Plexus](#) : CK(1) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Tetanus](#) : CK(61) : AC(8)

[Underestimation of central nervous system complications after pertussis immunization appears to be prevalent.](#) - GMI Summary

Pubmed Data : Acta Paediatr Jpn. 1991 Aug;33(4):421-7. PMID: [1792899](#)

Article Published Date : Aug 01, 1991

Authors : W Ehrengut

Study Type : Review

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: [Vaccination: Hepatitis B](#)

[Male newborns vaccinated with hepatitis B prior to 1999 had a 3-fold higher risk for parentally reported autism.](#) - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(24):1665-77. PMID: [21058170](#)

Article Published Date : Jan 01, 2010

Authors : Carolyn M Gallagher, Melody S Goodman

Study Type : Meta Analysis

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Neonate exposure to thimerosal mercury from hepatitis B vaccines may be a significant problem.](#) - GMI Summary

Pubmed Data : AmJ Perinatol. 2009 Aug;26(7):523-7. Epub 2009 Mar 12. PMID: [19283656](#)

Article Published Date : Aug 01, 2009

Authors : José G Dórea, Rejane C Marques, Katiane G Brandão

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Infant Chemical Exposures : CK\(165\) : AC\(24\)](#), [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[There are no randomized controlled trials that assessed the effects of hepatitis B vaccine during pregnancy for preventing infant infection. - GMI Summary](#)

Pubmed Data : Cochrane Database Syst Rev. 2011(3):CD007879. Epub 2011 Mar 16. PMID: [21412913](#)

Article Published Date : Jan 01, 2011

Authors : Ussanee S Sangkomkamhang, Pisake Lumbiganon, Malinee Laopaiboon

Study Type : Meta Analysis

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Vaccination is associated with a rare autoimmune neurological condition transverse myelitis. - GMI Summary](#)

Pubmed Data : Lupus. 2009 Nov;18(13):1198-204. PMID: [19880568](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, S Kivity, M Szyper-Kravitz, Y Shoenfeld

Study Type : Meta Analysis

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination is associated with an increased risk for hemolytic anemia. - GMI Summary](#)

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7394-7. Epub 2009 Sep 18. PMID: [19766577](#)

Article Published Date : Dec 09, 2009

Authors : Allison L Naleway, Edward A Belongia, James G Donahue, Burney A Kieke, Jason M Glanz,

Study Type : Meta Analysis

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[When polled 5% of nonpediatricians would not use Haemophilus influenzae type b vaccine if they had a child born in 2004. - GMI Summary](#)

Pubmed Data : Pediatrics. 2005 Nov;116(5):e623-33. PMID: [16263976](#)

Article Published Date : Nov 01, 2005

Authors : Klara M Posfay-Barbe, Ulrich Heininger, Christoph Aebi, Daniel Desgrandchamps, Bernard Vaudaux, Claire-Anne Siegrist

Study Type : Meta Analysis

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Acute hepatitis B can occur in those who are vaccinated against it and who are exposed through unprotected sexual contact and iatrogenically. - GMI Summary](#)

Pubmed Data : Postgrad Med J. 2006 Mar;82(965):207-10. PMID: [16517803](#)

Article Published Date : Mar 01, 2006

Authors : G Rosner, Y Lurie, L Blendis, Z Halpern, R Oren

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Iatrogenic Disease : CK\(62\) : AC\(7\)](#)

Additional Keywords : [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[C-reactive protein \(CRP\) elevation occur in infants without sepsis after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : Eur J Pediatr. 2013 Jan 29. Epub 2013 Jan 29. PMID: [23358708](#)

Article Published Date : Jan 28, 2013

Authors : Istemi Han Celik, Gamze Demirel, Fuat Emre Canpolat, Omer Erdeve, Ugur Dilmen

Study Type : Human Study

Additional Links

Diseases : [Elevated CRP : CK\(82\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hair mercury in breast-fed infants exposed to thimerosal-preserved vaccines indicates significant levels of exposure.](#) - GMI Summary

Pubmed Data : Eur J Pediatr. 2007 Sep;166(9):935-41. Epub 2007 Jan 20. PMID: [17237965](#)

Article Published Date : Sep 01, 2007

Authors : Rejane C Marques, José G Dórea, Márlon F Fonseca, Wanderley R Bastos, Olaf Malm

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Therapeutic Actions : [Breastfeeding : CK\(739\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination coverage has fallen to beneath 30% in France due to concerns over safety.](#) - GMI Summary

Pubmed Data : J Clin Virol. 2009 Nov;46(3):202-5. Epub 2009 Aug 28. PMID: [19716764](#)

Article Published Date : Nov 01, 2009

Authors : Marta A Balinska

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination has been linked to autoimmune inflammatory polyneuropathy \(PN\).](#) - GMI Summary

Pubmed Data : J Peripher Nerv Syst. 2002 Sep;7(3):163-7. PMID: [12365564](#)

Article Published Date : Sep 01, 2002

Authors : Claude Vital, Anne Vital, Georges Gbikpi-Benissan, Maité Longy-Boursier, Marie-Thérèse Climas, Yves Castaing, Marie-Hélène Canon, Michel Le Bras, Klaus Petry

Study Type : Human Study

Additional Links

Diseases : [Acute Autoimmune Neuropathy : CK\(104\) : AC\(2\)](#), [Autoimmune inflammatory polyneuropathy \(PN\) : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination is associated with a wide range of autoimmune](#)

diseases. - GMI Summary

Pubmed Data : Clin Chim Acta. 2006 Feb;364(1-2):196-204. Epub 2005 Aug 10. PMID: [15638050](#)

Article Published Date : Feb 01, 2006

Authors : M R Geier, D A Geier

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Rheumatoid : CK\(295\) : AC\(53\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Myelitis : CK\(39\) : AC\(5\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Pancytopenia : CK\(12\) : AC\(2\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination is associated with an increased risk of CNS inflammatory demyelination after 3 years of age. - GMI Summary

Pubmed Data : Reprod Toxicol. 2002 May-Jun;16(3):237-43. PMID: [18843097](#)

Article Published Date : May 01, 2002

Authors : Yann Mikaeloff, Guillaume Caridade, Samy Suissa, Marc Tardieu

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Inflammation : CK\(1125\) : AC\(377\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination is associated with potentially neurotoxic mercury exposure in infants. - GMI Summary

Pubmed Data : Chin Med. 2008 Mar 29;3:4. PMID: [10802503](#)

Article Published Date : Mar 29, 2008

Authors : G V Stajich, G P Lopez, S W Harry, W R Sexson

Study Type : Human Study

Additional Links

Diseases : [Mercury Poisoning : CK\(172\) : AC\(45\)](#), [Premature Birth : CK\(414\) : AC\(44\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination may contribute to autoimmune demyelinating complications due to immunological cross-reactivity between Hepatitis B virus surface antigen and myelin basic protein. - GMI Summary

Pubmed Data : Clin Dev Immunol. 2005 Sep;12(3):217-24. PMID: [16295528](#)

Article Published Date : Sep 01, 2005

Authors : Dimitrios-Petrou Bogdanos, Heather Smith, Yun Ma, Harold Baum, Giorgina Mieli-Vergani, Diego Vergani

Study Type : Human Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Hepatitis B Vaccine : CK\(30\) : AC\(2\)](#), [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Hepatitis B vaccination significantly increases the risk of a wide range of autoimmune diseases. - GMI Summary

Pubmed Data : Autoimmunity. 2005 Jun;38(4):295-301. PMID: [16206512](#)

Article Published Date : Jun 01, 2005

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Alopecia : CK\(131\) : AC\(28\)](#), [Arthritis : CK\(1493\) : AC\(221\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination was statistically associated with gastrointestinal reactions including: hepatitis, gastrointestinal disease and liver function test abnormalities.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2002 Nov-Dec;49(48):1571-5. PMID: [12397738](#)

Article Published Date : Nov 01, 2002

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Gastrointestinal Diseases : CK\(38\) : AC\(14\)](#), [Hepatitis : CK\(64\) : AC\(24\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination with or without hepatitis B immunoglobulin at birth to babies born of HBsAg-positive mothers prevents overt HBV transmission but may not prevent occult HBV infection in babies: a randomized controlled trial.](#) - GMI Summary

Article Published Date : Oct 31, 2013

Authors : C Pande, S K Sarin, S Patra, A Kumar, S Mishra, S Srivastava, K Bhutia, E Gupta, C K Mukhopadhyay, A K Dutta, S S Trivedi

Study Type : Human Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Additional Keywords : [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Hepatitis Viruses : CK\(1\) : AC\(1\)](#)

[Hepatitis B vaccine is associated with an increased risk of liver problems in U.S. children less than 6 years old, 1993 and 1994.](#) - GMI Summary

Pubmed Data : Epidemiology. 1999 May;10(3):337-9. PMID: [10230847](#)

Article Published Date : May 01, 1999

Authors : M A Fisher, S A Eklund

Study Type : Human Study

Additional Links

Diseases : [Liver Disease : CK\(112\) : AC\(31\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine is positively associated with adverse health outcomes in the general population of US children.](#) - GMI Summary

Pubmed Data : Ann Epidemiol. 2001 Jan;11(1):13-21. PMID: [11164115](#)

Article Published Date : Jan 01, 2001

Authors : M A Fisher, S A Eklund, S A James, X Lin

Study Type : Human Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Arthritis: Juvenile Chronic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Arthritis: Juvenile Rheumatoid : CK\(10\) : AC\(1\)](#), [Ear Infection : CK\(259\) : AC\(32\)](#), [Pharyngeal Diseases : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) :](#)

[Hepatitis B vaccine may have a possible association with the development of uveitis in some patients.](#) - GMI Summary

Pubmed Data : Cutan Ocul Toxicol. 2010 Mar;29(1):26-9. PMID: [19947819](#)

Article Published Date : Mar 01, 2010

Authors : Frederick W Fraunfelder, Eric B Suhler, Frederick T Fraunfelder

Study Type : Human Study

Additional Links

Diseases : [Uveitis : CK\(73\) : AC\(11\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[In the US the highest number of cases of Guillain-Barre syndrome are associated with influenza and hepatitis B vaccines.](#) - GMI Summary

Pubmed Data : J Clin Neuromuscul Dis. 2009 Sep;11(1):1-6. PMID: [19730016](#)

Article Published Date : Sep 01, 2009

Authors : Nizar Souayah, Abu Nasar, M Fareed K Suri, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Systemic lupus erythematosus related to hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1192-7. PMID: [19880567](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, Y Zafrir, Z Paz, T Shilton, G Zandman-Goddard, Y Shoenfeld

Study Type : Human Study

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination for DPT, Hepatitis B and influenza has been reported to be associated with the development of erythema multiforme in an infant.](#) - GMI Summary

Pubmed Data : Indian J Dermatol Venereol Leprol. 2008 May-Jun;74(3):251-3. PMID: [18583795](#)

Article Published Date : May 01, 2008

Authors : Sarvjit Kaur, Sanjeev Handa

Study Type : Human Study

Additional Links

Diseases : [Erythema](#) : CK(44) : AC(6), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)
Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Influenza](#) : CK(356) : AC(37)

[A case of lethal inflammatory polyradiculoneuropathy with spinal cord involvement after hepatitis B vaccination.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2001 May 1;186(1-2):81-5. PMID: [11412876](#)

Article Published Date : May 01, 2001

Authors : E Sindern, J M Schröder, M Krismann, J P Malin

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Inflammatory Demyelinating Polyradiculoneuropathy](#) : CK(87) : AC(1),
[Polyradiculoneuropathy: Acute Inflammatory](#) : CK(87) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[A case of lethal status epilepticus and lymphocytic pneumonitis has been reported.](#) - GMI Summary

Pubmed Data : Eur J Intern Med. 2008 Jul;19(5):383-5. Epub 2007 Dec 4. PMID: [18549949](#)

Article Published Date : Jul 01, 2008

Authors : Jozélio Freire de Carvalho, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Epilepsy](#) : CK(128) : AC(29), [Pneumonitis](#) : CK(18) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Acute posterior multifocal placoid pigment epitheliopathy after hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Arch Ophthalmol. 1995 Mar;113(3):297-300. PMID: [7887843](#)

Article Published Date : Mar 01, 1995

Authors : A P Brézin, P Massin-Korobelnik, M Boudin, A Gaudric, P LeHoang

Study Type : Human: Case Report

Additional Links

Diseases : [Acute Posterior Multifocal Placoid Pigment Epitheliopathy \(APMPPE\)](#) : CK(3) : AC(1),
[Chorioretinitis](#) : CK(3) : AC(1)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Autoimmunity following hepatitis B vaccine has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 Feb ;21(2):146-52. PMID: [22235045](#)

Article Published Date : Jan 31, 2012

Authors : Y Zafrir, N Agmon-Levin, Z Paz, T Shilton, Y Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

[Bell's palsy is a possible complication of hepatitis B vaccination in children.](#) - GMI Summary

Pubmed Data : J Health Popul Nutr. 2009 Oct;27(5):707-8. PMID: [19902808](#)

Article Published Date : Oct 01, 2009

Authors : Handan Alp, Hüseyin Tan, Zerrin Orbak

Study Type : Human: Case Report

Additional Links

Diseases : [Bell's Palsy](#) : CK(13) : AC(3)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Cutaneous lupus erythematosus and buccal aphthosis after hepatitis B vaccination has been reported in a 6-year-old child](#) - GMI Summary

Pubmed Data : Ann Dermatol Venereol. 1996;123(10):657-9. PMID: [9615128](#)

Article Published Date : Jan 01, 1996

Authors : P Grézard, M Chefaï, V Philippot, H Perrot, M Faisant

Study Type : Human: Case Report

Additional Links

Diseases : [Aphthosis: Buccal](#) : CK(3) : AC(1), [Lupus Erythematosus: Cutaneous](#) : CK(17) : AC(4)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Guillain-Barré syndrome following hepatitis B vaccination has been reported.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2004 Nov-Dec;22(6):767-70. PMID: [15638054](#)

Article Published Date : Nov 01, 2004

Authors : M Khamaisi, Y Shoenfeld, H Orbach

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccination has been linked to anaphylactic shock and death in infants.](#) - GMI Summary

Pubmed Data : Adv Exp Med Biol. 1990;272:183-95. PMID: [20077677](#)

Article Published Date : Jan 01, 1990

Authors : Fu-Zhen Wang, Fu-Qiang Cui, Da-Wei Liu

Study Type : Human: Case Report

Additional Links

Diseases : [Anaphylaxis](#) : CK(53) : AC(15), [Infant Mortality](#) : CK(249) : AC(25), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine associated with dermatomyositis has been reported.](#) - GMI Summary

Pubmed Data : Rheumatol Int. 2008 Apr;28(6):609-12. Epub 2007 Nov 23. PMID: [18034245](#)

Article Published Date : Apr 01, 2008

Authors : Arie Altman, Martine Szyper-Kravitz, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Dermatomyositis](#) : CK(44) : AC(10), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50)

[Hepatitis B vaccine may induce myelitis in susceptible individuals.](#) - GMI Summary

Pubmed Data : Eur J Neurol. 2001 Nov;8(6):711-5. PMID: [11784358](#)

Article Published Date : Nov 01, 2001

Authors : F Karaali-Savrun, A Altıntaş, S Saip, A Siva

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Immune-mediated myelitis following hepatitis B vaccination has been reported.](#)**- GMI Summary**

Pubmed Data : Autoimmun Rev. 2012 Apr 1. Epub 2012 Apr 1. PMID: [22498789](#)

Article Published Date : Apr 01, 2012

Authors : Joerg-Patrick Stübgen

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Optic neuritis following hepatitis B vaccination has been reported.](#)**n - GMI Summary**

Pubmed Data : J Chin Med Assoc. 2009 Nov;72(11):594-7. PMID: [19948437](#)

Article Published Date : Nov 01, 2009

Authors : Muferet Erguven, Sirin Guven, Umit Akyuz, Olcay Bilgiç, Fuat Laloglu

Study Type : Human: Case Report

Additional Links

Diseases : [Optic Neuritis : CK\(23\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Simultaneous sudden infant death syndrome has been reported in twins two days after receiving mutple vaccinations.](#)**- GMI Summary**

Pubmed Data : J Forensic Leg Med. 2007 Feb;14(2):87-91. PMID: [17654772](#)

Article Published Date : Feb 01, 2007

Authors : Yasemin Balci, Mehmet Tok, B Kenan Kocaturk, Cinar Yenilmez, Coşkun Yirulmaz

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Systemic lupus erythematosus has been triggered by hepatitis B vaccine.](#)**- GMI Summary**

Pubmed Data : Clin Nephrol. 2010 Aug;74(2):150-3. PMID: [20630136](#)

Article Published Date : Aug 01, 2010

Authors : D Santoro, G Vita, R Vita, A Mallamace, V Savica, G Bellinghieri, S Benvenega, S Gangemi

Study Type : Human: Case Report

Additional Links

Diseases : [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year.](#)**- GMI Summary**

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine alters the expression of 144 genes in the mouse liver within 1 day of vaccination, 7 of which are related to inflammation and metabolism.](#) - GMI Summary

Pubmed Data : Mol Biol Rep. 2011 Jun 21. Epub 2011 Jun 21. PMID: [21691704](#)

Article Published Date : Jun 21, 2011

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccine induces cell death in liver cells and mouse liver.](#) - GMI Summary

Pubmed Data : Apoptosis. 2012 Jan 17. Epub 2012 Jan 17. PMID: [22249285](#)

Article Published Date : Jan 17, 2012

Authors : Heyam Hamza, Jianhua Cao, Xinyun Li, Changchun Li, Mengjin Zhu, Shuhong Zhao

Study Type : Animal Study

Additional Links

Diseases : [Liver Damage : CK\(648\) : AC\(226\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Problem Substances : [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

Adverse Pharmacological Actions : [Hepatotoxic : CK\(301\) : AC\(85\)](#)

[Newborn primates receiving mercury-containing hepatitis B vaccines exhibit neurodevelopmental delays.](#) - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(19):1298-313. PMID: [20711932](#)

Article Published Date : Jan 01, 2010

Authors : Laura Hewitson, Lisa A Houser, Carol Stott, Gene Sackett, Jaime L Tomko, David Atwood, Lisa Blue, E Railey White

Study Type : Animal Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccination has the potential to induce central demyelinating disorders such as multiple sclerosis.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2006;66(1):84-6. Epub 2005 Sep 19. PMID: [16176857](#)

Article Published Date : Jan 01, 2006

Authors : Yannick Comenge, Marc Girard

Study Type : Commentary

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccinations is associated with autoimmune hazards.](#) - GMI

Summary

Pubmed Data : Autoimmun Rev. 2005 Feb;4(2):96-100. PMID: [15722255](#)

Article Published Date : Feb 01, 2005

Authors : Marc Girard

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[Hepatitis B vaccines have a potential to occasionally trigger the onset of immune diseases in individuals with an underlying genetic or immunological susceptibility.](#) - GMI Summary

Pubmed Data : J Neurol Sci. 2010 May 15;292(1-2):1-4. Epub 2010 Mar 7. PMID: [20207367](#)

Article Published Date : May 15, 2010

Authors : Joerg-Patrick Stübgen

Study Type : Review

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Dermatomyositis : CK\(44\) : AC\(10\)](#), [Myasthenia Gravis : CK\(82\) : AC\(14\)](#), [Neuromuscular Diseases : CK\(16\) : AC\(4\)](#), [Neuropathies : CK\(436\) : AC\(72\)](#), [Polyarteritis Nodosa : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The demyelinating effect of hepatitis B vaccination could be due to the contamination of the vaccine by partial hepatitis B virus polymerase.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2005;65(3):509-20. PMID: [15908138](#)

Article Published Date : Jan 01, 2005

Authors : E Faure

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The hepatitis B vaccine may induce autoimmune demyelinating disease through the molecular mimicry that exists between the vaccine antigen, Epstein-Barr virus and human myelin.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2008;70(2):346-8. Epub 2007 Jul 13. PMID: [17630224](#)

Article Published Date : Jan 01, 2008

Authors : Burton A Waisbren

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Epstein-Barr Virus Infections : CK\(102\) : AC\(44\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994
Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) **- GMI Summary**

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Vaccination: Influenza](#)

[Inactivated flu vaccines have not been proven to be effective or safe in preventing influenza in healthy children under two.](#) - GMI Summary

Pubmed Data : Altern Ther Health Med. 2009 Sep-Oct;15(5):44-6. PMID: [18425905](#)

Article Published Date : Sep 01, 2009

Authors : Tom Jefferson, Alessandro Rivetti, Anthony Harnden, Carlo Di Pietrantonj, Vittorio Demicheli

Study Type : Meta Analysis

Additional Links

Diseases : [Cold and Flu: Infants & Children : CK\(62\) : AC\(6\)](#), [Infection: In Infants & Children : CK\(111\) : AC\(11\)](#), [Influenza A : CK\(292\) : AC\(77\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination for healthcare workers who work with the elderly has no effect on laboratory-proven influenza, pneumonia or deaths from pneumonia.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD005187. Epub 2010 Feb 17. PMID: [20166073](#)

Article Published Date : Jan 01, 2010

Authors : Roger E Thomas, Tom Jefferson, Toby J Lasserson

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Maternal influenza vaccination during pregnancy does not reduce the incidence](#)

[of acute respiratory illness visits among infants.](#) - GMI Summary

Pubmed Data : Cancer Sci. 2004 Jul;95(7):596-601. PMID: [17146026](#)

Article Published Date : Jul 01, 2004

Authors : Eric K France, Renae Smith-Ray, David McClure, Simon Hambidge, Stanley Xu, Kristi Yamasaki, David Shay, Eric Weintraub, Alicia M Fry, Steve B Black, Henry R Shinefield, John P Moolooly, Lisa A Jackson

Study Type : Meta Analysis

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[The effectiveness of the 2008-2009 seasonal flu vaccine in England was -6%.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jan 31. Epub 2011 Jan 31. PMID: [21292008](#)

Article Published Date : Jan 31, 2011

Authors : Richard Pebody, Nick Andrews, Pauline Waight, Rashmi Malkani, Christine McCartney, Joanna Ellis, Elizabeth Miller

Study Type : Meta Analysis

Additional Links

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is a lack of evidence for the effectiveness of influenza vaccines in adults aged 65 years or older.](#) - GMI Summary

Pubmed Data : Lancet Infect Dis. 2011 Oct 25. Epub 2011 Oct 25. PMID: [22032844](#)

Article Published Date : Oct 25, 2011

Authors : Michael T Osterholm, Nicholas S Kelley, Alfred Sommer, Edward A Belongia

Study Type : Meta Analysis

Additional Links

Diseases : [Elderly: Age Specific Diseases : CK\(442\) : AC\(38\)](#), [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is currently no evidence from randomised studies that influenza vaccine given to people with CF is of benefit to them.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2009 Oct 7;(4):CD001753. PMID: [19821281](#)

Article Published Date : Oct 07, 2009

Authors : Poonam Dharmaraj, Rosalind L Smyth

Study Type : Meta Analysis

Additional Links

Diseases : [Cystic Fibrosis : CK\(523\) : AC\(78\)](#)

Additional Keywords : [Vaccine Research : CK\(20\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is little evidence supporting the belief that vaccines are effective in preventing influenza in healthy adults.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(7):CD001269. Epub 2010 Jul 7. PMID: [20614424](#)

Article Published Date : Jan 01, 2010

Authors : Tom Jefferson, Carlo Di Pietrantonj, Alessandro Rivetti, Ghada A Bawazeer, Lubna A Al-Ansary, Eliana Ferroni

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Influenza B : CK\(72\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[There is no solid evidence available supporting the belief that vaccines are effective in preventing influenza in the elderly.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2010(2):CD004876. Epub 2010 Feb 17. PMID: [20166072](#)

Article Published Date : Jan 01, 2010

Authors : Tom Jefferson, Carlo Di Pietrantonj, Lubna A Al-Ansary, Eliana Ferroni, Sarah Thorning, Roger E Thomas

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[We concluded that there is no credible evidence that vaccination of healthy people under the age of 60, who are healthcare workers caring for the elderly, affects influenza complications in those cared for.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2006 ;3:CD005187. Epub 2006 Jul 19. PMID: [16856082](#)

Article Published Date : Jan 01, 2006

Authors : R E Thomas, T Jefferson, V Demicheli, D Rivetti

Study Type : Meta Analysis

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#)

Additional Keywords : [Influenza : CK\(656\) : AC\(99\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

["Chart-confirmed guillain-barre syndrome after 2009 H1N1 influenza vaccination among the Medicare population, 2009-2010."](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2013 Sep 15 ;178(6):962-73. Epub 2013 May 6. PMID: [23652165](#)

Article Published Date : Sep 14, 2013

Authors : Laura L Polakowski, Sukhminder K Sandhu, David B Martin, Robert Ball, Thomas E Macurdy, Riley L Franks, Jonathan M Gibbs, Garner F Kropp, Armen Avagyan, Jeffrey A Kelman, Christopher M Worrall, Guoying Sun, Rebecca E Kliman, Dale R Burwen

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

["Risk of Guillain-Barré syndrome after 2010-2011 influenza vaccination."](#) - GMI Summary

Pubmed Data : Eur J Epidemiol. 2013 May ;28(5):433-44. Epub 2013 Mar 31. PMID: [23543123](#)

Article Published Date : Apr 30, 2013

Authors : Francesca Galeotti, Marco Massari, Roberto D'Alessandro, Ettore Beghi, Adriano Chiò, Giancarlo Logroscino, Graziella Filippini, Maria Donata Benedetti, Maura Pugliatti, Carmela Santuccio, Roberto Raschetti,

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[An association between Pandemrix vaccination and narcolepsy has been observed in Finland and Sweden](#) - GMI Summary

Pubmed Data : Euro Surveill. 2014 ;19(17):15-25. Epub 2014 May 1. PMID: [24821121](#)

Article Published Date : Dec 31, 2013

Authors : D O'Flanagan, A S Barret, M Foley, S Cotter, C Bonner, C Crowe, B Lynch, B Sweeney, H Johnson, B McCoy, E Purcell

Study Type : Human Study

Additional Links

Diseases : [Narcolepsy](#) : CK(21) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)
Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

[Annual influenza vaccination hampers the development of virus-specific CD8\(+\) T cell responses necessary to protect against influenza infection.](#) - GMI

Summary

Pubmed Data : J Virol. 2011 Nov ;85(22):11995-2000. Epub 2011 Aug 31. PMID: [21880755](#)

Article Published Date : Nov 01, 2011

Authors : Rogier Bodewes, Pieter L A Fraaij, Martina M Geelhoed-Mieras, Carel A van Baalen, Harm A W M Tiddens, Annemarie M C van Rossum, Fiona R van der Klis, Ron A M Fouchier, Albert D M E Osterhaus, Guus F Rimmelzwaan

Study Type : Human Study

Additional Links

Diseases : [Cystic Fibrosis](#) : CK(523) : AC(78), [Influenza](#) : CK(656) : AC(99)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Immunosuppressive](#) : CK(156) : AC(26)

[Flu vaccination causes measurable increases in inflammation in pregnant women which may increase the risk of preeclampsia and adverse outcomes such as preterm birth.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Sep 20. Epub 2011 Sep 20. PMID: [21945263](#)

Article Published Date : Sep 20, 2011

Authors : Lisa M Christian, Jay D Iams, Kyle Porter, Ronald Glaser

Study Type : Human Study

Additional Links

Diseases : [CRP](#) : CK(30) : AC(3), [Elevated CRP](#) : CK(82) : AC(8), [Pre-Eclampsia](#) : CK(299) : AC(33), [Pregnancy: Vaccination](#) : CK(92) : AC(16), [Pregnancy Complications](#) : CK(168) : AC(20), [Preterm Birth: Prevention](#) : CK(111) : AC(9), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Interleukin-6 up-regulation](#) : CK(14) : AC(3), [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation](#) : CK(42) : AC(4)

[In the US the highest number of cases of Guillain-Barre syndrome are associated with influenza and hepatitis B vaccines.](#) - GMI Summary

Pubmed Data : J Clin Neuromuscul Dis. 2009 Sep;11(1):1-6. PMID: [19730016](#)

Article Published Date : Sep 01, 2009

Authors : Nizar Souayah, Abu Nasar, M Fareed K Suri, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Influenza](#) : CK(356) : AC(37)

[Increased risk \(4.4 fold\) of noninfluenza respiratory virus infections associated with receipt of inactivated influenza vaccine.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2012 Jun ;54(12):1778-83. Epub 2012 Mar 15. PMID: [22423139](#)

Article Published Date : May 31, 2012

Authors : Benjamin J Cowling, Vicky J Fang, Hiroshi Nishiura, Kwok-Hung Chan, Sophia Ng, Dennis K M Ip, Susan S Chiu, Gabriel M Leung, J S Malik Peiris

Study Type : Human Study

Additional Links

Diseases : [Upper Respiratory Infections](#) : CK(824) : AC(90)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Influenza](#) : CK(356) : AC(37)

Adverse Pharmacological Actions : [Immunotoxic](#) : CK(254) : AC(48)

Influenza A vaccination containing adjuvant causes cardiac autonomic dysfunction and inflammation which may transiently increase the risk of cardiovascular events. - GMI Summary

Pubmed Data : J Intern Med. 2010 Sep 1. Epub 2010 Sep 1. PMID: [20964738](#)

Article Published Date : Sep 01, 2010

Authors : Gaetano A Lanza, Lucy Barone, Giancarla Scalone, Dario Pitocco, Gregory A Sgueglia, Roberto Mollo, Roberto Nerla, Francesco Zaccardi, Giovanni Ghirlanda, Filippo Crea

Study Type : Human Study

Additional Links

Diseases : [C-Reactive Protein](#) : CK(879) : AC(84), [Cardiovascular Diseases](#) : CK(5342) : AC(665), [Diabetes Mellitus: Type 2](#) : CK(3603) : AC(359), [Influenza A](#) : CK(292) : AC(77), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Pharmacological Actions : [Interleukin-6 upregulation](#) : CK(26) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Influenza vaccination does not prevent ischemic stroke and it does not reduce the rate of acute previous infections in stroke patients. - GMI Summary

Pubmed Data : Cerebrovasc Dis. 2008;26(4):339-47. Epub 2008 Aug 27. PMID: [18728360](#)

Article Published Date : Jan 01, 2008

Authors : G Piñol-Ripoll, I de la Puerta, S Santos, F Purroy, E Mostacero

Study Type : Human Study

Additional Links

Diseases : [Stroke: Prevention](#) : CK(163) : AC(21)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Influenza vaccines may be causing vasculitis. - GMI Summary

Pubmed Data : J Ethnopharmacol. 2000 Aug;71(3):457-63. PMID: [19734734](#)

Article Published Date : Aug 01, 2000

Authors : Rainer Birck, Isabelle Kaelsch, Peter Schnuelle, Luis Felipe Flores-Suárez, Rainer Nowack

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Influenza vaccines were not shown to be effective among children 6 to 59 months of age during 2 influenza seasons. - GMI Summary

Pubmed Data : Anticancer Res. 2009 Nov;29(11):4629-32. PMID: [18838647](#)

Article Published Date : Nov 01, 2009

Authors : Peter G Szilagyi, Gerry Fairbrother, Marie R Griffin, Richard W Hornung, Stephanie Donauer, Ardythe Morrow, Mekibib Altaye, Yuwei Zhu, Sandra Ambrose, Kathryn M Edwards, Katherine A Poehling, Geraldine Lofthus, Michol Holloway, Lyn Finelli, Marika Iwane, Mary Allen Staat,

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections](#) : CK(275) : AC(29), [Influenza](#) : CK(656) : AC(99), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Influenza-related mortality is not prevented with increasing vaccination coverage. - GMI Summary

Pubmed Data : Vaccine. 2006 Oct 30;24(42-43):6468-75. Epub 2006 Jul 7. PMID: [16876293](#)

Article Published Date : Oct 30, 2006

Authors : Caterina Rizzo, Cécile Viboud, Emanuele Montomoli, Lone Simonsen, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Prior receipt of seasonal flu vaccine \(2008-09 \)was associated with increased risk of medically attended pandemic H1N1 illness \(2008-09\).](#) - GMI Summary

Pubmed Data : PLoS Med. 2010;7(4):e1000258. Epub 2010 Apr 6. PMID: [20386731](#)

Article Published Date : Jan 01, 2010

Authors : Danuta M Skowronski, Gaston De Serres, Natasha S Crowcroft, Naveed Z Janjua, Nicole Boulianne, Travis S Hottes, Laura C Rosella, James A Dickinson, Rodica Gilca, Pam Sethi, Najwa Ouhoumane, Donald J Willison, Isabelle Rouleau, Martin Petric, Kevin Fonseca, Steven J Drews, Anuradha Rebbapragada, Hugues Charest, Marie-Eve Hamelin, Guy Boivin, Jennifer L Gardy, Yan Li, Trijntje L Kwindt, David M Patrick, Robert C Brunham,

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Additional Keywords : [Immunosuppressive Flu Vaccines : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Seasonal influenza vaccine \(2008-2009\) is associated with an increased risk of influenza-like illness from pandemic H1N1 infection.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2010 Nov 1;51(9):1017-1027. PMID: [20887210](#)

Article Published Date : Nov 01, 2010

Authors : Naveed Z Janjua, Danuta M Skowronski, Travis S Hottes, William Osei, Evan Adams, Martin Petric, Suzana Sabaiduc, Tracy Chan, Annie Mak, Marcus Lem, Patrick Tang, David M Patrick, Gaston De Serres, David Bowering

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#)

Additional Keywords : [Immunosuppressive Flu Vaccines : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Thirty-five percent of children with juvenile idiopathic arthritis experienced flare of the disease after vaccination.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2012 Mar 15. Epub 2012 Mar 15. PMID: [22513085](#)

Article Published Date : Mar 15, 2012

Authors : Natasa Toplak, Vesna Subelj, Tanja Kveder, Sasa Cucnik, Katarina Prosenc, Alenka Trampus-Bakija, Ljupco Todorovski, Tadej Avcin

Study Type : Human Study

Additional Links

Diseases : [Arthritis: Juvenile Idiopathic : CK\(20\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Adverse Pharmacological Actions : [Tumor necrosis factor \$\alpha\$ \(TNF \$\alpha\$ \) up-regulation : CK\(42\) : AC\(4\)](#)

[Vaccination for DPT, Hepatitis B and influenza has been reported to be associated with the development of erythema multiforme in an infant.](#) - GMI Summary

Pubmed Data : Indian J Dermatol Venereol Leprol. 2008 May-Jun;74(3):251-3. PMID: [18583795](#)

Article Published Date : May 01, 2008

Authors : Sarvjit Kaur, Sanjeev Handa

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Widening influenza vaccine coverage is not correleated with declining mortality rates in any age group. The benefits of vaccination are substantially overestimated.](#) - GMI Summary

Pubmed Data : Arch Intern Med. 2005 Feb 14;165(3):265-72. PMID: [15710788](#)

Article Published Date : Feb 14, 2005

Authors : Lone Simonsen, Thomas A Reichert, Cecile Viboud, William C Blackwelder, Robert J Taylor, Mark A Miller

Study Type : Human Study

Additional Links

Diseases : [H1N1 Infection : CK\(468\) : AC\(88\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Influenza A : CK\(292\) : AC\(77\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Zinc supplementation has a beneficial effect on malaise, one of the influenza vaccine associated adverse events, and decrease serum TNF- \$\alpha\$ levels.](#) - GMI Summary

Pubmed Data : J Trace Elem Med Biol. 2011 Apr 21. Epub 2011 Apr 21. PMID: [21514808](#)

Article Published Date : Apr 21, 2011

Authors : S Songül Yalçın, Defne Engür-Karasınav, Dursun Alehan, Kadriye Yurdakök, Süheyla Ozkutlu, Turgay Coşkun

Study Type : Human Study

Additional Links

Substances : [Zinc : CK\(880\) : AC\(128\)](#)

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor : CK\(1021\) : AC\(365\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[A case of innfluenza vaccine induced have necrotizing glomerulonephritis in decursu vasculitis has been reported.](#) - GMI Summary

Pubmed Data : Pol Merkur Lekarski. 2005 Jul;19(109):75-7. PMID: [16194032](#)

Article Published Date : Jul 01, 2005

Authors : Lidia Hyla-Klekot, Grazyna Kucharska, Witold Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Glomerulonephritis : CK\(41\) : AC\(9\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Acute transverse myelitis after influenza vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Neuroimaging. 1996 Oct;6(4):248-50. PMID: [8903080](#)

Article Published Date : Oct 01, 1996

Authors : R Bakshi, J C Mazziotta

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Autoimmune hemolytic anemia following MF59-adjuvanted influenza vaccine has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2011 Jan;45(1):e8. Epub 2010 Dec 28. PMID: [21189364](#)

Article Published Date : Jan 01, 2011

Authors : Sabrina Montagnani, Marco Tuccori, Giuseppe Lombardo, Arianna Testi, Stefania Mantarro, Elisa Ruggiero, Corrado Blandizzi

Study Type : Human: Case Report

Additional Links

Diseases : [Hemolytic Anemia : CK\(75\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Case report: a shoulder injury related to vaccine administration.](#) - GMI Summary

Pubmed Data : J Am Board Fam Med. 2012 Nov ;25(6):919-22. PMID: [23136333](#)

Article Published Date : Oct 31, 2012

Authors : Matthew G Barnes, Christopher Ledford, Karen Hogan

Study Type : Human: Case Report

Additional Links

Diseases : [Shoulder Injuries : CK\(23\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Delayed focal lipomatrophy after AS03-adjuvanted influenza A \(H1N1\) 2009 vaccine has been reported.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Dec 17. Epub 2010 Dec 17. PMID: [21172376](#)

Article Published Date : Dec 17, 2010

Authors : Emilie Javelle, Benjamin Soulier, Christian Brosset, Solène Lorcy, Fabrice Simon

Study Type : Human: Case Report

Additional Links

Diseases : [Lipomatrophy : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Development of fulminant Type 1 diabetes with thrombocytopenia after influenza vaccination has been observed.](#) - GMI Summary

Pubmed Data : Diabet Med. 2011 Jul 22. Epub 2011 Jul 22. PMID: [21781156](#)

Article Published Date : Jul 22, 2011

Authors : H Yasuda, M Nagata, H Moriyama, H Kobayashi, T Akisaki, H Ueda, K Hara, K Yokono

Study Type : Human: Case Report

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Diabetes Mellitus: Type 1 : CK\(1197\) : AC\(235\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Guillain-Barré syndrome following H1N1 immunization in a pediatric patient has been reported.](#) - GMI Summary

Pubmed Data : Ann Pharmacother. 2010 Jul-Aug;44(7-8):1330-3. Epub 2010 May 18. PMID: [20484170](#)

Article Published Date : Jul 01, 2010

Authors : Marie-Eve Tremblay, Aurélie Closon, Guy D'Anjou, Jean-François Bussières

Study Type : Human: Case Report

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[H1N1 vaccination has been linked to possible new-onset seizure.](#) - GMI Summary

Pubmed Data : Pharmacotherapy. 2011 Jan;31(1):113. PMID: [21182364](#)

Article Published Date : Jan 01, 2011

Authors : [No authors listed]

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Seizures : CK\(135\) : AC\(33\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination did not reduce the risk of subsequent hospital admission among patients with vaccine failure. These findings do not support the hypothesis that vaccination mitigates influenza illness severity.](#) - GMI Summary

Pubmed Data : Vaccine. 2014 Jan 16 ;32(4):453-7. Epub 2013 Nov 26. PMID: [24291201](#)

Article Published Date : Jan 15, 2014

Authors : Huong Q McLean, Jennifer K Meece, Edward A Belongia

Study Type : Human: Case Report

Additional Links

Diseases : [Influenza : CK\(656\) : AC\(99\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccination has been reported to cause miller fisher syndrome.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1327-9. PMID: [21987549](#)

Article Published Date : Oct 01, 2011

Authors : Ashkan Shoamanesh, Kristine Chapman, Anthony Traboulsee

Study Type : Human: Case Report

Additional Links

Diseases : [Guillain Barre Syndrome: Miller Fisher Variant : CK\(13\) : AC\(2\)](#), [Miller Fisher Syndrome : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

[Influenza vaccine has been reported to be a possible trigger of rhabdomyolysis induced acute renal failure in those taking statin drugs.](#) - GMI Summary

Pubmed Data : Nephrol Dial Transplant. 2000 May ;15(5):740-1. PMID: [10809833](#)

Article Published Date : May 01, 2000

Authors : E Plotkin, J Bernheim, S Ben-Chetrit, A Mor, Z Korzets

Study Type : Human: Case Report

Additional Links

Diseases : [Rhabdomyolysis : CK\(165\) : AC\(38\)](#), [Statin-Induced Pathologies : CK\(1600\) : AC\(320\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#)

Problem Substances : [Statin Drugs : CK\(3971\) : AC\(475\)](#)

Adverse Pharmacological Actions : [Myotoxicity : CK\(327\) : AC\(80\)](#)

[ransverse myelitis has been reported in association with a nasal attenuated novel influenza A\(H1N1\) vaccine.](#) - GMI Summary

Pubmed Data : Arch Neurol. 2010 Aug;67(8):1018-20. PMID: [20697056](#)

Article Published Date : Aug 01, 2010

Authors : Wafa Akkad, Bassel Salem, Jerome W Freeman, Mark K Huntington

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Nasal : CK\(3\) : AC\(1\)](#)

Influenza vaccines may induce hepatitis-B virus-related vasculitis and severe neuropathy. - GMI Summary

Pubmed Data : J Cardiovasc Pharmacol. 2003 Sep;42(3):329-38. PMID: [18579284](#)

Article Published Date : Sep 01, 2003

Authors : Yuko Wada, Chie Yanagihara, Yo Nishimura, Nobuyuki Oka

Study Type : Commentary

Additional Links

Diseases : [Peripheral Neuropathies](#) : CK(191) : AC(31), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Swine flu vaccine adjuvants may cause harm in patients with autoimmune diseases such as multiple sclerosis. - GMI Summary

Pubmed Data : Med Hypotheses. 2010 Feb 18. Epub 2010 Feb 18. PMID: [20171793](#)

Article Published Date : Feb 18, 2010

Authors : Serefnur Oztürk

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Multiple Sclerosis](#) : CK(746) : AC(133)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Influenza](#) : CK(356) : AC(37)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: [Vaccination: Mumps-Measles-Rubella \(MMR\)](#)

"The design and reporting of safety outcomes in MMR vaccine studies, both pre- and post-marketing, are largely inadequate." - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2012 ;2:CD004407. Epub 2012 Feb 15. PMID: [22336803](#)

Article Published Date : Dec 31, 2011

Authors : Vittorio Demicheli, Alessandro Rivetti, Maria Grazia Debalini, Carlo Di Pietrantonj

Study Type : Meta Analysis

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Mumps](#) : CK(41) : AC(1), [Rubella](#) : CK(54) : AC(4)

Additional Keywords : [Rubella](#) : CK(54) : AC(4), [Vaccine Safety](#) : CK(21) : AC(2)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

Thimerosal-containing vaccines are associated with autism prevalence and

measles-containing vaccines are associated with serious neurological disorders. - GMI Summary

Pubmed Data : Med Sci Monit. 2004 Mar;10(3):PI33-9. Epub 2004 Mar 1. PMID: [14976450](#)

Article Published Date : Mar 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Meta Analysis

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Vaccination is associated with a rare autoimmune neurological condition transverse myelitis. - GMI Summary

Pubmed Data : Lupus. 2009 Nov;18(13):1198-204. PMID: [19880568](#)

Article Published Date : Nov 01, 2009

Authors : N Agmon-Levin, S Kivity, M Szyper-Kravitz, Y Shoenfeld

Study Type : Meta Analysis

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Administration of varicella vaccine before the age of 15 months, and the prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease. - GMI Summary

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Mullooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#), [Corticosteroid-Induced Toxicity : CK\(78\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Autistic children have elevated levels of measles antibodies indicating that measles vaccination may be causing autoimmunity in these children. - GMI Summary

Pubmed Data : Pediatr Neurol. 2003 Apr;28(4):292-4. PMID: [12849883](#)

Article Published Date : Apr 01, 2003

Authors : Vijendra K Singh, Ryan L Jensen

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Children vaccinated with MMR before age 10 are at significantly higher risk of multiple sclerosis. - GMI Summary

Pubmed Data : Eur J Epidemiol. 2009;24(9):541-52. Epub 2009 Jul 26. PMID: [19633994](#)

Article Published Date : Jan 01, 2009

Authors : Cecilia Ahlgren, Kjell Torén, Anders Odén, Oluf Andersen

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis](#) : CK(746) : AC(133), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures](#) : CK(83) : AC(5), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Varicella](#) : CK(50) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population.](#) - GMI Summary

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)

Article Published Date : Dec 31, 2013

Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8), [Mumps](#) : CK(41) : AC(1), [Rubella](#) : CK(54) : AC(4)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Brachytherapy](#) : CK(10) : AC(1), [Vaccination: Measles](#) : CK(157) : AC(16), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Fifty-one percent of cases of patients in a 1998/1999 mumps outbreak had at least one MMR vaccination, indicating their effectiveness may be overestimated.](#) - GMI Summary

Pubmed Data : Vaccine. 2005 Jul 1 ;23(31):4070-4. PMID: [15950329](#)

Article Published Date : Jun 30, 2005

Authors : Richard Harling, Joanne M White, Mary E Ramsay, Karen F Macsween, Corry van den Bosch

Study Type : Human Study

Additional Links

Diseases : [Mumps](#) : CK(41) : AC(1)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Incidence of adverse reactions to vaccines in pediatric populations are under-reported and may be as high as 43.4% for certain vaccine combinations.](#) - GMI Summary

Pubmed Data : Clin Drug Investig. 2004;24(8):457-63. PMID: [17523706](#)

Article Published Date : Jan 01, 2004

Authors : Pilar Carrasco-Garrido, Carmen Gallardo-Pino, Rodrigo Jiménez-García, Miguel A Tapias, Angel Gil de Miguel

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Measles virus DNA from the MMR vaccine has been found in peripheral mononuclear cells in patients with ulcerative colitis and children with autism, indicating its possible role in the pathogenesis of these disorders.](#) - GMI

Summary

Pubmed Data : Dig Dis Sci. 2000 Apr;45(4):723-9. PMID: [10759242](#)

Article Published Date : Apr 01, 2000

Authors : H Kawashima, T Mori, Y Kashiwagi, K Takekuma, A Hoshika, A Wakefield

Study Type : Human Study

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Inflammatory Bowel Diseases : CK\(686\) : AC\(106\)](#), [Ulcerative Colitis : CK\(200\) : AC\(40\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Measles, mumps, and rubella catch up immunisation in a measles epidemic did not appear to confer protection and was associated with a variety of new side effects of the vaccine.](#) - GMI Summary

Pubmed Data : BMJ. 1995 Jun 24 ;310(6995):1629-32. PMID: [7795447](#)

Article Published Date : Jun 23, 1995

Authors : R J Roberts, Q D Sandifer, M R Evans, M Z Nolan-Farrell, P M Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Measles-mumps-rubella vaccine that is given in the second year of life is associated with an increased risk of immune thrombocytopenia purpura.](#) - GMI Summary

Pubmed Data : Pediatrics. 2008 Mar;121(3):e687-92. PMID: [18310189](#)

Article Published Date : Mar 01, 2008

Authors : Eric K France, Jason Glanz, Stanley Xu, Simon Hambidge, Kristi Yamasaki, Steve B Black, Michael Marcy, John P Mullooly, Lisa A Jackson, James Nordin, Edward A Belongia, K Hohman, Robert T Chen, Robert Davis,

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccination is associated with an increased risk for idiopathic thrombocytopaenic purpura.](#) - GMI Summary

Pubmed Data : Br J Clin Pharmacol. 2003 Jan;55(1):107-11. PMID: [12534647](#)

Article Published Date : Jan 01, 2003

Authors : Corri Black, James A Kaye, Hershel Jick

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Thrombocytopenia : CK\(231\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccination is associated with an increased risk of developing acute immune thrombocytopenia in childhood.](#) - GMI Summary

Pubmed Data : Drug Saf. 2010;33(1):65-72. PMID: [20000868](#)

Article Published Date : Jan 01, 2010

Authors : Federica Bertuola, Carla Morando, Francesca Menniti-Ippolito, Roberto Da Cas, Annalisa Capuano, Giorgio Perilongo, Liviana Da Dalt

Study Type : Human Study

Additional Links

Diseases : [Thrombocytopenia](#) : CK(231) : AC(25)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) - GMI Summary

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Combinations](#) : CK(20) : AC(2), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Polio](#) : CK(94) : AC(15)

[The measles-mumps-rubella vaccine causes autoantibodies to be formed against myelin basic protein \(the protective coating of the nerves\) contributing to the pathogenesis of autism.](#) - GMI Summary

Pubmed Data : J Biomed Sci. 2002 Jul-Aug;9(4):359-64. PMID: [12145534](#)

Article Published Date : Jul 01, 2002

Authors : Vijendra K Singh, Sheren X Lin, Elizabeth Newell, Courtney Nelson

Study Type : Human Study

Additional Links

Diseases : [Autism](#) : CK(570) : AC(65), [Autism Spectrum Disorders](#) : CK(1160) : AC(112), [Autoimmune Diseases](#) : CK(5523) : AC(880), [Measles](#) : CK(278) : AC(8)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[There is evidence that measles vaccine recipients can shed measles vaccine.](#) - GMI Summary

Pubmed Data : J Clin Microbiol. 1995 Sep ;33(9):2485-8. PMID: [7494055](#)

Article Published Date : Aug 31, 1995

Authors : P A Rota, A S Khan, E Durigon, T Yuran, Y S Villamarzo, W J Bellini

Study Type : Human Study

Additional Links

Diseases : [Measles](#) : CK(278) : AC(8)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30), [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Measles](#) : CK(157) : AC(16), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Thrombocytopenic purpura following vaccination in early childhood has been reported.](#) - GMI Summary

Pubmed Data : J Chin Med Assoc. 2010 Dec;73(12):634-7. PMID: [21145511](#)

Article Published Date : Dec 01, 2010

Authors : Yuh-Lin Hsieh, Lung-Huang Lin

Study Type : Human Study

Additional Links

Diseases : [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[Vaccination timing and co-administration may be associated with increased mortality, especially in females.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 May 29;24(22):4701-8. Epub 2006 Mar 31. PMID: [16621182](#)

Article Published Date : May 29, 2006

Authors : Peter Aaby, Henrik Jensen, Gijs Walraven

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: BCG \(Tuberculosis\) : CK\(33\) : AC\(4\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Vaccination-associated adverse events occur in approximately 1 of every 6 toddlers receiving measles-mumps-rubella vaccine dose 1, with high fever occurring in 1 of 20](#) - GMI Summary

Pubmed Data : Pediatrics. 2006 Oct;118(4):1422-30. PMID: [17015532](#)

Article Published Date : Oct 01, 2006

Authors : Charles W LeBaron, Daoling Bi, Bradley J Sullivan, Carol Beck, Paul Gargiullo

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

["Mumps outbreak among vaccinated university students associated with a large party, the Netherlands, 2010."](#) - GMI Summary

Pubmed Data : Vaccine. 2012 Jun 29 ;30(31):4676-80. Epub 2012 May 8. PMID: [22579874](#)

Article Published Date : Jun 28, 2012

Authors : Katie Greenland, Jane Whelan, Ewout Fanoy, Marjon Borgert, Koen Hulshof, Kioe-Bing Yap, Corien Swaan, Tjibbe Donker, Rob van Binnendijk, Hester de Melker, Susan Hahné

Study Type : Human: Case Report

Additional Links

Diseases : [Mumps : CK\(41\) : AC\(1\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Antibodies formed to rubella virus induce demyelination in rat brain cells, indicating that infection with and/or vaccination against rubella may induce autoimmune demyelination.](#) - GMI Summary

Pubmed Data : J Neurosci Res. 2001 Sep 1;65(5):446-54. PMID: [11536329](#)

Article Published Date : Sep 01, 2001

Authors : C Besson Duvanel, P Honegger, J M Matthieu

Study Type : Animal Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Aborted fetal cells \(diploid\) have been used to create the rubella, measles, mumps, rabies, polio, smallpox, hepatitis A, chickenpox, and herpes zoster vaccines.](#) - GMI Summary

Pubmed Data : Cuad Bioet. 2008 May-Aug;19(66):321-53. PMID: [18611078](#)

Article Published Date : May 01, 2008

Authors : José Luís Redondo Calderón

Study Type : Review

Additional Links

Additional Keywords : [Diploid Cell Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: Measles : CK\(157\)](#)

: [AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Autoimmune autistic disorder, a major subset of autism, is associated with autoantibody formation caused by viral \(wild and vaccine-induced\) infection.](#) - GMI Summary

Pubmed Data : Ann Clin Psychiatry. 2009 Jul-Sep;21(3):148-61. PMID: [19758536](#)

Article Published Date : Jul 01, 2009

Authors : Vijendra K Singh

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Biological assays lend support to the association between measles virus or MMR and autism.](#) - GMI Summary

Pubmed Data : J Neurovirol. 2005 Feb ;11(1):1-10. PMID: [15804954](#)

Article Published Date : Jan 31, 2005

Authors : Jane E Libbey, Thayne L Sweeten, William M McMahon, Robert S Fujinami

Study Type : Review

Additional Links

Diseases : [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Identification of conformational neutralization sites on the fusion protein of mumps virus.](#) - GMI Summary

Pubmed Data : J Gen Virol. 2015 Jan 22. Epub 2015 Jan 22. PMID: [25614584](#)

Article Published Date : Jan 21, 2015

Authors : Maja Šantak, Claes Örvell, Tanja Košutić Gulija

Study Type : Review

Additional Links

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[MMR vaccine may induce autoantibody formation against the gut \(secretin or its receptor\) and/or the brain, contributing to the pathogenesis of autism-spectrum disorder.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2003 May;60(5):650-3. PMID: [12710897](#)

Article Published Date : May 01, 2003

Authors : Bijal K Mehta, Kerim M Munir

Study Type : Commentary

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Molecular Mimicry : CK\(47\) : AC\(10\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#)

- GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Vaccination: Measles](#)

["A history of prior vaccination is not always associated with immunity nor with the presence of specific antibodies."](#) - GMI Summary

Pubmed Data : Clin Invest Med. 1988 Aug ;11(4):304-9. PMID: [3168353](#)

Article Published Date : Jul 31, 1988

Authors : L Sekla, W Stackiw, G Eibisch, I Johnson

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[20.7% \(6 of 29\) of persons known to have received measles vaccine had non-protective titers.](#) - GMI Summary

Pubmed Data : Am J Trop Med Hyg. 2008 Nov;79(5):787-92. PMID: [18981523](#)

Article Published Date : Nov 01, 2008

Authors : Inácio M Mandomando, Denise Naniche, Marcela F Pasetti, Xavier Vallès, Lilian Cuberos, Ariel Nhacolo, Karen L Kotloff, Helder Martins, Myron M Levine, Pedro Alonso

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A 1993 outbreak of measles in a highly immunised Australian population.](#) - GMI Summary

Pubmed Data : Aust J Public Health. 1994 Sep ;18(3):249-52. PMID: [7841251](#)

Article Published Date : Aug 31, 1994

Authors : A Herceg, I Passaris, C Mead

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A low measles vaccine efficacy rate may explain the less-than-expected gains attributable to vaccination. - GMI Summary](#)

Pubmed Data : BMC Int Health Hum Rights. 2009 ;9 Suppl 1:S6. Epub 2009 Oct 14. PMID: [19828064](#)

Article Published Date : Dec 31, 2008

Authors : Robert J Ledogar, John Fleming, Neil Andersson

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A major measles epidemic occurred in 1989 in the region of Quebec despite a 99% vaccine coverage. - GMI Summary](#)

Pubmed Data : Can J Public Health. 1991 May-Jun;82(3):189-90. PMID: [1884314](#)

Article Published Date : Apr 30, 1991

Authors : N Boulianne, G De Serres, B Duval, J R Joly, F Meyer, P Déry, M Alary, D Le Hénaff, N Thériault

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak at a college with a prematriculation immunization requirement. - GMI Summary](#)

Pubmed Data : Am J Public Health. 1991 Mar ;81(3):360-4. PMID: [1994745](#)

Article Published Date : Feb 28, 1991

Authors : B S Hersh, L E Markowitz, R E Hoffman, D R Hoff, M J Doran, J C Fleishman, S R Preblud, W A Orenstein

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak in Montana in 1985 indicates vaccine failure. - GMI Summary](#)

Pubmed Data : Am J Epidemiol. 1987 Sep ;126(3):438-49. PMID: [3618578](#)

Article Published Date : Aug 31, 1987

Authors : R M Davis, E D Whitman, W A Orenstein, S R Preblud, L E Markowitz, A R Hinman

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[A measles outbreak was reported in a highly vaccinated population, San Diego, 2008 - GMI Summary](#)

Pubmed Data : Pediatrics. 2010 Apr ;125(4):747-55. Epub 2010 Mar 22. PMID: [20308208](#)

Article Published Date : Mar 31, 2010

Authors : David E Sugerman, Albert E Barskey, Maryann G Delea, Ismael R Ortega-Sanchez, Daoling Bi, Kimberly J Ralston, Paul A Rota, Karen Waters-Montijo, Charles W Lebaron

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[An outbreak of measles occurred in a high school with a documented vaccination level of 98 per cent. - GMI Summary](#)

Pubmed Data : Am J Public Health. 1987 Apr ;77(4):434-8. PMID: [3826461](#)

Article Published Date : Mar 31, 1987

Authors : B M Nkowane, S W Bart, W A Orenstein, M Baltier

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Despite a high coverage with measles vaccines in parts of west Africa, epidemics of measles occur with reduced severity in an increasing proportion of older children who have been vaccinated. - GMI Summary](#)

Pubmed Data : Lancet. 1999 Jan 9 ;353(9147):98-102. PMID: [10023894](#)

Article Published Date : Jan 08, 1999

Authors : H C Whittle, P Aaby, B Samb, H Jensen, J Bennett, F Simondon

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population. - GMI Summary](#)

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)

Article Published Date : Dec 31, 2013

Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Mumps : CK\(41\) : AC\(1\)](#), [Rubella : CK\(54\) : AC\(4\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Brachytherapy : CK\(10\) : AC\(1\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls. - GMI Summary](#)

Pubmed Data : Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18. PMID: [21093496](#)

Article Published Date : Jan 10, 2011

Authors : J Agergaard, E Nante, G Poulstrup, J Nielsen, K L Flanagan, L Østergaard, C S Benn, P Aaby

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Even though 95% of the children had measles antibodies after vaccination, vaccine efficacy was not more than 68%. - GMI Summary](#)

Pubmed Data : J Infect Dis. 1990 Nov ;162(5):1043-8. PMID: [2230232](#)

Article Published Date : Oct 31, 1990

Authors : P Aaby, K Knudsen, T G Jensen, J Thårup, A Poulsen, M Sodemann, M C da Silva, H Whittle

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[High titre measles vaccination increases female mortality in those receiving immunization in West Africa. - GMI Summary](#)

Pubmed Data : Int J Epidemiol. 1996 Jun;25(3):665-73. PMID: [8671571](#)

Article Published Date : Jun 01, 1996

Authors : K M Knudsen, P Aaby, H Whittle, M Rowe, B Samb, F Simondon, J Sterne, P Fine

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[High-titer measles vaccination before 9 months of age has been linked to increased female mortality. - GMI Summary](#)

Pubmed Data : Semin Pediatr Infect Dis. 2003 Jul;14(3):220-32. PMID: [12913835](#)

Article Published Date : Jul 01, 2003

Authors : Peter Aaby, Henrik Jensen, Francois Simondon, Hilton Whittle

Study Type : Human Study

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[In a measles outbreak from March 1991 to April 1992 in Rio de Janeiro 76.4% of those suspected to be infected had received measles vaccine before their first birthday. - GMI Summary](#)

Pubmed Data : Rev Soc Bras Med Trop. 1995 Oct-Dec;28(4):339-43. PMID: [8668833](#)

Article Published Date : Sep 30, 1995

Authors : S A de Oliveira, W N Soares, M O Dalston, M T de Almeida, A J Costa

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Laboratory characterization of measles virus infection in previously vaccinated and unvaccinated individuals. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2011 Jul ;204 Suppl 1:S549-58. PMID: [21666212](#)

Article Published Date : Jun 30, 2011

Authors : Carole J Hickman, Terri B Hyde, Sun Bae Sowers, Sara Mercader, Marcia McGrew, Nobia J Williams, Judy A Beeler, Susette Audet, Bryan Kiehl, Robin Nandy, Azaibi Tamin, William J Bellini

Study Type : Human Study

Additional Links

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles outbreak in a fully immunized secondary-school population with up to 99 percent vaccination.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1987 Mar 26 ;316(13):771-4. PMID: [3821823](#)

Article Published Date : Mar 25, 1987

Authors : T L Gustafson, A W Lievens, P A Brunell, R G Moellenberg, C M Buttery, L M Sehulster

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Mumps orchitis occurs vaccinated postpubertal males.](#) - GMI Summary

Pubmed Data : Korean J Urol. 2012 Dec ;53(12):865-9. Epub 2012 Dec 20. PMID: [23301132](#)

Article Published Date : Nov 30, 2012

Authors : Bum Sik Tae, Byeong Kuk Ham, Jae Heon Kim, Jae Young Park, Jae Hyun Bae

Study Type : Human Study

Additional Links

Diseases : [Orchitis : CK\(2\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Passive acquired immunity against measles in infants born to naturally infected and vaccinated mothers.](#) - GMI Summary

Pubmed Data : Med Sci Monit. 2003 Dec ;9(12):CR541-6. PMID: [14646978](#)

Article Published Date : Nov 30, 2003

Authors : Leszek Szenborn, Annedore Tischer, Jerzy Pejcz, Zbigniew Rudkowski, Marta Wójcik

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Passive immunity against measles is superior in infants of mothers who experienced naturally acquired measles infection versus those who were vaccinated.](#) - GMI Summary

Pubmed Data : Vaccine. 1997 Apr-May;15(6-7):620-3. PMID: [9178461](#)

Article Published Date : Mar 31, 1997

Authors : G De Serres, J R Joly, M Fauvel, F Meyer, B Mâsse, N Boulianne

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Health Myths Explored : CK\(22\) : AC\(4\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Primary and secondary vaccine failure may explain the 1992 measles epidemic in Cape Town.](#) - GMI Summary

Pubmed Data : S Afr Med J. 1994 Mar ;84(3):145-9. PMID: [7740350](#)

Article Published Date : Feb 28, 1994

Authors : N Coetzee, G D Hussey, G Visser, P Barron, A Keen

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[The occurrence of secondary vaccine failure and vaccine-modified measles in the United States may lead to underreporting of measles cases and result in overestimation of vaccine efficacy in h - GMI Summary](#)

Pubmed Data : JAMA. 1990 May 9 ;263(18):2467-71. PMID: [2278542](#)

Article Published Date : May 08, 1990

Authors : M B Edmonson, D G Addiss, J T McPherson, J L Berg, S R Circo, J P Davis

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Measles : CK\(278\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[There is evidence that measles vaccine recipients can shed measles vaccine. - GMI Summary](#)

Pubmed Data : J Clin Microbiol. 1995 Sep ;33(9):2485-8. PMID: [7494055](#)

Article Published Date : Aug 31, 1995

Authors : P A Rota, A S Khan, E Durigon, T Yuran, Y S Villamarzo, W J Bellini

Study Type : Human Study

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

[Case report: an outbreak of measles among persons with prior evidence of immunity, New York City, 2011. - GMI Summary](#)

Pubmed Data : Clin Infect Dis. 2014 May ;58(9):1205-10. Epub 2014 Feb 27. PMID: [24585562](#)

Article Published Date : Apr 30, 2014

Authors : Jennifer B Rosen, Jennifer S Rota, Carole J Hickman, Sun B Sowers, Sara Mercader, Paul A Rota, William J Bellini, Ada J Huang, Margaret K Doll, Jane R Zucker, Christopher M Zimmerman

Study Type : Human: Case Report

Additional Links

Diseases : [Measles : CK\(278\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Measles vaccine and glyphosate-induced parkinsonism has been reported. - GMI Summary](#)

Pubmed Data : Arq Neuropsiquiatr. 2003 Jun ;61(2B):381-6. Epub 2003 Jul 28. PMID: [12894271](#)

Article Published Date : Jun 01, 2003

Authors : Maria do Desterro Leiros da Costa, Lílian Regina Gonçalves, Egberto Reis Barbosa, Luiz Alberto Bacheschi

Study Type : Human: Case Report

Additional Links

Diseases : [Glyphosate Toxicity : CK\(29\) : AC\(14\)](#), [Parkinsonian Disorders : CK\(15\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)
Problem Substances : [Glyphosate : CK\(403\) : AC\(130\)](#)
Adverse Pharmacological Actions : [Neurotoxic : CK\(1116\) : AC\(188\)](#)

[In this animal study measles vaccine did not prevent infection or disease against wild type MeV. - GMI Summary](#)

Pubmed Data : MBio. 2014 ;5(2):e01047. Epub 2014 Apr 15. PMID: [24736226](#)
Article Published Date : Dec 31, 2013
Authors : Wen-Hsuan W Lin, Chien-Hsiung Pan, Robert J Adams, Beth L Laube, Diane E Griffin
Study Type : Animal Study
Additional Links
Diseases : [Measles : CK\(278\) : AC\(8\)](#)
Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Aborted fetal cells \(diploid\) have been used to create the rubella, measles, mumps, rabies, polio, smallpox, hepatitis A, chickenpox, and herpes zoster vaccines. - GMI Summary](#)

Pubmed Data : Cuad Bioet. 2008 May-Aug;19(66):321-53. PMID: [18611078](#)
Article Published Date : May 01, 2008
Authors : José Luís Redondo Calderón
Study Type : Review
Additional Links
Additional Keywords : [Diploid Cell Vaccines : CK\(1\) : AC\(1\)](#)
Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Development of a new live attenuated mumps virus vaccine in human diploid cells. - GMI Summary](#)

Pubmed Data : Biologicals. 1991 Jul ;19(3):203-11. PMID: [1954002](#)
Article Published Date : Jun 30, 1991
Authors : A Sassani, H Mirchamsy, A Shafyi, P Ahourai, J Razavi, M R Gholami, A Mohammadi, A Ezzi, M Rahmani, G Fateh
Study Type : Review
Additional Links
Additional Keywords : [Diploid Cell Vaccines : CK\(1\) : AC\(1\)](#)
Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[Live attenuated virus Vaccines produced on chicken-derived cells contain low levels of particle-associated reverse transcriptase \(RT\). - GMI Summary](#)

Pubmed Data : J Virol. 1997 Apr ;71(4):3005-12. PMID: [9060660](#)
Article Published Date : Mar 31, 1997
Authors : R N Weissmahr, J Schüpbach, J Böni
Study Type : Review
Additional Links
Diseases : [Endogenous avian retrovirus \(EAV-0\) : CK\(1\) : AC\(1\)](#), [Retroviruses : CK\(7\) : AC\(1\)](#)
Additional Keywords : [Cross-Species Infection : CK\(4\) : AC\(3\)](#), [Endogenous Retroviruses : CK\(53\) : AC\(12\)](#), [Live Attenuated Vaccines : CK\(5\) : AC\(2\)](#), [Retroviruses : CK\(10\) : AC\(10\)](#)
Anti Therapeutic Actions : [Vaccination: Measles : CK\(157\) : AC\(16\)](#)
Problem Substances : [Endogenous avian retrovirus \(EAV-0\) : CK\(3\) : AC\(1\)](#)

[Measles vaccination in developing countries has resulted in higher infant mortality rates. - GMI Summary](#)

Pubmed Data : BMJ. 1993 Nov 20;307(6915):1294-5. PMID: [8257878](#)
Article Published Date : Nov 20, 1993

Authors : A J Hall, F T Cutts

Study Type : Review

Additional Links

Diseases : [Child Mortality : CK\(64\) : AC\(8\)](#), [Measles : CK\(278\) : AC\(8\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

Topic: [Vaccination: Varicella \(Chicken pox\)](#)

[Administration of varicella vaccine before the age of 15 months, and the prescription of oral steroids, may be associated with a slightly increased risk of breakthrough disease. - GMI Summary](#)

Pubmed Data : Pediatrics. 2003 Aug;112(2):e98-103. PMID: [12897314](#)

Article Published Date : Aug 01, 2003

Authors : Thomas Verstraeten, Aisha O Jumaan, John P Moolooly, Jane F Seward, Hector S Izurieta, Frank DeStefano, Steven B Black, Robert T Chen,

Study Type : Human Study

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#), [Corticosteroid-Induced Toxicity : CK\(78\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Approximately 1 in every 5 children who receives 1 dose of varicella vaccine may develop varicella disease, also known as breakthrough disease, if exposed to varicella-zoster virus. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2008 Mar 1 ;197 Suppl 2:S127-31. PMID: [18419385](#)

Article Published Date : Feb 29, 2008

Authors : Sandra S Chaves, John Zhang, Rachel Civen, Barbara M Watson, Tina Carbajal, Dana Perella, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Between 1995 and 2005 25,306 adverse events were reported from varicella vaccine. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2008 Mar 1;197 Suppl 2:S170-7. PMID: [18419393](#)

Article Published Date : Mar 01, 2008

Authors : Sandra S Chaves, Penina Haber, Kimp Walton, Robert P Wise, Hector S Izurieta, D Scott Schmid, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Combined MMR and varicella live vaccine is associated with higher rates of febrile convulsion than giving the vaccines separately. - GMI Summary](#)

Pubmed Data : Vaccine. 2009 Jul 23;27(34):4656-61. Epub 2009 Jun 9. PMID: [19520201](#)

Article Published Date : Jul 23, 2009

Authors : Steven J Jacobsen, Bradley K Ackerson, Lina S Sy, Trung N Tran, Tonia L Jones, Janis F Yao, Fagen Xie, T Craig Cheetham, Patricia Saddier

Study Type : Human Study

Additional Links

Diseases : [Febrile Seizures : CK\(83\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Increasing varicella vaccine coverage in Australia between 1998-2009 corresponds with increased levels of herpes zoster \(shingles\) cases managed in the same time period.](#) - GMI Summary

Pubmed Data : Med J Aust. 2010 Jul 19;193(2):110-3. PMID: [20642419](#)

Article Published Date : Jul 19, 2010

Authors : Mark R Nelson, Helena C Britt, Christopher M Harrison

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Shingles : CK\(472\) : AC\(35\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Chicken Pox \(Varicella\) Shingles \(Herpes Zoster\) Connection : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Loss of vaccine-induced immunity to varicella over time.](#) - GMI Summary

Pubmed Data : N Engl J Med. 2007 Mar 15 ;356(11):1121-9. PMID: [17360990](#)

Article Published Date : Mar 14, 2007

Authors : Sandra S Chaves, Paul Gargiullo, John X Zhang, Rachel Civen, Dalya Guris, Laurene Mascola, Jane F Seward

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Near complete vaccination coverage for varicella does not prevent outbreaks in those treated.](#) - GMI Summary

Pubmed Data : Pediatrics. 2006 Jun;117(6):e1070-7. PMID: [16740809](#)

Article Published Date : Jun 01, 2006

Authors : Adriana S Lopez, Dalya Guris, Laura Zimmerman, Linda Gladden, Tamara Moore, Dirk T Haselow, Vladimir N Loparev, D Scott Schmid, Aisha O Jumaan, Sandra L Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy.](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease : CK\(32\) : AC\(9\)](#), [Neuropathy: Small Fiber : CK\(10\) : AC\(1\)](#), [Rabies : CK\(13\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella outbreaks occur in vaccinated populations, even when receiving 2 doses.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2009 Aug;28(8):678-81. PMID: [19593254](#)

Article Published Date : Aug 01, 2009

Authors : Philip L Gould, Jessica Leung, Connie Scott, D Scott Schmid, Helen Deng, Adriana Lopez, Sandra S Chaves, Meredith Reynolds, Linda Gladden, Rafael Harpaz, Sandra Snow

Study Type : Human Study

Additional Links

Diseases : [Varicella : CK\(50\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccination in South Korea, despite high compliance rates \(via mandatory vaccination\), has not eradicated the disease. - GMI Summary](#)

Pubmed Data : Clin Vaccine Immunol. 2014 May ;21(5):762-8. Epub 2014 Mar 26. PMID: [24671555](#)

Article Published Date : Apr 30, 2014

Authors : Sung Hee Oh, Eun Hwa Choi, Seon Hee Shin, Yun-Kyung Kim, Jin Keun Chang, Kyong Min Choi, Jae Kyun Hur, Kyung-Hyo Kim, Jae Youn Kim, Eun Hee Chung, Soo Young Lee, Su Eun Park, Sungho Cha, Kwang-Nam Kim, Sang Hyuk Ma, Byung Wook Eun, Nam Hee Kim, Dae Sun Jo, Bo Youl Choi, Shin Ah Kim

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been associated with viremia and streptococcal toxic shock syndrome. - GMI Summary](#)

Pubmed Data : Med J Aust. 2009 Apr 20;190(8):451-3. PMID: [19374621](#)

Article Published Date : Apr 20, 2009

Authors : Claire M Italiano, Cheryl S Toi, Simon P Chan, Dominic E Dwyer

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Viremia : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to cause chronic, acyclovir-resistant herpes zoster infection in an immunosuppressed child. - GMI Summary](#)

Pubmed Data : J Infect Dis. 2003 Oct 1;188(7):954-9. Epub 2003 Sep 26. PMID: [14513413](#)

Article Published Date : Oct 01, 2003

Authors : Myron J Levin, Karen M Dahl, Adriana Weinberg, Roger Giller, Amita Patel, Philip R Krause

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Acyclovir-Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine has been reported to viral meningitis in an immunocompetent child. - GMI Summary](#)

Pubmed Data : Ann Emerg Med. 2009 Jun;53(6):792-5. Epub 2008 Nov 22. PMID: [19028409](#)

Article Published Date : Jun 01, 2009

Authors : Sujit Iyer, Manoj K Mittal, Richard L Hodinka

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#), [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Additional Keywords : [Undefined : CK\(14\) : AC\(3\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine may be associated with aplastic anemia in children. - GMI Summary](#)

Pubmed Data : [Pediatr Infect Dis J. 2009 Aug;28\(8\):746-8. PMID: 19633522](#)

Article Published Date : Aug 01, 2009

Authors : Paola Angelini, Fotini Kavadas, Navneet Sharma, Susan E Richardson, Graham Tipples, Chaim Roifman, Yigal Dror, Yehuda Nofech-Mozes

Study Type : Human Study

Additional Links

Diseases : [Anemia: Aplastic : CK\(30\) : AC\(3\)](#), [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others - Article 2. - GMI Summary](#)

Pubmed Data : [J Infect Dis. 1997 Oct;176\(4\):1072-5. PMID: 9333170](#)

Article Published Date : Oct 01, 1997

Authors : P LaRussa, S Steinberg, F Meurice, A Gershon

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella vaccine virus can be contagious and infect others. - GMI Summary](#)

Pubmed Data : [Homeopathy. 2009 Apr;98\(2\):77-82. PMID: 9255208](#)

Article Published Date : Apr 01, 2009

Authors : M B Salzman, R G Sharrar, S Steinberg, P LaRussa

Study Type : Human Study

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Varicella-zoster vaccine has been linked to herpes zoster ophthalmicus and encephalitis as possible, though rare side effects. - GMI Summary](#)

Pubmed Data : [Pediatrics. 2010 Apr;125\(4\):e969-72. Epub 2010 Mar 1. PMID: 20194287](#)

Article Published Date : Apr 01, 2010

Authors : Giorgos Chouliaras, Vana Spoulou, Mark Quinlivan, Judith Breuer, Maria Theodoridou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis : CK\(23\) : AC\(4\)](#), [Herpes: Ocular : CK\(12\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[A chickenpox outbreak occurred in a school in which 97% of students without a prior history of chickenpox were vaccinated. - GMI Summary](#)

Pubmed Data : [Pediatrics. 2004 Mar ;113\(3 Pt 1\):455-9. PMID: 14993534](#)

Article Published Date : Feb 29, 2004

Authors : Barna D Tugwell, Lore E Lee, Hilary Gillette, Eileen M Lorber, Katrina Hedberg, Paul R Cieslak

Study Type : Human: Case Report

Additional Links

Diseases : [Chickenpox : CK\(110\) : AC\(8\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)
Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

"Varicella vaccination is less effective than the natural immunity that existed in prevaccine communities." - GMI Summary

Pubmed Data : Vaccine. 2012 Jun 1. Epub 2012 Jun 1. PMID: [22659447](#)

Article Published Date : May 31, 2012

Authors : G S Goldman, P G King

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Aborted fetal cells (diploid) have been used to create the rubella, measles, mumps, rabies, polio, smallpox, hepatitis A, chickenpox, and herpes zoster vaccines. - GMI Summary

Pubmed Data : Cuad Bioet. 2008 May-Aug;19(66):321-53. PMID: [18611078](#)

Article Published Date : May 01, 2008

Authors : José Luís Redondo Calderón

Study Type : Review

Additional Links

Additional Keywords : [Diploid Cell Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Viruses (wild-type or recombinant vaccine-type) can silently prime for and trigger central nervous system autoimmune disease. - GMI Summary

Pubmed Data : J Neurovirol. 2001 Jun;7(3):220-7. PMID: [11517396](#)

Article Published Date : Jun 01, 2001

Authors : D J Theil, I Tsunoda, F Rodriguez, J L Whitton, R S Fujinami

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Vaccination: Pertussis](#)

[The risk of adverse events from the pertussis outweighed the risk of pertussis infection during the period of 1970-83 in children living in non-deprived circumstances in Britain.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1985;61:395-405. PMID: [3835080](#)

Article Published Date : Jan 01, 1985

Authors : G T Stewart

Study Type : Meta Analysis

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

["Primary infections with either B. pertussis or Bordetella parapertussis stimulated a vigorous antibody response to ACT. In contrast, patients in whom DTP and DTaP vaccines failed had minimal ACT antibody responses."](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2004 Feb 15 ;38(4):502-7. Epub 2004 Jan 29. PMID: [14765342](#)

Article Published Date : Feb 14, 2004

Authors : James D Cherry, Dorothy X L Xing, Penny Newland, Kashmira Patel, Ulrich Heininger, Michael J Corbel

Study Type : Human Study

Additional Links

Diseases : [Parapertussis : CK\(10\) : AC\(1\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis \(Tdap\) vaccine in order to prevent pertussis infection in their offspring, it does not reduce](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[In Kings County Washington, between 2002-2007, of the 176 confirmed cases of pertussis in infants under age 1 seventy-seven percent were age-appropriately vaccinated.](#) - GMI Summary

Pubmed Data : Arch Pediatr Adolesc Med. 2011 Jul ;165(7):647-52. PMID: [21727277](#)

Article Published Date : Jul 01, 2011

Authors : Matthew P Hanson, Tao S Kwan-Gett, Atar Baer, Krista Rietberg, Mara Ohrt, Jeffrey S Duchin

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pertussis vaccination may activate a genetic predisposition for encephalopathy](#)

[in susceptible individuals.](#) - GMI Summary

Pubmed Data : Cytotechnology. 2002 Nov;40(1-3):139-49. PMID: [20447868](#)

Article Published Date : Nov 01, 2002

Authors : Anne M McIntosh, Jacinta McMahon, Leanne M Dibbens, Xenia Iona, John C Mulley, Ingrid E Scheffer, Samuel F Berkovic

Study Type : Human Study

Additional Links

Diseases : [Dravet syndrome](#) : CK(30) : AC(3), [Encephalitis](#) : CK(23) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Pertussis vaccine has been linked to hypotonic-hyporesponsive episodes \(HHE\) in infants and children.](#) - GMI Summary

Pubmed Data : Drug Saf. 2002;25(2):85-90. PMID: [11888351](#)

Article Published Date : Jan 01, 2002

Authors : Michael S Gold

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Serious adverse events associated with whole cell pertussis vaccine, e.g. sudden infant death syndrome and encephalopathy, may have occurred in metabolically vulnerable children.](#) - GMI Summary

Pubmed Data : Pharmazie. 2007 Apr;62(4):299-304. PMID: [19660877](#)

Article Published Date : Apr 01, 2007

Authors : Kumanan Wilson, Beth Potter, Douglas Manuel, Jennifer Keelan, Pranesh Chakraborty

Study Type : Human Study

Additional Links

Diseases : [Encephalopathy: Acute Necrotizing](#) : CK(20) : AC(2), [Sudden Infant Death Syndrome \(SIDS\)](#) : CK(138) : AC(18), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Since the 1993 pertussis epidemic in Cincinnati occurred primarily among children who had been appropriately immunized, it is clear that the whole-cell pertussis vaccine failed to give full protection against the disease.](#) - GMI Summary

Pubmed Data : N Engl J Med. 1994 Jul 7;331(1):16-21. PMID: [8202096](#)

Article Published Date : Jul 07, 1994

Authors : C D Christie, M L Marx, C D Marchant, S F Reising

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14), [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects.](#) - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance](#) : CK(148) : AC(37), [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Diphtheria](#) : CK(50) : AC(2)

Problem Substances : [Adjuvant](#) : CK(18) : AC(6), [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

[Vaccinated children and adults may serve as reservoirs for silent pertussis infection and become potential transmitters to unprotected infants.](#) - GMI Summary

Pubmed Data : Emerg Infect Dis. 2000 Sep-Oct;6(5):526-9. PMID: [10998384](#)

Article Published Date : Sep 01, 2000

Authors : I Srugo, D Benilevi, R Madeb, S Shapiro, T Shohat, E Somekh, Y Rimmar, V Gershtein, R Gershtein, E Marva, N Lahat

Study Type : Human Study

Additional Links

Diseases : [Pertussis](#) : CK(142) : AC(14), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Whooping Cough](#) : CK(66) : AC(7)

Additional Keywords : [Whooping Cough](#) : CK(66) : AC(7)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Whole cell pertussis vaccines may have been causing serious neurological disorders.](#) - GMI Summary

Pubmed Data : Brain Dev. 2004 Aug;26(5):296-300. PMID: [15165669](#)

Article Published Date : Aug 01, 2004

Authors : David A Geier, Mark R Geier

Study Type : Human Study

Additional Links

Diseases : [Infant Infections](#) : CK(410) : AC(44), [Infant Neurological Development](#) : CK(46) : AC(7), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Lactobacillus bulgaricus contains a substance which may improve immunogenicity and reduce the toxicity of pertussis vaccination \(whooping cough vaccine\).](#) - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 1986 Jan;(1):62-5. PMID: [3705806](#)

Article Published Date : Jan 01, 1986

Authors : I B Shepeleva, N S Zakharova, T N Remova, I G Bazhanova, M V Britsina

Study Type : Animal Study

Additional Links

Substances : [Lactobacillus bulgaricus](#) : CK(35) : AC(8)

Diseases : [Pertussis](#) : CK(142) : AC(14), [Whooping Cough](#) : CK(66) : AC(7)

Additional Keywords : [Vaccine Side Effect Attenuation](#) : CK(2) : AC(1)

Anti Therapeutic Actions : [Vaccination: Pertussis](#) : CK(116) : AC(14)

[Mice exhibit lung pathology after vaccination with pertussis vaccines.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Mar 8;25(12):2346-60. Epub 2006 Dec 12. PMID: [17224216](#)

Article Published Date : Mar 08, 2007

Authors : Rob J Vandebriel, Eric R Gremmer, Jolanda P Vermeulen, Sandra M M Hellwig, Jan A M A Dormans, Paul J M Roholl, Frits R Mooi

Study Type : Animal Study

Additional Links

Pharmacological Actions : [Tumor Necrosis Factor \(TNF\) Alpha Inhibitor](#) : CK(1021) : AC(365)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Pertussis](#) : CK(116) :

[Despite high coverage rates for primary immunization in infants and children pertussis incidence rates are increasing.](#) - GMI Summary

Pubmed Data : *Pediatr Infect Dis J.* 2005 May;24(5 Suppl):S10-8. PMID: [15876918](#)

Article Published Date : May 01, 2005

Authors : Tina Tan, Evelinda Trindade, Danuta Skowronski

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Additional Keywords : [Vaccine Resistance : CK\(11\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Pertussis vaccination and asthma: is there a link?](#) - GMI Summary

Pubmed Data : *JAMA.* 1994 Aug 24-31;272(8):592-3. PMID: [8057511](#)

Article Published Date : Aug 23, 1994

Authors : M R Odent, E E Culpin, T Kimmel

Study Type : Commentary

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Additional Keywords : [Diseases that are Linked : CK\(2142\) : AC\(272\)](#)

Anti Therapeutic Actions : [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

[Underestimation of central nervous system complications after pertussis immunization appears to be prevalent.](#) - GMI Summary

Pubmed Data : *Acta Paediatr Jpn.* 1991 Aug;33(4):421-7. PMID: [1792899](#)

Article Published Date : Aug 01, 1991

Authors : W Ehrengut

Study Type : Review

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#)

Topic: [Vaccination: Polio](#)

[Vaccination in infants less than 3 months is associated with an increased risk of sudden infant death syndrome.](#) - GMI Summary

Pubmed Data : *Fundam Clin Pharmacol.* 1995;9(3):263-70. PMID: [7557822](#)

Article Published Date : Jan 01, 1995

Authors : A P Jonville-Bera, E Autret, J Laugier

Study Type : Meta Analysis

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[At the present time, the only poliovirus-caused poliomyelitis cases reported in Brazil and other countries of the Americas are of vaccine etiology.](#) - GMI Summary

Pubmed Data : *Rev Panam Salud Publica.* 2000 Apr;7(4):219-24. PMID: [10846924](#)

Article Published Date : Apr 01, 2000

Authors : L H de Oliveira, C J Struchiner

Study Type : Human Study

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Additional Keywords : [Iatrogenic Poliomyelitis : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Oral Polio Vaccine : CK\(10\) : AC\(1\)](#), [Vaccination: Oral Polio Vaccine, Bivalent : CK\(10\) : AC\(1\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) - GMI Summary

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[The oral polio vaccine is unlikely to be able to eradicate polio from India.](#) - GMI Summary

Pubmed Data : Vaccine. 2008 Apr 16 ;26(17):2058-61. Epub 2008 Mar 14. PMID: [18378367](#)

Article Published Date : Apr 16, 2008

Authors : Yash Paul

Study Type : Human Study

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccination with measles after DTP and polio vaccine is associated with 2-fold increase in female mortality.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2007 Mar;26(3):247-52. PMID: [17484223](#)

Article Published Date : Mar 01, 2007

Authors : Peter Aaby, May-Lill Garly, Jens Nielsen, Henrik Ravn, Cesario Martins, Carlitos Balé, Amabelia Rodrigues, Christine Stabell Benn, Ida Maria Lisse

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccine-associated paralytic poliomyelitis \(VAPP\) has emerged as the](#)

[predominant form of the disease in the United States since 1980.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 1992 Feb;14(2):568-79. PMID: [1554844](#)

Article Published Date : Feb 01, 1992

Authors : P M Strebel, R W Sutter, S L Cochi, R J Biellik, E W Brink, O M Kew, M A Pallansch, W A Orenstein, A R Hinman

Study Type : Human Study

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Additional Keywords : [Iatrogenic Poliomyelitis : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Some oral poliovirus vaccines were contaminated with infectious SV40 after 1961.](#) - GMI Summary

Pubmed Data : Cancer Res. 2005 Nov 15 ;65(22):10273-9. PMID: [16288015](#)

Article Published Date : Nov 15, 2005

Authors : Rochelle Cutrone, John Lednicky, Glynis Dunn, Paola Rizzo, Maurizio Bocchetta, Konstantin Chumakov, Philip Minor, Michele Carbone

Study Type : Human In Vitro

Additional Links

Diseases : [Simian virus 40 \(SV40\) : CK\(7\) : AC\(5\)](#)

Additional Keywords : [Vaccine Contamination : CK\(5\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Problem Substances : [Simian virus 40 \(SV40\) : CK\(113\) : AC\(16\)](#)

[Case report: failure to clear persistent vaccine-derived neurovirulent poliovirus infection in an immunodeficient man.](#) - GMI Summary

Pubmed Data : Lancet. 2004 May 8 ;363(9420):1509-13. PMID: [15135598](#)

Article Published Date : May 07, 2004

Authors : Calman MacLennan, Glynis Dunn, Aarnoud P Huissoon, Dinakantha S Kumararatne, Javier Martin, Paula O'Leary, Ronald A Thompson, Husam Osman, Philip Wood, Philip Minor, David J Wood, Deenan Pillay

Study Type : Human: Case Report

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Simultaneous sudden infant death syndrome has been reported in twins two days after receiving mutiple vaccinations.](#) - GMI Summary

Pubmed Data : J Forensic Leg Med. 2007 Feb;14(2):87-91. PMID: [17654772](#)

Article Published Date : Feb 01, 2007

Authors : Yasemin Balci, Mehmet Tok, B Kenan Kocaturk, Cinar Yenilmez, Coşkun Yirulmaz

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

["New strategies for the elimination of polio from India."](#) - GMI Summary

Pubmed Data : Science. 2006 Nov 17 ;314(5802):1150-3. PMID: [17110580](#)

Article Published Date : Nov 17, 2006

Authors : Nicholas C Grassly, Christophe Fraser, Jay Wenger, Jagadish M Deshpande, Roland W Sutter, David L Heymann, R Bruce Aylward

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Differential diagnosis of acute flaccid paralysis and its role in poliomyelitis surveillance.](#) - GMI Summary

Pubmed Data : Epidemiol Rev. 2000 ;22(2):298-316. PMID: [11218380](#)

Article Published Date : Jan 01, 2000

Authors : A Marx, J D Glass, R W Sutter

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[In 2011, there were an extra 47,500 new cases of non-polio acute flaccid paralysis \(NPAFP\); Clinically indistinguishable from polio paralysis but twice as deadly, the incidence of NPAFP was directly proportional to doses of oral polio received.](#) - GMI Summary

Pubmed Data : Indian J Med Ethics. 2012 Apr-Jun;9(2):114-7. PMID: [22591873](#)

Article Published Date : Apr 01, 2012

Authors : Neetu Vashisht, Jacob Puliyeel

Study Type : Review

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Over 40,000 cases of AFP are reported annually since 2007 regardless of the number of actual polio cases.](#) - GMI Summary

Pubmed Data : BMC Public Health. 2012 ;12:229. Epub 2012 Mar 22. PMID: [22439606](#)

Article Published Date : Jan 01, 2012

Authors : Rie R Yotsu, Katharine Abba, Helen Smith, Abhijit Das

Study Type : Review

Additional Links

Diseases : [Acute Flaccid Paralysis : CK\(3\) : AC\(1\)](#), [Non-polio acute flaccid paralysis \(NPAFP\) : CK\(12\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Provocation by vaccine injections can increase the risk of paralytic poliomyelitis by up to 25 fold.](#) - GMI Summary

Pubmed Data : Dev Biol Stand. 1986;65:123-6. PMID: [3549394](#)

Article Published Date : Jan 01, 1986

Authors : H V Wyatt

Study Type : Review

Additional Links

Diseases : [Poliomyelitis : CK\(33\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Vaccine-derived poliovirus may become pathogenic in complex viral ecosystems, through frequent recombination events and mutations.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2012 May 1 ;205(9):1363-73. Epub 2012 Mar 29. PMID: [22457288](#)

Article Published Date : May 01, 2012

Authors : Marie-Line Joffret, Sophie Jégouic, Maël Bessaud, Jean Balanant, Coralie Tran, Valerie Caro, Barbara Holmblat, Richter Razafindratsimandresy, Jean-Marc Reynes, Mala Rakoto-Andrianarivelo, Francis Delpeyroux

Study Type : Review

Additional Links

Diseases : [Polio : CK\(19\) : AC\(8\)](#), [Polio: Vaccine-Related : CK\(1\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Vaccination: HPV (Gardasil)

An Italian study found that 61% of women experienced an adverse event after the administration of the first dose of HPV vaccine. - GMI Summary

Pubmed Data : Recent Prog Med. 2013 Jun ;104(6):262-6. PMID: [23801230](#)

Article Published Date : May 31, 2013

Authors : Stefania Spila-Alegiani, Roberto Da Cas, Cristina Giambi, Roberto Raschetti, Stefania Salmaso

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Erythema multiforme has been reported as a possible side effect of vaccination for human papillomavirus. - GMI Summary

Pubmed Data : Dermatology. 2010;220(1):60-2. Epub 2009 Nov 3. PMID: [19887766](#)

Article Published Date : Jan 01, 2010

Authors : A C Katoulis, A Liakou, E Bozi, M Theodorakis, A Alevizou, A Zafeiraki, M Mistidou, N G Stavrianeas

Study Type : Human Study

Additional Links

Diseases : [Erythema : CK\(44\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

HPV vaccination does not have a therapeutic effect in young women with pre-existing human papillomavirus infection. - GMI Summary

Pubmed Data : JAMA. 2007 Aug 15;298(7):743-53. PMID: [17699008](#)

Article Published Date : Aug 15, 2007

Authors : Allan Hildesheim, Rolando Herrero, Sholom Wacholder, Ana C Rodriguez, Diane Solomon, M Concepcion Bratti, John T Schiller, Paula Gonzalez, Gary Dubin, Carolina Porras, Silvia E Jimenez, Douglas R Lowy,

Study Type : Human Study

Additional Links

Diseases : [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

HPV vaccination has been linked to demyelination. - GMI Summary

Pubmed Data : J Child Neurol. 2010 Mar;25(3):321-7. PMID: [20189933](#)

Article Published Date : Mar 01, 2010

Authors : Francis J DiMario, Mirna Hajjar, Thomas Ciesielski

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

HPV vaccination is associated with reported side effects in (over) 23.5% of

[vaccinated girls studied.](#) - GMI Summary

Pubmed Data : Community Pract. 2010 Jun;83(6):30-3. PMID: [20586376](#)

Article Published Date : Jun 01, 2010

Authors : Virginia Paul-Ebhohimhen, Sara Huc, Helen Tissington, Ken Oates, Cameron Stark

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Human Papilloma Virus \(HPV\) vaccine is associated with demyelinating events.](#) - GMI Summary

Pubmed Data : Mult Scler. 2009 Jan;15(1):116-9. Epub 2008 Sep 19. PMID: [18805844](#)

Article Published Date : Jan 01, 2009

Authors : I Sutton, R Lahoria, Il Tan, P Clouston, Mh Barnett

Study Type : Human Study

Additional Links

Diseases : [Demyelinating Diseases : CK\(1309\) : AC\(247\)](#), [HPV : CK\(31\) : AC\(4\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [HPV Vaccine : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Noticeable adverse reactions to the HPV vaccine occurred in 22% of those polled.](#) - GMI Summary

Pubmed Data : Aten Primaria. 2010 Dec 14. Epub 2010 Dec 14. PMID: [21163554](#)

Article Published Date : Dec 14, 2010

Authors : M Amparo Torrecilla Rojas, Miguel Pedregal González, Fermín García Rodríguez, Josefa Ruiz Fernández

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Postlicensure safety surveillance has revealed a disproportionate reporting of syncope and venous thromboembolic events following quadrivalent HPV vaccination.](#) - GMI Summary

Pubmed Data : JAMA. 2009 Aug 19;302(7):750-7. PMID: [19690307](#)

Article Published Date : Aug 19, 2009

Authors : Barbara A Slade, Laura Leidel, Claudia Vellozzi, Emily Jane Woo, Wei Hua, Andrea Sutherland, Hector S Izurieta, Robert Ball, Nancy Miller, M Miles Braun, Lauri E Markowitz, John Iskander

Study Type : Human Study

Additional Links

Diseases : [Syncope : CK\(10\) : AC\(1\)](#), [Thromboembolism : CK\(205\) : AC\(16\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[The risk of miscarriage increases following HPV vaccination.](#) - GMI Summary

Pubmed Data : BMJ. 2010;340:c712. Epub 2010 Mar 2. PMID: [20197322](#)

Article Published Date : Jan 01, 2010

Authors : Sholom Wacholder, Bingshu Eric Chen, Allen Wilcox, George Macones, Paula Gonzalez, Brian Befano, Allan Hildesheim, Ana Cecilia Rodríguez, Diane Solomon, Rolando Herrero, Mark Schiffman,

Study Type : Human Study

Additional Links

Diseases : [Cervical Cancer : CK\(222\) : AC\(72\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[The way that the effectiveness of HPV vaccines are framed influences whether or not respondents believe they are effective and their acceptance level of vaccine mandate policies.](#) - GMI Summary

Pubmed Data : Patient Educ Couns. 2010 Sep 17. Epub 2010 Sep 17. PMID: [20851560](#)

Article Published Date : Sep 17, 2010

Authors : Cabral A Bigman, Joseph N Cappella, Robert C Hornik

Study Type : Human Study

Additional Links

Diseases : [HPV : CK\(31\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[There were 69 reports of Guillain-Barré Syndrome \(GBS\) after Gardasil vaccination that occurred in the United States between 2006 and 2009.](#) - GMI Summary

Pubmed Data : Vaccine. 2010 Sep 23. Epub 2010 Sep 23. PMID: [20869467](#)

Article Published Date : Sep 23, 2010

Authors : Nizar Souayah, P A Michas-Martin, Abu Nasar, Nataliya Krivitskaya, Hussam A Yacoub, Hafiz Khan, Adnan I Qureshi

Study Type : Human Study

Additional Links

Diseases : [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

["Human papilloma virus vaccine and primary ovarian failure: another facet of the autoimmune/inflammatory syndrome induced by adjuvants."](#) - GMI Summary

Pubmed Data : Am J Reprod Immunol. 2013 Oct ;70(4):309-16. Epub 2013 Jul 31. PMID: [23902317](#)

Article Published Date : Sep 30, 2013

Authors : Serena Colafrancesco, Carlo Perricone, Lucija Tomljenovic, Yehuda Shoenfeld

Study Type : Human: Case Report

Additional Links

Diseases : [Ovarian Failure : CK\(4\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[Possible systemic lupus erythematosus following HPV immunization has been reported.](#) - GMI Summary

Pubmed Data : Lupus. 2012 ;21(2):158-61. PMID: [22235047](#)

Article Published Date : Jan 01, 2012

Authors : Hf Soldevilla, Sfr Briones, Sv Navarra

Study Type : Human: Case Report

Additional Links

Diseases : [Lupus Erythematosus: Systemic : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

[The HPV16 vaccine carries with it significant cross-reactivity risk due to the homologies that exist between the HPV and human proteome.](#) - GMI Summary

Pubmed Data : J Exp Ther Oncol. 2009;8(1):65-76. PMID: [19827272](#)

Article Published Date : Jan 01, 2009

Authors : Darja Kanduc

Study Type : In Vitro Study

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Vaccination: Tetanus

DTP or tetanus vaccination increases the risk of allergies and related respiratory symptoms in children and adolescents. - GMI Summary

Pubmed Data : J Manipulative Physiol Ther. 2000 Feb;23(2):81-90. PMID: [10714532](#)

Article Published Date : Feb 01, 2000

Authors : E L Hurwitz, H Morgenstern

Study Type : Meta Analysis

Additional Links

Diseases : [Allergies : CK\(520\) : AC\(96\)](#), [Allergies: Childhood : CK\(70\) : AC\(5\)](#), [Asthma : CK\(918\) : AC\(140\)](#), [Hypersensitivity : CK\(64\) : AC\(15\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Despite the CDC's current recommendation to vaccinate postpartum women before hospital discharge with the tetanus and diphtheria toxoids and acellular pertussis (Tdap) vaccine in order to prevent pertussis infection in their offspring, it does not reduce - GMI Summary

Pubmed Data : Clin Infect Dis. 2011 Nov 10. Epub 2011 Nov 10. PMID: [22075790](#)

Article Published Date : Nov 10, 2011

Authors : Luis A Castagnini, C Mary Healy, Marcia A Rench, Susan H Wootton, Flor M Munoz, Carol J Baker

Study Type : Human Study

Additional Links

Diseases : [Pertussis : CK\(142\) : AC\(14\)](#), [Whooping Cough : CK\(66\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

Neonatal tetanus despite protective serum antitoxin concentration. - GMI Summary

Pubmed Data : FEMS Microbiol Immunol. 1991 Jun ;3(3):171-5. PMID: [1878260](#)

Article Published Date : May 31, 1991

Authors : S Y Maselle, R Matre, R Mbise, T Hofstad

Study Type : Human Study

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects. - GMI Summary](#)

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance : CK\(148\) : AC\(37\)](#), [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Pertussis : CK\(116\) : AC\(14\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Diphtheria : CK\(50\) : AC\(2\)](#)

Problem Substances : [Adjuvant : CK\(18\) : AC\(6\)](#), [Aluminum Hydroxide : CK\(56\) : AC\(14\)](#), [Vaccine Adjuvants : CK\(403\) : AC\(79\)](#)

[A case of Leukemia Cutis arising at the site of injection of a Tetanus Booster has been reported. - GMI Summary](#)

Pubmed Data : Actas Dermosifiliogr. 2010 Oct;101(8):727-9. PMID: [20965018](#)

Article Published Date : Oct 01, 2010

Authors : R M Guinovart, J M Carrascosa, C Ferrándiz

Study Type : Human: Case Report

Additional Links

Diseases : [Leukemia Cutis : CK\(3\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Severe tetanus has been reported in immunized patients with high anti-tetanus titers. - GMI Summary](#)

Pubmed Data : Neurology. 1992 Apr ;42(4):761-4. PMID: [1565228](#)

Article Published Date : Apr 01, 1992

Authors : N E Crone, A T Reder

Study Type : Human: Case Report

Additional Links

Diseases : [Tetanus : CK\(47\) : AC\(5\)](#)

Additional Keywords : [Antibody Theory Of Vaccinology : CK\(75\) : AC\(5\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Coriandrum sativum has antioxidant activity. - GMI Summary](#)

Pubmed Data : J Nutr Biochem. 2009 Nov;20(11):901-8. Epub 2008 Nov 6. PMID: [10549163](#)

Article Published Date : Nov 01, 2009

Authors : V Chithra, S Leelamma

Study Type : Animal Study

Additional Links

Substances : [Coriandrum sativum : CK\(51\) : AC\(26\)](#)

Diseases : [Oxidative Stress : CK\(2004\) : AC\(750\)](#)

Pharmacological Actions : [Antioxidants : CK\(3864\) : AC\(1373\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Tetanus vaccine given to Phillipino women of reproductive age may have been designed to induce an anti-fertility action. - GMI Summary](#)

Pubmed Data : Vaccine Wkly. 1995 May 29 - Jun 5:9-10. PMID: [12346214](#)

Article Published Date : May 29, 1995

Authors : [No authors listed]

Study Type : Commentary

Additional Links

Diseases : [Infertility: Female : CK\(238\) : AC\(40\)](#)

Additional Keywords : [Population Control : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[The Institute of Medicine determined that routine childhood vaccines are linked to a number of serious adverse reactions.](#) - GMI Summary

Pubmed Data : JAMA. 1994 May 25;271(20):1602-5. PMID: [8182813](#)

Article Published Date : May 25, 1994

Authors : K R Stratton, C J Howe, R B Johnston

Study Type : Review

Additional Links

Diseases : [Anaphylaxis : CK\(53\) : AC\(15\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Hepatitis B : CK\(219\) : AC\(37\)](#), [Neuritis: Brachial Plexus : CK\(1\) : AC\(1\)](#), [Poliomyelitis : CK\(33\) : AC\(4\)](#), [Purpura: Thrombocytopenic : CK\(231\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

[Topic: Vaccination: Smallpox](#)

[Adverse events following smallpox vaccination with ACAM2000 in a military population have been reported.](#) - GMI Summary

Pubmed Data : Arch Dermatol. 2010 Jun;146(6):656-61. PMID: [20566929](#)

Article Published Date : Jun 01, 2010

Authors : Thomas M Beachkofsky, Scott C Carrizales, Jeffrey J Bidinger, David E Hrncir, Darren E Whittemore, Chad M Hivnor

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Among US military personnel vaccinated against smallpox, myopericarditis](#)

occurred at a rate of 1 per 12,819 primary vaccinees, and 3.6 fold higher in those without previous vaccinia vaccination. - GMI Summary

Pubmed Data : JAMA. 2003 Jun 25;289(24):3283-9. PMID: [12824210](#)

Article Published Date : Jun 25, 2003

Authors : Jeffrey S Halsell, James R Riddle, J Edwin Atwood, Pierce Gardner, Robert Shope, Gregory A Poland, Gregory C Gray, Stephen Ostroff, Robert E Eckart, Duane R Hospenthal, Roger L Gibson, John D Grabenstein, Mark K Arness, David N Tornberg,

Study Type : Human Study

Additional Links

Diseases : [Myopericarditis : CK\(40\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

An economic analysis of mass smallpox vaccination reveals that cardiovascular adverse events would be sizeable and costly. - GMI Summary

Pubmed Data : J Rheumatol. 1994 Jul;21(7):1305-9. PMID: [18284356](#)

Article Published Date : Jul 01, 1994

Authors : Ismael R Ortega-Sanchez, Mercedes M Sniadack, Gina T Mootrey

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Myocarditis and pericarditis have been reported following smallpox vaccination in Europe, Australia and the United States. - GMI Summary

Pubmed Data : Clin Infect Dis. 2008 Mar 15;46 Suppl 3:S242-50. PMID: [18284365](#)

Article Published Date : Mar 15, 2008

Authors : Juliette Morgan, Martha H Roper, Laurence Sperling, Richard A Schieber, James D Heffelfinger, Christine G Casey, Jacqueline W Miller, Scott Santibanez, Barbara Herwaldt, Paige Hightower, Pedro L Moro, Beth F Hibbs, Nancy H Levine, Louisa E Chapman, John Iskander, J Michael Lane, Melinda Wharton, Gina T Mootrey, David L Swerdlow

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Smallpox vaccination has been associated with cardiac complications such as myopericarditis. - GMI Summary

Pubmed Data : South Med J. 2009 May 7. Epub 2009 May 7. PMID: [19434043](#)

Article Published Date : May 07, 2009

Authors : Luis F Mora, Akbar H Khan, Laurence S Sperling

Study Type : Human Study

Additional Links

Diseases : [Myocarditis : CK\(54\) : AC\(8\)](#), [Myopericarditis : CK\(40\) : AC\(4\)](#), [Pericarditis : CK\(35\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Smallpox vaccine caused iatrogenic vaccinia in children in Russia. - GMI Summary

Pubmed Data : Zh Mikrobiol Epidemiol Immunobiol. 2001 Mar-Apr(2):40-5. PMID: [11548257](#)

Article Published Date : Mar 01, 2001

Authors : G G Onishchenko, V I Markov, V N Ustiushin, S V Borisevich, G I Kuznetsova, S Ia Loginova, A M Berezhnoĭ, N T Vasil'ev, V A Maksimov, A A Makhlaĭ

Study Type : Human Study

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vaccinia virus : CK\(22\) : AC\(4\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Varciella vaccine has been reported to cause herpes zoster skin lesions and meningitis in a previously healthy boy.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2008 Nov 15;198(10):1444-7. PMID: [18826373](#)

Article Published Date : Nov 15, 2008

Authors : Myron J Levin, Roberta L DeBiasi, Vanda Bostik, D Scott Schmid

Study Type : Human Study

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Meningitis: Viral : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

[Review: possible adverse effects that are associated with smallpox vaccination.](#) - GMI Summary

Pubmed Data : MMWR Recomm Rep. 2003 Feb 21;52(RR-4):1-28. PMID: [12617510](#)

Article Published Date : Feb 21, 2003

Authors : Joanne Cono, Christine G Casey, David M Bell,

Study Type : Review

Additional Links

Diseases : [Smallpox : CK\(23\) : AC\(4\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Pharmacological Actions : [Antiviral Agents : CK\(634\) : AC\(296\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Smallpox : CK\(71\) : AC\(8\)](#)

Topic: [Vaccination: Anthrax](#)

[Anthrax vaccination contributes to joint related adverse reactions.](#) - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Mar-Apr;20(2):217-20. PMID: [12051402](#)

Article Published Date : Mar 01, 2002

Authors : D A Geier, M R Geier

Study Type : Human Study

Additional Links

Diseases : [Joint Diseases : CK\(10\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[Birth defects are more common in pregnant women who received the anthrax vaccine during their first trimester versus later in pregnancy.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2008 Aug 15 ;168(4):434-42. Epub 2008 Jul 2. PMID: [18599489](#)

Article Published Date : Aug 15, 2008

Authors : Margaret A K Ryan, Tyler C Smith, Carter J Sevick, William K Honner, Rosha A Loach, Cynthia A Moore, J David Erickson

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Birth Defects : CK\(204\) : AC\(39\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)
Adverse Pharmacological Actions : [Teratogenic : CK\(318\) : AC\(62\)](#)

[Injection site reactions occur in 28% of those who receive the anthrax vaccine,](#)

[with women having twice the incidence of reaction versus men.](#) - GMI Summary

Pubmed Data : Pharmacoepidemiol Drug Saf. 2007 Mar ;16(3):259-74. PMID: [17245803](#)

Article Published Date : Mar 01, 2007

Authors : Michael M McNeil, I-Shan Chiang, John T Wheeling, Yujia Zhang

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Gender Differences : CK\(63\) : AC\(8\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[Symptomatic Gulf War Syndrome is strongly associated with the presence of autoantibodies to squalene, an adjuvant used in vaccines.](#) - GMI Summary

Pubmed Data : Exp Mol Pathol. 2000 Feb;68(1):55-64. PMID: [10640454](#)

Article Published Date : Feb 01, 2000

Authors : P B Asa, Y Cao, R F Garry

Study Type : Human Study

Additional Links

Diseases : [Gulf War Syndrome : CK\(33\) : AC\(5\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The anthrax vaccine is one of the most reactogenic vaccines reported in the Vaccine Adverse Events Reporting System \(VAERS\) database.](#) - GMI Summary

Pubmed Data : Hepatogastroenterology. 2004 May-Jun;51(57):762-7. PMID: [15143911](#)

Article Published Date : May 01, 2004

Authors : Mark R Geier, David A Geier

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The vaccine adjuvant squalene in anthrax vaccines given to soldiers in the Gulf War resulted in the formation of antibodies to squalene which are associated with Gulf War Syndrome.](#) - GMI Summary

Pubmed Data : Neuropharmacology. 2011 Feb-Mar;60(2-3):252-8. Epub 2010 Sep 22. PMID: [12127050](#)

Article Published Date : Feb 01, 2011

Authors : Pamela B Asa, Russell B Wilson, Robert F Garry

Study Type : Human Study

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#), [Gulf War Syndrome : CK\(33\) : AC\(5\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Problem Substances : [Squalene, Adjuvant : CK\(2\) : AC\(1\)](#)

[Anthrax vaccine development suffers from a wide range of potentially insurmountable problems.](#) - GMI Summary

Pubmed Data : Przegl Epidemiol. 2009 ;63(4):505-12. PMID: [20120948](#)

Article Published Date : Jan 01, 2009

Authors : Dorota Zakowska, Janusz Kocik, Michał Bartoszcze

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

[The development of human vaccines for anthrax has suffered from a number of technical challenges.](#) - GMI Summary

Pubmed Data : Hum Vaccin. 2009 Dec ;5(12):806-16. Epub 2009 Dec 9. PMID: [19786839](#)

Article Published Date : Dec 01, 2009

Authors : Leslie W Baillie

Study Type : Review

Additional Links

Diseases : [Anthrax : CK\(43\) : AC\(6\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anthrax : CK\(62\) : AC\(8\)](#)

Topic: [Vaccination: Combinations](#)

[Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau.](#) - GMI Summary

Pubmed Data : [Vaccine](#). 2013 Dec 7. pii: S0264-410X(13)01663-0. doi: 10.1016/j.vaccine.2013.11.074.

Article Published Date : Dec 06, 2013

Authors : Ane Bærent Fisker, Henrik Ravn, Amabelia Rodrigues, Marie Drivsholm Ostergaard, Carlito Bale, Christine Stabell Benn, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#)

Anti Therapeutic Actions : [Vaccination: Combinations : CK\(20\) : AC\(2\)](#)

[Diphtheria-tetanus-pertussis vaccine administered simultaneously with measles vaccine is associated with increased morbidity and poor growth in girls.](#) - GMI Summary

Pubmed Data : Vaccine. 2011 Jan 10;29(3):487-500. Epub 2010 Nov 18. PMID: [21093496](#)

Article Published Date : Jan 10, 2011

Authors : J Agergaard, E Nante, G Poulstrup, J Nielsen, K L Flanagan, L Østergaard, C S Benn, P Aaby

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#)

[DTP with or after measles vaccination is associated with increased in-hospital mortality in Guinea-Bissau.](#) - GMI Summary

Pubmed Data : [Vaccine](#). 2007 Jan 26;25(7):1265-9. Epub 2006 Oct 18.

Article Published Date : Jan 25, 2007

Authors : Peter Aaby, Sidu Biai, Jens Erik Veirum, Morten Sodemann, Ida Lisse, May-Lill Garly, Henrik Ravn, Christine Stabell Benn, Amabelia Rodrigues

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality : CK\(249\) : AC\(25\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Combinations : CK\(20\) : AC\(2\)](#)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) - GMI Summary

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) :](#)

[AC\(2\), Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

Topic: [Vaccination: Pneumococcal](#)

[Immunization of mothers with pneumococcal capsular polysaccharide vaccine during pregnancy is ineffective for infants. - GMI Summary](#)

Pubmed Data : Braz J Infect Dis. 2009 Apr;13(2):104-6. PMID: [20140352](#)

Article Published Date : Apr 01, 2009

Authors : Claudia R C Lopes, Eitan N Berezin, Ting Hui Ching, Jaildo de Souza Canuto, Vanilda Oliveira da Costa, Erika Monteiro Klering

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Upper Respiratory Infections : CK\(824\) : AC\(90\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal conjugate vaccination is associated with higher levels of serious adverse respiratory events and nonrespiratory events in infants 6 weeks to 6 months of age. - GMI Summary](#)

Pubmed Data : Pediatr Infect Dis J. 2009 Jun;28(6):455-62. PMID: [19483514](#)

Article Published Date : Jun 01, 2009

Authors : Marilla G Lucero, Hanna Nohynek, Gail Williams, Veronica Tallo, Eric A F Simões, Socorro Lupisan, Diozele Sanvictores, Simon Forsyth, Taneli Puumalainen, Juanita Ugpo, Marites Lechago, Margaret de Campo, Erma Abucejo-Ladesma, Lydia Sombrero, Antti Nissinen, Anu Soinen, Petri Ruutu, Ian Riley, Helen P Mäkelä

Study Type : Human Study

Additional Links

Diseases : [Infant Infections : CK\(410\) : AC\(44\)](#), [Respiratory Diseases : CK\(174\) : AC\(29\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal conjugate vaccine is not effective to prevent ear infections in previously unvaccinated toddlers and children with a history of recurrent ear infections. - GMI Summary](#)

Pubmed Data : Lancet. 2003 Jun 28;361(9376):2189-95. PMID: [12842372](#)

Article Published Date : Jun 28, 2003

Authors : Reinier Veenhoven, Debby Bogaert, Cuno Uiterwaal, Carole Brouwer, Herma Kiezebrink, Jacob Bruin, Ed IJzerman, Peter Hermans, Ronald de Groot, Ben Zegers, Wietse Kuis, Ger Rijkers, Anne Schilder, Elisabeth Sanders

Study Type : Human Study

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines are ineffective in children with a history of recurrent acute ear infections - Article 2. - GMI Summary](#)

Pubmed Data : Int J Pediatr Otorhinolaryngol. 2006 Feb;70(2):275-85. Epub 2005 Sep 2. PMID: [16140397](#)

Article Published Date : Feb 01, 2006

Authors : Muriel J P van Kempen, Judith S Vermeiren, Mario Vaneechoutte, Geert Claeys, Reinier H Veenhoven, Ger T Rijkers, Elisabeth A M Sanders, Ingeborg J Dhooge

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines are ineffective in children with a history of recurrent acute ear infections.](#) - GMI Summary

Pubmed Data : Clin Infect Dis. 2004 Oct 1;39(7):911-9. Epub 2004 Sep 1. PMID: [15472839](#)

Article Published Date : Oct 01, 2004

Authors : Reinier H Veenhoven, Debby Bogaert, Anne G M Schilder, Ger T Rijkers, Cuno S P M Uiterwaal, Herma H Kiezebrink, Muriel J P van Kempen, Inge J Dhooge, Jacob Bruin, Ed P F Ijzerman, Ronald de Groot, Wietse Kuis, Peter W M Hermans, Elisabeth A M Sanders

Study Type : Human Study

Additional Links

Diseases : [Aging : CK\(1399\) : AC\(392\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Pneumococcal vaccines do not appear to reduce the risk of death from pneumonia in adult populations.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2003(4):CD000422. PMID: [14583920](#)

Article Published Date : Jan 01, 2003

Authors : K Dear, J Holden, R Andrews, D Tatham

Study Type : Human Study

Additional Links

Diseases : [Pneumococcal Infections : CK\(50\) : AC\(11\)](#), [Pneumonia : CK\(330\) : AC\(40\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[There has been a five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine.](#) - GMI Summary

Pubmed Data : Pediatr Infect Dis J. 2008 Nov;27(11):1030-2. PMID: [18845981](#)

Article Published Date : Nov 01, 2008

Authors : Debra J Hendrickson, Dean A Blumberg, Jesse P Joad, Sanjay Jhawar, Ruth J McDonald

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections : CK\(275\) : AC\(29\)](#), [Empyema : CK\(10\) : AC\(1\)](#), [Parapneumonic Empyema : CK\(10\) : AC\(1\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

[Review: based on currently available research pneumococcal vaccination should not be recommended for large scale use in ear infection prone populations.](#) - GMI Summary

Pubmed Data : Cochrane Database Syst Rev. 2002(2):CD001480. PMID: [12076412](#)

Article Published Date : Jan 01, 2002

Authors : M Straetemans, E A Sanders, R H Veenhoven, A G Schilder, R A Damoiseaux, G A Zielhuis

Study Type : Review

Additional Links

Diseases : [Ear Infection : CK\(259\) : AC\(32\)](#), [Pneumococcal Infections : CK\(50\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Pneumococcal : CK\(71\) : AC\(8\)](#)

Topic: [Vaccination: Haemophilus Influenzae](#)

[A Haemophilus b polysaccharide vaccine resulted in minus 58 percent efficacy in children in Minnesota in August 1985.](#) - GMI Summary

Pubmed Data : JAMA. 1988 Sep 9;260(10):1423-8. PMID: [3261350](#)

Article Published Date : Sep 09, 1988

Authors : M T Osterholm, J H Rambeck, K E White, J L Jacobs, L M Pierson, J D Neaton, C W Hedberg, K L MacDonald, D M Granoff

Study Type : Human Study

Additional Links

Diseases : [Haemophilus influenzae : CK\(54\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#)

[The combination of MMR and DTaP-Hib-IPV vaccination is associated with significantly increased rates of adverse effects.](#) - GMI Summary

Pubmed Data : J Radiol Prot. 2009 Sep;29(3):429-43. Epub 2009 Aug 18. PMID: [20166340](#)

Article Published Date : Sep 01, 2009

Authors : Elena Shneyer, Avshalom Strulov, Yaakov Rosenfeld

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Combinations : CK\(20\) : AC\(2\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Polio : CK\(94\) : AC\(15\)](#)

[Between May 1985 and September 1987, 228 reports of disease due to Haemophilus influenzae in vaccinated children were submitted to the FDA.](#) - GMI Summary

Pubmed Data : J Infect Dis. 1988 Aug ;158(2):343-8. PMID: [3261314](#)

Article Published Date : Jul 31, 1988

Authors : E E Hiner, C E Frasch

Study Type : Human: Case Report

Additional Links

Diseases : [Haemophilus influenzae : CK\(4\) : AC\(1\)](#)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#)

[Conjugate vaccines may predispose children to autism spectrum disorders.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2011 Oct 10. Epub 2011 Oct 10. PMID: [21993250](#)

Article Published Date : Oct 10, 2011

Authors : Brian J Richmand

Study Type : Review

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Conjugate Vaccines : CK\(1\) : AC\(1\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Streptococcus Pneumoniae : CK\(1\) : AC\(1\)](#)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: [Vaccination: Animal Model](#)

[Live attenuated influenza vaccines may cause shedding of the virus in children 6-59 monhts. - GMI Summary](#)

Pubmed Data : Vaccine. 2011 Apr 20. Epub 2011 Apr 20. PMID: [21513761](#)

Article Published Date : Apr 20, 2011

Authors : Raburn M Mallory, Tingting Yi, Christopher S Ambrose

Study Type : Human Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[A vaccine developed for bison resulted in inducing placentitis and abortion in pregnant cows. - GMI Summary](#)

Pubmed Data : Am J Vet Res. 1996 Nov;57(11):1604-7. PMID: [8915438](#)

Article Published Date : Nov 01, 1996

Authors : M V Palmer, S C Olsen, M J Gilsdorf, L M Philo, P R Clarke, N F Chevillie

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#),

[Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Experimental in utero inoculation of late-term swine fetuses with porcine circovirus type 2 results in a high rate of reproductive abnormalities, including mummification and stillbirth. - GMI Summary](#)

Pubmed Data : J Vet Diagn Invest. 2002 Nov;14(6):507-12. PMID: [12423036](#)

Article Published Date : Nov 01, 2002

Authors : Charles S Johnson, Han S Joo, Kochakorn Direksin, Kyoung-Jin Yoon, Young K Choi

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Fatal adverse pulmonary reaction in calves after inadvertent intravenous vaccination has been reported. - GMI Summary](#)

Pubmed Data : Vet Pathol. 2005 Jul;42(4):492-5. PMID: [16006609](#)

Article Published Date : Jul 01, 2005

Authors : J D Ramsay, C L Williams, E Simko

Study Type : Animal Study

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Maturational changes in amygdala volume and the binding capacity of an](#)

opioid antagonist in the amygdala was significantly altered in infant macaques receiving the vaccine schedule. - GMI Summary

Pubmed Data : Acta Neurobiol Exp (Wars). 2010 ;70(2):147-64. PMID: [20628439](#)

Article Published Date : Dec 31, 2009

Authors : Laura Hewitson, Brian J Lopresti, Carol Stott, N Scott Mason, Jaime Tomko

Study Type : Animal Study

Additional Links

Diseases : [Amygdala: Damage/Abnormalities : CK\(12\) : AC\(1\)](#), [Neurodevelopmental Disorders : CK\(124\) : AC\(13\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Problem Substances : [Thimerosal : CK\(367\) : AC\(23\)](#)

Newborn primates receiving mercury-containing hepatitis B vaccines exhibit neurodevelopmental delays. - GMI Summary

Pubmed Data : J Toxicol Environ Health A. 2010 Jan;73(19):1298-313. PMID: [20711932](#)

Article Published Date : Jan 01, 2010

Authors : Laura Hewitson, Lisa A Houser, Carol Stott, Gene Sackett, Jaime L Tomko, David Atwood, Lisa Blue, E Railey White

Study Type : Animal Study

Additional Links

Diseases : [Hepatitis B : CK\(219\) : AC\(37\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Porcine circovirus type 2 (PCV2) vaccination of pregnant pigs may result in vertical transmission of PCV2 to the offspring. - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2009 Jun;16(6):830-4. Epub 2009 Apr 8. PMID: [19357312](#)

Article Published Date : Jun 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Pregnant cows vaccinated against a Brucella strain experienced an abortion rate of 58%. - GMI Summary

Pubmed Data : J Wildl Dis. 1991 Apr;27(2):258-64. PMID: [1906114](#)

Article Published Date : Apr 01, 1991

Authors : D S Davis, J W Templeton, T A Ficht, J D Huber, R D Angus, L G Adams

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Pregnant cows vaccinated with live attenuated Smithburn Rift Valley virus had a high rate of abortions which were associated with elevations in IgG and IgM antibodies. - GMI Summary

Pubmed Data : J Med Virol. 2006 Jun;78(6):787-91. PMID: [16628582](#)

Article Published Date : Jun 01, 2006

Authors : Boulos Botros, Adel Omar, Khairat Elian, Gihan Mohamed, Atef Soliman, Adel Salib, Diaa Salman, Magdi Saad, Kenneth Earhart

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Rift Valley fever vaccine in goats cause severe deleterious pathological changes in liver especially in kids and causing abortion in pregnant does.](#) - GMI Summary

Pubmed Data : Virol J. 2009;6:94. Epub 2009 Jul 6. PMID: [19580675](#)

Article Published Date : Jan 01, 2009

Authors : Samia Ahmed Kamal

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Smithburn Rift Valley Fever : CK\(4\) : AC\(2\)](#), [Rift Valley Fever : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The intranasal inoculation of pregnant sows with porcine circovirus 2 results in abortion and reproductive failure.](#) - GMI Summary

Pubmed Data : J Nutr. 2009 Nov;139(11):2061-6. Epub 2009 Sep 23. PMID: [15737340](#)

Article Published Date : Nov 01, 2009

Authors : J-S Park, J Kim, Y Ha, K Jung, C Choi, J-K Lim, S-H Kim, C Chae

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[The vaccination of pregnant sheep resulted in abortions and hydranencephaly.](#) - GMI Summary

Pubmed Data : Int Immunopharmacol. 2005 Mar;5(3):555-69. PMID: [8825310](#)

Article Published Date : Mar 01, 2005

Authors : M Flanagan, S J Johnson

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Hydranencephaly : CK\(2\) : AC\(1\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccination of pregnant monkeys resulted in abortions in 2 out of 25.](#) - GMI Summary

Pubmed Data : Am J Trop Med Hyg. 1991 Apr;44(4):382-9. PMID: [2042705](#)

Article Published Date : Apr 01, 1991

Authors : A Escajadillo, J K Frenkel

Study Type : Animal Study

Additional Links

Diseases : [Abortion: Spontaneous : CK\(204\) : AC\(29\)](#), [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

[Vaccine-induced immunity in pregnant pigs is not effective in preventing viremia in offspring.](#) - GMI Summary

Pubmed Data : Theriogenology. 2009 Oct 1;72(6):747-54. Epub 2009 Jun 25. PMID: [19559470](#)

Article Published Date : Oct 01, 2009

Authors : D M Madson, A R Patterson, S Ramamoorthy, N Pal, X J Meng, T Opriessnig

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Vaccine-induced scrapie has been reported in animals. - GMI Summary

Pubmed Data : J Gen Virol. 2003 Apr;84(Pt 4):1047-52. PMID: [12655108](#)

Article Published Date : Apr 01, 2003

Authors : Gianluigi Zanusso, Cristina Casalone, Pierluigi Acutis, Elena Bozzetta, Alessia Farinazzo, Matteo Gelati, Michele Fiorini, Gianluigi Forloni, Man Sun Sy, Salvatore Monaco, Maria Caramelli

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Infectious : CK\(8\) : AC\(4\)](#), [Animal Diseases: Scrapie : CK\(4\) : AC\(2\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Vaccine-induced, simian immunodeficiency virus-specific CD8+ T cells reduce virus replication but do not protect from simian immunodeficiency virus disease progression. - GMI Summary

Pubmed Data : J Immunol. 2009 Jul 1;183(1):706-17. PMID: [19542473](#)

Article Published Date : Jul 01, 2009

Authors : Jessica C Engram, Richard M Dunham, George Makedonas, Thomas H Vanderford, Beth Sumpter, Nichole R Klatt, Sarah J Ratcliffe, Seema Garg, Mirko Paiardini, Monica McQuoid, John D Altman, Silvija I Staprans, Michael R Betts, David A Garber, Mark B Feinberg, Guido Silvestri

Study Type : Animal Study

Additional Links

Diseases : [Animal Diseases: Simian Immunodeficiency Virus \(SIV\) : CK\(2\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Feline injection site-associated sarcoma is a serious problem associated with malignancy. - GMI Summary

Pubmed Data : Vet Microbiol. 2006 Oct 5;117(1):59-65. PMID: [16769184](#)

Article Published Date : Oct 05, 2006

Authors : Jolle Kirpensteijn

Study Type : Review

Additional Links

Diseases : [Sarcoma : CK\(42\) : AC\(26\)](#), [Tumors : CK\(199\) : AC\(116\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Animal Model : CK\(41\) : AC\(17\)](#)

Topic: Vaccination: BCG (Tuberculosis)

Among female infants, those who receive both BCG and DTP vaccines experience higher mortality than those who receive only one of the two vaccines. - GMI Summary

Pubmed Data : Trop Med Int Health. 2005 Oct;10(10):947-55. PMID: [16185228](#)

Article Published Date : Oct 01, 2005

Authors : Lawrence H Moulton, Lakshmi Rahmathullah, Neal A Halsey, R D Thulasiraj, Joanne Katz, James M Tielsch

Study Type : Human Study

Additional Links

Diseases : [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31)

[BCG revaccination may raise mortality in young children.](#) - GMI Summary

Pubmed Data : BMJ. 2010;340:c671. Epub 2010 Mar 15. PMID: [20231251](#)

Article Published Date : Jan 01, 2010

Authors : Adam Edvin Roth, Christine Stabell Benn, Henrik Ravn, Amabelia Rodrigues, Ida Maria Lisse, Maria Yazdanbakhsh, Hilton Whittle, Peter Aaby

Study Type : Human Study

Additional Links

Diseases : [Childhood Infections](#) : CK(275) : AC(29), [Tuberculosis](#) : CK(244) : AC(42)

Anti Therapeutic Actions : [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4)

[Vaccination timing and co-administration may be associated with increased mortality, especially in females.](#) - GMI Summary

Pubmed Data : Vaccine. 2006 May 29;24(22):4701-8. Epub 2006 Mar 31. PMID: [16621182](#)

Article Published Date : May 29, 2006

Authors : Peter Aaby, Henrik Jensen, Gijs Walraven

Study Type : Human Study

Additional Links

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26)

[A case of extensive ulcerating vasculitis following a BCG vaccination has been reported.](#) - GMI Summary

Pubmed Data : J Plast Reconstr Aesthet Surg. 2009 Aug;62(8):e286-9. Epub 2007 Dec 31. PMID: [18166508](#)

Article Published Date : Aug 01, 2009

Authors : A Ghattaura, K A Eley, E Molenaar, G Smith

Study Type : Human: Case Report

Additional Links

Diseases : [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: BCG \(Tuberculosis\)](#) : CK(33) : AC(4)

Topic: [Vaccination: Rotavirus](#)

["Lack of correlation between serum rotavirus antibody titers and protection following vaccination with reassortant RRV vaccines."](#) - GMI Summary

Pubmed Data : Vaccine. 1995 Sep ;13(13):1226-32. PMID: [8578808](#)

Article Published Date : Aug 31, 1995

Authors : R L Ward, D I Bernstein

Study Type : Human Study

Additional Links

Diseases : [Rotavirus Infections](#) : CK(75) : AC(16)

Additional Keywords : [Antibody Theory Of Vaccinology](#) : CK(75) : AC(5)

Anti Therapeutic Actions : [Vaccination: Rotavirus](#) : CK(33) : AC(6)

[Rates of intussusception associated with rotavirus vaccines may be significantly underestimated.](#) - GMI Summary

Pubmed Data : J Infect Dis. 2009 Nov 1;200 Suppl 1:S264-70. PMID: [19817607](#)

Article Published Date : Nov 01, 2009

Authors : Margaret M Cortese, Mary Allen Staat, Geoffrey A Weinberg, Kathryn Edwards, Marilyn A Rice, Peter G Szilagyi, Caroline B Hall, Daniel C Payne, Umesh D Parashar

Study Type : Human Study

Additional Links

Diseases : [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[Rotavirus vaccination has been associated with increased risk for gastroenteritis and intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2004 Apr;113(4):e353-9. PMID: [15060267](#)

Article Published Date : Apr 01, 2004

Authors : Penina Haber, Robert T Chen, Lynn R Zanardi, Gina T Mootrey, Roseanne English, M Miles Braun,

Study Type : Human Study

Additional Links

Diseases : [Gastroenteritis : CK\(96\) : AC\(11\)](#), [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[Rotavirus vaccinations have a history of causing adverse effects such as intussusception.](#) - GMI Summary

Pubmed Data : Pediatrics. 2001 Jun;107(6):E97. PMID: [11389295](#)

Article Published Date : Jun 01, 2001

Authors : L R Zanardi, P Haber, G T Mootrey, M T Niu, M Wharton

Study Type : Human Study

Additional Links

Diseases : [Intussusception : CK\(30\) : AC\(3\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

["Viral nucleic acids in live-attenuated vaccines: detection of minority variants and an adventitious virus."](#) - GMI Summary

Pubmed Data : J Virol. 2010 Jun ;84(12):6033-40. Epub 2010 Apr 7. PMID: [20375174](#)

Article Published Date : May 31, 2010

Authors : Joseph G Victoria, Chunlin Wang, Morris S Jones, Crystal Jaing, Kevin McLoughlin, Shea Gardner, Eric L Delwart

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Additional Keywords : [Adventitious Viruses : CK\(18\) : AC\(9\)](#), [Iatrogenic Disease : CK\(226\) : AC\(26\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

[PCV2 infection is now widespread worldwide, and increasing numbers of disease conditions have been linked to PCV2 infection in pigs.](#) - GMI Summary

Pubmed Data : Virus Res. 2012 Mar ;164(1-2):1-3. Epub 2011 Dec 14. PMID: [22192532](#)

Article Published Date : Mar 01, 2012

Authors : Xiang-Jin Meng

Study Type : Review

Additional Links

Diseases : [Animal Diseases: Porcine Circovirus Type 2 \(PCV2\) : CK\(11\) : AC\(7\)](#)

Anti Therapeutic Actions : [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Rotavirus vaccines have been found contaminated with porcine circovirus. - GMI Summary

Pubmed Data : Biologicals. 2012 Mar 6. Epub 2012 Mar 6. PMID: [22402185](#)

Article Published Date : Mar 06, 2012

Authors : Sarah M Gilliland, Lindsay Forrest, Heather Carre, Adrian Jenkins, Neil Berry, Javier Martin, Philip Minor, Silke Schepelmann

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Guillain-Barre Syndrome : CK\(84\) : AC\(14\)](#), [Human Papillomavirus \(HPV\) : CK\(163\) : AC\(23\)](#), [Inflammatory Myopathy : CK\(81\) : AC\(5\)](#), [Macrophagic myofasciitis : CK\(15\) : AC\(3\)](#), [Multiple Sclerosis : CK\(746\) : AC\(133\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Systemic Lupus Erythematosus : CK\(381\) : AC\(52\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Vasculitis : CK\(48\) : AC\(11\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#), [Vaccination: HPV \(Gardasil\) : CK\(105\) : AC\(13\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Lyme disease : CK\(11\) : AC\(2\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Rotavirus : CK\(33\) : AC\(6\)](#), [Vaccination: Tetanus : CK\(61\) : AC\(8\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

Topic: Vaccination: Adult Rubella

Congenital malformation is a possible consequence of rubella vaccination during pregnancy. - GMI Summary

Pubmed Data : JAMA. 1981 Sep 25;246(13):1413-7. PMID: [7265443](#)

Article Published Date : Sep 25, 1981

Authors : S R Preblud, H C Stetler, J A Frank, W L Greaves, A R Hinman, K L Herrmann

Study Type : Human Study

Additional Links

Diseases : [Birth Defects : CK\(204\) : AC\(39\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

In one study on rubella vaccination in 19 pregnant women, 9 aborted, 8 induced and 1 spontaneously. - GMI Summary

Pubmed Data : Int Ophthalmol Clin. 1975;15(4):229-41. PMID: [773881](#)

Article Published Date : Jan 01, 1975

Authors : V Boniuk

Study Type : Human Study

Additional Links

Diseases : [Cataract : CK\(182\) : AC\(57\)](#), [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Adult rubella and adult hepatitis B vaccines were statistically associated with chronic arthritis which persisted for at least one year. - GMI Summary

Pubmed Data : Clin Exp Rheumatol. 2002 Nov-Dec;20(6):767-71. PMID: [12508767](#)

Article Published Date : Nov 01, 2002

Authors : D A Geier, M R Geier

Study Type : Animal Study

Additional Links

Diseases : [Arthritis : CK\(1493\) : AC\(221\)](#), [Autoimmune Diseases : CK\(5523\) : AC\(880\)](#), [Rheumatoid Arthritis : CK\(454\) : AC\(69\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hepatitis B : CK\(367\) : AC\(50\)](#)

Aborted fetal cells (diploid) have been used to create the rubella, measles, mumps, rabies, polio, smallpox, hepatitis A, chickenpox, and herpes zoster vaccines. - GMI Summary

Pubmed Data : Cuad Bioet. 2008 May-Aug;19(66):321-53. PMID: [18611078](#)

Article Published Date : May 01, 2008

Authors : José Luís Redondo Calderón

Study Type : Review

Additional Links

Additional Keywords : [Diploid Cell Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#), [Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#), [Vaccination: Rabies : CK\(4\) : AC\(3\)](#), [Vaccination: Varicella \(Chicken pox\) : CK\(174\) : AC\(21\)](#)

During the first five yeras of rubella immunizations in adults concerns emerged about the possibility that the vaccines do harm to the fetus in pregnant women. - GMI Summary

Pubmed Data : Am J Obstet Gynecol. 1976 Feb 15;124(4):327-32. PMID: [1251853](#)

Article Published Date : Feb 15, 1976

Authors : M Siegel

Study Type : Review

Additional Links

Diseases : [Pregnancy: Vaccination : CK\(92\) : AC\(16\)](#), [Rubella : CK\(54\) : AC\(4\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Adult Rubella : CK\(24\) : AC\(5\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#)

Topic: [Vaccinaton: Diptheria](#)

Diphtheria immunisation is weakly associated with an increased risk of asthma by age 7 years. - GMI Summary

Pubmed Data : Thorax. 2007 Mar;62(3):270-5. Epub 2006 Nov 7. PMID: [17090571](#)

Article Published Date : Mar 01, 2007

Authors : Kazunori Nakajima, Shyamali C Dharmage, John B Carlin, Cathryn L Wharton, Mark A Jenkins, Graham G Giles, Michael J Abramson, E Haydn Walters, John L Hopper

Study Type : Meta Analysis

Additional Links

Diseases : [Asthma : CK\(918\) : AC\(140\)](#), [Atopic Disease : CK\(91\) : AC\(9\)](#), [Hypersensitivity: Immediate : CK\(93\) : AC\(9\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccinaton: Diptheria : CK\(50\) : AC\(2\)](#)

The association with DTwP vaccines and increased infant mortality in females may be due to vaccine adjuvants and Th2 polarizing effects. - GMI Summary

Pubmed Data : J Trop Med. 2011 ;2011:706304. Epub 2011 May 5. PMID: [21760811](#)

Article Published Date : Jan 01, 2011

Authors : Mogens Helweg Claesson

Study Type : Human Study

Additional Links

Diseases : [Immune Dysregulation: TH1/TH2 imbalance](#) : CK(148) : AC(37), [Infant Mortality](#) : CK(249) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Pertussis](#) : CK(116) : AC(14), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Diphtheria](#) : CK(50) : AC(2)

Problem Substances : [Adjuvant](#) : CK(18) : AC(6), [Aluminum Hydroxide](#) : CK(56) : AC(14), [Vaccine Adjuvants](#) : CK(403) : AC(79)

Topic: [Vaccination: Oral Polio Vaccine](#)

[Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\)](#) : CK(12) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Oral Polio Vaccine](#) : CK(10) : AC(1), [Vaccination: Oral Polio Vaccine, Bivalent](#) : CK(10) : AC(1), [Vaccination: Polio](#) : CK(94) : AC(15)

["Outbreak of paralytic poliomyelitis in Oman: evidence for widespread transmission among fully vaccinated children."](#) - GMI Summary

Pubmed Data : Lancet. 1991 Sep 21 ;338(8769):715-20. PMID: [1679866](#)

Article Published Date : Sep 20, 1991

Authors : R W Sutter, P A Patriarca, S Brogan, P G Malankar, M A Pallansch, O M Kew, A G Bass, S L Cochi, J P Alexander, D B Hall

Study Type : Human: Case Report

Additional Links

Diseases : [Polio](#) : CK(19) : AC(8), [Polio: Vaccine-Related](#) : CK(1) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4)

Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine](#) : CK(10) : AC(1)

Topic: [Vaccination: Oral Polio Vaccine, Bivalent](#)

[Paralytic poliomyelitis associated with bivalent oral polio vaccines occurs at a rate over up to 70-fold higher than monovalent oral polio vaccine in Hungary.](#) - GMI Summary

Pubmed Data : Am J Epidemiol. 2011 Aug 1 ;174(3):316-25. Epub 2011 Jun 17. PMID: [21685412](#)

Article Published Date : Jul 31, 2011

Authors : Concepción F Estívariz, Zsuzsanna Molnár, Linda Venczel, Beatrix Kapusinszky, James A Zingeser, Galina Y Lipskaya, Olen M Kew, György Berencsi, Agnes Csohán

Study Type : Human Study

Additional Links

Diseases : [Non-polio acute flaccid paralysis \(NPAFP\)](#) : CK(12) : AC(1), [Poliomyelitis](#) : CK(33) : AC(4), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Oral Polio Vaccine](#) : CK(10) : AC(1), [Vaccination: Oral Polio Vaccine, Bivalent](#) : CK(10) : AC(1), [Vaccination: Polio](#) : CK(94) : AC(15)

Acute immune thrombocytopenic purpura as adverse reaction to oral polio vaccine (OPV). - GMI Summary

Pubmed Data : Hum Vaccin Immunother. 2013 Jun 4 ;9(8). Epub 2013 Jun 4. PMID: [23807364](#)

Article Published Date : Jun 03, 2013

Authors : Cheng-Qiang Jin, Hai-Xin Dong, Zhuo-Xiang Sun, Jian-Wei Zhou, Cui-Yun Dou, Shu-Hua Lu, Rui-Rui Yang

Study Type : Human: Case Report

Additional Links

Diseases : [Purpura: Thrombocytopenic](#) : CK(231) : AC(25), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180)

Anti Therapeutic Actions : [Vaccination: Oral Polio Vaccine, Bivalent](#) : CK(10) : AC(1)

Topic: Vaccination: Lyme disease

Vaccination for rabies, varicella or Lyme disease may result in acute or subacute post-vaccination small fiber neuropathy. - GMI Summary

Pubmed Data : Vaccine. 2009 Dec 9;27(52):7322-5. Epub 2009 Oct 4. PMID: [19808027](#)

Article Published Date : Dec 09, 2009

Authors : Nizar Souayah, Senda Ajroud-Driss, Howard W Sander, Thomas H Brannagan, Arthur P Hays, Russell L Chin

Study Type : Human Study

Additional Links

Diseases : [Lyme Disease](#) : CK(32) : AC(9), [Neuropathy: Small Fiber](#) : CK(10) : AC(1), [Rabies](#) : CK(13) : AC(3), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Varicella](#) : CK(50) : AC(5)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Vaccination may contribute to causing a wide variety of autoimmune disorders. - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)

Article Published Date : Feb 01, 2010

Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard

Study Type : Commentary

Additional Links

Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)

Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: Vaccination: Rabies

Rabies encephalitis in a child: a failure of rabies post exposure prophylaxis? - GMI Summary

Pubmed Data : BMJ Case Rep. 2015 ;2015. Epub 2015 Jan 14. PMID: [25589528](#)

Article Published Date : Dec 31, 2014

Authors : Faten Tinsa, Aida Borgi, Imen Jahouat, Khadija Boussetta

Study Type : Human: Case Report

Additional Links

Diseases : [Rabies](#) : CK(13) : AC(3)
Additional Keywords : [Vaccine Failure](#) : CK(244) : AC(30)
Anti Therapeutic Actions : [Vaccination: Rabies](#) : CK(4) : AC(3)

[Rabies vaccine may be ineffective during symptomatic rabies and may contribute to "early death."](#) - GMI Summary

Pubmed Data : Vaccine. 2009 Nov 27;27(51):7173-7. PMID: [19925949](#)
Article Published Date : Nov 27, 2009
Authors : Rodney E Willoughby
Study Type : Animal Study
Additional Links
Diseases : [Rabies](#) : CK(13) : AC(3)
Anti Therapeutic Actions : [Vaccination: Rabies](#) : CK(4) : AC(3)

[Aborted fetal cells \(diploid\) have been used to create the rubella, measles, mumps, rabies, polio, smallpox, hepatitis A, chickenpox, and herpes zoster vaccines.](#) - GMI Summary

Pubmed Data : Cuad Bioet. 2008 May-Aug;19(66):321-53. PMID: [18611078](#)
Article Published Date : May 01, 2008
Authors : José Luís Redondo Calderón
Study Type : Review
Additional Links
Additional Keywords : [Diploid Cell Vaccines](#) : CK(1) : AC(1)
Anti Therapeutic Actions : [Vaccination: Adult Rubella](#) : CK(24) : AC(5), [Vaccination: Measles](#) : CK(157) : AC(16), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

[Vaccination may contribute to causing a wide variety of autoimmune disorders.](#) - GMI Summary

Pubmed Data : Discov Med. 2010 Feb;9(45):90-7. PMID: [20193633](#)
Article Published Date : Feb 01, 2010
Authors : Hedi Orbach, Nancy Agmon-Levin, Gisele Zandman-Goddard
Study Type : Commentary
Additional Links
Diseases : [Autoimmune Diseases](#) : CK(5523) : AC(880), [Guillain-Barre Syndrome](#) : CK(84) : AC(14), [Human Papillomavirus \(HPV\)](#) : CK(163) : AC(23), [Inflammatory Myopathy](#) : CK(81) : AC(5), [Macrophagic myofasciitis](#) : CK(15) : AC(3), [Multiple Sclerosis](#) : CK(746) : AC(133), [Rheumatoid Arthritis](#) : CK(454) : AC(69), [Systemic Lupus Erythematosus](#) : CK(381) : AC(52), [Vaccine-induced Toxicity](#) : CK(1242) : AC(180), [Vasculitis](#) : CK(48) : AC(11)
Anti Therapeutic Actions : [Vaccination: All](#) : CK(4702) : AC(361), [Vaccination: Diphtheria-Pertussis-Tetanus](#) : CK(282) : AC(31), [Vaccination: Haemophilus Influenzae](#) : CK(25) : AC(4), [Vaccination: Hepatitis B](#) : CK(367) : AC(50), [Vaccination: HPV \(Gardasil\)](#) : CK(105) : AC(13), [Vaccination: Influenza](#) : CK(356) : AC(37), [Vaccination: Lyme disease](#) : CK(11) : AC(2), [Vaccination: Mumps-Measles-Rubella \(MMR\)](#) : CK(228) : AC(26), [Vaccination: Rabies](#) : CK(4) : AC(3), [Vaccination: Rotavirus](#) : CK(33) : AC(6), [Vaccination: Tetanus](#) : CK(61) : AC(8), [Vaccination: Varicella \(Chicken pox\)](#) : CK(174) : AC(21)

Topic: [Brachytherapy](#)

[Difficulties in eliminating measles and controlling rubella and mumps in a 99% measles vaccine compliant population.](#) - GMI Summary

Pubmed Data : PLoS One. 2014 ;9(2):e89361. Epub 2014 Feb 20. PMID: [24586717](#)
Article Published Date : Dec 31, 2013
Authors : Zhifang Wang, Rui Yan, Hanqing He, Qian Li, Guohua Chen, Shengxu Yang, Enfu Chen
Study Type : Human Study
Additional Links
Diseases : [Measles](#) : CK(278) : AC(8), [Mumps](#) : CK(41) : AC(1), [Rubella](#) : CK(54) : AC(4)

Additional Keywords : [Vaccine Failure : CK\(244\) : AC\(30\)](#)
Anti Therapeutic Actions : [Brachytherapy : CK\(10\) : AC\(1\)](#), [Vaccination: Measles : CK\(157\) : AC\(16\)](#),
[Vaccination: Mumps-Measles-Rubella \(MMR\) : CK\(228\) : AC\(26\)](#)

Topic: [Vaccination: Yellow Fever](#)

["Yellow fever vaccination and increased relapse rate in travelers with multiple sclerosis." - GMI Summary](#)

Pubmed Data : Arch Neurol. 2011 Oct ;68(10):1267-71. Epub 2011 Jun 13. PMID: [21670384](#)

Article Published Date : Oct 01, 2011

Authors : Mauricio F Farez, Jorge Correale

Study Type : Human Study

Additional Links

Diseases : [Multiple Sclerosis : CK\(746\) : AC\(133\)](#)

Anti Therapeutic Actions : [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Adverse Pharmacological Actions : [Immunotoxic : CK\(254\) : AC\(48\)](#)

["Adverse events associated with 17D-derived yellow fever vaccination--United States, 2001-2002." - GMI Summary](#)

Pubmed Data : MMWR Morb Mortal Wkly Rep. 2002 Nov 8 ;51(44):989-93. PMID: [12455906](#)

Article Published Date : Nov 08, 2002

Study Type : Review

Additional Links

Diseases : [Brain Inflammation : CK\(86\) : AC\(45\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

[From 1990 to the present, the number of cases \(n = 31\) and deaths \(n = 12\) from the yellow fever vaccine in travelers has exceeded the reports of YF \(n = 6\) acquired by natural infection. - GMI Summary](#)

Pubmed Data : Expert Rev Vaccines. 2012 Apr ;11(4):427-48. PMID: [22551029](#)

Article Published Date : Apr 01, 2012

Authors : Thomas P Monath

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#), [Yellow Fever : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

[Identification and characterization of avian retroviruses in chicken embryo-derived yellow fever vaccines: investigation of transmission to vaccine recipients. - GMI Summary](#)

Pubmed Data : J Virol. 2003 Jan ;77(2):1105-11. PMID: [12502826](#)

Article Published Date : Dec 31, 2002

Authors : Althaf I Hussain, Jeffrey A Johnson, Marcos Da Silva Freire, Walid Heneine

Study Type : In Vitro Study

Additional Links

Additional Keywords : [Iatrogenic Disease : CK\(226\) : AC\(26\)](#), [Retroviruses : CK\(10\) : AC\(10\)](#), [Vaccine Contamination : CK\(5\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Yellow Fever : CK\(13\) : AC\(2\)](#)

Topic: [Vaccination: Hexavalent](#)

[A case of sudden infant death associated with hexavalent immunization has](#)

been reported. - GMI Summary

Pubmed Data : Forensic Sci Int. 2008 Aug 6;179(2-3):e25-9. Epub 2008 Jun 6. PMID: [18538957](#)

Article Published Date : Aug 06, 2008

Authors : Stefano D'Errico, Margherita Neri, Irene Riezzo, Giuseppina Rossi, Cristoforo Pomara, Emanuela Turillazzi, Vittorio Fineschi

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination has been reported. - GMI Summary

Pubmed Data : Virchows Arch. 2006 Jan;448(1):100-4. Epub 2005 Oct 18. PMID: [16231176](#)

Article Published Date : Jan 01, 2006

Authors : Giulia Ottaviani, Anna Maria Lavezzi, Luigi Maturri

Study Type : Human: Case Report

Additional Links

Diseases : [Sudden Infant Death Syndrome \(SIDS\) : CK\(138\) : AC\(18\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Hexavalent : CK\(6\) : AC\(2\)](#)

Topic: Obstetric Interventions

The use of misoprostol for early pregnancy failure after failed expectant management is less costly than curettage. - GMI Summary

Pubmed Data : Hum Reprod. 2005 Apr;20(4):1067-71. Epub 2004 Dec 23. PMID: [15618248](#)

Article Published Date : Apr 01, 2005

Authors : G C M Graziosi, J W van der Steeg, P H W Reuwer, A P Drogtop, H W Bruinse, B W J Mol

Study Type : Human Study

Additional Links

Diseases : [Miscarriage : CK\(313\) : AC\(36\)](#), [Miscarriage: Medical Intervention : CK\(125\) : AC\(14\)](#)

Additional Keywords : [Surgical Alternatives : CK\(20\) : AC\(2\)](#)

Anti Therapeutic Actions : [Obstetric Interventions : CK\(1030\) : AC\(69\)](#), [Vaccination: Diphtheria-Pertussis-Tetanus : CK\(282\) : AC\(31\)](#)

Topic: Vaccination: Cholera

killed cholera vaccination generates an inferior immune response in comparison to patients with naturally acquired cholera. - GMI Summary

Pubmed Data : Clin Vaccine Immunol. 2011 May ;18(5):844-50. Epub 2011 Feb 23. PMID: [21346055](#)

Article Published Date : May 01, 2011

Authors : Mohammad Murshid Alam, M Asrafuzzaman Riyadh, Kaniz Fatema, Mohammad Arif Rahman, Nayeema Akhtar, Tanvir Ahmed, Mohiul Islam Chowdhury, Fahima Chowdhury, Stephen B Calderwood, Jason B Harris, Edward T Ryan, Firdausi Qadri

Study Type : Human Study

Additional Links

Diseases : [Cholera : CK\(27\) : AC\(17\)](#)

Additional Keywords : [Cholera : CK\(27\) : AC\(17\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Cholera : CK\(20\) : AC\(2\)](#)

Topic: Vaccination: Japanese Encephalitis Virus Vaccine

Neutralizing antibodies, elicited by the mouse brain-derived and formalin-inactivated JEV Nakayama vaccine among a limited number of vaccinees, have reduced neutralizing capacity against circulating GI virus. - GMI Summary

Pubmed Data : PLoS Negl Trop Dis. 2012 Sep ;6(9):e1834. Epub 2012 Sep 27. PMID: [23029592](#)

Article Published Date : Aug 31, 2012

Authors : Yi-Chin Fan, Jo-Mei Chen, Hsien-Chung Chiu, Yi-Ying Chen, Jen-Wei Lin, Chen-Chang Shih, Chih-Ming Chen, Chao-Chin Chang, Gwong-Jen J Chang, Shyan-Song Chiou

Study Type : Human Study

Additional Links

Diseases : [Encephalitis: Japanese : CK\(13\) : AC\(4\)](#)

Additional Keywords : [Encephalitis: Japanese : CK\(13\) : AC\(4\)](#), [Vaccine Failure : CK\(244\) : AC\(30\)](#)

Anti Therapeutic Actions : [Vaccination: Japanese Encephalitis Virus Vaccine : CK\(10\) : AC\(1\)](#)

Topic: Vaccination: Nasal

ransverse myelitis has been reported in association with a nasal attenuated novel influenza A(H1N1) vaccine. - GMI Summary

Pubmed Data : Arch Neurol. 2010 Aug;67(8):1018-20. PMID: [20697056](#)

Article Published Date : Aug 01, 2010

Authors : Wafa Akkad, Bassel Salem, Jerome W Freeman, Mark K Huntington

Study Type : Human: Case Report

Additional Links

Diseases : [Myelitis : CK\(39\) : AC\(5\)](#), [Swine Flu Associated Virus : CK\(145\) : AC\(32\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Influenza : CK\(356\) : AC\(37\)](#), [Vaccination: Nasal : CK\(3\) : AC\(1\)](#)

Topic: Vaccination: Plasmid DNA Vaccines

There is evidence that a DNA vaccine exhibits anti-fertility properties. - GMI Summary

Pubmed Data : Vaccine. 2011 Jul 12 ;29(31):4933-9. Epub 2011 May 17. PMID: [21596079](#)

Article Published Date : Jul 12, 2011

Authors : Meng-Fei Yu, Wen-Ning Fang, Gao-Feng Xiong, Ying Yang, Jing-Pian Peng

Study Type : Animal Study

Additional Links

Diseases : [Infertility : CK\(576\) : AC\(109\)](#), [Vaccination: Abortion : CK\(40\) : AC\(14\)](#), [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: Plasmid DNA Vaccines : CK\(3\) : AC\(2\)](#)

DNA plasmid vaccines may carry under reported risks associated with structural instability. - GMI Summary

Pubmed Data : Appl Microbiol Biotechnol. 2010 Aug;87(6):2157-67. Epub 2010 May 23. PMID: [20496146](#)

Article Published Date : Aug 01, 2010

Authors : Pedro H Oliveira, Kristala Jones Prather, Duarte M F Prazeres, Gabriel A Monteiro

Study Type : Review

Additional Links

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Plasmid DNA Vaccines : CK\(3\) : AC\(2\)](#)

Topic: Vaccination: GMO Vaccines

Comparative antitumor effect among GM-CSF, IL-12 and GM-CSF+IL-12

[genetically modified tumor cell vaccines.](#) - GMI Summary

Pubmed Data : Cancer Gene Ther. 2013 Aug 23. Epub 2013 Aug 23. PMID: [23969885](#)

Article Published Date : Aug 22, 2013

Authors : A Miguel, M J Herrero, L Sendra, R Botella, R Algás, M Sánchez, S F Aliño

Study Type : Animal Study

Additional Links

Anti Therapeutic Actions : [Vaccination: GMO Vaccines : CK\(1\) : AC\(1\)](#)

[Review: Biological safety concepts of genetically modified live bacterial vaccines.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Jul 26 ;25(30):5598-605. Epub 2006 Dec 5. PMID: [17239999](#)

Article Published Date : Jul 26, 2007

Authors : Joachim Frey

Study Type : Review

Additional Links

Additional Keywords : [GMO Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Genetically Modified Organisms : CK\(83\) : AC\(58\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: GMO Vaccines : CK\(1\) : AC\(1\)](#)

[Topic: Vaccination: Varicella Zoster \(Shingles\)](#)

[Reactivation of Herpes Zoster Keratitis in an Adult After Varicella Zoster Vaccination.](#) - GMI Summary

Pubmed Data : Cornea. 2012 Nov 26. Epub 2012 Nov 26. PMID: [23187165](#)

Article Published Date : Nov 25, 2012

Authors : Charles W Hwang, Walter A Steigleman, Erika Saucedo-Sanchez, Sonal S Tuli

Study Type : Human: Case Report

Additional Links

Diseases : [Herpes Zoster : CK\(472\) : AC\(35\)](#), [Herpes Zoster Keratitis : CK\(3\) : AC\(1\)](#)

Anti Therapeutic Actions : [Vaccination: Varicella Zoster \(Shingles\) : CK\(3\) : AC\(1\)](#)

[Topic: Genetically Modified Organisms](#)

[Review: Biological safety concepts of genetically modified live bacterial vaccines.](#) - GMI Summary

Pubmed Data : Vaccine. 2007 Jul 26 ;25(30):5598-605. Epub 2006 Dec 5. PMID: [17239999](#)

Article Published Date : Jul 26, 2007

Authors : Joachim Frey

Study Type : Review

Additional Links

Additional Keywords : [GMO Vaccines : CK\(1\) : AC\(1\)](#)

Anti Therapeutic Actions : [Genetically Modified Organisms : CK\(83\) : AC\(58\)](#), [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: GMO Vaccines : CK\(1\) : AC\(1\)](#)

[Topic: Vaccination: Anti-Fertility](#)

[Vaccination for contraception.](#) - GMI Summary

Pubmed Data : Aust N Z J Obstet Gynaecol. 1994 Jun;34(3):320-9. PMID: [7848209](#)

Article Published Date : Jun 01, 1994

Authors : W R Jones

Study Type : Review

Additional Links

Diseases : [Vaccine-induced Toxicity : CK\(1242\) : AC\(180\)](#)

Anti Therapeutic Actions : [Vaccination: All : CK\(4702\) : AC\(361\)](#), [Vaccination: Anti-Fertility : CK\(1\) : AC\(1\)](#)

Topic: [Vaccination: Conjugate Vaccines](#)

[Conjugate vaccines may predispose children to autism spectrum disorders.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2011 Oct 10. Epub 2011 Oct 10. PMID: [21993250](#)

Article Published Date : Oct 10, 2011

Authors : Brian J Richmand

Study Type : Review

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Conjugate Vaccines : CK\(1\) : AC\(1\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Streptococcus Pneumoniae : CK\(1\) : AC\(1\)](#)

Topic: [Vaccination: Streptococcus Pneumoniae](#)

[Conjugate vaccines may predispose children to autism spectrum disorders.](#) - GMI Summary

Pubmed Data : Med Hypotheses. 2011 Oct 10. Epub 2011 Oct 10. PMID: [21993250](#)

Article Published Date : Oct 10, 2011

Authors : Brian J Richmand

Study Type : Review

Additional Links

Diseases : [Autism : CK\(570\) : AC\(65\)](#), [Autism Spectrum Disorders : CK\(1160\) : AC\(112\)](#)

Anti Therapeutic Actions : [Vaccination: Conjugate Vaccines : CK\(1\) : AC\(1\)](#), [Vaccination: Haemophilus Influenzae : CK\(25\) : AC\(4\)](#), [Vaccination: Streptococcus Pneumoniae : CK\(1\) : AC\(1\)](#)

Exhibit A
List of Required Vaccinations
(July 1, 2020)

Hawaii law allows the Director of Health, in consultation with the State Epidemiologist, to adopt, amend or appeal as rules, the immunization recommendations of the United States Department of Health and Human Services, Advisory Committee on Immunization Practices, including interim recommendations, as they apply to the listed vaccines indicated below. **The United States Department of Health and Human Services’ Advisory Committee on Immunization Practices’ General Best Practice Guidelines for Immunization, attached as Exhibit B, is adopted as the requirements in the State of Hawaii for minimum age, required spacing between doses, and other conditions governing the acceptability of immunizations for these listed vaccines.**

Table 1 – List of Pediatric Vaccinations Required for Children in the State of Hawaii*
DTaP [Diphtheria-Tetanus-acellular Pertussis]
<i>Haemophilus influenzae</i> type b (Hib)
Hepatitis A
Hepatitis B
Influenza
MMR [Measles (Rubeola)-Mumps-Rubella]
Pneumococcal Conjugate Vaccine (PCV)
Polio (IPV [Inactivated Poliovirus Vaccine])
Rotavirus
Varicella (chickenpox)

*The immunizations specified in Table 1 are required for children born in Hawaii after January 1, 1998, and all children born elsewhere after January 1, 1998 who become residents of Hawaii. Hawaii-born children are required to receive these immunizations within twenty-four months of their date of birth, and children born elsewhere who become residents are required to receive them within two years of first residence, unless medically contraindicated.

Table 2 – List of Vaccinations Required for Child-Care Center Attendance
DTaP [Diphtheria-Tetanus-acellular Pertussis] or DTP [Diphtheria-Tetanus-Pertussis]
<i>Haemophilus influenzae</i> type b (Hib)
Hepatitis A
Hepatitis B
MMR [Measles (Rubeola)-Mumps-Rubella]
Pneumococcal Conjugate Vaccine (PCV)
Polio (IPV [Inactivated Poliovirus Vaccine] or OPV [Oral Poliovirus Vaccine])
Varicella (chickenpox)

Table 3 – List of Vaccinations Required for Kindergarten – 12th Grade Attendance
DTaP [Diphtheria-Tetanus-acellular Pertussis] or DTP [Diphtheria-Tetanus-Pertussis]
Hepatitis A
Hepatitis B
HPV[†] [Human Papillomavirus Vaccine]
MCV[†] [Meningococcal Conjugate Vaccine]
MMR [Measles (Rubeola)-Mumps-Rubella]
Polio (IPV [Inactivated Poliovirus Vaccine] or OPV [Oral Poliovirus Vaccine])
Tdap[†] [Tetanus-diphtheria-acellular pertussis]
Varicella (chickenpox)

[†]Only required for students first entering a Hawaii school in 7th grade or higher.

Table 4 – List of Vaccinations Required for 7th Grade Attendance[‡]
HPV [Human Papillomavirus Vaccine]
MCV [Meningococcal Conjugate Vaccine]
Tdap [Tetanus-diphtheria-acellular pertussis]

[‡]In addition to meeting the K-12 Immunization Requirements upon first school attendance listed in Table 3, all students must show evidence of receiving these immunizations prior to 7th grade attendance.

Table 5 – List of Vaccinations Required for Post-Secondary School Attendance
MCV^{**} [Meningococcal Conjugate Vaccine]
MMR[¶] [Measles (Rubeola)-Mumps-Rubella]
Tdap [Tetanus-diphtheria-acellular pertussis]
Varicella (chickenpox)

^{**}First-year students living in on-campus housing.

[¶]Students born prior to 1957 are exempt from the MMR vaccination requirement.

**General Best Practice Guidelines for
Immunization**

**Best Practices Guidance of the Advisory
Committee on Immunization Practices
(ACIP)**

Kroger AT, Duchin J, Vázquez M

General Best Practice Guidelines for Immunization: Introduction

Kroger AT, Duchin J, Vázquez M. General Best Practice Guidelines for Immunization. Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP). [www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf]. Accessed on August 1, 2018.

General Best Practice Guidelines for Immunization

Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)

Kroger AT, Duchin J, Vázquez M

1. Introduction

The Centers for Disease Control and Prevention (CDC) recommends routine vaccination to prevent 17 vaccine-preventable diseases that occur in infants, children, adolescents, or adults. This report provides information for clinicians and other health care providers about concerns that commonly arise when vaccinating persons of various ages.

Providers and patients must navigate numerous issues, such as the timing of each dose, screening for contraindications and precautions, the number of vaccines to be administered, the educational needs of patients and parents, and interpreting and responding to adverse events. Vaccination providers help patients understand the substantial body of (occasionally conflicting) information about vaccination.

This vaccination best practice guidance is intended for clinicians and other health care providers who vaccinate patients in varied settings, including hospitals, provider offices, pharmacies, schools, community health centers, and public health clinics. The updated guidelines include 1) new information on simultaneous vaccination and febrile seizures; 2) enhancement of the definition of a “precaution” to include any condition that might

confuse diagnostic accuracy; 3) confirmation that if a patient is not acutely moderately or severely ill, vaccination during hospitalization is a best practice; 4) more descriptive characterization of anaphylactic allergy; 5) incorporation of protocols for management of anaphylactic allergy; 6) allowances for alternate route (subcutaneous instead of intramuscular) for hepatitis A vaccination; 7) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine; 8) deletion of much of the content from storage and handling, including storage units, temperature monitoring, and expiration dates (because this content is now codified and continually updated in the CDC's Vaccine Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html.); 9) incorporation of Infectious Diseases Society of America guidance on vaccination of persons with altered immunocompetence; 10) timing of intramuscular administration in patients with bleeding disorders; 11) updated data on vaccination record policy; 12) additional impacts of the Affordable Care Act (1,2) on adult vaccination; and 13) updated programmatic contact information on source material for vaccine information.

The guidance is organized in the following 10 documents: 1) Timing and Spacing of Immunobiologics; 2) Contraindications and Precautions; 3) Preventing and Managing Adverse Reactions; 4) Vaccine Administration; 5) Storage and Handling of Immunobiologics; 6) Altered Immunocompetence; 7) Special Situations; 8) Vaccination Records; 9) Vaccination Programs; and 10) Vaccine Information Sources. A glossary follows (see Appendix 1: Glossary).

This report will help vaccination providers to assess vaccine benefits and risks, use recommended administration practices, understand the most effective strategies for ensuring that vaccination coverage in the population remains high, and communicate the importance of vaccination to reduce the effects of vaccine-preventable disease. These best practice guidelines are intended for use in the United States; vaccine availability, use, and epidemiologic circumstances might differ in other countries and might warrant different guidance.

REFERENCES

1. The Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (2010).
2. U.S. Department of Health and Human Services. Read the law: the Affordable Care Act, section by section. 2015; www.hhs.gov/healthcare/about-the-law/read-the-law/index.html. Accessed 9 March, 2017.

2. Methods

The Advisory Committee on Immunization Practices (ACIP) General Recommendations Work Group (GRWG) reviews the evidence for best practices regarding immunization and releases updated guidance every 3 to 5 years (see Appendix 2: Membership). Work group members are required to report conflicts of interests. Conflict of interest information for those individuals who must report is available upon request to the corresponding author. Relevant topics are those identified by ACIP as topics related to all vaccines, including timing and spacing of doses, vaccine administration, and vaccine storage and handling. New topics are added when ACIP decides previous ACIP good practice statements on general issues (such as combination vaccines, adolescent vaccination, or adult vaccination) should be revised and incorporated into the *General Best Practice Guidelines for Immunization*.

The best practice guidelines in this report update the previous ACIP *General Recommendations on Immunization (1)* and are based both on review and analysis of available scientific evidence and on expert opinion of the diverse group of health care providers and public health officials who are members of GRWG. This group includes professionals from academic medicine (pediatrics, family practice, and pharmacy); international (Canada), federal, and state public health professionals; and a member from the nongovernmental Immunization Action Coalition (see Appendix 2: Membership). This revision involved consensus-building based on new evidence from the published literature and opinion from subgroups of subject matter experts consulted on specific topics.

The process by which the guidelines were drafted varied for each document; each document is therefore discussed individually below. ACIP voted to accept the proposed guidance in October 2014; for additional information, see www.cdc.gov/vaccines/acip/meetings/meetings-info.html.

Timing and Spacing of Immunobiologics

GRWG met monthly beginning in January 2011, and formed a subgroup to focus on review of guidelines around administration of simultaneous vaccination and febrile seizures. Meetings were held in April, May, and June 2011 to discuss the evidence. Other issues related to timing and spacing of vaccinations were discussed between February 2012 and September 2014 over 7 meetings (in February 2012, June 2012, August 2012, November 2012, January 2013, January 2014, May 2014, and September 2014). The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of the evidence were made to ACIP in June 2011, October 2011, and February 2013. Major changes include 1) guidance for simultaneous vaccination in the context of a risk for febrile seizures and 2) clarification of the use of the grace period between doses of the measles, mumps, rubella, and varicella vaccine (MMRV).

Contraindications and Precautions

GRWG met monthly and focused on revisions to the Contraindications and Precautions section beginning in January 2012, over 6 meetings (January 2012, February 2012, June 2012, August 2012, November, 2012, December 2012, and January 2013; see www.cdc.gov/vaccines/acip/meetings/meetings-info.html). The evidence supporting this document is based on a review of the published literature. Publications about vaccination during surgery, hospitalization, and anesthesia were obtained from the databases PubMed and MDConsult, searched from 1973 to 2014 using the MeSH (medical subject headings) terms “anesthesia” and “immunization”. The search and selection of studies was limited to English-language and human studies. The search and selection process yielded 20 publications, including review articles, observational studies, and letters to the editor. Presentations of proposed best practices were made to ACIP in February 2013 and a vote from ACIP affirming the language below was made in October 2014. Major changes include 1) enhancement of the definition of a “precaution” to include any condition that might confuse diagnostic accuracy and 2) guidance to vaccinate during a hospitalization if a patient is not acutely moderately or severely ill.

Preventing and Managing Adverse Reactions

GRWG met monthly and focused on revisions to the Preventing and Managing Adverse Reactions section beginning in April 2013, following revision to the document by the Allergy Subgroup. Selected members from this subgroup participated in the April 2013 main work group call. GRWG then met again in May 2013. The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of proposed guidance were made to ACIP in June 2013, and a vote from ACIP affirming the language below was made in October 2014. Major changes included 1) more descriptive characterization of anaphylactic allergy and 2) incorporation of protocols for managing adverse reactions. ACIP voted to accept the proposed statement in October 2014.

Vaccine Administration

GRWG met monthly beginning in May 2013 to discuss Vaccine Administration and met for 4 additional meetings (July 2013, August 2013, December 2013 and September 2014). The evidence supporting this document is based on expert opinion and arrived at by consensus. Presentations of the proposed guidance were made to ACIP in October 2013, and a vote from ACIP affirming the language below was made in October 2014. Major changes from 2011 include 1) allowances for alternate administration route (subcutaneous instead of intramuscular) for hepatitis A vaccine and 2) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine if given in error. ACIP voted to accept the proposed statement in October 2014.

Storage and Handling of Immunobiologics

GRWG met in December 2013 to discuss Storage and Handling of Immunobiologics and met one additional time in January 2014. The evidence supporting this document is based on expert opinion and arrived at by consensus. A presentation of proposed language was made to ACIP in February 2014, and a vote from ACIP approving the language below was made in October 2014. Most of the 2011 language was removed because this content is now codified and continually updated in the CDC's Vaccine

Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html. This content included Storage Units, Monitoring Storage Temperature, Vaccine Inventory, and Vaccine Transport.

Altered Immunocompetence

GRWG met twice in March and April 2014 to discuss best practices guidance for Altered Immunocompetence. This section incorporates general content from the Infectious Diseases Society of America (IDSA) policy statement *2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host (2)*, to which CDC provided input in November 2011. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed statement in June 2015.

Special Situations

GRWG met in April 2012 and then in 4 follow-up meetings in May, August, and November 2012, and January 2013. A focal point of discussion involved best practices guidance for intramuscular administration of persons with increased bleeding risk. Subject matter experts from the National Center for Birth Defects and Developmental Disabilities (NCBDDD) were invited to a work group meeting, and revisions to the guidance involving the timing of intramuscular administration were made in collaboration with these subject matter experts, primarily to ensure that ACIP's best practices guidance does not conflict with NCBDDD recommendations regarding the timing of clotting factor deficiency replacement. The evidence supporting this document is based on expert opinion and arrived at by consensus.

GRWG presented the Special Situations section to ACIP in February 2013. ACIP voted to accept the proposed statement in June 2015.

Vaccination Records

GRWG met in August and September 2013, and presented the vaccination records language to ACIP in October 2013. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed best practices guidance in June 2015.

Vaccination Programs

GRWG met in April 2014. The major revision to this section is the addition of language related to Affordable Care Act (3,4) coverage of adult vaccination. The evidence supporting this document is based on expert opinion and arrived at by consensus. GRWG presented this section to ACIP in June 2014. ACIP voted to accept this proposed statement in June 2015.

Vaccination Information Sources

GRWG met in September 2014 and presented this section to ACIP. The evidence supporting this document is based on expert opinion and arrived at by consensus. ACIP voted to accept this proposed statement in June 2015.

REFERENCES

1. Kroger AT, Sumaya CV, Pickering LK, Atkinson WL. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2011;1-60.
2. Rubin L, Levin M, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis.* 2014;58(3):e44-100. DOI: 10.1093/cid/cit684
3. The Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (2010).
4. U.S. Department of Health and Human Services. Read the law: the Affordable Care Act, section by section. 2015; www.hhs.gov/healthcare/about-the-law/read-the-law/index.html. Accessed 9 March, 2017.

3. Timing and Spacing of Immunobiologics

Updates

Major changes to the best practice guidance for timing and spacing of immunobiologics include 1) guidance for simultaneous vaccination in the context of a risk for febrile seizures and 2) clarification of the use of the grace period between doses of MMRV.

General Principles for Vaccine Scheduling

Optimal response to a vaccine depends on multiple factors, including the type of vaccine, age of the recipient, and immune status of the recipient. Recommendations for the age at which vaccines are administered are influenced by age-specific risks for disease, age-specific risks for complications, age-specific responses to vaccination, and potential interference with the immune response by passively transferred maternal antibodies. Vaccines are generally recommended for members of the youngest age group at risk for experiencing the disease for which vaccine efficacy and safety have been demonstrated.

Tetanus and diphtheria toxoids require booster doses to maintain protective antibody concentrations (1). Unconjugated polysaccharide vaccines do not induce T-cell memory, and additional doses (although they elicit the same or a lower antibody concentration) might increase the duration of protection. Conjugation with a protein carrier improves the effectiveness of polysaccharide vaccines by inducing T-lymphocyte–dependent immunologic function (2). Many vaccines that stimulate both cell-mediated immunity and neutralizing antibodies (e.g., live, attenuated virus vaccines) can usually induce prolonged immunity, even if antibody titers decline over time (3). Subsequent exposure to such viruses usually results in a rapid anamnestic antibody response without viremia.

Approximately 90%-95% of recipients of a single dose of certain live vaccines administered by injection at the recommended age (i.e., measles, rubella, and yellow fever vaccines) develop protective antibodies, generally within 14 days of the dose. For varicella and mumps vaccines, 80%-85% of vaccinees are protected after a single dose. However, because a limited proportion (5%-20%) of measles, mumps, and rubella

(MMR) or varicella vaccinees fail to respond to 1 dose, a second dose is recommended to provide another opportunity to develop immunity (4). Of those who do not respond to the first dose of the measles component of MMR or varicella vaccine, 97%-99% respond to a second dose (5,6).

The *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* are revised annually. Physicians and other health-care providers should ensure that they are following the most up-to-date schedules, which are available from CDC at

www.cdc.gov/vaccines/schedules/hcp/index.html.

Spacing of Multiple Doses of the Same Antigen

Vaccination providers should adhere to recommended vaccination schedules (Table 3-1). Administration at recommended ages and in accordance with recommended intervals between doses of multidose antigens provides optimal protection.

Administration of doses of a multidose vaccine using intervals that are shorter than recommended might be necessary in certain circumstances, such as impending international travel or when a person is behind schedule on vaccinations but needs rapid protection. In these situations, an accelerated schedule can be implemented using intervals between doses that are shorter than intervals recommended for routine vaccination (7). The accelerated or minimum intervals and ages for scheduling catch-up vaccinations are available at www.cdc.gov/vaccines/schedules/hcp/index.html. Vaccine doses should not be administered at intervals less than these minimum intervals or at an age that is younger than the minimum age.*^(a)

Before administering a vaccine dose, providers might need to verify that all previous doses were administered after the minimum age and in accordance with minimum intervals (Table 3-1). In clinical practice, vaccine doses occasionally are administered at intervals less than the minimum interval or at ages younger than the minimum age. Doses administered too close together or at too young an age can lead to a suboptimal immune response. However, administering a dose a few days earlier than the minimum interval or age is unlikely to have a substantially negative effect on the immune response

to that dose. Known as the “grace period”, vaccine doses administered ≤ 4 days before the minimum interval or age are considered valid; however, local or state mandates might supersede this 4-day guideline (7).^(b) (Day 1 is the day before the day that marks the minimum age or minimum interval for a vaccine.) The scenario most applicable to the grace period is a visit to a provider several days prior to the date indicated by the minimum interval, such as for a mild illness. Follow-up is unlikely soon after or even for a longer period of time following this mild illness visit; this therefore raises the question of whether vaccines be administered during the mild illness visit to avoid missed opportunities to vaccinate. Because of the unique schedule for rabies vaccine, the 4-day guideline does not apply to this vaccine (8). Doses of any vaccine administered ≥ 5 days earlier than the minimum interval or age should not be counted as valid doses and should be repeated as age appropriate. The repeat dose should be spaced after the invalid dose by the recommended minimum interval (Table 3-1). For example, if the first and second doses of *Haemophilus influenzae* type b (Hib) were administered only 14 days apart, the second dose would be invalid and need to be repeated because the minimum interval from dose 1 to dose 2 is 4 weeks. The repeat dose should be administered ≥ 4 weeks after the invalid dose (in this case, the second) (7). The repeat dose is counted as the valid second dose. If the first and second doses of hepatitis A vaccine were administered less than 6 months apart, the second dose is invalid and should be repeated 6 months after the invalid second dose (7). However, if this repeat dose (the third dose) is administered anytime 6 months or more after the first dose, the series can be considered complete.

If the first dose in a series is given ≥ 5 days before the recommended minimum age, the dose should be repeated on or after the date when the child reaches at least the minimum age (7). If the vaccine is a live vaccine, ensuring that a minimum interval of 28 days has elapsed from the invalid dose is recommended (7). For example, if the first dose of varicella vaccine were inadvertently administered at age 10 months, the repeat dose would be administered no earlier than the child’s first birthday (the minimum age for the first dose). If the first dose of varicella vaccine were administered at age 11 months and 2 weeks, the repeat dose should be administered no earlier than 4 weeks thereafter, which would occur after the first birthday.

Certain vaccines (e.g., adult tetanus and diphtheria toxoids [Td], pediatric diphtheria and tetanus toxoids [DT], tetanus toxoid) produce increased rates of local or systemic reactions in certain recipients when administered more frequently than recommended (9,10). Careful record keeping, maintenance of patient histories, use of immunization information systems (IISs), and adherence to recommended schedules can decrease the incidence of such reactions without adversely affecting immunity.

Simultaneous Administration

Simultaneous administration of vaccines is defined as administering more than one vaccine on the same clinic day, at different anatomic sites, and not combined in the same syringe. Experimental evidence and extensive clinical experience provide the scientific basis for administering vaccines simultaneously (11). Simultaneously administering all vaccines for which a person is eligible at the time of a visit increases the probability that a child, adolescent, or adult will be vaccinated fully by the appropriate age (12). A study conducted during a measles outbreak demonstrated that approximately one-third of measles cases among unvaccinated but vaccine-eligible preschool children might have been prevented if MMR had been administered at the same visit when another vaccine was administered (13). Simultaneous administration also is critical when preparing for foreign travel in the near future and when a health-care provider is uncertain that a patient will return for additional doses of vaccine.

With some exceptions, simultaneously administering the most widely used live and inactivated vaccines has produced seroconversion rates and rates for adverse reactions similar to those observed when the vaccines are administered separately (11, 14-16). Routine administration of all age-appropriate doses of vaccines simultaneously is recommended for children for whom no specific contraindications exist at the time of the visit (7). MMR and varicella vaccine can be administered simultaneously (7). Live, attenuated influenza vaccine (LAIV) does not interfere with the immune response to MMR or varicella vaccines administered at the same visit (17). No data exist about the immunogenicity of oral Ty21a typhoid vaccine when administered concurrently or within 30 days of live-virus vaccines. In the absence of such data, if typhoid vaccination is warranted, administration should not be delayed because of recent administration of

live, attenuated virus vaccines (18). Simultaneous administration of pneumococcal polysaccharide vaccine (PPSV) and inactivated influenza vaccine elicits a satisfactory antibody response without increasing the incidence or severity of adverse reactions (19). Simultaneous administration of PPSV23 and inactivated influenza vaccine is recommended for all persons for whom both vaccines are indicated. Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) and inactivated influenza vaccine (IIV) can be administered simultaneously (20). Hepatitis B vaccine administered with yellow fever vaccine is as safe and immunogenic as when these vaccines are administered separately (21). Measles and yellow fever vaccines have been administered safely at the same visit and without reduction of immunogenicity of either component (22,23).

During the 2010-2011 influenza season, surveillance systems detected safety signals for febrile seizures in young children following IIV and PCV13 vaccines (24). CDC studied the health-care visit records of more than 200,000 vaccinated children ages 6 months through 59 months through the Vaccine Safety Datalink Project during the 2010-2011 influenza season. The analyses found that febrile seizures following IIV and PCV13 vaccines given to this age group were rare, but did occur at higher than expected rates. The risk for febrile seizures peaked in children age 16 months and were more common when the 2 vaccines were given during the same health-care visit. In this group, about one additional febrile seizure occurred among every 2,200 children vaccinated. After assessing benefits and risks, ACIP continues to recommend IIV and PCV13 be given concomitantly if both are recommended (24,25).

There are 2 exceptions to the recommendation that vaccines should be administered simultaneously. In persons with anatomic or functional asplenia, quadrivalent meningococcal conjugate vaccine (MCV4)-D (MenACWY-D, Menactra) and pneumococcal conjugate vaccine (PCV)13 (PCV13, Prevnar 13) should not be administered simultaneously (26). This is based on immunogenicity studies that showed reduced antibody concentrations for 3 serotypes of pneumococcus (subtypes 4, 6B, and 18C) when PCV7 was administered simultaneously with MenACWY-D. For persons with anatomic or functional asplenia, PCV13 should be administered first and MenACWY-D 4 weeks later.

In patients recommended to receive both PCV13 and PPSV23, the 2 vaccines should not be administered simultaneously (27). PCV13 should be administered first. If PPSV23 has been administered first, PCV13 should be administered no earlier than 8 weeks later in children 6-18 years, and one year later in adults 19 years and older. Immunogenicity studies evaluating responses to PCV13 and PPSV23 administered in series showed a better immune response when PCV13 was administered first. An evaluation of immune response after a second pneumococcal vaccination administered 1 year after the initial study doses showed that subjects who received PPSV23 as the initial study dose had lower antibody responses after subsequent administration of PCV13 than those who had received PCV13 as the initial dose followed by a dose of PPSV23, regardless of the level of the initial response to PPSV23 (28,29).

Depending on which vaccines are administered during the first year of life, a child might receive up to 9 injections at the 12- through 15-month visit (MMR, varicella, Hib, PCV13, pediatric diphtheria and tetanus toxoids and acellular pertussis [DTaP], inactivated poliovirus [IPV], hepatitis A, hepatitis B [HepB], and influenza vaccines). Although there is no exact limit on the number of injections, with a little flexibility, a provider can ensure that the primary series doses are given without administering too many injections at each visit. To reduce the number of injections at the 12- through 15-month visit, the hepatitis B series and 3 doses of IPV (30) can be administered before the child's first birthday.

There are many other examples of ways the vaccination schedule provides flexibility. The majority of children aged 1 year who have received 2 Hib vaccine doses (polyribosylribitol phosphate-meningococcal outer membrane protein [PRP-OMP]) or 3 Hib vaccine doses (PRP-tetanus [PRP-T]) and 3 previous doses of DTaP and PCV13 have protection against Hib, diphtheria, pertussis, tetanus, and pneumococcus, which lasts throughout infancy (2,31). The third (PRP-OMP) or fourth (PRP-T) dose of the Hib series and the fourth doses of DTaP and PCV13 are critical in boosting antibody titer and ensuring continued protection (2,32-34). The fourth dose of DTaP is recommended at age 15-18 months but may be administered as early as age 12 months if 6 months have elapsed since the third dose and if there is concern that the child might not return by age 18 months (32). For infants at low risk for infection with hepatitis B virus (i.e., mother

tested negative for hepatitis B surface antigen [HBsAg] at the time of delivery and is not in a high risk group), the hepatitis B series can be completed at any time for children aged 6-18 months (35). The minimum age for administration of combination vaccines is the oldest minimum age for any of the individual components; the minimum interval between doses is equal to the greatest minimum interval of any of the individual components. Recommended spacing of doses should be maintained (Table 3-1).

Combination Vaccines

Combination vaccines merge equivalent component vaccines into single products to prevent more than one disease or to protect against multiple strains of infectious agents causing the same disease. Licensed combination vaccines can be used whenever any components of the combination are indicated and its other components are not contraindicated and if licensed by the Food and Drug Administration (FDA) for that dose in the series. Use of combination vaccines can reduce the number of injections patients receive and alleviate concern associated with the number of injections (30,36,37). Studies have demonstrated that parents and providers might be uncomfortable with multiple injections during single visits (38-40). Potential advantages of combination vaccines include 1) improved vaccine coverage rates (41), 2) timely vaccination coverage for children who are behind in the schedule (42-43), 3) reduced shipping and stocking costs, 4) reduced costs for extra health care visits necessitated by deferral of vaccination, and 5) facilitation of additional new vaccines into vaccination programs.

Potential disadvantages of combination vaccines include the following: 1) adverse events that might occur more frequently after administration of a combination vaccine compared with administration of separate antigens at the same visit, such as fever that occurs with the combination MMRV vaccine and combination DTaP-HepB-IPV vaccine (44,45); 2) confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses, especially when vaccinations are given by multiple providers who might be using different products; 3) reduced pathogen coverage if the combination product covers fewer types of one particular vaccine-preventable disease-causing agent (46); 4) extra doses of certain antigens in the combination product (e.g., a

provider who administers 4 doses of DTaP-HepB-IPV vaccine will give an extra dose of hepatitis B component); and 5) a shorter shelf-life than the individual component vaccines. The economic impact of the use of combination vaccines is unclear because combination products have the potential for either increased or decreased costs compared with single-antigen component vaccines. The price of a combination vaccine might exceed the total price of separate vaccines containing the same antigens. However, combination vaccines might represent a better overall economic value if the direct and indirect costs of extra injections, delayed or missed vaccinations, and additional handling and storage are taken into consideration (47).

Licensed Combination Vaccines

In this report, a combination vaccine is defined as a product containing components that can be divided equally into independently available routine vaccines. A dash (-) between vaccine products indicates that products are supplied in their final form by the manufacturer and do not require mixing or reconstitution by the user. A slash (/) indicates that the products must be mixed or reconstituted by the user. Seven combination vaccines for which separate antigens or antigen combinations exist have been licensed by FDA since 1996 in the United States (Table 3-2) (48-54). In the future, combination vaccines might include increasing numbers of components in different arrays to protect against these and other diseases. (The status of licensure and recommendations for new vaccines is available at <http://aapredbook.aappublications.org/news/vaccstatus.shtml>.) The use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines (55). Considerations should include provider assessment,^(c) patient preference, and the potential for adverse events. An exception is the first dose of MMRV. Unless the parent or caregiver expresses a preference for MMRV vaccine, MMR and varicella vaccine should be administered for the first dose for children aged 12-47 months (see Contraindications and Precautions) (44).

Situations might arise in which one component of a combination vaccine is specifically preferred to another component in that same vaccine. Future research considerations for newly licensed combination vaccines should focus on safety of doses that are not

needed because a patient is already vaccinated against the agents, whether the combination vaccine will improve the timeliness of vaccination, and potential reduced costs from disease prevention resulting from timely vaccination.

Combination Vaccines and FDA Licensure

Only combination vaccines licensed by FDA should be used (55). Vaccination providers should not combine separate vaccines into the same syringe to administer together unless mixing is indicated for the patient's age and is explicitly specified on the FDA-approved product label inserts. Only 2 combination vaccines, (DTaP-IPV/Hib vaccine, marketed as Pentacel, and Hib-MenCY, marketed as MenHibrix) contain separate antigen components for which FDA approves mixing by the user. The safety, immunogenicity, and effectiveness of unlicensed combinations are unknown.

Interchangeability of Formulations

FDA generally licenses a combination vaccine based on studies demonstrating that the product's immunogenicity (or efficacy) and safety are comparable or equivalent to monovalent or combination products licensed previously (37). FDA licensure also generally indicates that a combination vaccine may be used interchangeably with monovalent formulations and other combination products with similar component antigens produced by the same manufacturer to continue the vaccination series. For example, DTaP, DTaP-IPV/Hib, DTaP-HepB-IPV, and future DTaP vaccines that contain similar acellular pertussis antigens from the same manufacturer may be used interchangeably if licensed and indicated for the patient's age (34).

Interchangeability of Combination Vaccines from Different Manufacturers

Licensure of a vaccine by FDA does not necessarily indicate that the vaccine is interchangeable with products from other manufacturers. Such data are ascertained and interpreted more readily for diseases with known correlates of protective immunity (e.g., specific serologic markers). For diseases without such surrogate laboratory markers, prelicensure field vaccine efficacy (phase III) trials or postlicensure surveillance generally are required to determine protection (56). ACIP prefers that doses

of vaccine in a series come from the same manufacturer; however, if this is not possible or if the manufacturer of doses given previously is unknown, providers should administer the vaccine that they have available.

Vaccine Supply

Although vaccination providers should stock sufficient quantities of combination and monovalent vaccines needed to vaccinate children, adolescents, and adults against all diseases for which vaccines are recommended (30,37), all available types or brand-name products need not be stocked. Potential advantages of stocking a limited number of vaccines include 1) reducing confusion and potential errors when staff members must handle redundant products and formulations, 2) minimizing waste when less commonly used products expire, 3) decreasing cold storage capacity requirements, and 4) minimizing administrative costs related to accounting, purchasing, and handling. The National Pediatric Vaccine Stockpile exists to offset supply challenges (57).

Extra Doses of Vaccine Antigens

Administering extra antigens contained in a combination vaccine should be avoided in most situations (55). Using combination vaccines containing certain antigens not indicated at the time of administration to a patient might be justified when 1) the extra antigen is not contraindicated, 2) products that contain only the needed antigens are not readily available, and 3) potential benefits to the patient outweigh the potential risk for adverse events associated with the extra antigens. An extra dose of many live-virus vaccines and Hib or hepatitis B vaccine has not been found to be harmful (58,59). However, the risk for an adverse event might increase when extra doses are administered at an earlier time than the recommended interval for certain vaccines (e.g., tetanus toxoid vaccines and PPSV) (19,32,60).

A vaccination provider might not have vaccines available that contain only the antigens needed as indicated by a child's vaccination history. Alternatively, although the indicated vaccines might be available, the provider might prefer to use a combination vaccine to reduce the required number of injections. In such cases, the benefits and risks of administering the combination vaccine with an unneeded antigen should be carefully considered and discussed with the patient or parent.

When inactivated (i.e., killed) or subunit vaccines (which are often adsorbed to aluminum-salt adjuvants) are administered, the reactogenicity of the vaccine must be considered in balancing the benefits and risks of extra doses (55). Because clinical experience suggests low reactogenicity, an extra dose of Hib or hepatitis B vaccine may be administered as part of a combination vaccine to complete a vaccination series for another component of the combination. Administration of extra doses of tetanus toxoid vaccines earlier than the recommended intervals can increase the risk for severe local reactions (20,33). Examples of such vaccines include DTaP, DT (for children), and Td (for adolescents and adults). Extra doses of tetanus-toxoid–containing vaccines might be appropriate for certain patients, including for children who previously received DT or Td vaccine and need protection from pertussis (in DTaP or Tdap) or for immigrants with uncertain vaccination histories.

Conjugate Vaccine Carrier Proteins

Protein conjugates used in Hib conjugate vaccines produced in the United States include tetanus toxoid (in PRP-T) which is also used as a component of DTaP and Tdap vaccines (61). Simultaneous or sequential vaccination with Hib and these tetanus-toxoid containing vaccines is recommended when both are indicated (55). MCV4 and PCV13 both contain diphtheria-toxoid conjugates. There has been concern about simultaneous administration of vaccines containing like conjugates. One brand of MCV4, MenACWY-D (Menactra), demonstrates reduced immunogenicity of the antibody response to Streptococcal pneumonia strains when administered simultaneously with PCV13 compared with separate administration. It is recommended to space these vaccines by 28 days in a person with anatomic asplenia (46). Simultaneous or sequential vaccination of MCV4-CRM (Menveo), PCV13, and Tdap (33,61), all of which contain diphtheria toxoid, is not associated with reduced immunogenicity or increase in local adverse events.

Nonsimultaneous Administration

There is no evidence that inactivated vaccines interfere with the immune response to other inactivated vaccines or to live vaccines. Any inactivated vaccine can be administered either simultaneously or at any time before or after a different inactivated

vaccine or live vaccine ([Table 3-3](#)). The 2 exceptions, as mentioned above, are a 4-week interval between PCV13 and MenACWY-D in a person with anatomic asplenia and the separation of doses between PCV13 and PPSV23 (6-12 months recommended for non-high risk, 8 week minimum) if PCV13 is given first, 8 weeks in children 6-18 years, and 1 year minimum in adults 19 years and older if PPSV23 is given first (26).

Limited data are available regarding interference between live vaccines used in the United States. The immune response to one live-virus vaccine might be impaired if administered within 28 days (i.e., 4 weeks) of another live-virus vaccine (62,63). In a study conducted in 2 U.S. health maintenance organizations, the risk for varicella vaccine failure (i.e., varicella disease in a vaccinated person) among persons who received varicella vaccine within 28 days of MMR vaccination was threefold higher than among persons who received varicella vaccine >28 days after MMR vaccination (64). Another study determined that the response to yellow fever vaccine is not affected by monovalent measles vaccine administered 1-27 days earlier (22). The effect of nonsimultaneous administration of rubella, mumps, varicella, and yellow fever vaccines is unknown.

Two or more injectable or nasally administered live vaccines not administered on the same day should be separated by at least 4 weeks ([Table 3-3](#)), to minimize the potential risk for interference. If 2 such vaccines are separated by <4 weeks, the second vaccine administered should not be counted and the dose should be repeated at least 4 weeks later. On the day a live injectable or intranasal vaccine will be administered, providers should ensure that no live injectable or intranasal vaccine was given in the previous 28 days.

The 4-day grace period discussed earlier, which may be used to shorten the minimum interval between doses of the same vaccine, should not be applied to this 4-week interval between 2 different live vaccines (55). Confusion about this prohibition may arise when 2 live vaccines whose intervals are identical are administered simultaneously. For example, if MMR and varicella vaccines are administered on the same day, the second dose of each vaccine could come due 4 weeks later (depending on the patient's age). If either vaccine had been given alone at both time points, the 4-day grace period could be applied to the second dose. But in this situation the live vaccine rule prevents the grace

period from being applied to the second dose of either vaccine, because Varicella-2, if administered earlier than 4 weeks, could potentially be affected by MMR1, and likewise MMR2 could be affected by Varicella-1. Note that this prohibition also applies if the combination MMRV is used rather than individual MMR and varicella vaccines.

The oral vaccines Ty21a typhoid vaccine and rotavirus can be administered simultaneously with or at any interval before or after other live vaccines (injectable or intranasal) if indicated (65).

Spacing of Vaccines and Antibody-Containing Products

Live Vaccines

Ty21a typhoid, yellow fever, LAIV, zoster, and rotavirus vaccines may be administered at any time before, concurrent with, or after administration of any antibody-containing preparation such as immune globulin, hyperimmune globulin, or intravenous immune globulin (IGIV) (66). Blood (e.g., whole blood, packed red blood cells, and plasma) and other antibody-containing blood products (e.g., immune globulin, hyperimmune globulin, and IGIV) can inhibit the immune response to measles and rubella vaccines for ≥ 3 months. The effect of blood and immune globulin preparations on the response to mumps and varicella vaccines is unknown; however, commercial immune globulin preparations contain antibodies to these viruses. Blood products available in the United States are unlikely to contain a substantial amount of antibody to yellow fever virus. The length of time that interference with injectable live-virus vaccine (other than yellow fever) can persist after the antibody-containing product is a function of the amount of antigen-specific antibody contained in the product (67-69). Therefore, after an antibody-containing product is received, live vaccines (other than Ty21a typhoid, yellow fever, LAIV, zoster, and rotavirus vaccines) should be delayed until the passive antibody has degraded (Table 3-4). If a dose of injectable live-virus vaccine (other than yellow fever and zoster) is administered after an antibody-containing product but at an interval shorter than recommended in this report, the vaccine dose should be repeated unless serologic testing is feasible and indicates a response to the vaccine. The repeat dose or serologic testing should be performed after the interval indicated for the antibody-containing product (Table 3-5).

Although passively acquired antibodies can interfere with the response to rubella vaccine, the low dose of anti-Rho(D) globulin or any other blood product administered to postpartum women have not been demonstrated to reduce the response to the RA27/3 strain rubella vaccine (70). Congenital rubella syndrome and congenital varicella are conditions with considerable morbidity and represent a true risk in future pregnancies. Because of the importance of rubella and varicella immunity among women of child-bearing age (4,71), the postpartum vaccination of women without evidence of immunity to rubella or varicella with MMR, varicella, or MMRV vaccines should not be delayed because of receipt of anti-Rho(D) globulin or any other blood product during the last trimester of pregnancy or at delivery. Any reduction in immunity caused by anti-Rho(D) globulin or other blood products is outweighed by the opportunity to generate immunity. These women should be vaccinated immediately after giving birth and, if possible, tested ≥ 3 months later to ensure immunity to rubella and, if appropriate, to measles (2). Measles and rubella serologies have a low false-positive rate and are therefore acceptable for use in this limited postpartum context. Interference might occur if administration of an antibody-containing product becomes necessary after administration of MMR or varicella vaccines. Usually, vaccine virus replication and stimulation of immunity occurs 1-2 weeks after vaccination. If the interval between administration of any of these vaccines and subsequent administration of an antibody-containing product is < 14 days, vaccination should be repeated after the recommended interval (Tables 3-4 and 3-5) unless serologic testing indicates a protective antibody response (7).

A humanized mouse monoclonal antibody product (palivizumab) is available as prophylaxis for serious lower respiratory tract disease from respiratory syncytial virus among infants and young children. This product contains only antibody to respiratory syncytial virus and does not interfere with the immune response to licensed live or inactivated vaccines.

Inactivated Vaccines

Antibody-containing products interact less with inactivated, recombinant subunit, and polysaccharide vaccines and toxoids than with live vaccines (72). Therefore,

administering inactivated vaccines and toxoids either simultaneously with or at any interval before or after receipt of an antibody-containing product should not substantially impair development of a protective antibody response ([Table 3-4](#)). The vaccine or toxoid and antibody preparation should be administered at different sites using the standard recommended dose.

Interchangeability of Single-Component Vaccines from Different Manufacturers

Certain vaccines that provide protection from the same diseases are available from different manufacturers, and these vaccines usually are not identical in antigen content or in amount or method of formulation. Manufacturers use different production processes, and their products might contain different concentrations of antigen per dose or a different stabilizer or preservative.

Available data indicate that infants who receive sequential doses of different Hib conjugate, hepatitis B, and hepatitis A vaccines produce a satisfactory antibody response after a complete primary series (73-76). All brands of Hib conjugate, hepatitis B,^(d) hepatitis A, rotavirus,^(e) and quadrivalent meningococcal conjugate vaccines are interchangeable within their respective series. If different brands of a particular vaccine require a different number of doses for series completion (e.g., Hib and rotavirus vaccines) and a provider mixes brands in the primary series, the higher number of doses is recommended for series completion (e.g., doses of either rotavirus or Hib vaccine). For Hib vaccines, any monovalent or combination conjugate vaccine is acceptable for the booster dose of the series, if only one product was used for the primary series (55).

Limited data are available about the safety, immunogenicity, and efficacy of using acellular pertussis (i.e., DTaP) vaccines from different manufacturers for successive doses of the pertussis series. Data from one study indicate that for the first 3 doses of the DTaP series, 1-2 doses of Tripedia (Sanofi Pasteur) followed by Infanrix (GlaxoSmithKline) for the remaining dose (or doses) is comparable to 3 doses of Tripedia with regard to immunogenicity, as measured by antibodies to diphtheria, tetanus, and pertussis toxoids, and filamentous hemagglutinin (77). However, in the absence of a clear serologic correlate of protection for pertussis, the relevance of these

immunogenicity data for protection against pertussis is unknown. When feasible, the same brand of DTaP vaccine should be used for all doses of the vaccination series (55). If vaccination providers do not know or have available the type of DTaP vaccine previously administered to a child, any DTaP vaccine may be used to continue or complete the series (55). For a child who needs 2 doses of influenza vaccine (IIV or LAIV), it is preferable to use the same type of vaccine for both doses. However, if the child is eligible for either IIV or LAIV, and the type of vaccine used for the first dose is not available, either vaccine can be used for the second dose (55). In a postlicensure study, meningococcal conjugate vaccines from different manufacturers were evaluated for successive doses of meningococcal conjugate vaccine. Persistence of antibodies were studied in recipients of MCV4-CRM after previous receipt of either MCV4-CRM or MenACWY-D. The percentage of persons with protective titers were the same for all serogroups. No data exist on the use of MenACWY-D after MCV4-CRM. Health-care providers should use every opportunity to provide a dose when indicated, regardless of the vaccine brand used for the previous dose or doses. For vaccines in general, vaccination should not be deferred because the brand used for previous doses is not available or is unknown (30,78).

Lapsed Vaccination Schedule

Vaccination providers should administer vaccines as close to the recommended intervals as possible. However, intervals between doses that are longer than recommended typically do not reduce final antibody concentrations, although protection might not be attained until the recommended number of doses has been administered. With some exceptions (e.g. oral typhoid vaccine) an interruption in the vaccination schedule does not require restarting the entire series of a vaccine or toxoid or addition of extra doses (7).

Unknown or Uncertain Vaccination Status

Vaccination providers frequently encounter persons who do not have adequate documentation of vaccinations. With the exception of influenza vaccine and PPSV23, providers should only accept written, dated records as evidence of vaccination; self-reported doses of influenza vaccine and PPSV23 are acceptable (60,79). The rationale

for acceptance for influenza vaccine is that the time period of recall is one year or less, making it very likely that correct recall will occur. The rationale for acceptance for PPSV23 is high frequency of vaccination leads to an increased rate of local reactions due to the reactogenicity of this vaccine. Although vaccinations should not be postponed if records cannot be found, an attempt to locate missing records should be made by contacting previous health care providers, reviewing state or local IISs, and searching for a personally held record. If records cannot be located within a reasonable time, these persons should be considered susceptible and started on the age-appropriate vaccination schedule. Serologic testing for immunity is an alternative to vaccination for certain antigens (e.g., measles, rubella, hepatitis A, and tetanus). However, commercial serologic testing might not always be sufficiently sensitive or standardized for detection of vaccine-induced immunity (with the exception of hepatitis B vaccination at 1-2 months after the final dose), and research laboratory testing might not be readily available.

^(a) During measles outbreaks, if cases are occurring among infants aged <12 months, measles vaccination of infants as young as 6 months can be used as an outbreak control measure. However, doses administered at ages <12 months should not be counted as part of the series (80).

^(b) In certain situations, local or state requirements might mandate that doses of selected vaccines be administered on or after specific ages. For example, a school entry requirement might not accept a dose of MMR or varicella vaccine administered before the child's first birthday. ACIP recommends that physicians and other health-care providers comply with local or state vaccination requirements when scheduling and administering vaccines.

^(c) Provider assessment should include number of injections, vaccine availability, likelihood of improved coverage, likelihood of patient return, and storage and cost considerations.

^(d) The exception is the 2-dose hepatitis B vaccination series for adolescents aged 11-15 years. Only Recombivax HB (Merck Vaccine Division) should be used in the schedule. Engerix-B (GlaxoSmithKline) is not approved by FDA for this schedule.

^(e)Based on expert opinion.

TABLE 3-1. Recommended and minimum ages and intervals between vaccine doses^{(a),(b),(c),(d)}

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
DTaP-1 ^(e)	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months ^(f)	6 months ^(f)
DTaP-4	15-18 months	15 months ^(f)	3 years	6 months
DTaP-5 ^(g)	4-6 years	4 years	—	—
HepA-1 ^(e)	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	—	—
HepB-1 ^(h)	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3 ⁽ⁱ⁾	6-18 months	24 weeks	—	—
Hib-1 ^(j)	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3 ^(k)	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	—	—
HPV-1 ^(l)	11-12 years	9 years	8 weeks	4 weeks
HPV-2	11-12 years (+2 months)	9 years (+4 weeks)	4 months	12 weeks ^(l)
HPV-3 ^{(l), (m)}	11-12 years (+6 months)	9 years (+5 months)	—	—
Influenza, inactivated ⁽ⁿ⁾	≥6 months	6 months ^(o)	4 weeks	4 weeks
IPV-1 ^(e)	2 months	6 weeks	8 weeks	4 weeks
IPV-2	4 months	10 weeks	8 weeks-14 months	4 weeks

IPV-3	6-18 months	14 weeks	3-5 years	6 months
IPV-4 ^(p)	4-6 years	4 years	—	—
LAIV ⁽ⁿ⁾	2-49 years	2 years	4 weeks	4 weeks
MenACWY-1 ^(q)	11-12 years	6 weeks ^(r)	4-5 years	8 weeks
MenACWY-2	16 years	11 years (+8 weeks) ^(s)	—	—
MMR-1 ^(t)	12-15 months	12 months	3-5 years	4 weeks
MMR-2 ^(t)	4-6 years	13 months	—	—
PCV13-1 ^(j)	2 months	6 weeks	8 weeks	4 weeks
PCV13-2	4 months	10 weeks	8 weeks	4 weeks
PCV13-3	6 months	14 weeks	6 months	8 weeks
PCV13-4	12-15 months	12 months	—	—
PPSV-1	—	2 years	5 years	5 years
PPSV-2 ^(u)	—	7 years	—	—
Rotavirus-1 ^(v)	2 months	6 weeks	8 weeks	4 weeks
Rotavirus-2	4 months	10 weeks	8 weeks	4 weeks
Rotavirus-3 ^(v)	6 months	14 weeks	—	—
Td	11-12 years	7 years	10 years	5 years
Tdap ^(w)	≥11 years	7 years	—	—
Varicella-1 ^(t)	12-15 months	12 months	3-5 years	12 weeks ^(x)
Varicella-2 ^(t)	4-6 years	15 months ^(y)	—	—
ZVL ^(z)	≥60 years	60 years ^(aa)	—	—
RZV - 1	≥50 years	50 years ^(bb)	2-6 months	4 weeks
RZV - 2	≥50 years (+ 2-6 months)	50 years	—	—

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = Haemophilus influenzae type b; HPV = human papillomavirus; IPV = inactivated poliovirus;

LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23 = pneumococcal polysaccharide vaccine; PRP-OMP = polyribosylribitol phosphate-meningococcal outer membrane protein conjugate; RZV = recombinant zoster vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; ZVL = zoster vaccine live.

(a) Combination vaccines are available. Use of licensed combination vaccines is generally preferred to separate injections of their equivalent component vaccines. When administering combination vaccines, the minimum age for administration is the oldest age for any of the individual components. The minimum interval between doses is equal to the greatest interval of any of the individual components.

(b) Information on travel vaccines, including typhoid, Japanese encephalitis, and yellow fever, is available at <https://www.cdc.gov/travel>. Information on other vaccines that are licensed in the United States but not distributed, including anthrax and smallpox, is available at <http://emergency.cdc.gov/bioterrorism/>.

(c) “Months” refers to calendar months.

(d) Within a number range, a hyphen (-) should be read as “through.”

(e) Combination vaccines containing the hepatitis B component are available (see Table 3-2). These vaccines should not be administered to infants aged <6 weeks because of the other vaccine components (i.e., Hib, DTaP, HepA, and IPV).

(f) The minimum recommended interval between DTaP-3 and DTaP-4 is 6 months. However, DTaP-4 need not be repeated if administered at least 4 months after DTaP-3. This is a special grace period of 2 months which can be used if evaluating records retrospectively. An additional 4 days should not be added to this grace period prospectively, but can be added retrospectively.

(g) If a fourth dose of DTaP is given on or after the fourth birthday, a fifth dose is not needed

(h) Adjuvanted Hepatitis B vaccine (HepB-CgG) can be administered to adults 18 years old and older on a two dose schedule, the first and second dose separated by 4 weeks.

(i) HepB-3 should be administered at least 8 weeks after HepB-2 and at least 16 weeks after HepB-1 and should not be administered before age 24 weeks.

(j) For Hib and PCV13, children receiving the first dose of vaccine at age ≥ 7 months require fewer doses to complete the series.

(k) If PRP-OMP (Pedvax-Hib, Merck Vaccine Division) was administered at ages 2 and 4 months, a dose at age 6 months is not necessary. The final dose has a minimum age of 12 months.

(l) Quadrivalent and nine-valent HPV vaccines are approved for males and females aged 9-26 years. The minimum age for HPV-3 is based on the baseline minimum age for the first dose (i.e., 9 years) and the minimum interval of 5 months between the first and third dose. Dose 3 need not be repeated if it is administered at least 5 months after the first dose and the intervals between dose 1 and dose 2, and dose 2 and dose 3, are maintained at 4 weeks and 12 weeks, respectively.

(m) A two-dose schedule of HPV vaccine is recommended for most persons beginning the series between 9 through 14 years of age. See HPV vaccine-specific recommendations for details. www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6549a5.pdf

(n) One dose of influenza vaccine per season is recommended for most persons. To determine which children younger than 9 years should receive 2 doses in a single season, please see influenza vaccine-specific recommendations (81).

(o) The minimum age for inactivated influenza vaccine varies by vaccine manufacturer. See package insert for vaccine-specific minimum ages.

(p) A fourth dose is not needed if the third dose was administered at ≥ 4 years and at least 6 months after the previous dose.

(q) Revaccination with meningococcal vaccine is recommended for previously vaccinated persons who remain at high risk for meningococcal disease (46).

(r) MenACWY-D (Menactra) can be given as young as 9 months for high-risk persons. MenACWY-CRM (Menveo) can be given as young as 2 months for high-risk persons. Hib-MenCY can be given as young as 6 weeks for high-risk persons. Hib-MenCY is given as a 4-dose series at 2 months, 4 months, 6 months and 12-18 months.

- (s) For routine non-high risk adolescent vaccination, the minimum age for the booster dose is 16 years.
- (t) Combination MMRV vaccine can be used for children aged 12 months-12 years. See text for details.
- (u) A second dose of PPSV23 5 years after the first dose is recommended for persons aged ≤ 65 years at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody concentration (60).
- (v) The first dose of rotavirus must be administered at age 6 weeks through 14 weeks and 6 days. The vaccine series should not be started for infants aged ≥ 15 weeks, 0 days. Rotavirus should not be administered to children older than 8 months, 0 days of age regardless of the number of doses received between 6 weeks and 8 months, 0 days of age. If 2 doses of Rotarix (GlaxoSmithKline) are administered as age appropriate, a third dose is not necessary.
- (w) Only 1 dose of Tdap is recommended. Subsequent doses should be given as Td. For management of a tetanus-prone wound in persons who have received a primary series of tetanus-toxoid-containing vaccine, the minimum interval after a previous dose of any tetanus-containing vaccine is 5 years.
- (x) A special grace period of 2 months, based on expert opinion, can be applied to the minimum interval of 3 months, when evaluating records retrospectively, which results in an acceptable minimum interval of 4 weeks. An additional 4 days should not be added on to this grace period.
- (y) A special grace period of 2 months, based on expert opinion, can be applied to the minimum age of 15 months when evaluating records retrospectively, which results in an acceptable minimum age of 13 months. An additional 4 days should not be added on to this grace period.
- (z) Zoster vaccine live is recommended as a single dose for persons aged ≥ 60 years.
- (aa) If a dose of zoster vaccine live is administered to someone 50-59 years of age, the dose does not need to be repeated. A 4 day grace period can be added to the absolute minimum age of 50 years when evaluating records retrospectively.
- (bb) If a 1st dose of recombinant zoster vaccine is administered to someone 18 – 49 years of age, the dose does not need to be repeated. A 4 day grace period can be added to the absolute minimum age of 18 years when evaluating records retrospectively.

TABLE 3-2. FDA-licensed combination vaccines^(a)

Vaccine^(b)	Trade name (year licensed)	Age range	Routinely recommended ages
HepA-HepB	Twinrix (2001)	≥18 years	Three doses on a schedule of 0, 1, and 6 months
DTaP-HepB-IPV	Pediarix (2002)	6 weeks-6 years	Three-dose series at 2, 4, and 6 months of age
MMRV	ProQuad (2005)	12 months-12 years	Two doses, the first at 12-15 months, the second at 4-6 years
DTaP-IPV	Kinrix (2008)	4-6 years	Fifth dose of DTaP and fourth dose of IPV
DTaP-IPV/Hib	Pentacel (2008)	6 weeks-4 years	Four-dose schedule at 2, 4, 6, and 15-18 months of age
Hib-MenCY	MenHibrix (2012)	6 weeks-18 months	Four-dose schedule at 2, 4, 6, and 12-15 months of age ^(c)
DTaP-IPV	Quadracel (2015)	4-6 years	Fifth dose of DTaP and fourth or fifth dose of IPV
<p>Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; FDA = Food and Drug Administration; HepA = hepatitis A; HepB = hepatitis B; Hib = Haemophilus influenzae type b; IPV = inactivated poliovirus; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.</p> <p>Source: (82).</p> <p>(a) Although MMR, DTaP, DT, Td, and Tdap are combination vaccines, they are not included on this list because they are not available in the United States as single-antigen products.</p> <p>(b) In descriptions of combination vaccines, dash (-) indicates products in which the active components are supplied in their final (combined) form by the manufacturer; slash (/) indicates products in which active components must be mixed by the user.</p> <p>(c) Hib-MenCY can be used for routine dosing of Hib vaccine but is recommended only for meningococcal vaccination in persons at high-risk of meningococcal disease.</p>			

TABLE 3-3. Guidelines for spacing of live and inactivated antigens

Antigen combination	Recommended minimum interval between doses
Two or more inactivated ^{(a),(b)}	May be administered simultaneously or at any interval between doses
Inactivated and live ^(c)	May be administered simultaneously or at any interval between doses
Two or more live injectable ^(c)	28 days minimum interval, if not administered simultaneously

Source: (82).

^(a) Certain experts suggest a 28-day interval between tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine and tetravalent meningococcal conjugate vaccine if they are not administered simultaneously.

^(b) In persons with functional or anatomic asplenia, MCV-D and PCV13 should not be administered simultaneously and should be spaced by 4 weeks. Likewise for persons with immunosuppressive high-risk conditions indicated for PCV13 and PPSV23, PCV13 should be administered first, and PPSV23 should be administered no earlier than 8 weeks later. For persons 65 years old or older indicated for PCV13 and PPSV23, PCV13 should be administered first and PPSV23 should be administered 6-12 months later.

^(c) The live oral vaccines Ty21a typhoid vaccine and rotavirus vaccine may be administered simultaneously with or at any interval before or after inactivated or live injectable vaccines.

TABLE 3-4. Guidelines for administering antibody-containing products^(a) and vaccines

Type of administration	Products administered		Recommended minimum interval between doses
Simultaneous (during the same clinic day)	Antibody-containing products and inactivated antigen		Can be administered simultaneously at different anatomic sites or at any time interval between doses
	Antibody-containing products and live antigen		Should not be administered simultaneously. ^(b) If simultaneous administration of measles-containing vaccine or varicella vaccine is unavoidable, administer at different sites and revaccinate or test for seroconversion after the recommended interval (see Table 3-5)
Nonsimultaneous	Administered first	Administered second	
	Antibody-containing products	Inactivated antigen	No interval necessary
	Inactivated antigen	Antibody-containing products	No interval necessary
	Antibody-containing products	measles, mumps, rubella vaccine, varicella vaccine, and combined measles, mumps, rubella, varicella vaccine antigens	Dose related ^{(b),(c)}

	MMR vaccine, varicella vaccine, and combined measles, mumps, rubella, varicella vaccine antigens	Antibody-containing products	2 weeks^(b)
--	---	-------------------------------------	------------------------------

^(a) Blood products containing substantial amounts of immune globulin include intramuscular, subcutaneous, and intravenous immune globulin, specific hyperimmune globulin (e.g., hepatitis B immune globulin, tetanus immune globulin, varicella zoster immune globulin, and rabies immune globulin), whole blood, packed red blood cells, plasma, and platelet products.

^(b) Yellow fever vaccine; rotavirus vaccine; oral Ty21a typhoid vaccine; live, attenuated influenza vaccine; and zoster vaccine are exceptions to these recommendations. These live, attenuated vaccines can be administered at any time before or after or simultaneously with an antibody-containing product.

^(c) The duration of interference of antibody-containing products with the immune response to the measles component of measles-containing vaccine, and possibly varicella vaccine, is dose related (see Table 3-5).

TABLE 3-5. Recommended intervals between administration of antibody-containing products and measles- or varicella-containing vaccine, by product and indication for vaccination

Product/Indication	Dose (mg IgG/kg) and route^(a)	Recommended interval before measles- or varicella-containing vaccine^(b) administration (months)
Blood transfusion		
RBCs, washed	10 mL/kg, negligible IgG/kg IV	None
RBCs, adenine-saline added	10 mL/kg (10 mg IgG/kg) IV	3
Packed RBCs (hematocrit 65%) ^(c)	10 mL/kg (60 mg IgG/kg) IV	6
Whole blood (hematocrit 35%-50%) ^(c)	10 mL/kg (80-100 mg IgG/kg) IV	6
Plasma/platelet products	10 mL/kg (160 mg IgG/kg) IV	7
Botulinum Immune Globulin Intravenous (Human)	1.0 mL/kg (50 mg IgG/kg) IV	6
Cytomegalovirus IGIV	150 mg/kg maximum	6
Hepatitis A IG		
Contact prophylaxis	0.1 mL/kg (3.3 mg IgG/kg) IM	3
International travel, <2 month stay	0.1 mL/kg (3.3 mg IgG/kg) IM	3
International travel, ≥2 month stay	0.2 mL/kg (10 mg IgG/kg) IM	3
Hepatitis B IG	0.06 mL/kg (10 mg IgG/kg) IM	3
IGIV		

Replacement therapy for immune deficiencies ^(d)	300-400 mg/kg IV ^(d)	8
Immune thrombocytopenic purpura treatment	400 mg/kg IV	8
Postexposure varicella prophylaxis	400 mg/kg IV	8
Postexposure measles prophylaxis for immunocompromised contacts	400 mg/kg IV	8
Immune thrombocytopenic purpura treatment	1000 mg/kg IV	10
Kawasaki disease	2 g/kg IV	11
Measles prophylaxis IG		
Standard (i.e., nonimmunocompromised) contact	0.50 mL/kg (80 mg IgG/kg) IM	6
Monoclonal antibody to respiratory syncytial virus F protein (e.g., Synagis [MedImmune])^(e)	15 mg/kg IM	None
Rabies IG	20 IU/kg (22 mg IgG/kg) IM	4
Tetanus IG	250 units (10 mg IgG/kg) IM	3
Varicella IG	125 units/10 kg (60-200 mg IgG/kg) IM, maximum 625 units	5

Abbreviations: HIV = human immunodeficiency virus; IG = immune globulin; IgG = immune globulin G; IGIV = intravenous immune globulin; mg IgG/kg = milligrams of immune globulin G per kilogram of body weight; IM = intramuscular; IV = intravenous; RBCs = red blood cells.

(a) This table is not intended for determining the correct indications and dosages for using antibody-containing products. Unvaccinated persons might not be protected fully against measles during the entire recommended interval, and additional doses of IG or measles vaccine might be indicated after measles exposure. Concentrations of measles antibody in an IG preparation can vary by manufacturer's lot. Rates of antibody clearance after receipt of an IG preparation also might vary. Recommended intervals are extrapolated from an estimated half-life of 30 days for passively acquired antibody and an observed interference with the immune response to measles vaccine for 5 months after a dose of 80 mg IgG/kg.

(b) Does not include zoster vaccine. Zoster vaccine may be given with antibody-containing blood products.

(c) Assumes a serum IgG concentration of 16 mg/mL.

(d) Measles vaccination is recommended for children with mild or moderate immunosuppression from HIV infection, and varicella vaccination may be considered for children with mild or moderate immunosuppression from HIV infection, but both are contraindicated for persons with severe immunosuppression from HIV or any other immunosuppressive disorder.

(e) Contains antibody only to respiratory syncytial virus.

REFERENCES

1. CDC. Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1991;40(RR-10):1-28.
2. CDC. *Haemophilus b* conjugate vaccines for prevention of *Haemophilus influenzae* type b disease among infants and children two months of age and older. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1991;40(RR-1):1-7.
3. Plotkin SA. Immunologic correlates of protection induced by vaccination. *Pediatr Infect Dis J.* 2001;20(1):63-75. DOI: 10.1097/00006454-200101000-00013
4. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1998;47(RR-8):1-57.
5. Watson JC, Pearson JA, Markowitz LE, et al. An evaluation of measles revaccination among school-entry-aged children. *Pediatrics.* 1996;97(5):613-618.
6. Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2007;56(RR-4):1-40.
7. Atkinson WL, Pickering LK, Schwartz B, Weniger BG, Iskander JK, Watson JC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). *MMWR Recomm Rep.* 2002;51(RR-2):1-35.
8. Manning SE, Rupprecht CE, Fishbein D, et al. Human rabies prevention—United States, 2008: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep.* 2008;57(RR-3):1-28.

9. Levine L, Edsall G. Tetanus toxoid: what determines reaction proneness? *J Infect Dis*. 1981;144(4):376. DOI: 10.1093/infdis/144.4.376
10. Edsall G, Elliott MW, Peebles TC, Eldred MC. Excessive use of tetanus toxoid boosters. *JAMA*. 1967;202(1):111-113. DOI: 10.1001/jama.1967.03130140075009
11. King GE, Hadler SC. Simultaneous administration of childhood vaccines: an important public health policy that is safe and efficacious. *Pediatr Infect Dis J*. 1994;13(5):394-407.
12. National Vaccine Advisory Committee. Standards for child and adolescent immunization practices. *Pediatrics*. 2003;112(4):958-963.
13. Hutchins SS, Escolan J, Markowitz LE, et al. Measles outbreak among unvaccinated preschool-aged children: opportunities missed by health care providers to administer measles vaccine. *Pediatrics*. 1989;83(3):369-374.
14. Deforest A, Long SS, Lischner HW, et al. Simultaneous administration of measles-mumps-rubella vaccine with booster doses of diphtheria-tetanus-pertussis and poliovirus vaccines. *Pediatrics*. 1988;81(2):237-246.
15. Dashefsky B, Wald E, Guerra N, Byers C. Safety, tolerability, and immunogenicity of concurrent administration of *Haemophilus influenzae* type b conjugate vaccine (meningococcal protein conjugate) with either measles-mumps-rubella vaccine or diphtheria-tetanus-pertussis and oral poliovirus vaccines in 14- to 23-month-old infants. *Pediatrics*. 1990;85(4 Pt 2):682-689.
16. Giammanco G, Li Volti S, Mauro L, et al. Immune response to simultaneous administration of a recombinant DNA hepatitis B vaccine and multiple compulsory vaccines in infancy. *Vaccine*. 1991;9(10):747-750. DOI: 10.1016/0264-410X(91)90291-D
17. Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 influenza season. *MMWR Morb Mortal Wkly Rep*. 2015;64(30):818-825.

18. CDC. Typhoid immunization: recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1990;39(RR-10):1-5.
19. DeStefano F, Goodman RA, Noble GR, McClary GD, Smith S, Broome CV. Simultaneous administration of influenza and pneumococcal vaccines. *JAMA.* 1982;247(18):2551-2554. DOI: 10.1001/jama.1982.03320430055032
20. Kretsinger K, Broder KR, Cortese MM, et al. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. *MMWR Recomm Rep.* 2006;55(RR-17):1-37.
21. Yvonnnet B, Coursaget P, Deubel V, Diop-Mar I, Digoutte JP, Chiron JP. Simultaneous administration of hepatitis B and yellow fever vaccines. *J Med Virol.* 1986;19(4):307-311. DOI: 10.1002/jmv.1890190403
22. Stefano I, Sato HK, Pannuti CS, et al. Recent immunization against measles does not interfere with the sero-response to yellow fever vaccine. *Vaccine.* 1999;17(9-10):1042-1046. DOI: 10.1016/S0264-410X(98)00320-X
23. Staples JE, Gershman M, Fischer M. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-7):1-27.
24. Leroy Z, Broder K, Menschik D, Shimabukuro T, Martin D. Febrile seizures after 2010-2011 influenza vaccine in young children, United States: a vaccine safety signal from the vaccine adverse event reporting system. *Vaccine.* 2012;30(11):2020-2023. DOI: 10.1016/j.vaccine.2011.12.042
25. Tse A, Tseng HF, Greene SK, Vellozzi C, Lee GM. Signal identification and evaluation for risk of febrile seizures in children following trivalent inactivated influenza vaccine in the Vaccine Safety Datalink Project, 2010-2011. *Vaccine.* 2012;30(11):2024-2031. DOI: 10.1016/j.vaccine.2012.01.027
26. CDC. Recommendation of the Advisory Committee on Immunization Practices (ACIP) for use of quadrivalent meningococcal conjugate vaccine

- (MenACWY-D) among children aged 9 through 23 months at increased risk for invasive meningococcal disease. *MMWR Morb Mortal Wkly Rep.* 2011;60(40):1391-1392.
27. CDC. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 2012;61(40):816-819.
 28. CDC. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among children aged 6-18 years with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 2013;62(25):521-524.
 29. Tomczyk S, Bennett NM, Stoecker C, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥ 65 years: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 2014;63(37):822-825.
 30. CDC. Recommended immunization schedules for persons aged 0 through 18 years—United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2011;60(5):1-4.
 31. Shinefield HR, Black S, Ray P, et al. Safety and immunogenicity of heptavalent pneumococcal CRM197 conjugate vaccine in infants and toddlers. *Pediatr Infect Dis J.* 1999;18(9):757-763. DOI: 10.1097/00006454-199909000-00004
 32. CDC. Pertussis vaccination: use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-7):1-25.
 33. Broder KR, Cortese MM, Iskander JK, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-3):1-34.

34. Nuorti JP, Whitney CG. Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-11):1-18.
35. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep.* 2005;54(RR-16):1-31.
36. Committee on Infectious Diseases. Recommended childhood and adolescent immunization schedules—United States, 2010. *Pediatrics.* 2010;125(1):195-196. DOI: 10.1542/peds.2009-3194
37. CDC. Recommended adult immunization schedule—United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2011;60(4):1-4.
38. Woodin KA, Rodewald LE, Humiston SG, Carges MS, Schaffer SJ, Szilagyi PG. Physician and parent opinions. Are children becoming pincushions from immunizations? *Arch Pediatr Adolesc Med.* 1995;149(8):845-849. DOI: 10.1001/archpedi.1995.02170210019003
39. Kuppermann M, Nease RF, Jr., Ackerson LM, Black SB, Shinefield HR, Lieu TA. Parents' preferences for outcomes associated with childhood vaccinations. *Pediatr Infect Dis J.* 2000;19(2):129-133. DOI: 10.1097/00006454-200002000-00010
40. Meyerhoff A, Jacobs RJ, Greenberg DP, Yagoda B, Castles CG. Clinician satisfaction with vaccination visits and the role of multiple injections, results from the COVISE Study (Combination Vaccines Impact on Satisfaction and Epidemiology). *Clin Pediatr (Phila).* 2004;43(1):87-93.
41. Marshall GS, Happe LE, Lunacsek OE, et al. Use of combination vaccines is associated with improved coverage rates. *Pediatr Infect Dis J.* 2007;26(6):496-500. DOI: 10.1097/INF.0b013e31805d7f17
42. Kalies H, Grote V, Verstraeten T, Hessel L, Schmitt HJ, von Kries R. The use of combination vaccines has improved timeliness of vaccination in children.

- Pediatr Infect Dis J.* 2006;25(6):507-512. DOI: 10.1097/01.inf.0000222413.47344.23
43. Happe LE, Lunacsek OE, Kruzikas DT, Marshall GS. Impact of a pentavalent combination vaccine on immunization timeliness in a state Medicaid population. *Pediatr Infect Dis J.* 2009;28(2):98-101. DOI: 10.1097/INF.0b013e318187d047
 44. Marin M, Broder KR, Temte JL, Snider DE, Seward JF. Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-3):1-12.
 45. Thompson LA, Irigoyen M, Matiz LA, LaRussa PS, Chen S, Chimkin F. The impact of DTaP-IPV-HB vaccine on use of health services for young infants. *Pediatr Infect Dis J.* 2006;25(9):826-831. DOI: 10.1097/01.inf.0000232635.81312.06
 46. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-2):1-28.
 47. Weniger BG, Chen RT, Jacobson SH, et al. Addressing the challenges to immunization practice with an economic algorithm for vaccine selection. *Vaccine.* 1998;16(19):1885-1897. DOI: 10.1016/S0264-410X(98)00170-4
 48. Liang J, Wallace G, Mootrey G. Licensure of a diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine and guidance for use as a booster dose. *MMWR Morb Mortal Wkly Report* 2015;64: 948-9.
 49. CDC. FDA approval of a Haemophilus b Conjugate Vaccine combined by reconstitution with an acellular pertussis vaccine. *MMWR Morb Mortal Wkly Rep.* 1996;45(45):993-995.
 50. CDC. FDA approval for a combined hepatitis A and B vaccine. *MMWR Morb Mortal Wkly Rep.* 2001;50(37):806-807.
 51. CDC. FDA licensure of diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and poliovirus vaccine combined,

- (PEDIARIX) for use in infants. *MMWR Morb Mortal Wkly Rep.* 2003;52(10):203-204.
52. CDC. Licensure of a combined live attenuated measles, mumps, rubella, and varicella vaccine. *MMWR Morb Mortal Wkly Rep.* 2005;54(47):1212-1214.
 53. CDC. Licensure of a diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine and guidance for use as a booster dose. *MMWR Morb Mortal Wkly Rep.* 2008;57(39):1078-1079.
 54. CDC. Licensure of a diphtheria and tetanus toxoids and acellular pertussis adsorbed, inactivated poliovirus, and haemophilus B conjugate vaccine and guidance for use in infants and children. *MMWR Morb Mortal Wkly Rep.* 2008;57(39):1079-1080.
 55. Kroger AT, Sumaya CV, Pickering LK, Atkinson WL. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2011:1-60.
 56. Plotkin SA. Vaccines: correlates of vaccine-induced immunity. *Clin Infect Dis.* 2008;47(3):401-409. DOI: 10.1086/589862
 57. Lane KS, Chu SY, Santoli JM. The United States pediatric vaccine stockpile program. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America.* 2006;42 Suppl 3:S125-129. DOI: 10.1086/499591
 58. Midthun K, Horne AD, Goldenthal KL. Clinical safety evaluation of combination vaccines. *Dev Biol Stand.* 1998;95:245-249.
 59. Pichichero ME, Blatter MM, Reisinger KS, et al. Impact of a birth dose of hepatitis B vaccine on the reactogenicity and immunogenicity of diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-*Haemophilus influenzae* type b combination vaccination. *Pediatr Infect Dis J.* 2002;21(9):854-859. DOI: 10.1097/01.inf.0000027669.37444.24
 60. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1-24.

61. Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2005;54(RR-7):1-21.
62. Petralli JK, Merigan TC, Wilbur JR. Action of endogenous interferon against vaccinia infection in children. *Lancet.* 1965;2(7409):401-405. DOI: 10.1016/S0140-6736(65)90755-5
63. Petralli JK, Merigan TC, Wilbur JR. Circulating interferon after measles vaccination. *N Engl J Med.* 1965;273:198-201. DOI: 10.1056/nejm196507222730405
64. Verstraeten T, Jumaan AO, Mullooly JP, et al. A retrospective cohort study of the association of varicella vaccine failure with asthma, steroid use, age at vaccination, and measles-mumps-rubella vaccination. *Pediatrics.* 2003;112(2):e98-103. DOI: 10.1542/peds.112.2.e98
65. CDC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1994;43(RR-1):1-38.
66. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2008;57(RR-5):1-30; quiz CE32-34.
67. Siber GR, Werner BG, Halsey NA, et al. Interference of immune globulin with measles and rubella immunization. *J Pediatr.* 1993;122(2):204-211. DOI: 10.1016/S0022-3476(06)80114-9
68. Mason WH, Schneider TL, Takahashi M. Duration of passively acquired measles antibody and response to live virus vaccination allowing gamma globulin therapy for Kawasaki syndrome. *Prog Pediatr Cardiol.* 1992;1(1):82. DOI: 10.1016/S1058-9813(06)80067-6
69. Kaplan JE, Nelson DB, Schonberger LB, et al. The effect of immune globulin on the response to trivalent oral poliovirus and yellow fever vaccinations. *Bull World Health Organ.* 1984;62(4):585-590.
70. Black NA, Parsons A, Kurtz JB, McWhinney N, Lacey A, Mayon-White RT. Post-partum rubella immunisation: a controlled trial of two vaccines. *Lancet.* 1983;2(8357):990-992. DOI: 10.1016/S0140-6736(83)90979-0

71. CDC. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR Recomm Rep.* 2001;50(RR-12):1-23.
72. Siber GR, Snyderman DR. Use of immune globulin in the prevention and treatment of infections. In: Remington J, Swartz M, eds. *Current clinical topics in infectious diseases*. Vol 12. Malden, MA: Blackwell Science; 1992.
73. Greenberg DP, Lieberman JM, Marcy SM, et al. Enhanced antibody responses in infants given different sequences of heterogeneous *Haemophilus influenzae* type b conjugate vaccines. *J Pediatr.* 1995;126(2):206-211. DOI: 10.1016/S0022-3476(95)70546-5
74. Anderson EL, Decker MD, Englund JA, et al. Interchangeability of conjugated *Haemophilus influenzae* type b vaccines in infants. *JAMA.* 1995;273(11):849-853. DOI: 10.1001/jama.1995.03520350031024
75. Piazza M, Abrescia N, Picciotto L, et al. [Demonstration of the interchangeability of 2 types of recombinant anti-hepatitis-B vaccine]. *Boll Soc Ital Biol Sper.* 1993;69(4):273-280.
76. Bryan JP, Henry CH, Hoffman AG, et al. Randomized, cross-over, controlled comparison of two inactivated hepatitis A vaccines. *Vaccine.* 2000;19(7-8):743-750. DOI: 10.1016/S0264-410X(00)00301-7
77. Greenberg DP, Pickering LK, Senders SD, et al. Interchangeability of 2 diphtheria-tetanus-acellular pertussis vaccines in infancy. *Pediatrics.* 2002;109(4):666-672. DOI: 10.1542/peds.109.4.666
78. CDC. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2000;49(RR-13):1-8.
79. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep.* 2010;59(RR-8):1-62.
80. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary

- recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-4):1-34.
81. Grohskopf LA, Olsen SJ, Sokolow LZ, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2014-15 influenza season. *MMWR Morb Mortal Wkly Rep.* 2014;63(32):691-697.
 82. American Academy of Pediatrics. Active Immunization. In: Pickering L, Baker C, Kimberlin D, Long S, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases.* 28th ed. Elk Grove Village, IL: American Academy of Pediatric; 2012.

4. Contraindications and Precautions

Updates

Major changes to the best practice guidance in this section include 1) enhancement of the definition of a “precaution” to include any condition that might confuse diagnostic accuracy and 2) recommendation to vaccinate during a hospitalization if a patient is not acutely moderately or severely ill.

General Principles

Contraindications (conditions in a recipient that increases the risk for a serious adverse reaction) and precautions to vaccination are conditions under which vaccines should not be administered. Because the majority of contraindications and precautions are temporary, vaccinations often can be administered later when the condition leading to a contraindication or precaution no longer exists. A vaccine should not be administered when a contraindication is present; for example, MMR vaccine should not be administered to severely immunocompromised persons (1). However, certain conditions are commonly misperceived as contraindications (i.e., are not valid reasons to defer vaccination).

National standards for pediatric vaccination practices have been established and include descriptions of valid contraindications and precautions to vaccination (2). Persons who administer vaccines should screen patients for contraindications and precautions to the vaccine before each dose of vaccine is administered (Table 4-1). Screening is facilitated by consistent use of screening questionnaires, which are available from certain state vaccination programs and other sources (e.g., the Immunization Action Coalition, <http://www.immunize.org>).

Severely immunocompromised persons generally should not receive live vaccines (3). Because of the theoretical risk to the fetus, women known to be pregnant generally should not receive live, attenuated virus vaccines (4). Persons who experienced

encephalopathy within 7 days after administration of a previous dose of pertussis-containing vaccine not attributable to another identifiable cause should not receive additional doses of a vaccine that contains pertussis (4,5). Severe Combined Immunodeficiency (SCID) disease and a history of intussusception are both contraindications to the receipt of rotavirus vaccines (6).

A precaution is a condition in a recipient that might increase the risk for a serious adverse reaction, might cause diagnostic confusion, or might compromise the ability of the vaccine to produce immunity (e.g., administering measles vaccine to a person with passive immunity to measles from a blood transfusion administered up to 7 months prior) (7). A person might experience a more severe reaction to the vaccine than would have otherwise been expected; however, the risk for this happening is less than the risk expected with a contraindication. In general, vaccinations should be deferred when a precaution is present. However, a vaccination might be indicated in the presence of a precaution if the benefit of protection from the vaccine outweighs the risk for an adverse reaction.

The presence of a moderate or severe acute illness with or without a fever is a precaution to administration of all vaccines ([Table 4-1](#)). The decision to administer or delay vaccination because of a current or recent acute illness depends on the severity of symptoms and etiology of the condition. The safety and efficacy of vaccinating persons who have mild illnesses have been documented (8-11). Vaccination should be deferred for persons with a moderate or severe acute illness. This precaution avoids causing diagnostic confusion between manifestations of the underlying illness and possible adverse effects of vaccination or superimposing adverse effects of the vaccine on the underlying illness. After they are screened for contraindications, persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved. Studies indicate that failure to vaccinate children with minor illnesses can impede vaccination efforts (12-14). Among persons whose compliance with medical care cannot be ensured, use of every opportunity to administer appropriate vaccines is critical.

Hospitalization should be used as an opportunity to provide recommended vaccinations. Health-care facilities are held to standards of offering influenza vaccine for hospitalized patients, so providers are incentivized to vaccinate these patients at some point during hospitalization (15). Likewise, patients admitted for elective procedures will not be acutely ill during all times during their hospitalization. Most studies that have explored the effect of surgery or anesthesia on the immune system were observational, included only infants and children, and were small and indirect, in that they did not look at the immune effect on the response to vaccination specifically (16-35). They do not provide convincing evidence that recent anesthesia or surgery significantly affect response to vaccines. Current, recent, or upcoming anesthesia/surgery/hospitalization is not a contraindication to vaccination (16-35). Efforts should be made to ensure vaccine administration during the hospitalization or at discharge. For patients who are deemed moderately or severely ill throughout the hospitalization, vaccination should occur at the earliest opportunity (i.e., during immediate post-hospitalization follow-up care, including home or office visits) when patients' clinical symptoms have improved.

A personal or family history of seizures is a precaution for MMRV vaccination; this is because a recent study found an increased risk for febrile seizures in children 12-23 months who receive MMRV compared with MMR and varicella vaccine (36).

Clinicians or other health-care providers might misperceive certain conditions or circumstances as valid contraindications or precautions to vaccination when they actually do not preclude vaccination (2) ([Table 4-2](#)). These misperceptions result in missed opportunities to administer recommended vaccines (37).

Routine physical examinations and procedures (e.g., measuring temperatures) are not prerequisites for vaccinating persons who appear to be healthy. The provider should ask the parent or guardian if the child is ill. If the child has a moderate or severe illness, the vaccination should be postponed.

TABLE 4-1. Contraindications and precautions^(a) to commonly used vaccines

Vaccine	Citation	Contraindications	Precautions
DT, Td	(4)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	GBS <6 weeks after previous dose of tetanus-toxoid-containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid-containing or tetanus-toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine Moderate or severe acute illness with or without fever
DTaP	(38)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP or DTaP	Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, progressive encephalopathy; defer DTaP until neurologic status clarified and stabilized Temperature of $\geq 40.5^{\circ}\text{C}$ ($\geq 105^{\circ}\text{F}$) within 48 hours after vaccination with a previous dose of DTP or DTaP GBS <6 weeks after previous dose of tetanus-toxoid-containing vaccine History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid-containing or tetanus-toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine Moderate or severe acute illness with or without fever
Hepatitis A	(39)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever

Hepatitis B	(40)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Hypersensitivity to yeast	Moderate or severe acute illness with or without fever
Hib	(41)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component Age <6 weeks	Moderate or severe acute illness with or without fever
HPV	(42)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Pregnancy Moderate or severe acute illness with or without fever
IIV	(43)	Severe allergic reaction (e.g., anaphylaxis) after previous dose of influenza vaccine or to vaccine component.	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever Egg allergy other than hives, e.g., angioedema, respiratory distress, lightheadedness, recurrent emesis; or required epinephrine or another emergency medical intervention (IIV may be administered in an inpatient or outpatient medical setting and under the supervision of a health care provider who is able to recognize and manage severe allergic conditions).
IPV	(44)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Pregnancy Moderate or severe acute illness with or without fever
LAIV ^(b)	(43)	Severe allergic reaction (e.g., anaphylaxis) after a vaccine component, including egg protein Concomitant use of aspirin or aspirin-containing medication	GBS <6 weeks after a previous dose of influenza vaccine Asthma in persons aged 5 years old or older Medical conditions which might predispose to higher risk of

		<p>in children and adolescents</p> <p>LAIV4 should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours.</p>	<p>complications attributable to influenza^(c)</p> <p>Moderate or severe acute illness with or without fever</p>
MenACWY	(45)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MenB	(46,47)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
MMR ^{(d),(e)}	(1)	<p>Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component</p> <p>Pregnancy</p> <p>Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy^(f) or patients with HIV infection who are severely immunocompromised)</p> <p>Family history of altered immunocompetence^(g)</p>	<p>Recent (≤ 11 months) receipt of antibody-containing blood product (specific interval depends on product)</p> <p>History of thrombocytopenia or thrombocytopenic purpura</p> <p>Need for tuberculin skin testing or interferon-gamma release assay (IGRA) testing^(h)</p> <p>Moderate or severe acute illness with or without fever</p>
MPSV4	(48)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever

PCV13	(49)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose of PCV13 or any diphtheria-toxoid-containing vaccine or to a component of a vaccine (PCV13 or any diphtheria-toxoid-containing vaccine)	Moderate or severe acute illness with or without fever
PPSV23	(50)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever
RIV	(43)	Severe allergic reaction (e.g., anaphylaxis) to any component of the vaccine	GBS <6 weeks after a previous dose of influenza vaccine Moderate or severe acute illness with or without fever
Rotavirus	(6)	Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component SCID History of intussusception	Altered immunocompetence other than SCID Chronic gastrointestinal disease ⁽¹⁾ Spina bifida or bladder exstrophy ⁽¹⁾ Moderate or severe acute illness with or without fever

Tdap	(51)	<p>Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component</p> <p>Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP, DTaP, or Tdap</p>	<p>GBS <6 weeks after a previous dose of tetanus-toxoid-containing vaccine</p> <p>Progressive or unstable neurological disorder, uncontrolled seizures, or progressive encephalopathy until a treatment regimen has been established and the condition has stabilized</p> <p>History of Arthus-type hypersensitivity reactions after a previous dose of diphtheria-toxoid-containing or tetanus-toxoid-containing vaccine; defer vaccination until at least 10 years have elapsed since the last tetanus-toxoid-containing vaccine</p> <p>Moderate or severe acute illness with or without fever</p>
Varicella ^{(d),(e)}	(52)	<p>Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component</p> <p>Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy^(f) or patients with HIV infection who are severely immunocompromised)^(e)</p> <p>Pregnancy</p> <p>Family history of altered immunocompetence^(g)</p>	<p>Recent (≤ 11 months) receipt of antibody-containing blood product (specific interval depends on product)</p> <p>Moderate or severe acute illness with or without fever</p> <p>Receipt of specific antiviral drugs (acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vaccination)</p> <p>Use of aspirin or aspirin-containing products⁽ⁱ⁾</p>

Zoster	(53)	<p>Severe allergic reaction (e.g., anaphylaxis) after a previous dose or to a vaccine component</p> <p>Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy^(f) or patients with HIV infection who are severely immunocompromised)^(e)</p> <p>Pregnancy</p>	<p>Moderate or severe acute illness with or without fever</p> <p>Receipt of specific antiviral drugs (acyclovir) 14 days after vaccination)</p>
--------	------	--	---

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; GBS = Guillain-Barré syndrome; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; RIV=recombinant influenza vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

(a) Events or conditions listed as precautions should be reviewed carefully. Benefits of and risks for administering a specific vaccine to a person under these circumstances should be considered. If the risk from the vaccine is believed to outweigh the benefit, the vaccine should not be administered. If the benefit of vaccination is believed to outweigh the risk, the vaccine should be administered. Whether and when to administer DTaP to children with proven or suspected underlying neurologic disorders should be decided on a case-by-case basis.

(b) In addition, ACIP recommends LAIV not be used for pregnant women, immunosuppressed persons, persons with egg allergy, and children aged 2-4 years who have asthma or who have had a wheezing episode noted in the medical record within the past 12 months, or for whom parents report that a health-care provider stated that they had wheezing or asthma within the last 12 months. LAIV should not be administered to persons who have taken influenza antiviral medications within the previous 48 hours. Persons who care for severely immunosuppressed persons who require a protective environment should not receive LAIV, or should avoid contact with such persons for 7 days after receipt.

(c) **Source:** (52).

(d) HIV-infected children may receive varicella vaccine if CD4+ T-lymphocyte count is $\geq 15\%$ and should receive MMR vaccine if they are aged ≥ 12 months and do not have evidence of current severe immunosuppression (i.e., individuals aged ≤ 5 years must have CD4+T lymphocyte [CD4] percentages $\geq 15\%$ for ≥ 6 months; and individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) or other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤ 5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥ 6 months above age-specific CD4+count criteria: CD4+count > 750 lymphocytes/mm³ while aged ≤ 12 months and CD4+count ≥ 500 lymphocytes/mm³ while aged 1 through 5 years.

Sources: (1,50).

(e) MMR and varicella-containing vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.

(f) A substantially immunosuppressive steroid dose is considered to be ≥ 2 weeks of daily receipt of 20 mg or 2 mg/kg body weight of prednisone or equivalent.

(g) family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings), unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory

(h) If active tuberculosis is suspected, MMR should be delayed. Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin or IGRA testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for ≥ 4 weeks after the vaccination. If an urgent need exists to skin test or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.

(i) For details, see (55).

(j) No adverse events associated with the use of aspirin or aspirin-containing products after varicella vaccination have been reported; however, the vaccine manufacturer recommends that vaccine recipients avoid using aspirin or aspirin-containing products for 6 weeks after receiving varicella vaccines because of the association between aspirin use and Reye syndrome after varicella. Vaccination with subsequent close monitoring should be considered for children who have rheumatoid arthritis or other conditions requiring therapeutic aspirin. The risk for serious complications associated with aspirin is likely to be greater in children in whom natural varicella develops than it is in children who receive the vaccine containing attenuated VZV. No association has been documented between Reye syndrome and analgesics or antipyretics that do not contain aspirin.”

TABLE 4-2. Conditions incorrectly perceived as contraindications or precautions to vaccination (i.e., vaccines may be given under these conditions)

Vaccine	Conditions commonly misperceived as contraindications or precautions
General for all vaccines, including DTaP, pediatric DT, adult Td, adolescent-adult Tdap, IPV, MMR, Hib, hepatitis A, hepatitis B, varicella, rotavirus, PCV13, IIV, LAIV, PPSV23, MenACWY, MPSV4, HPV, and herpes zoster	Mild acute illness with or without fever Mild to moderate local reaction (i.e., swelling, redness, soreness); low-grade or moderate fever after previous dose Lack of previous physical examination in well-appearing person Current antimicrobial therapy ^(a) Convalescent phase of illness Preterm birth (hepatitis B vaccine is an exception in certain circumstances) ^(b) Recent exposure to an infectious disease History of penicillin allergy, other nonvaccine allergies, relatives with allergies, or receiving allergen extract immunotherapy History of GBS ^(c)
DTaP	Collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP Seizure ≤ 3 days after receiving a previous dose of DTP/DTaP Persistent, inconsolable crying lasting ≥ 3 hours within 48 hours after receiving a previous dose of DTP/DTaP Family history of seizures Family history of sudden infant death syndrome Family history of an adverse event after DTP or DTaP administration Stable neurologic conditions (e.g., cerebral palsy, well-controlled seizures, or developmental delay)
Hepatitis B	Pregnancy Autoimmune disease (e.g., systemic lupus erythematosus or rheumatoid arthritis)
HPV	Immunosuppression Previous equivocal or abnormal Papanicolaou test Known HPV infection Breastfeeding History of genital warts
IIV	Nonsevere (e.g., contact) allergy to latex, thimerosal, or egg Concurrent administration of Coumadin (generic: warfarin) or aminophylline
IPV	Previous receipt of ≥ 1 dose of oral polio vaccine

LAIV	<p>Health-care providers that see patients with chronic diseases or altered immunocompetence (an exception is providers for severely immunocompromised patients requiring care in a protected environment)</p> <p>Breastfeeding</p> <p>Contacts of persons with chronic disease or altered immunocompetence (an exception is contacts of severely immunocompromised patients requiring care in a protected environment)</p>
MMR ^{(d),(e)}	<p>Positive tuberculin skin test</p> <p>Simultaneous tuberculin skin or interferon-gamma release assay (IGRA) testing^(f)</p> <p>Breastfeeding</p> <p>Pregnancy of recipient's mother or other close or household contact</p> <p>Recipient is female of child-bearing age</p> <p>Immunodeficient family member or household contact</p> <p>Asymptomatic or mildly symptomatic HIV infection</p> <p>Allergy to eggs</p>
PPSV23	History of invasive pneumococcal disease or pneumonia
Rotavirus	<p>Prematurity</p> <p>Immunosuppressed household contacts</p> <p>Pregnant household contacts</p>
Tdap	<p>History of fever of $\geq 40.5^{\circ}\text{C}$ ($\geq 105^{\circ}\text{F}$) for <48 hours after vaccination with a previous dose of DTP or DTaP</p> <p>History of collapse or shock-like state (i.e., hypotonic hyporesponsive episode) within 48 hours after receiving a previous dose of DTP/DTaP</p> <p>History of seizure <3 days after receiving a previous dose of DTP/DTaP</p> <p>History of persistent, inconsolable crying lasting >3 hours within 48 hours after receiving a previous dose of DTP/DTaP</p> <p>History of extensive limb swelling after DTP/DTaP/Td that is not an Arthus-type reaction</p> <p>History of stable neurologic disorder</p> <p>History of brachial neuritis</p> <p>Latex allergy that is not anaphylactic</p> <p>Breastfeeding</p> <p>Immunosuppression</p>
Varicella	<p>Pregnancy of recipient's mother or other close or household contact</p> <p>Immunodeficient family member or household contact^(g)</p> <p>Asymptomatic or mildly symptomatic HIV infection</p> <p>Humoral immunodeficiency (e.g., agammaglobulinemia)</p>

Zoster	<p>Therapy with low-dose methotrexate (≤ 0.4 mg/kg/week), azathioprine (≤ 3.0 mg/kg/day), or 6-mercaptopurine (≤ 1.5 mg/kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, or other conditions</p> <p>Health-care providers of patients with chronic diseases or altered immunocompetence</p> <p>Contacts of patients with chronic diseases or altered immunocompetence</p> <p>Unknown or uncertain history of varicella in a U.S.-born person</p>
<p>Abbreviations: DT = diphtheria and tetanus toxoids; DTP = diphtheria toxoid, tetanus toxoid, and pertussis; DTaP = diphtheria and tetanus toxoids and acellular pertussis; GBS = Guillain-Barré syndrome; HBsAg = hepatitis B surface antigen; Hib = <i>Haemophilus influenzae</i> type b; HIV = human immunodeficiency virus; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MMR = measles, mumps, and rubella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV = pneumococcal conjugate vaccine; PPSV23 = pneumococcal polysaccharide vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.</p> <p>(a) Antibacterial drugs might interfere with Ty21a oral typhoid vaccine, and certain antiviral drugs might interfere with varicella-containing vaccines and LAIV4.</p> <p>(b) Hepatitis B vaccination should be deferred for infants weighing $< 2,000$ g if the mother is documented to be HBsAg negative. Vaccination should commence at chronological age 1 month or at hospital discharge. For infants born to HBsAg-positive women, hepatitis B immune globulin and hepatitis B vaccine should be administered within 12 hours after birth, regardless of weight.</p> <p>(c) An exception is Guillain-Barré syndrome within 6 weeks of a dose of influenza vaccine or tetanus-toxoid-containing vaccine, which are precautions for influenza vaccines and tetanus-toxoid containing vaccines, respectively.</p> <p>(d) MMR and varicella vaccines can be administered on the same day. If not administered on the same day, these vaccines should be separated by at least 28 days.</p> <p>(e) HIV-infected children should receive immune globulin after exposure to measles. HIV-infected children can receive varicella and measles vaccine if CD4+ T-lymphocyte count is $> 15\%$. (54).</p> <p>(f) Measles vaccination might suppress tuberculin reactivity temporarily. Measles-containing vaccine can be administered on the same day as tuberculin skin or IGRA testing. If testing cannot be performed until after the day of MMR vaccination, the test should be postponed for at least 4 weeks after the vaccination. If an urgent need exists to skin test or IGRA, do so with the understanding that reactivity might be reduced by the vaccine.</p> <p>(g) If a vaccinee experiences a presumed vaccine-related rash 7-25 days after vaccination, the person should avoid direct contact with immunocompromised persons for the duration of the rash.</p>	

REFERENCES

1. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-4):1-34.
2. National Vaccine Advisory Committee. Standards for child and adolescent immunization practices. *Pediatrics.* 2003;112(4):958-963.
3. Rubin L, Levin M, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis.* 2014;58(3):e44-100. DOI: 10.1093/cid/cit684
4. Kroger A, Atkinson W, Pickering L. General immunization practices. In: Plotkin S, Orenstein W, Offit P, eds. *Vaccines.* 6th ed. China: Elsevier Saunders; 2013:88-111.
5. CDC. Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1991;40(RR-10):1-28.
6. CDC. Addition of history of intussusception as a contraindication for rotavirus vaccination. *MMWR Morb Mortal Wkly Rep.* 2011;60(41):1427.
7. Siber GR, Werner BG, Halsey NA, et al. Interference of immune globulin with measles and rubella immunization. *J Pediatr.* 1993;122(2):204-211. DOI: 10.1016/S0022-3476(06)80114-9
8. Halsey NA, Boulos R, Mode F, et al. Response to measles vaccine in Haitian infants 6 to 12 months old. Influence of maternal antibodies, malnutrition, and concurrent illnesses. *N Engl J Med.* 1985;313(9):544-549. DOI: 10.1056/nejm198508293130904
9. Ndikuyeze A, Munoz A, Stewart J, et al. Immunogenicity and safety of measles vaccine in ill African children. *Int J Epidemiol.* 1988;17(2):448-455. DOI: 10.1093/ije/17.2.448
10. Lindegren ML, Atkinson WL, Farizo KM, Stehr-Green PA. Measles vaccination in pediatric emergency departments during a measles outbreak. *JAMA.* 1993;270(18):2185-2189. DOI: 10.1001/jama.1993.03510180055033

11. Atkinson W, Markowitz L, Baughman A, et al. Serologic response to measles vaccination among ill children [Abstract 422]. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy; 1992; Anaheim, CA.
12. Orenstein W, Rodewald L, Hinman A, Schuchat A. Immunization in the United States. In: Plotkin S, Orenstein W, Offit P, eds. *Vaccines*. 5th ed. China: Saunders/Elsevier; 2008:1479-1510.
13. Lewis T, Osborn LM, Lewis K, Brockert J, Jacobsen J, Cherry JD. Influence of parental knowledge and opinions on 12-month diphtheria, tetanus, and pertussis vaccination rates. *Am J Dis Child*. 1988;142(3):283-286. DOI: 10.1001/archpedi.1988.02150030053018
14. Farizo KM, Stehr-Green PA, Markowitz LE, Patriarca PA. Vaccination levels and missed opportunities for measles vaccination: a record audit in a public pediatric clinic. *Pediatrics*. 1992;89(4 Pt 1):589-592.
15. Centers for Medicare & Medicaid Services. Overview of specifications of measures displayed on hospital compare as of December 14, 2006. 2006; <http://www.cms.hhs.gov/HospitalQualityInits/downloads/HospitalOverviewOfSpecs200512.pdf>. Accessed 9 March, 2017.
16. Donovan R, Soothill JF. Immunological studies in children undergoing tonsillectomy. *Clin Exp Immunol*. 1973;14(3):347-357.
17. Puri P, Reen DJ, Browne O, Blake P, Guiney EJ. Lymphocyte response after surgery in the neonate. *Arch Dis Child*. 1979;54(8):599-603. DOI: 10.1136/ad.54.8.599
18. Mollitt DL, Steele RW, Marmer DJ, Stevers Golladay E, Costas S. Surgically induced immunologic alterations in the child. *J Pediatr Surg*. 1984;19(6):818-822. DOI: 10.1016/S0022-3468(84)80376-0
19. Mollitt DL, Marmer DJ, Steele RW. Age-dependent variation of lymphocyte function in the postoperative child. *J Pediatr Surg*. 1986;21(7):633-635. DOI: 10.1016/S0022-3468(86)80420-1
20. Kurz R, Pfeiffer KP, Sauer H. Immunologic status in infants and children following surgery. *Infection*. 1983;11(2):104-113. DOI: 10.1007/BF01641075

21. Merry C, Puri P, Reen DJ. Effect of major surgery on neutrophil chemotaxis and actin polymerization in neonates and children. *J Pediatr Surg.* 1997;32(6):813-817. DOI: 10.1016/S0022-3468(97)90626-6
22. Platt MP, Lovat PE, Watson JG, Aynsley-Green A. The effects of anesthesia and surgery on lymphocyte populations and function in infants and children. *J Pediatr Surg.* 1989;24(9):884-887. DOI: 10.1016/S0022-3468(89)80588-3
23. Mattila-Vuori A, Salo M, Iisalo E. Immune response in infants undergoing application of cast: comparison of halothane and balanced anesthesia. *Can J Anaesth.* 1999;46(11):1036-1042. DOI: 10.1007/bfo3013198
24. Espanol T, Todd GB, Soothill JF. The effect of anaesthesia on the lymphocyte response to phytohaemagglutinin. *Clin Exp Immunol.* 1974;18(1):73-79.
25. Hauser GJ, Chan MM, Casey WF, Midgley FM, Holbrook PR. Immune dysfunction in children after corrective surgery for congenital heart disease. *Crit Care Med.* 1991;19(7):874-881.
26. Puri P, Lee A, Reen DJ. Differential susceptibility of neonatal lymphocytes to the immunosuppressive effects of anesthesia and surgery. *Pediatr Surg Int.* 1992;7(1):47-50. DOI: 10.1007/bfo0181002
27. Hansen TG, Tonnesen E, Andersen JB, Toft P, Bendtzen K. The peri-operative cytokine response in infants and young children following major surgery. *Eur J Anaesthesiol.* 1998;15(1):56-60. DOI: 10.1046/j.1365-2346.1998.00230.x
28. Mattila-Vuori A, Salo M, Iisalo E, Pajulo O, Viljanto J. Local and systemic immune response to surgery under balanced anaesthesia in children. *Paediatr Anaesth.* 2000;10(4):381-388. DOI: 10.1046/j.1460-9592.2000.00505.x
29. Romeo C, Cruccetti A, Turiaco A, et al. Monocyte and neutrophil activity after minor surgical stress. *J Pediatr Surg.* 2002;37(5):741-744. DOI: 10.1053/jpsu.2002.32268
30. Vuori A, Salo M, Viljanto J, Pajulo O, Pulkki K, Nevalainen T. Effects of post-operative pain treatment using non-steroidal anti-inflammatory analgesics, opioids or epidural blockade on systemic and local immune responses in children. *Acta Anaesthesiol Scand.* 2004;48(6):738-749. DOI: 10.1111/j.1399-6576.2004.00404.x

31. Siebert JN, Posfay-Barbe KM, Habre W, Siegrist CA. Influence of anesthesia on immune responses and its effect on vaccination in children: review of evidence. *Paediatr Anaesth.* 2007;17(5):410-420. DOI: 10.1111/j.1460-9592.2006.02120.x
32. Currie J. Vaccination: is it a real problem for anesthesia and surgery? *Paediatr Anaesth.* 2006;16(5):501-503. DOI: 10.1111/j.1460-9592.2006.01898.x
33. Siebert J, Posfay-Barbe KM, Habre W, Siegrist C-A. Author's reply. *Paediatr Anaesth.* 2007;17(12):1218-1220. DOI: 10.1111/j.1460-9592.2007.02369.x
34. Nafiu OO, Lewis I. Vaccination and anesthesia: more questions than answers. *Paediatr Anaesth.* 2007;17(12):1215-1215. DOI: 10.1111/j.1460-9592.2007.02318.x
35. Short JA, Van Der Walt JH, Zoanetti DC. Author's reply. *Paediatr Anaesth.* 2007;17(12):1215-1216. DOI: 10.1111/j.1460-9592.2007.02321.x
36. Marin M, Broder KR, Temte JL, Snider DE, Seward JF. Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-3):1-12.
37. Szilagyi PG, Rodewald LE. Missed opportunities for immunizations: a review of the evidence. *J Public Health Manag Pract.* 1996;2(1):18-25. DOI: 10.1097/00124784-199600210-00005
38. CDC. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2000;49(RR-13):1-8.
39. Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-7):1-23.
40. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep.* 2005;54(RR-16):1-31.
41. Briere EC, Rubin L, Moro PL, Cohn A, Clark T, Messonnier N. Prevention and control of *Haemophilus influenzae* type b disease: recommendations of the

- advisory committee on immunization practices (ACIP). *MMWR Recomm Rep.* 2014;63(RR-1):1-14.
42. Markowitz L, Dunne E, Saraiya M, et al. Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2014;63(RR-05):1-30.
 43. Grohskopf LA, Sokolow LZ, Olsen SJ, et al. Prevention and Control of Seasonal Influenza with Vaccines Recommendations of the Advisory Committee on Immunization Practices – United States, 2016–17 Influenza Season. *MMWR Recomm Rep* 2016;65(No. RR-5):1-54.
 44. Prevots DR, Burr RK, Sutter RW, Murphy TV. Poliomyelitis prevention in the United States. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2000;49(RR-5):1-22; quiz CE21-27.
 45. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-2):1-28.
 46. Bexsero Package Insert. Available at www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm431374.htm (accessed 05/04/17)
 47. Trumenba Package Insert. Available at www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM421139.pdf (accessed 05/04/17)
 48. Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2005;54(RR-7):1-21.
 49. Advisory Committee on Immunization Practices. Preventing pneumococcal disease among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep.* 2000;49(RR-9):1-35.
 50. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1-24.

51. Broder KR, Cortese MM, Iskander JK, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-3):1-34.
52. Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2007;56(RR-4):1-40.
53. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2008;57(RR-5):1-30; quiz CE32-34.
54. Grohskopf LA, Olsen SJ, Sokolow LZ, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2014-15 influenza season. *MMWR Morb Mortal Wkly Rep.* 2014;63(32):691-697.
55. Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2009;58(RR-2):1-25.
56. American Academy of Pediatrics. Passive immunization. In: Pickering L, Baker C, Kimberlin D, Long S, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.

5. Preventing and Managing Adverse Reactions

Updates

Major changes to the best practice guidance include 1) more descriptive characterization of anaphylactic allergy and 2) incorporation of protocols for managing adverse reactions.

Benefit and Risk Communication

Parents, guardians, legal representatives, and adolescent and adult patients should be informed about the benefits of and risks from vaccines in language that is culturally sensitive and at an appropriate educational level. Opportunity for questions should be provided before each vaccination. Discussion of the benefits of and risks from vaccination is sound medical practice and is required by law.

The National Childhood Vaccine Injury Act of 1986 (1) requires that vaccine information materials be developed for each vaccine covered by the Act (uscode.house.gov). These materials, known as vaccine information statements (VISs), must be provided by all public and private vaccination providers each time a vaccine is administered. Copies of VISs are available from state health authorities responsible for vaccination and from CDC (www.cdc.gov/vaccines/hcp/vis/index.html). Translations of VISs into languages other than English are available from certain state vaccination programs and from the Immunization Action Coalition website (<http://www.immunize.org>). The act does not require that a signature be obtained; however, documentation of consent might be recommended or required by certain state or local health authorities or school authorities.

Some parents or patients question the need for or safety of vaccinations and want to discuss the risks from and benefits of certain vaccines. Some refuse certain vaccines or reject all vaccinations for personal or religious reasons. Having a basic understanding of

how patients and parents of patients view vaccine risk and developing effective approaches to address vaccine safety concerns are imperative for vaccination providers.

Each person understands and reacts to vaccine information on the basis of different factors, including previous experience, education, personal values, method of data presentation, perceptions of the risk for disease and perceived ability to control these risks, and risk tolerance. In some circumstances, decisions about vaccination are based on inaccurate information about risk provided by the media and certain websites. Websites and other sources of vaccine information may be inaccurate or incomplete. Health care providers can be a pivotal source of science-based credible information by discussing with parents and patients the risks from and benefits of vaccines, which helps patients make informed decisions.

When a parent or patient initiates a discussion about a perceived vaccine adverse reaction, the health care provider should discuss the specific concerns and provide factual information, using appropriate language. Effective, empathetic vaccine risk communication is essential in responding to misinformation and concerns, with health care providers recognizing that risk assessment and decision-making can be difficult and confusing. Certain vaccines might be acceptable to a parent who is resistant to other vaccines. This partial acceptance can be used to facilitate additional communication. Their concerns can be addressed using the VIS and offering other resource materials (e.g., vaccination information from CDC: www.cdc.gov/vaccines/hcp/vis/index.html).

The American Academy of Pediatrics (AAP) does not recommend that providers exclude from their practice patients whose parents or guardians question or refuse vaccination. However, an effective public health strategy is to identify common ground and discuss measures that need to be followed if the decision is to defer vaccination (2). Health care providers should reinforce key points about each vaccine, including safety, and emphasize risks for disease among unvaccinated children.

Parents should be advised of state laws regarding entry to schools or child-care facilities, which might require that unvaccinated children be excluded from the facility during outbreaks (www.cdc.gov/vaccines/imz-managers/coverage/schoolvaxview/requirements/index.html). These discussions should be documented in the patient's medical record, including the refusal to receive certain vaccines (i.e., informed refusal). When a vaccine is refused when first offered the provider should take the opportunity to offer the vaccine again at the next visit.

Preventing Adverse Reactions

Vaccines are intended to produce active immunity to specific antigens. An adverse reaction is an undesirable side effect that occurs after a vaccination. Vaccine adverse reactions are classified as 1) local, 2) systemic, or 3) allergic (additional information is available at

<https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm>. Local reactions (e.g., redness) are usually the least severe and most frequent. Systemic reactions (e.g., fever) occur less frequently than local reactions, and severe allergic reactions (e.g., anaphylaxis) are the least frequent reactions. Severe adverse reactions are rare (3).

Some of the systemic reactions may be complicated by the onset of syncope. Syncope (vasovagal or vasodepressor reaction) can occur after vaccination and is most common among adolescents and young adults. In 2005, the Vaccine Adverse Event Reporting System (VAERS) began detecting a trend of increasing syncope reports that coincided with the licensure of 3 vaccines for adolescents: human papillomavirus (HPV), MenACWY, and Tdap (4). Of particular concern among adolescents has been the risk for serious secondary injuries, including skull fracture and cerebral hemorrhage. Of 463 VAERS reports of syncope during January 1, 2005, to July 31, 2007, a total of 41 listed syncope with secondary injury with information on the timing after vaccination, and the majority of these syncope reports (76%) occurred among adolescents.

Among all age groups, 80% of reported syncope episodes occur within 15 minutes of vaccine administration (additional information is available at www.cdc.gov/vaccinesafety/concerns/fainting.html). Providers should take appropriate measures to prevent injuries if a patient becomes weak or dizzy or loses consciousness. Adolescents and adults should be seated or lying down during vaccination. Vaccine providers, particularly when vaccinating adolescents, should consider observing patients (with patients seated or lying down) for 15 minutes after vaccination to decrease the risk for injury should they faint (4). If syncope develops, patients should be observed until the symptoms resolve.

Although allergic reactions are a common concern for vaccine providers, these reactions are uncommon and anaphylaxis following vaccines is rare, occurring at a rate of approximately one per million doses for many vaccines (5). Epinephrine and equipment for managing an airway should be available for immediate use (6). The best practice to prevent allergic reactions is to identify individuals at increased risk by obtaining a history of allergy to previous vaccinations and vaccine components that might indicate an underlying hypersensitivity. Acute allergic reactions following vaccinations might be caused by the vaccine antigen, residual animal protein, antimicrobial agents, preservatives, stabilizers, or other vaccine components (7). Components of each vaccine are listed in the respective package insert. An extensive list of vaccine components and their use, as well as the vaccines that contain each component, has been published (8) and also is available from CDC (www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf). Additional information and tables of potential allergens in different vaccines are available at (www.vaccinesafety.edu/components-Allergens.htm). The allergens identified in the history can be cross-checked against the allergens identified in package inserts.

Managing Acute Vaccine Reactions

Vaccine providers should be familiar with identifying immediate-type allergic reactions, including anaphylaxis, and be competent in treating these events at the time of vaccine administration. Providers should also have a plan in place to contact emergency medical services immediately in the event of a severe acute vaccine reaction.

Allergic reactions can include: local or generalized urticaria (hives) or angioedema; respiratory compromise due to wheezing or swelling of the throat; hypotension; and shock. Immediate-immunoglobulin E (IgE)–mediated (type 1) immune reactions, such as anaphylaxis, usually occur within minutes of parenteral administration and involve specific IgE interactions with discrete antigens (9,10). Rapid recognition and initiation of treatment are required to prevent possible progression to respiratory failure or cardiovascular collapse. It is important to note that urticaria may not be present in all cases of anaphylaxis. For respiratory or cardiovascular symptoms, or other signs or symptoms of anaphylaxis, immediate intramuscular epinephrine is the treatment of choice (11,12). Additional doses of epinephrine as well as other drugs also might be indicated ([Tables 5-1 and 5-2](#)) (12). If hypotension is present, the patient should be placed in a recumbent position with the legs elevated. Maintenance of the airway, oxygen administration, and intravenous normal saline might be necessary. After the patient is stabilized, arrangements should be made for immediate transfer to an emergency facility for additional evaluation and treatment. Because anaphylaxis may recur after patients begin to recover, monitoring in a medical facility for several hours is advised, even after complete resolution of symptoms and signs. Additional information on management of patients with anaphylaxis has been published (9).

Persons Who Have Had an Allergic Reaction Following a Previous Immunization

For an individual patient who has experienced an immediate reaction to immunization, it is important to identify the type of reaction that occurred, obtain a history of prior allergic reactions, and try to identify the particular agent responsible. An algorithm

approach to these patients has been published (13) and additional advice is available for allergists on the evaluation of these adverse events (10). In general, a history of a severe allergic reaction to a vaccine should be considered a contraindication to additional doses of the same vaccine (13). Referral of the individual to an allergist for evaluation is usually indicated to possibly determine the component responsible, before making decisions regarding administration of the additional doses of the same vaccine or other vaccines that have the same components. Patients who have not had a severe allergic reaction following a vaccine, but who have a history of possible allergy to a vaccine component can often be vaccinated safely after careful evaluation (6).

Influenza Vaccination of Persons with a History of Egg Allergy

Severe allergic and anaphylactic reactions can occur in response to a number of influenza vaccine components, but such reactions are rare (6). All but the recombinant inactivated influenza vaccine may have come into contact with egg protein. The use of influenza vaccines for persons with a history of egg allergy has been reviewed recently by ACIP (14). VAERS data mining did not identify a higher than expected proportion of serious allergic events after influenza vaccination during the 2011-2012 season, relative to all other reported vaccines and adverse events in the database. Persons with a history of egg allergy should receive recombinant inactivated vaccine (if 18 years or older), or IIV.

Other measures, such as dividing and administering the vaccine by a 2-step approach and skin testing with vaccine, are not recommended (10).

All vaccines should be administered in settings in which personnel and equipment for rapid recognition and treatment of anaphylaxis are available. ACIP recommends that all vaccination providers be certified in cardiopulmonary resuscitation (CPR), have an office emergency plan, and ensure that all staff are familiar with the plan (6). Some persons who report allergy to egg might not be egg-allergic. Those who are able to eat lightly cooked egg (e.g., scrambled egg) without reaction are unlikely to be allergic.

Egg-allergic persons might tolerate egg in baked products (e.g., bread or cake). Tolerance to egg-containing foods does not exclude the possibility of egg allergy (15). Egg allergy can be confirmed by a consistent medical history of adverse reactions to eggs and egg-containing foods, plus skin and/or blood testing for IgE antibodies to egg proteins.

A previous severe allergic reaction to influenza vaccine, regardless of the component suspected to be responsible for the reaction, is a contraindication to future receipt of the vaccine (14).

Yellow Fever Vaccination of Persons with a History of Egg Allergy

Yellow fever vaccine contains egg protein. There have been insufficient studies to determine which patients with egg allergy may be able to receive yellow fever vaccine, but there are reports of patients with true egg allergy safely receiving yellow fever vaccine after evaluation by specialists with expertise in the management of allergic reactions (16,17). According to the manufacturer, persons who are able to eat eggs or egg products may receive the vaccine (18). However, potential hypersensitivity reactions might occur in persons with a history of minor reactions to eggs. For egg-sensitive persons, a scratch test or intradermal test can be performed before administering the vaccine to check for reactivity. If a person has a severe egg-sensitivity or has a positive skin test to the vaccine, but the vaccination is recommended because of their travel destination-specific risk, desensitization can be performed under direct supervision of a physician experienced in the management of anaphylaxis. The desensitization procedure is detailed in the product insert (see yellow fever recommendations at www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm094074.htm).

Vaccines with MMR or Varicella Components and Persons with a History of Egg Allergy

Varicella vaccine is grown in human diploid cell cultures and can safely be administered to persons with a severe allergy to eggs or egg proteins (19). Measles and mumps vaccine viruses are grown in chick embryo fibroblast tissue culture. However, persons with a severe egg allergy can receive measles- or mumps-containing vaccines in the usual manner because the content of these proteins is extremely low (20). The rare severe allergic reactions after measles- or mumps-containing vaccines or varicella are thought to be caused by other components of the vaccine (e.g., gelatin) (21-24). MMR, MMRV, varicella and other vaccines contain hydrolyzed gelatin as a stabilizer.

Vaccines and Persons with a History of Allergy to Substances Other than Eggs

Persons who have had an anaphylactic reaction to gelatin or gelatin-containing products should be evaluated by an allergist prior to receiving gelatin-containing vaccines (6).

Certain vaccines contain trace amounts of antimicrobial agents or other preservatives (e.g., neomycin or thimerosal), although allergies to these are rare. No licensed vaccine contains penicillin or penicillin derivatives.

Most often, neomycin hypersensitivity manifests as contact dermatitis, a delayed-type (cell-mediated) immune response rather than immediate-hypersensitivity (IgE-mediated allergy)–type response (25,26). A history of delayed-type reactions to neomycin is not a contraindication for administration of neomycin-containing vaccines. There has only been 1 reported case of immediate hypersensitivity reaction following a neomycin-containing vaccine (27). Persons who have had anaphylactic reactions to neomycin should be evaluated by an allergist prior to receiving vaccines containing neomycin (6).

Thimerosal, an organic mercurial compound in use since the 1930s, is added to certain immunobiologics as a preservative. Since mid-2001, vaccines routinely recommended for infants younger than 6 months of age have been manufactured without thimerosal as a preservative (14). Live, attenuated vaccines have never contained thimerosal.

Thimerosal-free formulations of inactivated influenza vaccine are available. Inactivated influenza vaccine also is available in formulations with only trace amounts of thimerosal, which remains as a manufacturing residual but is not added at the higher concentration that would be necessary for it to function as a preservative. Thimerosal at a preservative concentration is present in certain other vaccines that can be administered to children (e.g., Td and DT). Information about the thimerosal content of vaccines is available from FDA at <http://www.fda.gov/cber/vaccine/thimerosal.htm>.

Reactions to thimerosal have been described as local delayed-type hypersensitivity reactions with only rare reports of immediate reactions (28-31). Thimerosal elicits positive delayed-type hypersensitivity patch tests in 1%-18% of persons tested; however, these tests have no relevance to acute allergic reactions that might occur within minutes or hours after immunization (32,33). The majority of persons do not experience reactions to thimerosal administered as a component of vaccines even when patch or intradermal tests for thimerosal indicate hypersensitivity (31). A local or delayed-type hypersensitivity reaction to thimerosal is not a contraindication to receipt of a vaccine that contains thimerosal (34).

Latex is sap from the rubber tree. Latex contains naturally occurring plant proteins that can be responsible for immediate-type allergic reactions. Latex is processed to form either natural rubber latex products such as gloves or dry, natural rubber products such as syringe plunger tips and vial stoppers. Synthetic rubber is also used in gloves, syringe plungers, and vial stoppers but does not contain the latex proteins linked to immediate-type allergic reactions. Natural rubber latex or dry, natural rubber used in vaccine packaging generally is noted in the manufacturers' package inserts.

Immediate-type allergic reactions due to latex allergy have been described after vaccination, but such reactions are rare (35).

If a person reports a severe anaphylactic allergy to latex, vaccines supplied in vials or syringes that contain natural rubber latex should be avoided if possible (6). If not, if the decision is made to vaccinate, providers should be prepared to treat immediate allergic reactions due to latex, including anaphylaxis. The most common type of latex hypersensitivity is a delayed-type (type 4, cell-mediated) allergic contact dermatitis (36). For patients with a history of contact allergy to latex, vaccines supplied in vials or syringes that contain dry natural rubber or natural rubber latex may be administered.

Reporting Adverse Events After Vaccination

Modern vaccines are safe and effective; however, adverse events have been reported after administration of all vaccines (3). More complete information about adverse reactions to a specific vaccine is available in the package insert for each vaccine and from CDC at <https://www.cdc.gov/vaccines/vac-gen/side-effects.htm>. An adverse event is an untoward event that occurs after a vaccination that might be caused by the vaccine product or vaccination process. These events range from common, minor, local reactions to rare, severe, allergic reactions (e.g., anaphylaxis). Reporting to VAERS helps establish trends, identify clusters of adverse events, or generate hypotheses. However, establishing evidence for cause and effect on the basis of case reports and case series alone is usually not possible, because health problems that have a temporal association with vaccination do not necessarily indicate causality.

Many adverse events require more detailed epidemiologic studies to compare the incidence of the event among vaccinees with the incidence among unvaccinated persons. Potential causal associations between reported adverse events after vaccination can be assessed through epidemiologic or clinical studies.

The National Childhood Vaccine Injury Act of 1986 (1) requires health care personnel and vaccine manufacturers to report to VAERS specific adverse events that occur after vaccination. The reporting requirements are different for manufacturers and health care personnel. Manufacturers are required to report all adverse events that occur after vaccination to VAERS, whereas health care providers are required to report events that

appear in the reportable events table on the VAERS website at

[https://vaers.hhs.gov/docs/VAERS Table of Reportable Events Following Vaccination.pdf](https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf).

In addition to the mandated reporting of events listed on the reportable events table, health care personnel should report to VAERS all events listed in product inserts as contraindications, as well as all clinically significant adverse events, even if they are uncertain that the adverse event is related causally to vaccination (6). Persons other than health care personnel also can report adverse events to VAERS.

General information on VAERS is available at <https://vaers.hhs.gov/index.html>.

Specific information for healthcare providers is available at

<https://vaers.hhs.gov/resources/infoproviders.html>. Reporting to VAERS is fully electronic and can be done using an online reporting tool or a writable PDF; instructions are available at <https://vaers.hhs.gov/reportevent.html>. Further assistance on VAERS reporting is available through email at info@VAERS.org and the VAERS toll free number 1-800-822-7967.

National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program, established by the National Childhood Vaccine Injury Act of 1986 (1), is a no-fault system in which persons thought to have experienced an injury or to have died as a result of administration of a covered vaccine can seek compensation. The program became operational on October 1, 1988, and is intended as an alternative to civil litigation under the traditional tort system in that negligence need not be proven. Claims arising from covered vaccines must first be adjudicated through the program before civil litigation can be pursued.

The program relies on the Vaccine Injury Table, which lists the vaccines covered by the program and the injuries (including death), disabilities, illnesses, and conditions for which compensation might be awarded. The table defines the time during which the first

symptom or substantial aggravation of an injury must appear after vaccination to be eligible. Successful claimants receive a legal presumption of causation if a condition listed in the table is proven, thus avoiding the need to prove actual causation in an individual case. Claimants also can prevail for conditions not listed in the reportable events table if they prove causation for covered vaccines. Additional information is available from the Health Resources and Services Administration (HRSA at www.hrsa.gov/vaccine-compensation/index.html or by telephone at 800-338-2382). Persons who would like to file a claim for vaccine injury should contact the U.S. Court of Federal Claims (717 Madison Place, N.W., Washington, DC 20005; telephone: 202-357-6400).

TABLE 5-1: Rapid overview: Emergent management of anaphylaxis in infants and children^(a)	
Diagnosis is made clinically:	The most common signs and symptoms are cutaneous (eg, sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20% of patients have no skin findings.
	Danger signs: Rapid progression of symptoms, evidence of respiratory distress (e.g., stridor, wheezing, dyspnea, increased work of breathing, retractions, persistent cough, cyanosis), signs of poor perfusion, abdominal pain, vomiting, dysrhythmia, hypotension, collapse.
Acute management:	The first and most important therapy in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis.
	Airway: Immediate intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
	IM epinephrine (1 mg/mL preparation): Epinephrine 0.01 mg/kg should be injected intramuscularly in the midouter thigh. For large children (>50 kg), the maximum is 0.5 mg per dose. If there is no response or the response is inadequate, the injection can be repeated in 5 to 15 minutes (or more frequently). If epinephrine is injected promptly IM, patients respond to one, two, or at most, three injections. If signs of poor perfusion are present or symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below).
	Place patient in recumbent position, if tolerated, and elevate lower extremities.
	Oxygen: Give 8 to 10 L/minute via facemask or up to 100% oxygen, as needed.
	Normal saline rapid bolus: Treat poor perfusion with rapid infusion of 20 mL/kg. Reevaluate and repeat fluid boluses (20 mL/kg), as needed. Massive fluid shifts with severe loss of intravascular volume can occur. Monitor urine output.
	Albuterol: For bronchospasm resistant to IM epinephrine, give albuterol 0.15 mg/kg (minimum dose: 2.5 mg) in 3 mL saline inhaled via nebulizer. Repeat, as needed.
	H1 antihistamine: Consider giving diphenhydramine 1 mg/kg (max 40 mg) IV.
	H2 antihistamine: Consider giving ranitidine 1 mg/kg (max 50 mg) IV.
	Glucocorticoid: Consider giving methylprednisolone 1 mg/kg (max 125 mg) IV.
Monitoring: Continuous noninvasive hemodynamic monitoring and pulse oximetry monitoring should be performed. Urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock.	
Treatment of refractory symptoms:	Epinephrine infusion: ^(b) In patients with inadequate response to IM epinephrine and IV saline, give epinephrine continuous infusion at 0.1 to 1 mcg/kg/minute, titrated to effect.
	Vasopressors: ^(b) Patients may require large amounts of IV crystalloid to maintain blood pressure. Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according

	to blood pressure and cardiac rate/function monitored continuously and oxygenation monitored by pulse oximetry
IM: intramuscular; IV: intravenous.	
(a) A child is defined as a prepubertal patient weighing less than 40 kg. (b) All patients receiving an infusion of epinephrine and/or another vasopressor require continuous noninvasive monitoring of blood pressure, heart rate and function, and oxygen saturation. We suggest that pediatric centers provide instructions for preparation of standard concentrations and also provide charts for established infusion rate for epinephrine and other vasopressors in infants and children.	

Table 5-2: Rapid overview: Emergency management of anaphylaxis in adults	
Diagnosis is made clinically:	The most common signs and symptoms are cutaneous (e.g., sudden onset of generalized urticaria, angioedema, flushing, pruritus). However, 10 to 20% of patients have no skin findings.
	Danger signs: Rapid progression of symptoms, respiratory distress (e.g., stridor, wheezing, dyspnea, increased work of breathing, persistent cough, cyanosis), vomiting, abdominal pain, hypotension, dysrhythmia, chest pain, collapse.
Acute management:	The first and most important treatment in anaphylaxis is epinephrine. There are NO absolute contraindications to epinephrine in the setting of anaphylaxis. Airway: Immediate intubation if evidence of impending airway obstruction from angioedema. Delay may lead to complete obstruction. Intubation can be difficult and should be performed by the most experienced clinician available. Cricothyrotomy may be necessary.
Promptly and simultaneously, give:	IM epinephrine (1 mg/mL preparation): Give epinephrine 0.3 to 0.5 mg intramuscularly, preferably in the midouter thigh. Can repeat every 5 to 15 minutes (or more frequently), as needed. If epinephrine is injected promptly IM, most patients respond to one, two, or at most, three doses. If symptoms are not responding to epinephrine injections, prepare IV epinephrine for infusion (see below). Place patient in recumbent position, if tolerated, and elevate lower extremities. Oxygen: Give 8 to 10 L/minute via facemask or up to 100% oxygen, as needed. Normal saline rapid bolus: Treat hypotension with rapid infusion of 1 to 2 liters IV. Repeat, as needed. Massive fluid shifts with severe loss of intravascular volume can occur. Albuterol (salbutamol): For bronchospasm resistant to IM epinephrine, give 2.5 to 5 mg in 3 mL saline via nebulizer. Repeat, as needed.
Adjunctive therapies:	H1 antihistamine: ^(a) Consider giving diphenhydramine 25 to 50 mg IV (for relief of urticaria and itching only). H2 antihistamine: ^(a) Consider giving ranitidine 50 mg IV. Glucocorticoid: ^(a) Consider giving methylprednisolone 125 mg IV. Monitoring: Continuous noninvasive hemodynamic monitoring and pulse oximetry monitoring should be performed. Urine output should be monitored in patients receiving IV fluid resuscitation for severe hypotension or shock.
Treatment of refractory symptoms:	Epinephrine infusion ^(b) : For patients with inadequate response to IM epinephrine and IV saline, give

	epinephrine continuous infusion, beginning at 0.1 mcg/kg/minute by infusion pump ^(c) . Titrate the dose continuously according to blood pressure, cardiac rate and function, and oxygenation.
	Vasopressors ^(b) : Some patients may require a second vasopressor (in addition to epinephrine). All vasopressors should be given by infusion pump, with the doses titrated continuously according to blood pressure and cardiac rate/function and oxygenation monitored by pulse oximetry.
	Glucagon: Patients on beta blockers may not respond to epinephrine and can be given glucagon 1 to 5 mg IV over 5 minutes, followed by infusion of 5 to 15 mcg/minute. Rapid administration of glucagon can cause vomiting.
Instructions on how to prepare and administer epinephrine for IV continuous infusions are available as separate tables in UpToDate.	
IM: intramuscular; IV: intravenous.	
^(a) These medications should not be used as initial or sole treatment. ^(b) All patients receiving an infusion of epinephrine and another vasopressor require continuous noninvasive monitoring of blood pressure, heart rate and function, and oxygen saturation. ^(c) For example, the initial infusion rate for a 70 kg patient would be 7 mcg/minute. This is consistent with the recommended range for non–weight-based dosing for adults, which is 2 to 10 mcg/minute. Non–weight-based dosing can be used if the patient's weight is not known and cannot be estimated.	

Reproduced with permission from: Campbell RL, Kelso JM. Anaphylaxis: Emergency treatment. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on 03/08/2017) Copyright © 2017 UpToDate, Inc. For more information visit www.uptodate.com.

Source: (37).

REFERENCES

1. National Childhood Vaccine Injury Act, 42 U.S.C. Sect. 300aa-1 to 300aa-34 (1986).
2. Opel DJ, Heritage J, Taylor JA, et al. The architecture of provider-parent vaccine discussions at health supervision visits. *Pediatrics*. 2013;2013-2037. DOI: 10.1542/peds.2013-2037
3. CDC. Update: vaccine side effects, adverse reactions, contraindications, and precautions. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 1996;45(RR-12):1-35.
4. CDC. Syncope after vaccination—United States, January 2005–July 2007. *MMWR Morb Mortal Wkly Rep*. 2008;57(17):457-460.
5. Bohlke K, Davis RL, Marcy SM, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics*. 2003;112(4):815-820. DOI: 10.1542/peds.112.4.815
6. Kroger A, Atkinson W, Pickering L. General immunization practices. In: Plotkin S, Orenstein W, Offit P, eds. *Vaccines*. 6th ed. China: Elsevier Saunders; 2013:88-111.
7. Grabenstein JD. Clinical management of hypersensitivities to vaccine components. *Hospital Pharmacy*. 1997;32:77-87.
8. Grabenstein JD. *ImmunoFacts: Vaccines and Immunologic Drugs—2013*. 38th ed. St. Louis, MO: Lippincott Williams & Wilkins; 2012.
9. Lieberman P, Nicklas RA, Oppenheimer J, et al. The diagnosis and management of anaphylaxis practice parameter: 2010 update. *J Allergy Clin Immunol*. 2010;126(3):477-480.e471-442. DOI: 10.1016/j.jaci.2010.06.022
10. Kelso JM, Greenhawt MJ, Li JT, et al. Adverse reactions to vaccines practice parameter 2012 update. *J Allergy Clin Immunol*. 2012;130(1):25-43. DOI: 10.1016/j.jaci.2012.04.003
11. Ruggeberg JU, Gold MS, Bayas JM, et al. Anaphylaxis: case definition and guidelines for data collection, analysis, and presentation of immunization safety data. *Vaccine*. 2007;25(31):5675-5684. DOI: 10.1016/j.vaccine.2007.02.064

12. Sampson HA, Munoz-Furlong A, Bock SA, et al. Symposium on the definition and management of anaphylaxis: summary report. *J Allergy Clin Immunol*. 2005;115(3):584-591. DOI: 10.1016/j.jaci.2005.01.009
13. Wood RA, Berger M, Dreskin SC, et al. An algorithm for treatment of patients with hypersensitivity reactions after vaccines. *Pediatrics*. 2008;122(3):e771-777. DOI: 10.1542/peds.2008-1002
14. Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 influenza season. *MMWR Morb Mortal Wkly Rep*. 2015;64(30):818-825.
15. Erlewyn-Lajeunesse M, Brathwaite N, Lucas JS, Warner JO. Recommendations for the administration of influenza vaccine in children allergic to egg. *BMJ*. 2009;339:b3680. DOI: 10.1136/bmj.b3680
16. Mosimann B, Stoll B, Francillon C, Pecoud A. Yellow fever vaccine and egg allergy. *J Allergy Clin Immunol*. 1995;95(5 Pt 1):1064. DOI: 10.1016/S0091-6749(95)70118-4
17. Munoz-Cano R, Sanchez-Lopez J, Bartra J, Valero A. Yellow fever vaccine and egg allergy: really a problem? *Allergy*. 2010;65(4):533-534. DOI: 10.1111/j.1398-9995.2009.02205.x
18. Sanofi Pasteur Inc. *Yellow fever vaccine: YF-VAX® [Package insert]*. Swiftwater, PA: Sanofi Pasteur Inc.; 2015. Available at: <http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM142831.pdf>. Accessed 02 Feb 2017.
19. Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2007;56(RR-4):1-40.
20. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 1998;47(RR-8):1-57.

21. Kelso JM, Jones RT, Yunginger JW. Anaphylaxis to measles, mumps, and rubella vaccine mediated by IgE to gelatin. *J Allergy Clin Immunol*. 1993;91(4):867-872. DOI: 10.1016/0091-6749(93)90344-F
22. Sakaguchi M, Nakayama T, Inouye S. Food allergy to gelatin in children with systemic immediate-type reactions, including anaphylaxis, to vaccines. *J Allergy Clin Immunol*. 1996;98(6 Pt 1):1058-1061. DOI: 10.1016/S0091-6749(96)80191-6
23. Sakaguchi M, Ogura H, Inouye S. IgE antibody to gelatin in children with immediate-type reactions to measles and mumps vaccines. *J Allergy Clin Immunol*. 1995;96(4):563-565. DOI: 10.1016/S0091-6749(95)70304-7
24. Sakaguchi M, Yamanaka T, Ikeda K, et al. IgE-mediated systemic reactions to gelatin included in the varicella vaccine. *J Allergy Clin Immunol*. 1997;99(2):263-264. DOI: 10.1016/S0091-6749(97)70108-8
25. Rietschel RL, Bernier R. Neomycin sensitivity and the MMR vaccine. *JAMA*. 1981;245(6):571. DOI: 10.1001/jama.1981.03310310017008
26. Elliman D, Dhanraj B. Safe MMR vaccination despite neomycin allergy. *Lancet*. 1991;337(8737):365. DOI: 10.1016/0140-6736(91)90995-2
27. Kwittken PL, Rosen S, Sweinberg SK. MMR vaccine and neomycin allergy. *Am J Dis Child*. 1993;147(2):128-129. DOI: 10.1001/archpedi.1993.02160260018005
28. Aberer W. Vaccination despite thimerosal sensitivity. *Contact Dermatitis*. 1991;24(1):6-10. DOI: 10.1111/j.1600-0536.1991.tb01621.x
29. Cox NH, Forsyth A. Thiomersal allergy and vaccination reactions. *Contact Dermatitis*. 1988;18(4):229-233. DOI: 10.1111/j.1600-0536.1988.tb02809.x
30. Kirkland LR. Ocular sensitivity to thimerosal: a problem with hepatitis B vaccine? *South Med J*. 1990;83(5):497-499.
31. Zheng W, Dreskin SC. Thimerosal in influenza vaccine: an immediate hypersensitivity reaction. *Ann Allergy Asthma Immunol*. 2007;99(6):574-575. DOI: 10.1016/s1081-1206(10)60391-2
32. Wantke F, Demmer CM, Götz M, Jarisch R. Contact dermatitis from thimerosal. *Contact Dermatitis*. 1994;30(2):115. DOI: 10.1111/j.1600-0536.1994.tb00580.x

33. Moller H. All these positive tests to thimerosal. *Contact Dermatitis*. 1994;31(4):209-213. DOI: 10.1111/j.1600-0536.1994.tb01989.x
34. Russell M, Pool V, Kelso JM, Tomazic-Jezic VJ. Vaccination of persons allergic to latex: a review of safety data in the Vaccine Adverse Event Reporting System (VAERS). *Vaccine*. 2004;23(5):664-667. DOI: 10.1016/j.vaccine.2004.06.042
35. Lear JT, English JS. Anaphylaxis after hepatitis B vaccination. *Lancet*. 1995;345(8959):1249. DOI: 10.1016/S0140-6736(95)92039-0
36. Slater JE. Latex allergy. *J Allergy Clin Immunol*. 1994;94(2 Pt 1):139-149; quiz 150. DOI: 10.1053/ai.1994.v94.a55437
37. Adapted from: Simons FER. Anaphylaxis. *J Allergy Clin Immunol*. 2010;125:S161.

6. Vaccine Administration

Updates

Major changes to the best practice guidance include 1) allowances for alternate administration route (subcutaneous instead of intramuscular) for hepatitis A vaccine and 2) an age cutoff of 12 years through 17 years of age for validating a dose of intradermal influenza vaccine if given in error.

Infection Control and Sterile Technique

General Precautions

Persons administering vaccinations should follow appropriate precautions to minimize risk for disease exposure and spread. Hands should be cleansed with an alcohol-based waterless antiseptic hand rub or washed with soap and water before preparing vaccines for administration and between each patient contact (1). Occupational Safety and Health Administration (OSHA) regulations do not require gloves to be worn when administering vaccinations, unless persons administering vaccinations have open lesions on their hands or are likely to come into contact with a patient's body fluids (2). If worn, gloves should be changed between patients.

Vaccine Administration: Preparation and Timely Disposal

Vaccines should be drawn up in a designated clean medication area that is not adjacent to areas where potentially contaminated items are placed. Multi-dose vials to be used for more than one patient should not be kept or accessed in the immediate patient treatment area. This is to prevent inadvertent contamination of the vial through direct or indirect contact with potentially contaminated surfaces or equipment that could then lead to infections in subsequent patients (3).

Different vaccines should never be mixed in the same syringe unless specifically licensed for such use (4). Single-dose vials and manufacturer-filled syringes are designed for single-dose administration and should be discarded if vaccine has been withdrawn or reconstituted and subsequently not used within the time frame specified by the manufacturer. Syringes that are prefilled by the manufacturer and activated (i.e., syringe cap removed or needle attached) but unused should be discarded at the end of the clinic day. For inactivated vaccines manufacturers, typically recommend use within the same day that a vaccine is withdrawn or reconstituted. When in doubt about the appropriate handling of a vaccine, vaccination providers should contact that vaccine's manufacturer.

ACIP discourages the routine practice of providers' prefilling syringes for several reasons. Because the majority of vaccines have a similar appearance after being drawn into a syringe, prefilling might result in administration errors. Because unused prefilled syringes also typically must be discarded if not used within the same day that they are filled, vaccine wastage might occur. The FDA does not license administration syringes for vaccine storage.

In certain circumstances in which a single vaccine type is being used (e.g., in preparation for a community influenza vaccination campaign), filling a small number (10 or fewer) of syringes may be considered (5). The doses should be administered as soon as possible after filling, by the same person who filled the syringes. Unused syringes that are prefilled by the manufacturer and activated (i.e., syringe cap removed or needle attached) should be discarded at the end of the clinic day.

Safe Use of Needles and Syringes

Needles and syringes used for vaccine injections must be sterile and disposable. A separate needle and syringe should be used for each injection. Changing needles between drawing vaccine from a vial and injecting it into a recipient is not necessary unless the needle has been damaged or contaminated (6).

Bloodborne diseases (e.g., hepatitis B, hepatitis C, human immunodeficiency virus [HIV]) are occupational hazards for clinicians and other health-care providers. The Needlestick Safety and Prevention Act (2) was enacted in 2000 to reduce the incidence of needlestick injury and the consequent risk for bloodborne diseases acquired from patients. The act directed OSHA to strengthen its existing bloodborne pathogen standards. The revised standards became effective in 2001 (2). These federal regulations require the use of engineering and work practice controls to eliminate or minimize employee exposure to bloodborne pathogens (see <https://www.osha.gov/SLTC/bloodbornepathogens/standards.html>). Engineering controls means controls (e.g., sharps disposal containers, self-sheathing needles, safer medical devices, such as sharps with engineered sharps injury protections and needleless systems) that isolate or remove the bloodborne pathogens hazard from the workplace (see https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051). Needle-shielding or needle-free devices that might satisfy the occupational safety regulations for administering injectable vaccines are available in the United States (7-8). The regulations also require maintenance of records documenting injuries caused by needles and other medical sharp objects and that nonmanagerial employees be involved in the evaluation and selection of safety-engineered devices before they are procured. Additional information about implementation and enforcement of these regulations is available from OSHA.

To prevent inadvertent needlestick injury or reuse, safety mechanisms should be deployed after use and needles and syringes should be discarded immediately in labeled, puncture-proof containers located in the same room where the vaccine is administered (5). Used needles should never be recapped.

Route of Administration

Injectable Route

Routes of administration are recommended by the manufacturer for each immunobiologic ([Table 6-1](#)). With the exceptions of bacille Calmette-Guérin (BCG) vaccine and smallpox vaccine (administered intraepidermally), injectable vaccines are administered by the intramuscular, subcutaneous, or intradermal route. Deviation from the recommended route of administration might reduce vaccine efficacy (*9, 10*) or increase the risk for local adverse reactions (*11-13*).

The method of administration of injectable vaccines is determined, in part, by the inclusion of adjuvants in some vaccines. An adjuvant is a vaccine component distinct from the antigen that enhances the immune response to the antigen, but might also increase risk of adverse reactions. To decrease risk of local adverse events, inactivated vaccines containing an adjuvant should be injected into a muscle. Administering a vaccine containing an adjuvant either subcutaneously or intradermally can cause local irritation, induration, skin discoloration, inflammation, and granuloma formation.

Intramuscular Injections

Needle Length

Injectable immunobiologics should be administered where local, neural, vascular, or tissue injury is unlikely. Use of longer needles has been associated with less redness or swelling than occurs with shorter needles because of injection into deeper muscle mass (*11*). Appropriate needle length depends on age and body mass. Injection technique is the most important parameter to ensure efficient intramuscular vaccine delivery.

For all intramuscular injections, the needle should be long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underlying nerves, blood vessels, or bone (*10,14-16*). Vaccinators should be

familiar with the anatomy of the area into which they are injecting vaccine. Intramuscular injections are administered at a 90-degree angle to the skin, preferably into the anterolateral aspect of the thigh or the deltoid muscle of the upper arm, depending on the age of the patient ([Table 6-2](#)).

The needle gauge for intramuscular injection is 22-25 gauge. A decision on needle length and site of injection must be made for each person on the basis of the size of the muscle, the thickness of adipose tissue at the injection site, the volume of the material to be administered, injection technique, and the depth below the muscle surface into which the material is to be injected ([Figure 1](#)). Some experts allow intramuscular injection with a $\frac{5}{8}$ -inch needle but ONLY if the skin is stretched flat (*16*). If the subcutaneous and muscle tissue are bunched to minimize the chance of striking bone (*14*), a 1-inch needle or larger is required to ensure intramuscular administration. Aspiration before injection of vaccines or toxoids (i.e., pulling back on the syringe plunger after needle insertion but before injection) is not necessary because no large blood vessels are present at the recommended injection sites, and a process that includes aspiration might be more painful for infants (*17*).

Infants (Aged <12 Months)

For the majority of infants, the anterolateral aspect of the thigh is the recommended site for injection because it provides comparatively larger muscle mass than the deltoid ([Figure 2](#)) (*18*). In certain circumstances (e.g., physical obstruction to other sites and no reasonable indication to defer doses), the gluteal muscle can be used. If the gluteal muscle must be used, care should be taken to define the anatomic landmarks.^(a) For the majority of infants, a 1-inch needle is sufficient to penetrate the thigh muscle.

Toddlers (Aged 12 Months-2 Years)

For toddlers, the anterolateral thigh muscle is preferred, and when this site is used, the needle should be at least 1 inch long. The deltoid muscle can be used if the muscle mass is adequate. If 2 vaccines are to be administered in a single limb, they should be spaced an inch apart (*4,19*).

Children (Aged 3-10 Years)

The deltoid muscle is preferred for children aged 3-10 years (18); the needle length for deltoid site injections can range from 5/8 to 1 inch on the basis of technique. The anterolateral thigh can also be used (20). In this case the needle length should be 1 inch to 1.25 inches. Knowledge of body mass can be useful for estimating the appropriate needle length (21).

Young Adolescents (Aged 11-18 years)

The deltoid muscle is preferred for adolescents 11-18 years of age. The anterolateral thigh can also be used. For injection into the anterolateral thigh, most adolescents will require a 1-1.5-inch needle to ensure intramuscular administration (21).

Adults (Aged ≥19 Years)

For adults, the deltoid muscle is recommended for routine intramuscular vaccinations (18) (Figure 3). The anterolateral thigh also can be used. For adults a measurement of body mass/weight is allowable prior to vaccination, understanding that resources to measure body mass/weight are not available in all clinical settings. For men and women who weigh <130 lbs (<60 kg), a 5/8-inch needle is sufficient to ensure intramuscular injection in the deltoid muscle if the injection is made at a 90-degree angle and the tissue is not bunched. For men and women who weigh 130-152 lbs (60-70 kg), a 1-inch needle is sufficient. For women who weigh 152-200 lbs (70-90 kg) and men who weigh 152-260 lbs (70-118 kg), a 1- to 1.5-inch needle is recommended. For women who weigh >200 lbs (>90 kg) or men who weigh >260 lbs (>118 kg), a 1.5-inch needle is recommended (Table 6-2) (15).

Subcutaneous Injections

Subcutaneous injections are administered at a 45-degree angle, usually into the thigh for infants aged <12 months and in the upper-outer triceps area of persons aged ≥12 months. Subcutaneous injections may be administered into the upper-outer triceps area of an infant if necessary. A 5/8-inch, 23- to 25-gauge needle should be inserted into the subcutaneous tissue ([Figures 4 and 5](#)) (4).

Intradermal Injections

One brand of injectable influenza vaccine is licensed to be administered intradermally. It is packaged as a pre-filled 3/50-inch microneedle injector system and approved for persons 18-64 years of age. The approved site is the skin over the deltoid muscle.

Intradermal influenza vaccine injection of someone 12-17 years of age can be counted as a valid dose on the presumption that their skin thickness is similar to someone 18-64 years of age. A dose of intradermal vaccine given to someone younger than 12 years of age or older than 64 years of age should not be counted as valid (personal communication with manufacturer).

Oral Route

Rotavirus, adenovirus, cholera vaccine, and oral typhoid vaccines are the only vaccines administered orally in the United States. Oral typhoid capsules should be administered as directed by the manufacturer. The capsules should not be opened or mixed with any other substance. Rotavirus vaccines are licensed for infants. There are 2 brands of rotavirus vaccine, and they have different types of applicators. Providers should consult package inserts for details. A dose of rotavirus vaccine need not be repeated if the vaccine is spit up or vomited. The infant should receive the remaining recommended doses of rotavirus vaccine following the routine schedule (5).

Intranasal Route

LAIV is approved for healthy nonpregnant persons aged 2-49 years and is the only vaccine administered by the intranasal route. The administration device is a nasal sprayer with a dose-divider clip that allows introduction of one 0.1-mL spray into each naris. The tip should be inserted slightly into the naris before administration. Even if the person coughs or sneezes immediately after administration or the dose is expelled any other way, the vaccine dose need not be repeated (5).

Severely immunosuppressed persons (i.e., those who require care in a protected environment, e.g., bone marrow transplant patients, patients with severe combined immunodeficiency disease) should not administer LAIV. It would be uncommon for persons with these conditions to be in a role administering vaccines. Other persons at increased risk for influenza complications can administer LAIV. These include persons with underlying medical conditions placing them at higher risk or who are likely to be at risk, including pregnant women, persons with asthma, and persons aged ≥ 50 years (22).

Multiple Injections

If multiple vaccines are administered at a single visit, administer each preparation at a different anatomic site (23). The location of all injection sites with the corresponding vaccine injected should be documented in each patient's medical record. Health-care practices should consider using a vaccination site map so that all persons administering vaccines routinely use a particular anatomic site for each particular vaccine.

For infants and younger children, if more than 2 vaccines are injected in a single limb, the thigh is the preferred site because of the greater muscle mass; the injections should be sufficiently separated (separate anatomic sites [i.e. ≥ 1 inch] if possible) so that any local reactions can be differentiated (8,24). For older children and adults, the deltoid muscle can be used for more than one intramuscular injection. If a vaccine and an immune globulin preparation are administered simultaneously (e.g., Td/Tdap and

tetanus immune globulin [TIG], hepatitis A and IG, hepatitis B and hepatitis B immunoglobulin [HBIG]), separate limbs should be used for each injection (25,26).

Jet Injections

Jet injectors are needle-free devices that pressurize liquid medication, forcing it through a nozzle orifice into a narrow stream capable of penetrating skin to deliver a drug or vaccine into intradermal, subcutaneous, or intramuscular tissues (27,28). Immune responses generated by jet injectors against both attenuated and inactivated viral and bacterial antigens are usually equivalent to, and occasionally greater than, immune responses induced by needle injection. However, local reactions or injuries (e.g., skin laceration, transient neuropathy, hematoma) are sometimes more frequent on delivery of vaccine by jet injectors compared with needle injection, depending on the inherent irritability of the vaccine and operator technique (28).

Multiple use jet injectors using the same nozzle for consecutive injections without intervening sterilization were used in mass vaccination campaigns from the 1950s through the 1990s (28); however, these were found to be unsafe because of the possibility of bloodborne pathogen transmission (29-32) and should not be used. A new generation of jet injectors with disposable cartridges and syringes has been developed since the 1990s. With a new, sterile dose chamber and nozzle for each patient and correct use, these devices do not have the same safety concerns as multiple-use nozzle jet injectors. Several of the newer devices have been approved by FDA for sale in the United States (28) and for use with individual vaccines. Jet injectors prevent needlestick injuries to health-care providers (2) and can overcome improper, unsterile reuse and other drawbacks of needles and syringes in developing countries (7,33,34).

Methods for Alleviating Discomfort and Pain Associated with Vaccination

Comfort measures, such as distraction (e.g., playing music or pretending to blow away the pain), cooling of the injection site(s), topical analgesia, ingestion of sweet liquids,

breastfeeding, swaddling, and slow, lateral swaying can help infants or children cope with the discomfort associated with vaccination (35-37). Pretreatment (30-60 minutes before injection) with a 5% topical lidocaine-prilocaine emulsion might decrease the pain of vaccination by causing superficial anesthesia (38,39). Evidence indicates that this cream does not interfere with the immune response to MMR (40). Topical lidocaine-prilocaine emulsion should not be used on infants aged <12 months who are receiving treatment with methemoglobin-inducing agents (e.g., acetaminophen, amyl nitrate, nitroprusside, dapsone) because of the possible development of methemoglobinemia (41). Use of a topical refrigerant (vapocoolant) spray immediately before vaccination can reduce the short-term pain associated with injections and can be as effective as lidocaine-prilocaine cream (42). Evidence does not support use of antipyretics before or at the time of vaccination; however, they can be used for the treatment of fever and local discomfort that might occur following vaccination. Studies of children with previous febrile seizures have not demonstrated antipyretics to be effective in the prevention of febrile seizures (43).

Clinical Implications of Nonstandard Vaccination Practices

Best practice guidance for route, site, and dosage of immunobiologics is derived from data from clinical trials, practical experience, normal periodicity of health-care visits, and theoretical considerations. ACIP discourages variations from the recommended route, site, volume, or number of doses of any vaccine.

Variation from the recommended route and site can result in inadequate protection. In adults (but not in infants) (44), the immunogenicity of hepatitis B is substantially lower when the gluteal rather than the deltoid site is used for administration (6). Hepatitis B administered intradermally might result in a lower seroconversion rate and final titer of hepatitis B surface antibody than when administered by the deltoid intramuscular route (45,46). Hepatitis B administered by any route other than intramuscular, or in adults at any site other than the deltoid or anterolateral thigh, should not be counted as valid and should be repeated (6). Similarly, doses of rabies vaccine administered in the gluteal site should not be counted as valid doses and should be repeated (47). Hepatitis A vaccine

and meningococcal conjugate vaccine do not need to be repeated if administered by the subcutaneous route (48-49). However, for DTaP, Hib, and PCV13, there is no evidence related to immunogenicity of these 3 vaccines given subcutaneously. Providers should address circumstances in which dose(s) of these vaccines have been administered subcutaneously on a case-by-case basis. Inactivated influenza vaccine is immunogenic when administered in a lower-than-standard dose by the intradermal route to healthy adult volunteers. Intradermal injection produced antibody responses similar to intramuscular injection in vaccinees aged 18-60 years (50). However, the immunogenicity for persons aged ≥ 65 years is inadequate, and varying the recommended route and dose either with the intradermal product licensed through 64 years of age or with other influenza vaccines is not recommended (19).

Live, attenuated injectable vaccines (e.g., MMR, varicella, yellow fever) and certain inactivated vaccines (e.g., meningococcal polysaccharide) are recommended by the manufacturers to be administered by subcutaneous injection. PPSV23 and IPV are recommended by the manufacturer to be administered by the subcutaneous or intramuscular route. Response to vaccines recommended by the subcutaneous route is unlikely to be affected if the vaccines are administered by the intramuscular rather than subcutaneous route. Repeating doses of vaccine administered by the intramuscular route when recommended to be by the subcutaneous route is not necessary (6).

Administering volumes smaller than recommended (e.g., inappropriately divided doses) might result in inadequate protection. Using reduced doses administered at multiple vaccination visits that equal a full dose or using smaller divided doses is not recommended (4). Any vaccination using less than the standard dose should not be counted, and the person should be revaccinated according to age unless serologic testing indicates that an adequate response has developed. However, if 2 half-volume formulations of vaccine have already been administered on the same clinic day to a patient recommended for the full volume formulation, these 2 doses can count as one full dose. If less than a full recommended dose of a vaccine is administered because of syringe, applicator, or needle leakage, the dose should be repeated (5). Using larger-

than-recommended dosages can be hazardous because of excessive local or systemic concentrations of antigens or other vaccine constituents.

^(a) If the gluteal muscle is chosen, injection should be administered lateral and superior to a line between the posterior superior iliac spine and the greater trochanter or in the ventrogluteal site, the center of a triangle bounded by the anterior superior iliac spine, the tubercle of the iliac crest, and the upper border of the greater trochanter.

TABLE 6-1. Dose and route of administration for selected vaccines

Vaccine	Dose	Route
DTaP, DT, Td, Tdap	0.5 mL	IM
DTaP-HepB-IPV	0.5 mL	IM
DTaP/Hib	0.5 mL	IM
DTaP-IPV/Hib	0.5 mL	IM
DTaP-IPV	0.5 mL	IM
Hib	0.5 mL	IM
Hib-MenCY	0.5 mL	IM
HepA	≤18 years: 0.5 mL ≥19 years: 1.0 mL	IM
HepB	≤19 years: 0.5 mL ^(a) ≥20 years: 1.0 mL	IM
HepA-HepB	≥18 years: 1.0 mL	IM
LAIV	0.2 mL divided dose between nares	Intranasal spray
IIV	6-35 months: 0.25 mL or 0.5 mL ≥3 years: 0.5 mL 18-64 years: 0.1 mL	IM ID
MMR	0.5 mL	Subcut
MMRV	0.5 mL	Subcut
MenACWY	0.5 mL	IM
PCV13	0.5 mL	IM
PPSV23	0.5 mL	IM or Subcut
HPV	0.5 mL	IM
IPV	0.5 mL	IM or Subcut
Rotavirus (RV1 or RV5)	(1.0 mL or 2.0 mL)	Oral

Varicella	0.5 mL	Subcut
ZVL	0.65 mL	Subcut
RZV	0.5 mL ^(b)	IM

Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IM = intramuscular; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MenCY = bivalent meningococcal conjugate vaccine component; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; RV1 = live, attenuated monovalent rotavirus vaccine; RV5 = live, reassortment pentavalent rotavirus vaccine; RZV = recombinant adjuvanted zoster vaccine; Subcut = subcutaneous; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis; ZVL = zoster vaccine live.

Source: Adapted from Immunization Action Coalition: <http://www.immunize.org>.

- (a) Persons aged 11-15 years may be administered Recombivax HB (Merck), 1.0 mL (adult formulation) on a 2-dose schedule.
- (b) Do not withdraw more than 0.5 mL from the reconstituted product, even if some product is left in the vial.

TABLE 6-2. Needle length and injection site of IM injections for children aged ≤18 years (by age) and adults aged ≥19 years (by sex and weight)

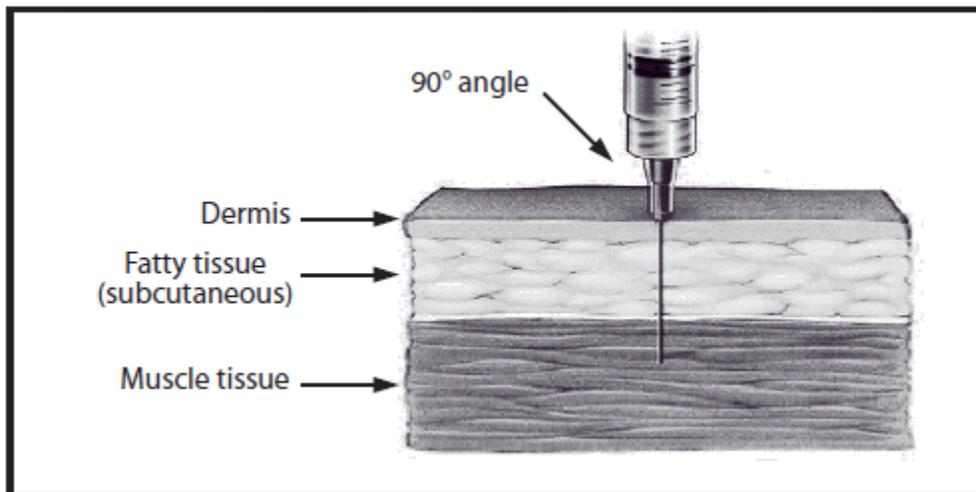
Age group	Needle length	Injection site
Children (birth-18 years)		
Neonates ^(a)	5/8 inch (16 mm) ^(b)	Anterolateral thigh
Infants, 1-12 months	1 inch (25 mm)	Anterolateral thigh
Toddlers, 1-2 years	1-1.25 inch (25-32 mm)	Anterolateral thigh ^(c)
	5/8 ^(b) -1 inch (16-25 mm)	Deltoid muscle of arm
Children, 3-10 years	5/8 ^(b) -1 inch (16-25 mm)	Deltoid muscle of arm ^(c)
	1-1.25 inches (25-32 mm)	Anterolateral thigh
Children, 11-18 years	5/8 ^(b) -1 inch (16-25 mm)	Deltoid muscle of arm ^(c)
	1-1.5 inches (25-38 mm)	Anterolateral thigh
Adults (≥19 years)		
Men and women, <60 kg (130 lbs)	1 inch (25 mm) ^(d)	Deltoid muscle of arm
Men and women, 60-70 kg (130-152 lbs)	1 inch (25 mm)	
Men, 70-118 kg (152-260 lbs)	1-1.5 inches (25-38 mm)	
Women, 70-90 kg (152-200 lbs)		
Men, >118 kg (260 lbs)	1.5 inches (38 mm)	
Women, >90 kg (200 lbs)		

Abbreviation: IM = intramuscular.

Source: (14).

- (a) First 28 days of life.
- (b) If skin is stretched tightly and subcutaneous tissues are not bunched.
- (c) Preferred site.
- (d) Some experts recommend a 5/8-inch needle for men and women who weigh <60 kg, if used, skin must be stretched tightly (do not bunch subcutaneous tissue)

Figure 1. Intramuscular needle insertion



Source: Adapted from California Immunization Branch.

Alternate Text: This drawing shows intramuscular needle insertion into a cross-section of skin. The needle is inserted at a 90-degree angle and penetrates the dermis, fatty tissue (subcutaneous), and muscle tissue.

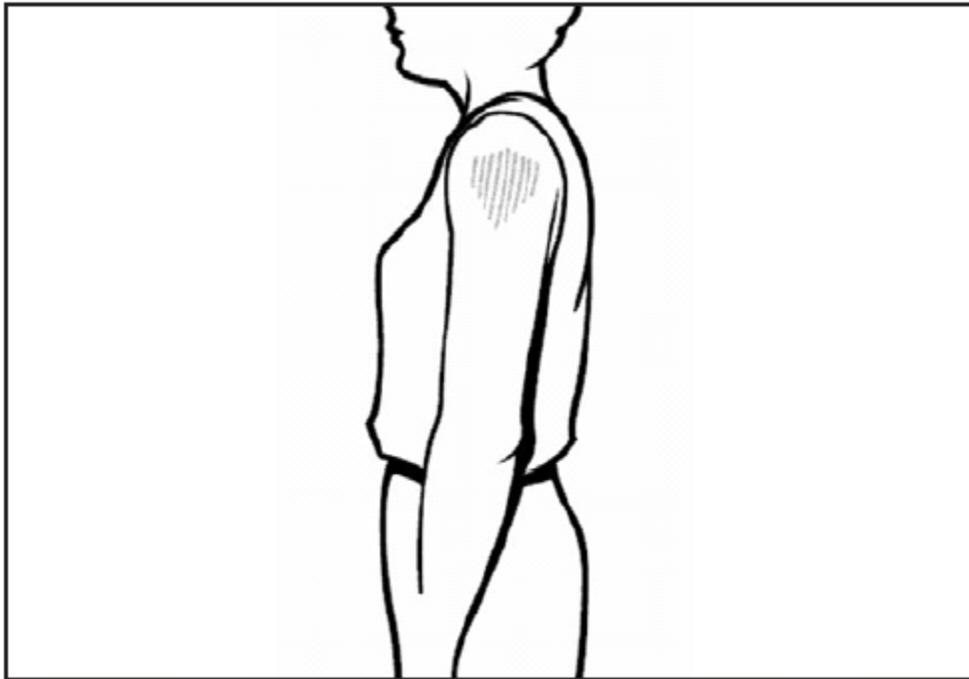
Figure 2. Intramuscular/subcutaneous site of administration: anterolateral thigh



Source: Adapted from Minnesota Department of Health.

Alternate Text: This drawing shows a mother holding an infant. The anterolateral aspect of the infant's thigh is shaded, showing the proper site for intramuscular/subcutaneous vaccine administration.

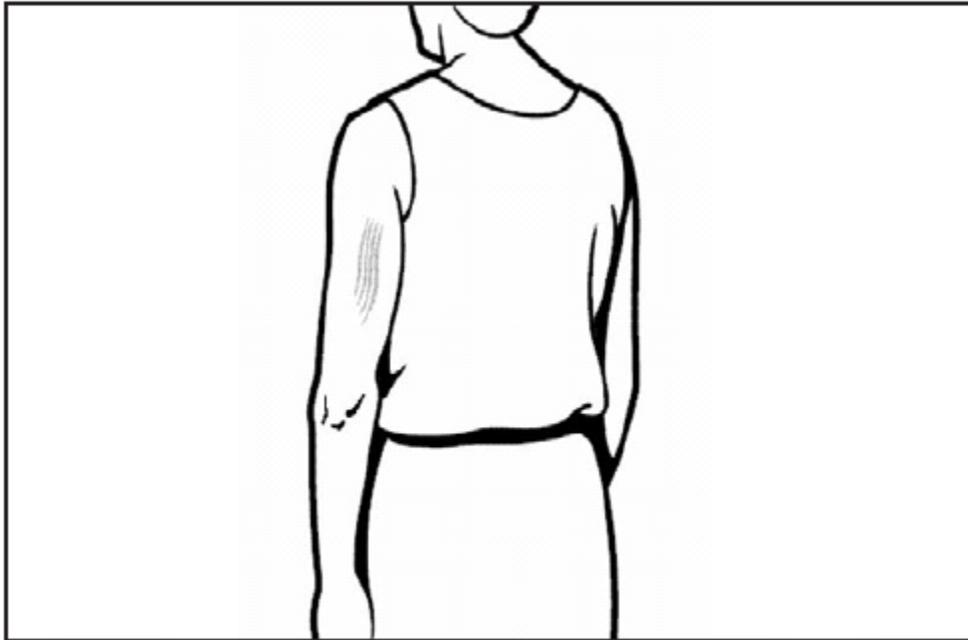
Figure 3. Intramuscular site of administration: deltoid



Source: Adapted from Minnesota Department of Health.

Alternate Text: This line drawing is a side view of an adult. The deltoid muscle of the arm is shaded, showing the proper site for intramuscular vaccine administration.

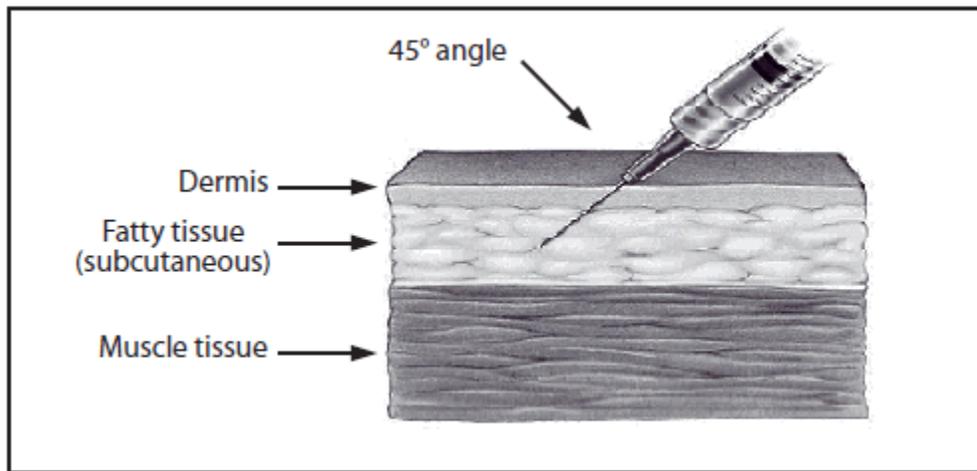
Figure 4. Subcutaneous site of administration: triceps



Source: Adapted from the Minnesota Department of Health.

Alternate Text: This line drawing is a rear/dorsal view of an adult. The triceps muscle of the arm is shaded, showing the proper site for subcutaneous vaccine administration.

Figure 5. Subcutaneous needle insertion



Source: Adapted from California Immunization Branch.

Alternate Text: This drawing shows subcutaneous needle insertion into a cross-section of skin. The needle is inserted at a 45-degree angle and penetrates the dermis and fatty tissue (subcutaneous) but not the muscle tissue.

REFERENCES

1. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. *MMWR Recomm Rep.* 2002;51(RR-16):1-45, quiz CE41-44.
2. Occupational Health and Safety Administration. Occupational exposure to bloodborne pathogens; needlesticks and other sharps injuries; Final Rule (29 CFR Part 1910). *Fed Regist.* 2001;66(12):5318-5325.
3. Siegel J, Rhinehart E, Jackson M, Chiarello L, the Healthcare Infection Control Practices Advisory Committee. *2007 guideline for isolation precautions: preventing transmission of infectious agents in healthcare settings* Atlanta, GA: CDC;2007.
4. CDC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1994;43(RR-1):1-38.
5. Kroger AT, Sumaya CV, Pickering LK, Atkinson WL. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2011;1-60.
6. Atkinson WL, Pickering LK, Schwartz B, Weniger BG, Iskander JK, Watson JC. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians (AAFP). *MMWR Recomm Rep.* 2002;51(RR-2):1-35.
7. Drucker E, Alcabes PG, Marx PA. The injection century: massive unsterile injections and the emergence of human pathogens. *Lancet.* 2001;358(9297):1989-1992. DOI: 10.1016/s0140-6736(01)06967-7
8. International Health Care Worker Safety Center. List of safety-engineered sharp devices and other products designed to prevent occupational exposures to bloodborne pathogens. 2003;

- <https://www.medicalcenter.virginia.edu/epinet/safetydevice.html>. Accessed 07 Feb 2017.
9. Shaw FE, Jr., Guess HA, Roets JM, et al. Effect of anatomic injection site, age and smoking on the immune response to hepatitis B vaccination. *Vaccine*. 1989;7(5):425-430. DOI: 10.1016/0264-410X(89)90157-6
 10. Zuckerman JN. The importance of injecting vaccines into muscle. Different patients need different needle sizes. *BMJ*. 2000;321(7271):1237-1238. DOI: 10.1136/bmj.321.7271.1237
 11. Ipp MM, Gold R, Goldbach M, et al. Adverse reactions to diphtheria, tetanus, pertussis-polio vaccination at 18 months of age: effect of injection site and needle length. *Pediatrics*. 1989;83(5):679-682.
 12. Michaels L, Poole RW. Injection granuloma of the buttock. *Can Med Assoc J*. 1970;102(6):626-628.
 13. Haramati N, Lorans R, Lutwin M, Kaleya RN. Injection granulomas. Intramuscle or intrafat? *Arch Fam Med*. 1994;3(2):146-148.
 14. Bergeson PS, Singer SA, Kaplan AM. Intramuscular injections in children. *Pediatrics*. 1982;70(6):944-948.
 15. Poland GA, Borrud A, Jacobson RM, et al. Determination of deltoid fat pad thickness. Implications for needle length in adult immunization. *JAMA*. 1997;277(21):1709-1711. DOI: 10.1001/jama.1997.03540450065037
 16. Groswasser J, Kahn A, Bouche B, Hanquinet S, Perlmutter N, Hessel L. Needle length and injection technique for efficient intramuscular vaccine delivery in infants and children evaluated through an ultrasonographic determination of subcutaneous and muscle layer thickness. *Pediatrics*. 1997;100(3 Pt 1):400-403. DOI: 10.1542/peds.100.3.400
 17. Ipp M, Taddio A, Sam J, Gladbach M, Parkin PC. Vaccine-related pain: randomised controlled trial of two injection techniques. *Arch Dis Child*. 2007;92(12):1105-1108. DOI: 10.1136/adc.2007.118695
 18. CDC. Recommendation of the Immunization Practices Advisory Committee: general recommendations on immunization *MMWR Morb Mortal Wkly Rep*. 1983;32(1):1-16.

19. Kroger AT, Atkinson WL, Marcuse EK, Pickering LK. General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2006;55(RR-15):1-48.
20. Jackson LA, Yu O, Nelson JC, et al. Injection site and risk of medically attended local reactions to acellular pertussis vaccine. *Pediatrics.* 2011;127(3):e581-587. DOI: 10.1542/peds.2010-1886
21. Middleman AB, Anding R, Tung C. Effect of needle length when immunizing obese adolescents with hepatitis B vaccine. *Pediatrics.* 2010;125(3):e508-512. DOI: 10.1542/peds.2009-1592
22. Fiore AE, Uyeki TM, Broder K, et al. Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR Recomm Rep.* 2010;59(RR-8):1-62.
23. CDC. General recommendations on immunization: recommendations of the Public Health Service Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep.* 1976;25(44):1-3.
24. Scheifele D, Bjornson G, Barreto L, Meekison W, Guasparini R. Controlled trial of *Haemophilus influenzae* type B diphtheria toxoid conjugate combined with diphtheria, tetanus and pertussis vaccines, in 18-month-old children, including comparison of arm versus thigh injection. *Vaccine.* 1992;10(7):455-460. DOI: 10.1016/0264-410X(92)90394-Y
25. CDC. Diphtheria, tetanus, and pertussis: recommendations for vaccine use and other preventive measures. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1991;40(RR-10):1-28.
26. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep.* 2005;54(RR-16):1-31.

27. Hingson RA, Davis HS, Rosen M. Historical development of jet injection and envisioned uses in mass immunization and mass therapy based upon 2 decades experience. *Mil Med.* 1963;128(6):516-524.
28. Weniger B, Papania M. Alternative vaccine delivery methods. In: Plotkin S, Orenstein W, Offit P, eds. *Vaccines*. 5th ed. China: Saunders/Elsevier; 2008:1357-1392.
29. CDC. Hepatitis B associated with jet gun injection—California. *MMWR Morb Mortal Wkly Rep.* 1986;35(23):373-376.
30. Canter J, Mackey K, Good LS, et al. An outbreak of hepatitis B associated with jet injections in a weight reduction clinic. *Arch Intern Med.* 1990;150(9):1923-1927. DOI: 10.1001/archinte.1990.00390200105020
31. Hoffman PN, Abuknesha RA, Andrews NJ, Samuel D, Lloyd JS. A model to assess the infection potential of jet injectors used in mass immunisation. *Vaccine.* 2001;19(28-29):4020-4027. DOI: 10.1016/S0264-410X(01)00106-2
32. Kelly K, Loskutov A, Zehrunge D, et al. Preventing contamination between injections with multiple-use nozzle needle-free injectors: a safety trial. *Vaccine.* 2008;26(10):1344-1352. DOI: 10.1016/j.vaccine.2007.12.041
33. Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of bloodborne pathogens: a review. *Bull World Health Organ.* 1999;77(10):789-800.
34. Kane A, Lloyd J, Zaffran M, Simonsen L, Kane M. Transmission of hepatitis B, hepatitis C and human immunodeficiency viruses through unsafe injections in the developing world: model-based regional estimates. *Bull World Health Organ.* 1999;77(10):801-807.
35. Gray L, Watt L, Blass EM. Skin-to-skin contact is analgesic in healthy newborns. *Pediatrics.* 2000;105(1):e14. DOI: 10.1542/peds.105.1.e14
36. Gray L, Miller LW, Philipp BL, Blass EM. Breastfeeding is analgesic in healthy newborns. *Pediatrics.* 2002;109(4):590-593. DOI: 10.1542/peds.109.4.590
37. Harrington JW, Logan S, Harwell C, et al. Effective analgesia using physical interventions for infant immunizations. *Pediatrics.* 2012;129(5):815-822. DOI: 10.1542/peds.2011-1607

38. Taddio A, Nulman I, Goldbach M, Ipp M, Koren G. Use of lidocaine-prilocaine cream for vaccination pain in infants. *J Pediatr*. 1994;124(4):643-648. DOI: 10.1016/S0022-3476(05)83150-6
39. Uhari M. A eutectic mixture of lidocaine and prilocaine for alleviating vaccination pain in infants. *Pediatrics*. 1993;92(5):719-721.
40. Halperin SA, McGrath P, Smith B, Houston T. Lidocaine-prilocaine patch decreases the pain associated with the subcutaneous administration of measles-mumps-rubella vaccine but does not adversely affect the antibody response. *J Pediatr*. 2000;136(6):789-794. DOI: 10.1016/S0022-3476(00)64169-0
41. Frayling IM, Addison GM, Chattergee K, Meakin G. Methaemoglobinaemia in children treated with prilocaine-lignocaine cream. *BMJ*. 1990;301(6744):153-154. DOI: 10.1136/bmj.301.6744.153
42. Reis EC, Holubkov R. Vapocoolant spray is equally effective as EMLA cream in reducing immunization pain in school-aged children. *Pediatrics*. 1997;100(6):E5. DOI: 10.1542/peds.100.6.e5
43. American Academy of Pediatrics Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures. Febrile seizures: clinical practice guideline for the long-term management of the child with simple febrile seizures. *Pediatrics*. 2008;121(6):1281-1286. DOI: 10.1542/peds.2008-0939
44. Cook IF, Murtagh J. Comparative immunogenicity of hepatitis B vaccine administered into the ventrogluteal area and anterolateral thigh in infants. *J Paediatr Child Health*. 2002;38(4):393-396. DOI: 10.1046/j.1440-1754.2002.00013.x
45. Redfield RR, Innis BL, Scott RM, Cannon HG, Bancroft WH. Clinical evaluation of low-dose intradermally administered hepatitis B virus vaccine. A cost reduction strategy. *JAMA*. 1985;254(22):3203-3206. DOI: 10.1001/jama.1985.03360220069031

46. Coleman PJ, Shaw FE, Jr., Serovich J, Hadler SC, Margolis HS. Intradermal hepatitis B vaccination in a large hospital employee population. *Vaccine*. 1991;9(10):723-727. DOI: 10.1016/0264-410X(91)90287-G
47. Fishbein DB, Sawyer LA, Reid-Sanden FL, Weir EH. Administration of human diploid-cell rabies vaccine in the gluteal area. *N Engl J Med*. 1988;318(2):124-125. DOI: 10.1056/nejm198801143180219
48. CDC. Inadvertent misadministration of meningococcal conjugate vaccine—United States, June-August 2005. *MMWR Morb Mortal Wkly Rep*. 2006;55(37):1016-1017.
49. Ragni MV, Lusher JM, Koerper MA, Manco-Johnson M, Krause DS. Safety and immunogenicity of subcutaneous hepatitis A vaccine in children with haemophilia. *Haemophilia*. 2000;6(2):98-103. DOI: 10.1046/j.1365-2516.2000.00386.x
50. Belshe RB, Newman FK, Cannon J, et al. Serum antibody responses after intradermal vaccination against influenza. *N Engl J Med*. 2004;351(22):2286-2294. DOI: 10.1056/NEJMoa043555

7. Storage and Handling of Immunobiologics

Updates

Most of the 2011 language was removed because this content is now codified and continually updated in the CDC's Vaccine Storage and Handling Toolkit, available at www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html. This content included Storage Units, Monitoring Storage Temperature, Vaccine Inventory, and Vaccine Transport.

General Principles

Failure to adhere to recommended specifications for storage and handling of immunobiologics can reduce or destroy their potency, resulting in inadequate or no immune response in the recipient (www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html). Recommendations in the product package inserts, including methods for reconstitution of the vaccine, should be followed carefully. Maintenance of vaccine quality is the shared responsibility of all handlers of vaccines from the time a vaccine is manufactured until administration. All vaccines should be inspected on delivery and monitored during storage to ensure that the recommended storage temperatures are maintained. Vaccines should continue to be stored at recommended temperatures immediately upon receipt until use. Inadequate vaccine storage also can result in significant costs to replace vaccine inventory (www.cdc.gov/vaccines/hcp/admin/storage/toolkit/index.html).

Storage Temperature

Vaccines licensed for refrigerator storage should be stored at 36°F-46°F (2°C-8°C). Liquid vaccines containing an aluminum adjuvant permanently lose potency when exposed to freezing temperatures. Inactivated vaccines that are stored in a liquid state (i.e., non-lyophilized [freeze-dried]) but that do not contain aluminum adjuvants should also generally be kept at refrigerator temperature, although whether or not they lose

potency when frozen is not known. Inactivated lyophilized vaccines generally do not need to be frozen, but lyophilized varicella-containing vaccines that are recommended to be stored frozen lose potency when exposed to higher temperatures because the viruses degrade more quickly at storage temperatures that are warmer than recommended ([Table 7-1](#)). These varicella-containing vaccines also can be prone to losses in sterility if kept too cold, due to increased gas permeability of the rubber vaccine vial (observed with use of dry ice at temperatures below -58°F or -50°C [personal communication, manufacturer]).

Response to Out-of-Range Temperature Reading

An out-of-range temperature reading should prompt immediate action. A plan should be developed ahead of time to address various types of emergencies that might require removal of vaccine from the original storage unit. Transfer of vaccines to a predesignated alternative emergency storage site might be necessary if a temperature problem cannot be resolved immediately (e.g., plugging in an unplugged unit or closing a door that has been left open). It is critical to avoid freezing vaccine during transport (improperly packing vaccine with ice can damage vaccines). Vaccine should be marked “do not use” and moved to the alternate site after verifying that the alternate unit is at the proper temperature. Determinations of vaccine viability in practice include consideration of both time and magnitude of temperature excursions and should be made in consultation with state/local public health departments or the vaccine manufacturer, as one or both of these groups may have additional information based on a broad international perspective. Damage to the immunogenicity of a vaccine exposed to temperatures outside of the recommended range might not be apparent visually. As a general rule, vaccines that have been stored at inappropriate temperatures should not be administered unless public health authorities or the manufacturer determine it is safe and effective to do so. If such vaccines already have been administered, vaccine exposed to inappropriate temperatures that is inadvertently administered should generally be repeated. Clinicians should consult promptly with state or local health departments in these situations. Consultation with CDC is available when necessary.

TABLE 7-1. Vaccine storage temperature recommendations**Nonlyophilized, aluminum-adjuvanted vaccines**

Vaccines	Vaccine storage temperature	Diluent storage temperature
Diphtheria-tetanus-containing vaccines (DT, Td) or pertussis-containing vaccines (DTaP, Tdap)	2°C-8°C (36°F-46°F) Do not freeze	No diluent ^(a)
HepA and HepB	2°C-8°C (36°F-46°F) Do not freeze	No diluent
MenB ^(b)	2°C-8°C (36°F-46°F) Do not freeze	No diluent
PCV13	2°C-8°C (36°F-46°F) Do not freeze	No diluent
HPV ^(b)	2°C-8°C (36°F-46°F) Do not freeze	No diluent

Nonlyophilized, nonaluminum-adjuvanted vaccines

Vaccines	Vaccine storage temperature	Diluent storage temperature
PRP-OMP Hib	2°C-8°C (36°F-46°F)	No diluent
IPV ^(b)	2°C-8°C (36°F-46°F)	No diluent
MenACWY ^{(b),(c)}	2°C-8°C (36°F-46°F)	No diluent
PPSV	2°C-8°C (36°F-46°F)	No diluent
IIV ^(b)	2°C-8°C (36°F-46°F)	No diluent
RZV ^(b)	2°C-8°C (36°F-46°F) Do not freeze	2°C-8°C (36°F-46°F) Do not freeze

Lyophilized (non-varicella) vaccines		
Vaccines	Vaccine storage temperature	Diluent storage temperature
PRP-T Hib ^(b)	2°C-8°C (36°F-46°F) ^(d)	2°C-8°C (36°F-46°F) Do not freeze
MMR ^(b)	2°C-8°C (36°F-46°F) ^(d)	(2°C-25°C) 35°F-77°F Can be refrigerated or stored at room temperature
Varicella-containing vaccines		
Vaccines	Vaccine storage temperature	Diluent storage temperature
MMRV ^(b)	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Varicella ^(b)	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Herpes zoster ^(b)	-58°F-5°F (-50°C to -15°C)	35°F-77°F (2°C-25°C) Can be refrigerated or stored at room temperature
Noninjectable vaccines		
Vaccines	Vaccine storage temperature	Diluent storage temperature
RV5 vaccine ^(b)	2°C-8°C (36°F-46°F) Do not freeze	No diluent
RV1 vaccine ^(b)	2°C-8°C (36°F-46°F) Do not freeze	The diluent may be stored at a controlled room temperature 20°C-25°C (68°F-77°F). Do not freeze
LAIV ^(b)	2°C-8°C (36°F-46°F)	No diluent
<p>Abbreviations: DT = diphtheria and tetanus toxoids; DTaP = diphtheria and tetanus toxoids and acellular pertussis; HepA = hepatitis A; HepB = hepatitis B; Hib = <i>Haemophilus influenzae</i> type b; HPV = human papillomavirus; IIV = inactivated influenza vaccine; IPV = inactivated poliovirus; LAIV = live, attenuated influenza vaccine; MenACWY = quadrivalent meningococcal conjugate vaccine; MenB = Serogroup B meningococcal vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent</p>		

meningococcal polysaccharide vaccine; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; PRP-OMP = polyribosylribitol phosphate-meningococcal outer membrane protein conjugate; PRP-T = polyribosylribitol phosphate polysaccharide conjugated to a tetanus toxoid; PRP-T Hib = polyribosylphosphate tetanus-toxoid conjugate Hib vaccine; PRP-T Hib-MenCY = polyribosylphosphate-tetanus-toxoid Hib vaccine with a bivalent Meningococcal vaccine; RV = rotavirus; RV1 = live, attenuated monovalent rotavirus vaccine; RV5 = live, reassortment pentavalent rotavirus vaccine; Td = tetanus and diphtheria toxoids; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

Sources: (1,2).

(a) DTaP-Daptacel is sometimes used as a diluent for ActHib.

(b) Protect from light.

(c) There are 2 meningococcal conjugate vaccines; Menactra is nonlyophilized, and Menveo is lyophilized. Both powder and diluent should be stored at 35°F-46°F.

(d) The lyophilized pellet may be stored at freezer temperature; the reconstituted vaccine should be stored at refrigerator temperature.

REFERENCES

1. Kroger A, Atkinson W, Pickering L. General immunization practices. In: Plotkin S, Orenstein W, Offit P, eds. *Vaccines*. 6th ed. China: Elsevier Saunders; 2013:88-111.
2. CDC. Guidelines for maintaining and managing the vaccine cold chain. *MMWR Morb Mortal Wkly Rep*. 2003;52(42):1023-1025.

8. Altered Immunocompetence

Updates

This section incorporates general content from the Infectious Diseases Society of America policy statement, *2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host (1)*, to which CDC provided input in November 2011. The evidence supporting this guidance is based on expert opinion and arrived at by consensus.

General Principles

Altered immunocompetence, a term often used synonymously with immunosuppression, immunodeficiency, and immunocompromise, can be classified as primary or secondary. Primary immunodeficiencies generally are inherited and include conditions defined by an inherent absence or quantitative deficiency of cellular, humoral, or both components that provide immunity. Examples include congenital immunodeficiency diseases such as X-linked agammaglobulinemia, SCID, and chronic granulomatous disease. Secondary immunodeficiency is acquired and is defined by loss or qualitative deficiency in cellular or humoral immune components that occurs as a result of a disease process or its therapy. Examples of secondary immunodeficiency include HIV infection, hematopoietic malignancies, treatment with radiation, and treatment with immunosuppressive drugs. The degree to which immunosuppressive drugs cause clinically significant immunodeficiency generally is dose related and varies by drug. Primary and secondary immunodeficiencies might include a combination of deficits in both cellular and humoral immunity. Certain conditions like asplenia and chronic renal disease also can cause altered immunocompetence.

Determination of altered immunocompetence is important to the vaccine provider because incidence or severity of some vaccine-preventable diseases is higher in persons with altered immunocompetence; therefore, certain vaccines (e.g., inactivated influenza vaccine, pneumococcal vaccines) are recommended specifically for persons with these

diseases (2,3). Administration of live vaccines might need to be deferred until immune function has improved. This is primarily a safety concern, because persons who have altered immunocompetence and receive live vaccines might be at increased risk for an adverse reaction because of uninhibited growth of the attenuated live virus or bacteria. Vaccines might be less effective during the period of altered immunocompetence. Inactivated vaccines might best be deferred during a period of altered immunocompetence; in this circumstance, the concern is with effectiveness and not safety. Additionally, if an inactivated vaccine is administered during the period of altered immunocompetence, it might need to be repeated after immune function has improved.

The degree of altered immunocompetence in a patient should be determined by a physician. The challenge for clinicians and other health care providers is assessing the safety and effectiveness of vaccines for conditions associated with primary or secondary immunodeficiency, especially when new therapeutic modalities are being used and information about the safety and effectiveness of vaccines has not been characterized fully in persons receiving these drugs ([Table 8-1](#)). Laboratory studies can be useful for assessing the effects of a disease or drug on the immune system. Tests useful to assess humoral immunity include immunoglobulin (and immunoglobulin subset) levels and specific antibody levels (e.g., tetanus and diphtheria). Tests that demonstrate the status of cellular immunity include lymphocyte numbers (i.e., a complete blood count with differential), a test that delineates concentrations and proportions of lymphocyte subsets (i.e., B and T lymphocytes, CD4+ B lymphocytes versus CD8+ T lymphocytes), and tests that measure T-cell proliferation or function in response to specific or nonspecific stimuli (e.g., lymphocyte proliferation assays) (4,5). The ability to characterize a drug or disease condition as affecting cellular or humoral immunity is only the first step; using this information to draw inferences about whether particular vaccines are indicated or whether caution is advised with use of live or inactivated vaccines is more complicated and might require consultation with an infectious diseases or immunology specialist.

Altered Immunocompetence as an Indication to Receive a Vaccine Outside of Routinely Recommended Age Groups

This section describes situations in which vaccines are recommended outside of the routine-age-based recommendation because the risk for vaccine-preventable disease is increased due to altered immunocompetence. Persons with altered immunocompetence generally are recommended to receive polysaccharide-based vaccines (PCV13, PPSV23, and Hib), on the basis of increased risk for disease if the vaccine is withheld. For certain specific categories of altered immunocompetence, patients are also recommended to receive polysaccharide based vaccines (MenACWY, Hib-MenCY, and MPSV4).

Pneumococcal Vaccines

Two types of vaccine against invasive pneumococcal disease are available in the United States: PCV13 and PPSV23. PCV13 is recommended routinely for all children beginning at age 2 months through age 59 months and for adults aged 65 years or older. PCV13 is also recommended for children, adolescents, and adults with conditions that place them at high risk for invasive disease from *Streptococcus pneumoniae*. PCV13 is recommended for persons aged 6-64 years who have not previously received PCV13 and have congenital immunodeficiency disorders (including B- or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders), anatomic or functional asplenia (including sickle cell disease and other hemoglobinopathies), HIV infection, cochlear implant, cerebrospinal fluid leak, chronic renal failure, nephrotic syndrome, iatrogenic immunosuppression, or other immunocompromising conditions.

PPSV23 is licensed for use in persons aged ≥ 2 years and recommended routinely for adults aged 65 years and older. PPSV23 is also recommended for persons age 2 through 64 years with congenital immunodeficiency disorders, anatomical and functional asplenia, HIV infection, cochlear implant, cerebrospinal fluid leak, and iatrogenic immunosuppression. Complete recommendations on use of PCV13 and PPSV23 are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule (2,6)*.

Meningococcal Vaccines

Three types of meningococcal vaccines are licensed in the United States: meningococcal conjugate (MenACWY and Hib-MenCY), meningococcal polysaccharide (MPSV4), and serogroup B meningococcal (MenB) vaccines. Persons with functional or anatomic asplenia (including sickle cell disease) and persistent complement component deficiency (including persons taking eculizumab [Soliris]) (7) are at increased risk for meningococcal disease and should receive both MenACWY and MenB vaccines. For children 2 months through 23 months of age, an age-appropriate series of meningococcal conjugate vaccine should be administered. If MenACWY-D (Menactra) is administered to a child with asplenia, it should be after 2 years of age and at least 4 weeks after the completion of all PCV13 doses. A 2-dose primary series of either MenACWY-CRM (Menveo) or MenACWY-D (Menactra) should be administered to persons 2 years of age or older with asplenia or complement deficiency. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for persons who received their previous dose at younger than 7 years. A 5-year interval is recommended for persons who received their previous dose at age 7 years or older. Although MPSV4 is the only meningococcal vaccine licensed for persons older than 55 years of age, adults 56 years and older with asplenia or complement deficiency should be vaccinated with MenACWY-CRM or MenACWY-D rather than MPSV4 (8). Meningococcal serogroup B vaccines are licensed for persons 10-25 years of age and are recommended for persons 10 years of age or older for persons with high-risk conditions like functional or anatomic asplenia or persistent complement component deficiency. There are presently no recommendations for booster doses of either MenB vaccine (9,10). Complete recommendations for use of meningococcal vaccines are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Schedule* (2,6).

Hib Vaccines

Hib conjugate vaccines are available in single or combined antigen preparations. Hib vaccine is recommended routinely for all children through age 59 months. Children 12 through 59 months who are at high risk for invasive Hib disease (i.e., recipients of chemotherapy or radiation for malignant neoplasms, recipients of hematopoietic cell transplant, or those with functional or anatomic asplenia, HIV infection, immunoglobulin deficiency, or early complement component deficiency) and who are unvaccinated or received only one dose of Hib disease before 12 months of age should receive 2 additional doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose. A child younger than 5 years of age receiving chemotherapy or radiation therapy should have Hib doses repeated if the doses were received during therapy or within 14 days of starting therapy; repeat doses should be started at least 3 months after completion of therapy. Recipients of hematopoietic cell transplants should be revaccinated with 3 doses of Hib vaccine, starting 6-12 months after successful transplant, regardless of vaccination history or age. Children 5-18 years of age with HIV who are unimmunized^(a) should receive a dose of Hib vaccine; Hib vaccination is not recommended in HIV-infected adults. Unimmunized^(a) asplenic patients older than 59 months of age or adults should receive a dose of Hib vaccine. Anyone 15 months of age or older who is undergoing a splenectomy and is unimmunized^(a) should receive a dose of Hib vaccine (11). Complete recommendations for use of Hib vaccine are available in the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* and the *Recommended Adult Immunization Schedule* (2,6).

Vaccination of Contacts of Persons with Altered Immunocompetence

Household contacts and other close contacts of persons with altered immunocompetence should receive all age- and exposure-appropriate vaccines, with the exception of smallpox vaccine (12,13). Receipt of vaccines will prevent the vaccine-preventable disease, so there can be no potential transmission to the contact with altered immunocompetence. The live MMR, varicella, and rotavirus vaccines should be administered to susceptible household contacts and other close contacts of immunocompromised patients when indicated. Zoster vaccine can be administered when indicated. MMR vaccine viruses are not transmitted to contacts, and transmission of varicella-zoster virus vaccine strain is rare (14,15). No specific precautions are needed unless the varicella vaccine recipient has a rash after vaccination, in which case direct contact with susceptible household contacts with altered immunocompetence should be avoided until the rash resolves (14,15). All members of the household should wash their hands after changing the diaper of an infant who received rotavirus vaccine. This minimizes rotavirus transmission, as shedding may occur up to one month after the last dose (16,17). Household and other close contacts of persons with altered immunocompetence should receive annual influenza vaccination. Introduction of low levels of vaccine viruses into the environment likely is unavoidable when administering LAIV. LAIV vaccine viruses are cold-adapted, so they can replicate in the nose and generate an immune response without entering the lungs (i.e., they are temperature sensitive and replicate poorly at core body temperatures). No instances have been reported of illness caused by attenuated vaccine virus infections among health care providers or immunocompromised patients. LAIV may be administered to healthy household and other close contacts of persons with altered immunocompetence unless the person with altered immunocompetence is in a protective environment, typically defined as a specialized patient-care area with a positive airflow relative to the corridor, high-efficiency particulate air filtration, and frequent air changes (3). No preference exists for inactivated influenza vaccine use by health care workers or other persons who have close contact with persons with lesser degrees of immunosuppression (e.g.,

persons with diabetes, persons with asthma taking high-dose corticosteroids, or persons infected with HIV), and no preference exists for inactivated influenza vaccine use by health care workers or other healthy persons aged 5-49 years in close contact with all other groups at high risk.

Inactivated Vaccines: Safety

All inactivated vaccines can be administered safely to persons with altered immunocompetence, whether the vaccine is a killed whole-organism or a recombinant, subunit, split-virus, toxoid, polysaccharide, or polysaccharide protein-conjugate vaccine.

Inactivated Vaccines: Effectiveness

Except for inactivated influenza vaccine, vaccination during chemotherapy or radiation therapy should be avoided if possible because antibody response might be suboptimal. Patients vaccinated within a 14-day period before starting immunosuppressive therapy or while receiving immunosuppressive therapy should be considered unimmunized and should be revaccinated at least 3 months after therapy is discontinued if immune competence has been restored. Patients who have quantitative B-cell deficiencies and are receiving immunoglobulin therapy should not receive either inactivated or live vaccines while receiving the immunoglobulin therapy because of concerns about effectiveness of the vaccines. Patients on chemotherapy with anti-B cell antibodies (e.g., rituximab) should wait at least 6 months after therapy before being vaccinated with inactivated vaccines. Some experts recommended longer than 6 months for some anti-B cell antibodies. For other forms of altered immunocompetence, if inactivated vaccines are indicated, the usual schedules are recommended. However, the effectiveness of such vaccinations might be suboptimal (1).

Live, Attenuated Viral and Bacterial Vaccines: Effectiveness

The same rationale regarding effectiveness that exists with inactivated vaccines also exists with live vaccines.

Live, Attenuated Viral and Bacterial Vaccines: Safety

Severe complications have followed vaccination with certain live, attenuated viral and live, attenuated bacterial vaccines among persons with altered immunocompetence (18-26). Persons with most forms of altered immunocompetence should not receive live vaccines (MMR, varicella, MMRV, LAIV, zoster, yellow fever, Ty21a oral typhoid, BCG, smallpox, and rotavirus). However, exceptions exist, and are discussed in this section.

Patients with any defect in phagocytic function (e.g., chronic granulomatous disease, leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live bacterial vaccines. Patients with a specific type of defect in phagocytic function—chronic granulomatous disease—should receive otherwise indicated live attenuated viral vaccines in addition to inactivated vaccines but should NOT receive live bacterial vaccines. Patients with defects in phagocytic function that are undefined or known to be accompanied by defects in T-cell and natural killer cell function (e.g., leukocyte adhesion deficiency, myeloperoxidase deficiency, Chediak-Higashi syndrome) should NOT receive live attenuated viral or bacterial vaccines. These conditions include specific deficits in T-cell and natural killer cell function, reducing the response to live viral vaccine antigens to an extent not seen in chronic granulomatous disease (1). Children with deficiencies in complement should receive otherwise indicated live, attenuated viral and live, attenuated bacterial vaccines. Children with asplenia should not receive LAIV, but can receive other indicated live, attenuated viral and live, attenuated bacterial vaccines.

Persons with severe cell-mediated immunodeficiency should not receive live, attenuated viral or bacterial vaccines. Patients with defects of the interferon-gamma/interleukin-12 axis should not receive live bacterial vaccines. Patients with deficiencies of interferon-gamma or interferon-alpha should not receive live viral or live bacterial vaccine. These defects involve a deficiency in cytokine production which affects the immune response to a wide scope of antigens, both bacterial and viral (1). Two factors support vaccination of HIV-exposed or HIV-infected infants with rotavirus vaccines: 1) the HIV diagnosis might not be established in infants born to HIV-infected mothers before the age of the first rotavirus vaccine dose (only 1.5%-3% of HIV-exposed infants in the United States will be determined to be HIV-infected), and 2) the vaccine strains of rotavirus are considerably attenuated. Patients taking exogenous interferon as therapy should not receive live bacterial or live viral vaccines.

Children with HIV infection are at increased risk for complications from varicella and herpes zoster infection compared with immunocompetent children (27,28). Limited data among HIV-infected children younger than 8 years (specifically, those individuals with CDC class N, A, or B with age-specific CD4+ T-lymphocyte percentages of $\geq 15\%$) indicate that single-component varicella vaccine is immunogenic, effective, and safe (14,28). Data on use of varicella vaccine in HIV-infected adolescents and adults are lacking. However, on the basis of expert opinion, the safety of varicella vaccine in HIV-infected persons older than 8 years with comparable levels of immune function (CD4+T-lymphocyte count greater than 200 cells/mm³) is likely to be similar to that of children aged younger than 8 years (14). Varicella vaccine should be considered for persons who meet these criteria. Eligible HIV-infected persons 12 months of age or older should receive 2 doses of single-component varicella vaccine with a 3-month interval between doses (14,28). Doses separated by <3 months are invalid for persons with HIV infection. MMRV vaccine should not be administered to any HIV-infected person.

Persons with HIV infection are at increased risk for severe complications if infected with measles. No severe or unusual adverse events have been reported after measles vaccination among HIV-infected persons who did not have evidence of severe

immunosuppression (29-32). Two doses of MMR vaccine are recommended for all HIV-infected individuals aged ≥ 12 months who do not have evidence of current severe immunosuppression (i.e., individuals aged ≤ 5 years must have CD4+T lymphocyte [CD4+] percentages $\geq 15\%$ for ≥ 6 months, and individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) and do not have current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those > 5 years, the assessment of severe immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤ 5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥ 6 months above age-specific CD4+count criteria: CD4+count > 750 lymphocytes/mm³ while aged ≤ 12 months and CD4+count ≥ 500 lymphocytes/mm³ while aged 1 through 5 years (33). Similarly, repeat doses of MMR vaccination are recommended for individuals with perinatal HIV infection who were vaccinated prior to establishment of effective combination antiretroviral therapy (cART). They should receive 2 appropriately spaced doses of MMR vaccine once effective cART has been established (individuals aged ≤ 5 years must have CD4+percentages $\geq 15\%$ for ≥ 6 months; individuals aged > 5 years must have CD4+percentages $\geq 15\%$ and CD4+ ≥ 200 lymphocytes/mm³ for ≥ 6 months) unless they have other acceptable current evidence of measles, rubella, and mumps immunity.

HIV-infected persons who are receiving regular doses of IGIV are unlikely to respond to varicella vaccine or MMR vaccine because of the continued presence of passively acquired antibody. However, because of the potential benefit, MMR and varicella vaccines should be considered approximately 14 days before the next scheduled dose of IGIV (if not otherwise contraindicated), although an optimal immune response might not occur depending on the presence of neutralizing antibodies against the vaccine virus. Vaccination should be repeated (if not otherwise contraindicated) after the recommended interval (see [Table 3-5](#) in the Timing and Spacing of Immunobiologics of this document). In most cases, this is after the therapy has been discontinued.

Patients with leukemia, lymphoma, or other malignancies whose disease is in remission, who have restored immunocompetence, and whose chemotherapy has been discontinued for at least 3 months can receive live-virus vaccines. Persons with impaired humoral immunity (e.g., hypogammaglobulinemia or dysgammaglobulinemia) may be vaccinated with varicella vaccine (14). However, most persons with these disorders also receive periodic doses of IGIV. Appropriate spacing should be maintained between administration of IGIV and varicella vaccine in an attempt to prevent an inadequate response to vaccination caused by the presence of neutralizing antibodies from the IGIV.

Zoster incidence is higher in persons with altered immunocompetence (34). Adults with most types of altered immunocompetence are expected to maintain residual immunity to varicella-zoster virus because of chronic latent infection that protects against primary varicella but provides incomplete protection against zoster. Zoster vaccine is contraindicated in persons with primary or acquired immunodeficiency (e.g., lymphoma, leukemia, tumors involving bone marrow, and patients receiving chemotherapy) and some HIV infected patients (34). Zoster vaccine may be administered to certain persons age 60 or older with altered immunocompetence, such as persons receiving low dosages of immunosuppressive medications, those with isolated B-cell deficiencies (i.e., impaired humoral immunity), or those with HIV infection who have CD4+ T-lymphocyte counts >200 cells/mm³.

Recipients of Hematopoietic Cell Transplants

A hematopoietic cell transplant (HCT) results in immunosuppression because of the hematopoietic ablative therapy administered before the transplant, drugs used to prevent or treat graft-versus-host disease, and, in some cases, from the underlying disease process necessitating transplantation (35-37). HCT involves ablation of the bone marrow followed by reimplantation of the person's own stem cells or stem cells from a donor. Antibody titers to vaccine-preventable diseases (e.g., tetanus, poliovirus, measles, mumps, rubella, and encapsulated bacteria) decrease 1-4 years after autologous or allogeneic HCT if the recipient is not revaccinated. HCT recipients of all ages are at increased risk for certain vaccine-preventable diseases, including diseases caused by

encapsulated bacteria (i.e., pneumococcal, meningococcal, and Hib infections). As a result, HCT recipients who received vaccines prior to their HCT should be revaccinated routinely after HCT, regardless of the source of the transplanted stem cells (35-37). Vaccination or revaccination doses of pneumococcal vaccines, DTaP vaccine, Hib vaccine, hepatitis A vaccine, hepatitis B vaccine, meningococcal vaccines, IPV, inactivated influenza vaccines, and human papillomavirus (HPV) vaccines (for individuals aged 9-26 years) are recommended after HCT (1,35). Varicella, zoster, and MMR vaccines may be administered after HCT if 24 months have passed since HCT, the patient does NOT have graft-vs-host disease, and is considered immunocompetent. Yellow fever vaccine, rabies vaccine, tick-borne encephalitis vaccine, and Japanese encephalitis vaccine are not routinely administered vaccines, so their use post-HCT will be driven by a disease-specific risk such as exposure or travel. If someone has received yellow fever vaccine prior to an HCT, another dose should be administered post-HCT (38). BCG, LAIV, typhoid vaccine, and rotavirus vaccine are not recommended after HCT. Most inactivated vaccines should be initiated 6 months after the HCT (37). Inactivated influenza vaccine should be administered beginning at least 6 months after HCT and annually thereafter for the life of the patient. A dose of inactivated influenza vaccine can be given as early as 4 months after HCT, but a second dose should be considered in this situation (37). A second dose is recommended routinely for all children younger than 9 years receiving influenza vaccine for the first time. Sequential administration of 3 doses of pneumococcal conjugate vaccine is recommended, beginning 3-6 months after the transplant, followed by a dose of PPSV23 (35). Some sources state a 4-week interval between these doses as reasonable with the dose of PPSV23 being replaced by a dose of PCV13 in the context of graft-versus-host disease (35). Others sources support 3 doses of PCV13 at 8-week intervals, with a dose of PPSV23 recommended 8 weeks after the last dose of PCV13 and 12 months after the HCT (1). A 3-dose regimen of Hib vaccine should be administered beginning 6 months after transplant; at least 1 month should separate the doses (37). This series should be given regardless of whether or not vaccine doses were administered prior to the HCT. The revaccination schedule for pertussis-containing vaccines includes 3 doses of DTaP for patients <7 years (14). For patients ≥ 7 years, providers have 3 options for

revaccination: 1) 3 doses of DTaP; 2) one dose of Tdap and 2 doses of DT; or 3) one dose of Tdap and 2 doses of Td (16).

Providers need to make a clinical judgment whether they will follow the revaccination schedule described above, even if doses were not administered prior to the HCT. There are specific recommendations for Hib and pertussis-containing vaccines. Use of the 3-dose Hib schedule following HCT is supported for both patients that received Hib prior to HCT and those who did not receive Hib prior to HCT (6,11). For children >6 years who did not receive previous doses of pertussis-containing vaccine prior to the HCT, the preferred schedule following HCT is a dose of Tdap followed by 2 doses of Td (personal communication, subject matter experts). This is identical to one of the alternative regimens for revaccination doses, described above.

Conditions or Drugs that Might Cause Immunodeficiencies

Asplenia and use of corticosteroids or certain drugs have the potential to be immunosuppressive and are presumed to cause some degree of altered immunocompetence.

Anatomic or Functional Asplenia

Persons with anatomic asplenia (e.g., surgical removal or congenital absence of the spleen) or functional asplenia (as occurs in persons with sickle cell disease) are at increased risk for infection by encapsulated bacteria, especially *S. pneumoniae* (pneumococcus), *N. meningitidis* (meningococcus), and Hib (7,8,39). Children should receive an age-appropriate series of PCV13. Unvaccinated children 2-5 years should receive 2 doses of PCV13. Children ≥ 6 years should receive a dose of PCV13 if they have not previously received a dose of PCV13. Persons aged ≥ 2 years should receive 2 doses of PPSV23 separated by 5 years, beginning 8 or more weeks after completing all recommended doses of PCV13 (6,7,40,41). In circumstances where both PCV13 and PPSV23 are indicated, doses of PCV13 should be administered first followed by PPSV23 8 weeks after the last dose of PCV13.

Meningococcal conjugate (MenACWY) and serogroup B (MenB) vaccines are recommended for persons with anatomic or functional asplenia (including sickle cell disease). For children 2-23 months of age, a series of MenACWY-CRM (Menveo) or Hib-MenCY (MenHibrix) should be administered. For persons ≥ 2 years of age, a 2-dose primary series of either MenACWY-CRM or MenACWY-D (Menactra) should be administered. If a person with functional or anatomic asplenia is catching up on pneumococcal conjugate vaccine (PCV13), and the provider only carries MenACWY-D, indicated doses of PCV13 should be completed first and MenACWY-D should be given 4 weeks after the PCV13 series is completed. Following the primary series of vaccine, a 3-year interval to the next dose is recommended for asplenic children who received their last previous dose at age younger than 7 years. A 5-year interval for asplenic persons is recommended for persons who received their last previous dose at age 7 years or older. Meningococcal B (MenB) vaccine should be administered as either a 2-dose series of MenB-4C (Bexsero) or a 3-dose series of MenB-FHbp (Trumenba). The same vaccine product must be used for all doses. Based on available data and expert opinion, MenB-4C or MenB-FHbp may be administered concomitantly with MenACWY vaccines, but at a different anatomic site, if feasible. There are presently no recommendations for booster doses of either MenB vaccine.

Hib vaccine is recommended routinely for all children through age 59 months. Children 12-59 months with functional or anatomic asplenia and who are unvaccinated or who received only one dose of Hib disease before 12 months of age should receive 2 doses of Hib vaccine; those who received 2 or more doses of Hib before 12 months of age should receive one additional dose. Unimmunized^(a) asplenic patients older than 59 months of age should receive one dose of Hib vaccine. Anyone ≥ 15 months of age who is undergoing a splenectomy and is unimmunized^(a) should receive one dose of Hib vaccine.

Pneumococcal, meningococcal, and Hib vaccinations should be administered at least 14 days before elective splenectomy, if possible. If the vaccinations are not administered before surgery, they should be administered after the procedure as soon as the patient's condition is stable.

Corticosteroids

The amount of systemically absorbed corticosteroids and the duration of administration needed to suppress the immune system of an otherwise immunocompetent person are not well defined. Although the immunosuppressive effects of steroid treatment vary, the majority of clinicians consider a dose equivalent to either ≥ 2 mg/kg of body weight or ≥ 20 mg/day of prednisone or equivalent for persons who weigh >10 kg when administered for ≥ 14 consecutive days as sufficiently immunosuppressive to raise concern about the safety of vaccination with live-virus vaccines (37). This dosage is referred to as “high-dose corticosteroids”. Corticosteroids used in greater than physiologic doses also can reduce the immune response to vaccines. Vaccination providers should defer live-virus vaccination for at least 1 month after discontinuation of high-dose systemically absorbed corticosteroid therapy administered for ≥ 14 days. Following vaccination, the decision needs to be made when to restart immunosuppressive therapy. There are no specific recommendations about when to restart immunosuppressive medicines. However, when initiating immunosuppressive therapy, providers should wait 4 weeks after a live vaccine and 2 weeks after an inactivated vaccine. However, if patients require therapy for chronic inflammatory conditions, this therapy should not be delayed because of past administration of vaccines (1).

Corticosteroid therapy usually is not a contraindication to administering live-virus vaccine when administration is 1) short term (i.e., <14 days); 2) a low to moderate dose (i.e., <20 mg of prednisone or equivalent per day or <2 mg/kg body weight per day for a young child); 3) long-term, alternate-day treatment with short-acting preparations; 4) maintenance physiologic doses (replacement therapy); or 5) topical (skin or eyes), inhaled, or by intra-articular, bursal, or tendon injection (37). No evidence of an increased risk for more severe reactions to live, attenuated viral vaccines has been reported among persons receiving corticosteroid therapy by aerosol, and such therapy is not a reason to delay vaccination.

Other Immunosuppressive Drugs

When feasible, clinicians should administer all indicated vaccines before initiation of chemotherapy, before treatment with other immunosuppressive drugs, and before radiation or splenectomy. Persons receiving chemotherapy or radiation for leukemia and other hematopoietic malignancies, or for solid tumors, should be assumed to have altered immunocompetence. Live, attenuated vaccines should not be administered for at least 3 months after such immunosuppressive therapy. Inactivated vaccines administered during chemotherapy should be readministered after immune competence is regained. Children vaccinated before receiving chemotherapy for leukemia, lymphoma, other malignancies, or radiation generally are thought to retain immune memory after treatment, although revaccination with the common childhood vaccines after chemotherapy for acute lymphoblastic leukemia might be indicated (42). In general, revaccination of a person after chemotherapy or radiation therapy is considered unnecessary if the previous vaccination occurred before therapy and not during therapy, with the exception of recipients of HCT, who should be revaccinated as recommended previously. Determination of the level of immune memory and the need for revaccination should be made by the treating physician.

Certain immunosuppressive medications are administered to prevent solid organ transplant rejection. Live vaccines should be withheld for 2 months following discontinuation of anti-rejection therapies in patients with a solid organ transplant. Zoster vaccine should be withheld one month following discontinuation of anti-rejection therapies (34).

Other immunosuppressive medications include human immune mediators like interleukins and colony-stimulating factors, immune modulators, and medicines like tumor necrosis factor-alpha inhibitors and anti-B cell antibodies. Inactivated and live vaccines should be administered 2 or more weeks before initiating such therapies. Live vaccines should be withheld 3 months following such therapies, and both inactivated and live vaccines should be withheld at least 6 months following therapy with anti-B cell antibodies. Some experts recommend longer than 6 months following anti-B cell

antibodies. Anti-B cell antibodies suppress antibody-producing cells for a prolonged duration, hence the longer interval recommended before administering vaccines (17). Zoster vaccine is an exception and should be withheld 1 month following anti-B cell antibodies.

^(a) Patients who have not received a primary series and booster dose or at least 1 dose of Hib vaccine after 14 months of age are considered unimmunized.

TABLE 8-1. Vaccination of persons with primary and secondary immunodeficiencies

Primary	Specific immunodeficiency	Contraindicated vaccines ^(a)	Risk-specific recommended vaccines ^(a)	Effectiveness and comments
B-lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	OPV ^(b) Smallpox ^(c) LAIV BCG Ty21a (live typhoid) Yellow fever MMR MMRV	Pneumococcal Hib (children 12-59 months of age) ^(d)	The effectiveness of any vaccine is uncertain if it depends only on the humoral response (e.g., PPSV23 or MPSV4) IGIV interferes with the immune response to measles vaccine and possibly varicella vaccine
	Less severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency)	OPV ^(b) BCG Yellow fever ^(e) Other live vaccines appear to be safe	Pneumococcal Hib (children 12-59 months of age) ^(d)	All vaccines likely effective; immune response might be attenuated
T-lymphocyte (cell-mediated and humoral)	Complete defects (e.g., SCID disease, complete DiGeorge syndrome)	All live vaccines ^{(f),(g),(h)}	Pneumococcal Hib (children 12-59 months of age) ^(d)	Vaccines likely to be effective

	Partial defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines ^{(f),(g),(h)}	Pneumococcal Meningococcal Hib (children 12-59 months of age) ^(d)	Effectiveness of any vaccine depends on degree of immune suppression
	Interferon-gamma/ Interleukin 12 axis deficiencies	All live bacterial vaccines (All live vaccines contraindicated in Interferon-gamma or interferon-alpha deficiencies)	None	
Complement	Persistent complement, properdin, or factor B deficiency;	None	Pneumococcal Meningococcal Hib (children 12-59 months of age) ^(d)	All routine vaccines likely effective
	Taking eculizumab (Soliris)	None	Meningococcal	
Phagocytic function	Chronic granulomatous disease	Live bacterial vaccines ^(f)	None	Live viral vaccines likely safe and effective

	Phagocytic deficiencies that are undefined or accompanied by defects in T-cell and NK cell dysfunction (such as a Chediak-Higashi syndrome, Leukocyte Adhesion Deficiency [LAD], and myeloperoxidase deficiency)	MMR MMRV Varicella OPV ^(b) Smallpox BCG LAIV Ty21a Yellow Fever and bacterial vaccines ^{(f), (g)}	Pneumococcal	All inactivated vaccines safe and likely effective
Secondary	HIV/AIDS	OPV ^(b) Smallpox BCG LAIV MMRV Withhold MMR, varicella, and zoster in severely immunocompromised persons Yellow fever vaccine might have a contraindication or a precaution depending on clinical parameters of immune function ⁽ⁱ⁾	Pneumococcal Hib ^{(d), (j)} HepB	MMR and Varicella vaccine in those with mild immunosuppression, rotavirus, and all inactivated vaccines, including inactivated influenza as per routine vaccination schedule, might be effective ^(k)
	Generalized malignant neoplasm, transplantation, immunosuppression	Live viral and bacterial, depending on immune status ^{(f), (g), (l)}	Pneumococcal Hib ^(m)	Effectiveness of any vaccine depends on degree of

	sive or radiation therapy			immune suppression
	Asplenia	LAIV	Pneumococcal Meningococcal Hib ^{(d),(n)}	All routine vaccines likely effective
	Chronic renal disease	LAIV	Pneumococcal HepB ^(o)	All routine vaccines likely effective

Abbreviations: AIDS = acquired immunodeficiency syndrome; BCG = bacille Calmette-Guérin; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HIV = human immunodeficiency virus; IG = immunoglobulin; IGIV = immune globulin intravenous; IgA = immune globulin A; IgG = immune globulin G; LAIV = live, attenuated influenza vaccine; MMR = measles, mumps, and rubella; MMRV = measles, mumps, rubella, and varicella; MPSV4 = quadrivalent meningococcal polysaccharide vaccine; OPV = oral poliovirus vaccine (live); PPSV23 = pneumococcal polysaccharide vaccine; SCID = severe combined immunodeficiency; Ty21a = live oral typhoid vaccine.

Source: (43).

- (a) Other vaccines that are universally or routinely recommended should be given if not contraindicated. An exception is patients with B-cell deficiencies receiving immunoglobulins, who should not receive either live or inactivated vaccines, due to safety (live vaccines) and efficacy (live and inactivated vaccines) concerns.
- (b) OPV is no longer available in the United States.
- (c) This table refers to contraindications for nonemergency vaccination (i.e., the ACIP recommendations); emergency response recommendations are addressed in the clinical guidance for smallpox vaccine use in an emergency.
- (d) Children 12-59 months: if unimmunized or received zero or only 1 dose, and that dose was administered before 12 months of age, should receive 2 Hib doses, 8 weeks apart; if received 2 or more doses before age 12 months, and none after 12 months, should receive 1 Hib dose 8 weeks after the last dose; if completed a primary series and received a booster dose at age 12 months or older, no additional Hib doses are recommended.
- (e) There are no data to support IgA deficiency as a contraindication for yellow fever vaccine.
- (f) Live bacterial vaccines: BCG, adenovirus, and oral Ty21a *Salmonella Typhi* vaccine.
- (g) Live viral vaccines: MMR, MMRV, OPV, LAIV, yellow fever, zoster, rotavirus, varicella, and vaccinia (smallpox). Nonemergency smallpox vaccination is not recommended for children younger than 18 years or the general public.
- (h) Regarding T-lymphocyte immunodeficiency as a contraindication for rotavirus vaccine, data exist only for SCID.
- (i) Symptomatic HIV infection or CD4+ T-lymphocyte count of <200/mm³ or <15% of total lymphocytes for children aged <6 years is a contraindication to yellow fever vaccine administration. Asymptomatic HIV infection with CD4+ T-lymphocyte count of 200-499/mm³ for persons aged ≥6 years or 15%-24% of total lymphocytes for children aged <6 years is a precaution for yellow fever vaccine administration. Details of yellow fever vaccine recommendations are available from CDC (44)
- (j) Patients 5-18 years of age who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.
- (k) HIV-infected children should be considered for varicella vaccine if CD4+ T-lymphocyte count is ≥15% and should receive MMR vaccine if they are aged ≥12 months and do not have 1) evidence of current severe immunosuppression (i.e., individuals aged ≤5 years must have CD4+T lymphocyte [CD4] percentages ≥15% for ≥6 months; and individuals aged >5 years must have CD4+percentages ≥15% and CD4+≥200 lymphocytes/mm³ for ≥6 months) and 2) other current evidence of measles, rubella, and mumps immunity. In cases when only CD4+cell counts or only CD4+percentages are available for those older than age 5 years, the assessment of severe

immunosuppression can be based on the CD4+values (count or percentage) that are available. In cases when CD4+percentages are not available for those aged ≤ 5 years, the assessment of severe immunosuppression can be based on age-specific CD4+counts at the time CD4+counts were measured; i.e., absence of severe immunosuppression is defined as ≥ 6 months above age-specific CD4+count criteria: CD4+count >750 lymphocytes/ mm^3 while aged ≤ 12 months and CD4+count ≥ 500 lymphocytes/ mm^3 while aged 1 through 5 years (33).

^(l) Withholding inactivated vaccines also is recommended with some forms of immunosuppressive therapy, like anti-CD20 antibodies, induction or consolidation chemotherapy, or patients with major antibody deficiencies receiving immunoglobulins. Inactivated influenza vaccine is an exception, but consideration should be given to repeating doses of any inactivated vaccine administered during these therapies.

^(m) Persons younger than 60 months undergoing chemotherapy or radiation therapy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age; HCT patients of any ages, regardless of Hib vaccine history.

⁽ⁿ⁾ Persons older than 59 months who are asplenic and persons 15 months or older who are undergoing elective splenectomy who have not received a Hib primary series and a booster dose or at least one Hib dose after 14 months of age.

^(o) Indicated based on the risk from dialysis-based bloodborne transmission.

REFERENCES

1. Rubin L, Levin M, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58(3):e44-100. DOI: 10.1093/cid/cit684
2. Kim DK, Bridges CB, Harriman KH. Advisory committee on immunization practices recommended immunization schedule for adults aged 19 years or older—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(4):91-92.
3. Grohskopf LA, Olsen SJ, Sokolow LZ, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP)—United States, 2014-15 influenza season. *MMWR Morb Mortal Wkly Rep*. 2014;63(32):691-697.
4. Markert ML, Hummell DS, Rosenblatt HM, et al. Complete DiGeorge syndrome: persistence of profound immunodeficiency. *J Pediatr*. 1998;132(1):15-21. DOI: 10.1016/S0022-3476(98)70478-0
5. Jeffrey Modell Foundation Medical Advisory Board. 10 warning signs of primary immunodeficiency [Poster]. 2009; [http:// www.info4pi.org/library/educational-materials/10-warning-signs](http://www.info4pi.org/library/educational-materials/10-warning-signs). Accessed 9 March, 2017.
6. Strikas RA. Advisory committee on immunization practices recommended immunization schedules for persons aged 0 through 18 years—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(4):93-94.
7. Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2005;54(RR-7):1-21.
8. Cohn AC, MacNeil JR, Clark TA, et al. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2013;62(RR-2):1-28.
9. Folaranmi T, Rubin L, Martin SW, Patel M, MacNeil JR. Use of serogroup B meningococcal vaccines in persons aged ≥ 10 years at increased risk for serogroup B meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(22):608-612.

10. MacNeil JR, Rubin L, Folaranmi T, Ortega-Sanchez IR, Patel M, Martin SW. Use of serogroup B meningococcal vaccines in adolescents and young adults: recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64(41):1171-1176. DOI: 10.15585/mmwr.mm6441a3
11. Briere EC, Rubin L, Moro PL, Cohn A, Clark T, Messonnier N. Prevention and control of *Haemophilus influenzae* type b disease: recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep.* 2014;63(RR-1):1-14.
12. Petersen BW, Harms TJ, Reynolds MG, Harrison LH. Use of vaccinia virus smallpox vaccine in laboratory and health care personnel at risk for occupational exposure to orthopoxviruses - recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. *MMWR Morb Mortal Wkly Rep.* 2016;65(10):257-262. DOI: 10.15585/mmwr.mm6510a2
13. Petersen BW, Damon IK, Pertowski CA, et al. Clinical guidance for smallpox vaccine use in a postevent vaccination program. *MMWR Recomm Rep.* 2015;64(RR-2):1-26.
14. Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2007;56(RR-4):1-40.
15. Grossberg R, Harpaz R, Rubtcova E, Loparev V, Seward JF, Schmid DS. Secondary transmission of varicella vaccine virus in a chronic care facility for children. *J Pediatr.* 2006;148(6):842-844. DOI: 10.1016/j.jpeds.2006.01.038
16. Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2009;58(RR-2):1-25.
17. Anderson EJ. Rotavirus vaccines: viral shedding and risk of transmission. *Lancet Infect Dis.* 2008;8(10):642-649. DOI: 10.1016/s1473-3099(08)70231-7
18. Sixbey JW. Routine immunizations and the immunosuppressed child. *Adv Pediatr Infect Dis.* 1987;2:79-114.

19. Wright PF, Hatch MH, Kasselberg AG, Lowry SP, Wadlington WB, Karzon DT. Vaccine-associated poliomyelitis in a child with sex-linked agammaglobulinemia. *J Pediatr*. 1977;91(3):408-412. DOI: 10.1016/S0022-3476(77)81309-7
20. Wyatt HV. Poliomyelitis in hypogammaglobulinemics. *J Infect Dis*. 1973;128(6):802-806. DOI: 10.1093/infdis/128.6.802
21. Davis LE, Bodian D, Price D, Butler IJ, Vickers JH. Chronic progressive poliomyelitis secondary to vaccination of an immunodeficient child. *N Engl J Med*. 1977;297(5):241-245. DOI: 10.1056/nejm197708042970503
22. CDC. Disseminated *Mycobacterium bovis* infection from BCG vaccination of a patient with acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep*. 1985;34(16):227-228.
23. Ninane J, Grymonprez A, Burtonboy G, Francois A, Cornu G. Disseminated BCG in HIV infection. *Arch Dis Child*. 1988;63(10):1268-1269. DOI: 10.1136/adc.63.10.1268
24. Redfield RR, Wright DC, James WD, Jones TS, Brown C, Burke DS. Disseminated vaccinia in a military recruit with human immunodeficiency virus (HIV) disease. *N Engl J Med*. 1987;316(11):673-676. DOI: 10.1056/nejm198703123161106
25. CDC. Measles pneumonitis following measles-mumps-rubella vaccination of a patient with HIV infection, 1993. *MMWR Morb Mortal Wkly Rep*. 1996;45(28):603-606.
26. Cono J, Casey CG, Bell DM. Smallpox vaccination and adverse reactions. Guidance for clinicians. *MMWR Recomm Rep*. 2003;52(RR-4):1-28.
27. Derryck A, LaRussa P, Steinberg S, Capasso M, Pitt J, Gershon AA. Varicella and zoster in children with human immunodeficiency virus infection. *Pediatr Infect Dis J*. 1998;17(10):931-933. DOI: 10.1097/00006454-199810000-00023
28. Levin MJ, Gershon AA, Weinberg A, Song LY, Fentin T, Nowak B. Administration of live varicella vaccine to HIV-infected children with current or past significant depression of CD4(+) T cells. *J Infect Dis*. 2006;194(2):247-255. DOI: 10.1086/505149

29. Sprauer MA, Markowitz LE, Nicholson JK, et al. Response of human immunodeficiency virus-infected adults to measles-rubella vaccination. *J Acquir Immune Defic Syndr*. 1993;6(9):1013-1016.
30. McLaughlin M, Thomas P, Onorato I, et al. Live virus vaccines in human immunodeficiency virus-infected children: a retrospective survey. *Pediatrics*. 1988;82(2):229-233.
31. Onorato IM, Markowitz LE, Oxtoby MJ. Childhood immunization, vaccine-preventable diseases and infection with human immunodeficiency virus. *Pediatr Infect Dis J*. 1988;7(8):588-595.
32. Palumbo P, Hoyt L, Demasio K, Oleske J, Connor E. Population-based study of measles and measles immunization in human immunodeficiency virus-infected children. *Pediatr Infect Dis J*. 1992;11(12):1008-1014.
33. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2013;62(RR-4):1-34.
34. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2008;57(RR-5):1-30; quiz CE32-34.
35. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238. DOI: 10.1016/j.bbmt.2009.06.019
36. Ljungman P, Cordonnier C, Einsele H, et al. Vaccination of hematopoietic cell transplant recipients. *Bone Marrow Transplant*. 2009;44(8):521-526. DOI: 10.1038/bmt.2009.263
37. American Academy of Pediatrics. Immunization in special clinical circumstances. In: Pickering L, Baker C, Kimberlin D, Long S, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.

38. Staples JE, Bocchini JA, Jr., Rubin L, Fischer M. Yellow fever vaccine booster doses: Recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64(23):647-650.
39. CDC. *Haemophilus b* conjugate vaccines for prevention of *Haemophilus influenzae* type b disease among infants and children two months of age and older. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep.* 1991;40(RR-1):1-7.
40. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1-24.
41. Nuorti JP, Whitney CG. Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-11):1-18.
42. Brodtman DH, Rosenthal DW, Redner A, Lanzkowsky P, Bonagura VR. Immunodeficiency in children with acute lymphoblastic leukemia after completion of modern aggressive chemotherapeutic regimens. *J Pediatr.* 2005;146(5):654-661. DOI: 10.1016/j.jpeds.2004.12.043
43. American Academy of Pediatrics. Passive immunization. In: Pickering L, Baker C, Kimberlin D, Long S, eds. *Red Book: 2012 Report of the Committee on Infectious Diseases.* 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.
44. Staples JE, Gershman M, Fischer M. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2010;59(RR-7):1-27.

9. Special Situations

Updates

Major revisions to this section of the best practices guidance include the timing of intramuscular administration and the timing of clotting factor deficiency replacement.

Concurrent Administration of Antimicrobial Agents and Vaccines

With a few exceptions, use of an antimicrobial agent does not interfere with the effectiveness of vaccination. Antibacterial agents have no effect on inactivated, recombinant subunit, or polysaccharide vaccines or toxoids. They also have no effect on response to live, attenuated vaccines, except live oral Ty21a typhoid and BCG vaccines. Ty21a typhoid vaccine should not be administered to persons receiving antimicrobial agents until 72 hours after the last dose of antimicrobial (1). If feasible, to avoid a possible reduction in vaccine effectiveness, antibacterial drugs should not be started or resumed until 1 week after the last dose of Ty21a. Antimicrobial or immunosuppressive agents may interfere with the immune response to BCG and should only be used under medical supervision (for additional information, see http://www.merck.com/product/usa/pi_circulars/b/bcg/bcg_pi.pdf).

Antiviral drugs used for treatment or prophylaxis of influenza virus infections have no effect on the response to inactivated influenza vaccine (2). However, live, attenuated influenza vaccine should not be administered until 48 hours after cessation of therapy with antiviral influenza drugs. If feasible, to avoid possible reduction in vaccine effectiveness, antiviral medication should not be administered for 14 days after LAIV administration (2). If influenza antiviral medications are administered within 2 weeks after receipt of LAIV, the LAIV dose should be repeated 48 or more hours after the last dose of antiviral medication. Alternatively, persons receiving antiviral drugs within the period 2 days before to 14 days after vaccination with LAIV may be revaccinated with another approved vaccine formulation (e.g., IIV or recombinant influenza vaccine). Antiviral drugs active against herpesviruses (e.g., acyclovir or valacyclovir) might reduce

the efficacy of vaccines containing live, attenuated varicella zoster virus (i.e., Varivax, ProQuad, and Zostavax) (3,4). These drugs should be discontinued at least 24 hours before administration, if possible. If clinically appropriate, delay use or resumption of antiviral therapy for 14 days after vaccination. No data exist to suggest that commonly used antiviral drugs have an effect on rotavirus vaccine or MMR.

Administration of Live Vaccines and Tuberculin Skin Tests (TSTs) and Interferon-gamma Release Assays (IGRAs)

Measles illness, severe acute or chronic infections, HIV infection, and malnutrition can create a relatively anergic state during which the TST might have a false-negative reaction (5-7). Although live, attenuated measles vaccine theoretically can suppress TST reactivity, the degree of suppression is likely less than that occurring from acute infection from wild-type measles virus. Screening children for tuberculosis exposure is accomplished by medical history rather than TST testing; universal TST screening of all children is no longer recommended, though TST screening is sometimes indicated (e.g., for persons at increased risk for tuberculosis exposure based on medical history, or for employees for occupational health reasons).

In a general screening situation, a TST may be administered simultaneously with live vaccines, or should be deferred for 28 days after vaccination. The TST and measles-containing vaccine can be administered at the same visit (this is the preferred option). Simultaneously administering the TST and measles-containing vaccine does not interfere with reading the TST result at 48-72 hours and ensures that the person has received measles vaccine. If the measles-containing vaccine has been administered recently, TST screening should be delayed for at least 4 weeks after vaccination. A delay in performing the TST removes the concern of any theoretical transient suppression of TST reactivity. Some providers choose to perform TST screening and then delay the vaccine until the patient returns to have the TST read. This option is the least favored because it delays receipt of the measles-containing vaccine and risks having neither the TST nor vaccination completed if the patient does not return.

Because of similar concerns about smallpox vaccine and TST suppression, a TST should not be performed until 4 weeks after smallpox vaccination (8). No data exist regarding the potential degree of TST suppression that might be associated with other live, attenuated virus vaccines (e.g., varicella or yellow fever). However, in the absence of data, following guidelines for measles-containing vaccine when scheduling TST screening and administering other live, attenuated virus vaccines is prudent. If the opportunity to vaccinate might be missed, vaccination should not be delayed only because of these theoretical considerations. TST can be repeated 4 weeks after vaccination if it is negative and concern for TB infection persists.

Interferon gamma release assays (IGRAs), such as the QuantiFERON-TB Gold In-Tube test and the T-Spot TB test, are blood-test alternatives to the TST for detecting *Mycobacterium tuberculosis* infection. The IGRA requires only a single visit to complete and may be less affected by previous BCG vaccination (9). The same timing guidelines that apply to the interval between a live vaccine and TST apply to IGRA (i.e., 28 days between live vaccine and IGRA if they do not occur on the same day), because IGRA (like TST) might be suppressed through immunologic mechanisms. The potential for a previous TST to cause boosting of future TST results should be considered in adults who have a negative initial TST (9). Two-step testing, in which TST is repeated in a short time frame (e.g., 1 to 3 weeks) after an initial negative TST, can illicit boosting and identify persons whose immune response may have waned with time since infection or BCG vaccination. For people undergoing serial screening for infection, for instance health care personnel who are tested yearly, differentiation of positive tests due boosting versus new infection is important (9). The 2-step test, in which the test is given twice in a short time frame, reduces the chance of these false negatives, which are important to identify among adults who may have had or plan to have repeat testing anyway—for example, health care personnel who are tested yearly (9). Because this test consists of 2 TSTs separated by an interval of 1-3 weeks, there is a greater window of time during which live vaccine replication could suppress reactivity. If a live vaccine is administered, the first dose of a 2-step TST should be delayed for 4 weeks, and if additional doses of live vaccines are indicated thereafter, they should be delayed until the second TST is measured.

TST or IGRA reactivity in the absence of active tuberculosis is not a contraindication to administration of any vaccine, including live, attenuated virus vaccines.

Note that TST screening of an asymptomatic individual is clinically different than testing a person suspected to have active tuberculosis. If a person is suspected to have active tuberculosis, MMR vaccine is typically not administered. Active tuberculosis should be considered severe acute illness, and moderate or severe acute illness is a precaution for vaccination.

Although no studies have reported on the effects of MMR vaccine on persons with active untreated tuberculosis, a theoretical basis exists for concern that measles vaccine might exacerbate active tuberculosis (10). As a result, before administering MMR to persons with untreated active tuberculosis, initiating antituberculosis therapy is advisable (10). Considering whether concurrent immunosuppression (e.g., immunosuppression caused by HIV infection) is present before administering live, attenuated vaccines also is necessary, because immunosuppression is a contraindication to MMR vaccine.

Vaccination of Preterm Infants

In the majority of cases, preterm infants (infants born before 37 weeks' gestation), regardless of birth weight, should be vaccinated at the same chronological age and according to the same schedule and using the same precautions as for full-term infants and children. Birth weight and size are not factors in deciding whether to vaccinate a clinically stable preterm infant (11-15), except for hepatitis B vaccination. The full recommended dose of each vaccine should be used. Divided or reduced doses are not recommended.

Decreased seroconversion rates might occur among certain preterm infants (i.e., those with low birth weights [$<2,000$ g]) after administration of hepatitis B vaccine at birth (16). However, by the chronological age of 1 month, all preterm infants, regardless of initial birth weight, are likely to respond as adequately as larger infants (17-19). Infants weighing $<2,000$ g born to HBsAg-negative mothers should receive the first dose of the hepatitis B vaccine series at chronological age 1 month or hospital discharge, if hospital

discharge occurs when the infant is younger than one month of age. Preterm low-birth-weight–infants born to HBsAg-positive mothers should receive immunoprophylaxis with hepatitis B vaccine within 12 hours after birth. The initial vaccine dose should not be counted toward completion of the hepatitis B series, and 3 additional doses of hepatitis B vaccine should be administered, beginning when the infant is aged 1 month. For mothers with unknown HBsAg status, hepatitis B vaccine is recommended within 12 hours of birth regardless of low-birth-weight status.

In addition to hepatitis B vaccines, hepatitis B Immunoglobulin (HBIG) is recommended for infants whose mothers are HBsAg positive or unknown. If the mother is HBsAg positive, HBIG must be given within 12 hours of birth. If the mother's HBsAg status is unknown, providers should first attempt to determine the mother's status. Regardless, if the infant is preterm or low birth weight, HBIG must be given within 12 hours of birth. If the infant is neither preterm nor low birth weight, providers have up to 7 days from birth to determine if the mother is HBsAg negative; because the protective efficacy of HBIG declines the longer that administration is delayed, if results are unlikely to be known by day 7 of life, HBIG should be given no later than day 7 if not earlier. If the mother is determined to be HBsAg positive, HBIG should be administered as soon as possible (20).

If a child aged at least 6 weeks has been in the hospital since birth, deferral of rotavirus vaccine is recommended until the time of discharge. If an infant were to be vaccinated with rotavirus vaccine while still needing care in the NICU or nursery, at least a theoretic risk exists for vaccine virus being transmitted to infants in the same unit who are acutely ill and to preterm infants who are not age-eligible for vaccine (21). The rotavirus vaccine series should not be initiated for infants aged ≥ 15 weeks, 0 days.

Breastfeeding and Vaccination

With 2 exceptions, neither inactivated nor live-virus vaccines administered to a lactating woman affect the safety of breastfeeding for women or their infants. Although live viruses in vaccines can replicate in the mother, the majority of live viruses in vaccines

have been demonstrated not to be excreted in human milk. Varicella vaccine virus has not been found in human milk (22). Although rubella vaccine virus has been excreted in human milk, the virus usually does not infect the infant. If infection does occur, it is well tolerated because the virus is attenuated (23). Inactivated, recombinant, subunit, polysaccharide, and conjugate vaccines, as well as toxoids, pose no risk for mothers who are breastfeeding or for their infants. Breastfeeding is a contraindication for smallpox vaccination of the mother because of the theoretical risk for contact transmission from mother to infant. Yellow fever vaccine should be avoided in breastfeeding women, because 2 cases (one confirmed, one probable) of yellow-fever vaccine associated acute neurotropic disease (YEL-AND) have been detected in infants whose mothers were vaccinated but were not vaccinated themselves. In both infants, vaccine virus was recovered from the cerebrospinal fluid of the infant, but the exact mode of transmission was not precisely determined because vaccine virus was not recovered from breast milk (24). However, when nursing mothers cannot avoid or postpone travel to areas endemic for yellow fever in which risk for acquisition is high, these women should be vaccinated.

Limited data indicate that breastfeeding can enhance the response to certain vaccine antigens (25). There are no data to suggest that passive transfer of antibodies in human milk can affect the efficacy of live-virus vaccines. Breastfed infants should be vaccinated according to the recommended schedule (26-28).

Vaccination During Pregnancy

No evidence exists of risk to the fetus from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids (29,30). In spite of the lack of evidence of risk, HPV vaccine, an inactivated vaccine, is not recommended during pregnancy. Live vaccines administered to a pregnant woman pose a theoretical risk to the fetus; therefore, live, attenuated virus and live bacterial vaccines generally are contraindicated during pregnancy. Women should avoid conception for 4 weeks after vaccination with live vaccines. However, benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high, when infection would pose a risk to the mother or fetus, and when the vaccine is unlikely to cause harm.

Recommendations for vaccination during pregnancy are developed using ACIP's *Guiding Principles for Development of ACIP Recommendations for Vaccination During Pregnancy and Breastfeeding* (31).

Women who are pregnant should receive a dose of Tdap for the prevention of infant pertussis whether or not they have previously received Tdap. Vaccination of the mother generates antibodies that pass transplacentally to the fetus (32). Vaccination in the third trimester optimizes the duration of this antibody protection until after birth.

Additionally, preventing pertussis in the mother reduces the risk that the infant is exposed to pertussis after birth (33). Health care personnel should administer Tdap during pregnancy, preferably during the third trimester. If Tdap is not administered during pregnancy to women who have never received it, it should be administered immediately postpartum. Pregnant women who are not vaccinated or are only partially vaccinated against tetanus should complete the primary series (34). Women for whom Td is indicated but who did not complete the recommended 3-dose series during pregnancy should receive follow-up after delivery to ensure the series is completed. One dose of the tetanus vaccine series should be Tdap, if Tdap has not already been received.

Pregnant and postpartum women are at higher risk for severe illness and complications from influenza than women who are not pregnant (2,35). Pregnant women have protective levels of anti-influenza antibodies after vaccination (36,37). Passive transfer of anti-influenza antibodies that might provide protection from vaccinated women to neonates has been reported (36,38-41). Routine vaccination with inactivated influenza vaccine is recommended for all women who are or will be pregnant (in any trimester) during influenza season.

IPV can be administered to pregnant women who are at risk for exposure to wild-type poliovirus. This includes travelers to areas or countries where polio is epidemic or endemic; members of communities or specific population groups with disease caused by wild polioviruses; laboratory workers who handle specimens that might contain polioviruses; health care personnel who have close contact with patients who might be excreting wild polioviruses; and unvaccinated persons whose children will be receiving

oral poliovirus vaccine (42). Hepatitis A, pneumococcal polysaccharide, meningococcal conjugate, and meningococcal polysaccharide vaccines should be considered for women at increased risk for those infections (43-45). Pregnant women who must travel to areas where there is a risk for acquiring yellow fever should receive yellow fever vaccine, because the limited theoretical risk from vaccination is outweighed substantially by the risk for yellow fever infection (24,46). Hepatitis B vaccine is not contraindicated in pregnancy and should be given to a pregnant woman for whom it is indicated (20,47).

Pregnancy is a contraindication for smallpox (vaccinia) vaccine and measles-, mumps-, rubella-, and varicella-containing vaccines. Smallpox vaccine is the only vaccine known to harm a fetus when administered to a pregnant woman. In addition, smallpox vaccine should not be administered to a household contact of a pregnant woman (8). Women who are pregnant should not have close contact with anyone who has recently (within the last 28 days) received the smallpox vaccine. Data from studies of children born to mothers inadvertently vaccinated with rubella vaccine during pregnancy demonstrate rubella antibody in unvaccinated infants. This could represent passive transfer of maternal antibody or a fetal antibody response to vaccine virus infection in the fetus. No cases of congenital rubella or varicella syndrome or abnormalities attributable to fetal infection have been observed among infants born to susceptible women who inadvertently received rubella or varicella vaccines during pregnancy (48-50). Because of the importance of protecting women of childbearing age against rubella and varicella, reasonable practices in any vaccination program include asking women if they are pregnant or might become pregnant in the next 4 weeks; not vaccinating women who state that they are or plan to become pregnant within that interval; explaining the theoretical risk for the fetus if MMR, varicella, or MMRV vaccine were administered to a woman who is pregnant; and counseling women who are vaccinated not to become pregnant during the 4 weeks after MMR, varicella, or MMRV vaccination (10,48-51). MMRV is an unlikely option for a pregnant woman because the vaccine is only licensed through 12 years of age. Routine pregnancy testing of women of childbearing age before administering a live-virus vaccine is not recommended (3,10). If a pregnant woman is inadvertently vaccinated or becomes pregnant within 4 weeks after MMR or varicella vaccination, she should be counseled about the theoretical basis of concern for the fetus;

however, MMR or varicella vaccination during pregnancy should not be considered a reason to terminate pregnancy (3,10,50).

Persons who receive MMR vaccine do not transmit the vaccine viruses to contacts (10). Transmission of varicella vaccine virus to contacts is exceedingly rare (3). MMR and varicella vaccines should be administered when indicated to children and other household contacts of pregnant women (10). Infants living in households with pregnant women should be vaccinated with rotavirus vaccine according to the same schedule as infants in households without pregnant women.

Pregnant women should be evaluated for evidence of immunity to rubella and varicella and be tested for the presence of HBsAg during every pregnancy (10,20,52). Women without evidence of immunity to rubella and varicella should be vaccinated immediately after delivery. A second dose of varicella vaccine should be administered 4-8 weeks later. A woman found to be HBsAg positive should be followed-up carefully to ensure that the infant receives HBIG and begins the hepatitis B vaccine series no later than 12 hours after birth and that the infant completes the recommended hepatitis B vaccine series on schedule (20). No known risk exists for the fetus from passive immunization of pregnant women with immune globulin preparations.

Persons Vaccinated Outside the United States

Clinicians have a limited ability to determine whether persons are protected on the basis of their country of origin and their vaccination records alone. Vaccines administered outside the United States generally can be accepted as valid if the schedule (i.e., minimum ages and intervals) is similar to that recommended in the United States. With the exception of influenza vaccine, only written documentation should be accepted as evidence of previous vaccination. Written records are more likely to predict protection if the vaccines, dates of administration, intervals between doses, and age at the time of vaccination are comparable to U.S. recommendations. Although vaccines with inadequate potency have been produced in other countries (53,54), the majority of

vaccines used worldwide are produced with adequate quality control standards and are potent.

Persons vaccinated outside of the United States can enter the country through a number of different mechanisms. Those seeking to immigrate to the United States may be vaccinated under the authority of a civil surgeon or a panel physician. Some enter the United States as refugees and are vaccinated under the authority of the Office of Refugee Resettlement, part of the Administration for Children and Families, in the Department of Health and Human Services.

Adopted children's birth countries often have vaccination schedules that differ from the recommended childhood vaccination schedule in the United States. Differences in the U.S. schedule and those used in other countries include the vaccines administered, the recommended ages of administration, and the number and timing of doses.

Data are inconclusive regarding the extent to which an internationally adopted child's vaccination record reflects the child's protection. A child's record might indicate administration of MMR vaccine when only single-antigen measles vaccine was administered. A study of children adopted from orphanages in the People's Republic of China, Russia, and countries in Eastern Europe determined that 67% of children with documentation of >3 doses of DTP before adoption had nonprotective titers to these antigens (54). In contrast, children adopted from these countries who received vaccination in the community (not only from orphanages) and had documentation of ≥ 1 doses of DTP exhibited protective titers 67% of the time (54). However, antibody testing was performed by using a hemagglutination assay, which tends to underestimate protection and cannot directly be compared with antibody concentration (55). Data are likely to remain limited for areas other than the People's Republic of China, Russia, and Eastern Europe. Health care providers should ensure that household contacts of international adoptees are vaccinated adequately, particularly for measles, hepatitis A, and hepatitis B (56).

Health care providers may use one of multiple approaches if the immunogenicity of vaccines or the completeness of series administered to persons outside the United States is in question. Repeating the vaccinations is an acceptable option that usually is safe and prevents the need to obtain and interpret serologic tests. If avoiding unnecessary injections is desired, judicious use of serologic testing might help determine which vaccinations are needed. For some vaccines, the most readily available serologic tests cannot document protection against infection. This best practices document provides guidance on possible approaches to evaluation and revaccination for each vaccine recommended in the United States ([Table 9-1](#)).

DTaP Vaccine

Vaccination providers can revaccinate children younger than 7 years of age with DTaP vaccine without regard to recorded doses; however, data indicate increased rates of local adverse reactions after the fourth and fifth doses of DTaP (57). If a revaccination approach is adopted and a severe local reaction occurs, serologic testing for specific IgG antibody to tetanus and diphtheria toxins can be measured before administering additional doses. Protective concentration^(a) indicates that additional doses are unnecessary and subsequent vaccination should occur as age appropriate. No established serologic correlates exist for protection against pertussis.

For a child whose record indicates receipt of ≥ 3 doses of DTP or DTaP, serologic testing for specific IgG antibody to both diphtheria and tetanus toxin before additional doses is a reasonable approach. If a protective concentration is present, recorded doses are considered valid, and the vaccination series should be completed as age appropriate. An indeterminate antibody concentration might indicate immunologic memory but waning antibody; serologic testing can be repeated after a booster dose if vaccination providers or parents want to avoid revaccination with a complete series.

Alternately, for a child whose records indicate receipt of ≥ 3 doses, a single booster dose can be administered followed by serologic testing after 1 month for specific IgG antibody to both diphtheria and tetanus toxins. If the child has a protective concentration, the

recorded doses are considered valid, and the vaccination series should be completed as age appropriate. Children with an indeterminate concentration after a booster dose should be revaccinated with a complete series.

Hepatitis A Vaccine

Children aged 12-23 months without documentation of hepatitis A vaccination or serologic evidence of immunity should be vaccinated on arrival in the United States (45). Persons who have received 1 dose should receive the second dose if 6-18 months have passed since the first dose was administered.

Hepatitis B Vaccine

Persons not known to be vaccinated for hepatitis B should receive an age-appropriate series of hepatitis B vaccine. A person whose records indicate receipt of ≥ 3 doses of vaccine is considered protected, and additional doses are not needed if ≥ 1 dose was administered at age ≥ 24 weeks. Persons who received their last hepatitis B vaccine dose at an age < 24 weeks should receive an additional dose at age ≥ 24 weeks. People who have received < 3 doses of vaccine should complete the series at the recommended intervals and ages.

All foreign-born persons and immigrants, refugees, and internationally adopted children born in Asia, the Pacific Islands, Africa, and other regions of high or intermediate hepatitis B endemicity should be tested for HBsAg, regardless of vaccination status (58). Those determined to be HBsAg positive should be monitored for development of liver disease. Household members of HBsAg-positive children or adults should be vaccinated if they are not already immune.

Hib Vaccine

Interpretation of a serologic test to verify whether children who were vaccinated > 2 months previously are protected against Hib bacteria can be difficult. Because the number of vaccinations needed for protection decreases with age and because adverse

events are rare (59), age-appropriate vaccination should be provided. Hib vaccination is not recommended routinely for persons aged ≥ 5 years (59).

Meningococcal Vaccine

Quadrivalent meningococcal conjugate vaccines are not routinely used in other countries in adolescents (the United Kingdom is the exception). Unless patients have documented receipt they should be considered unvaccinated and receive the age-appropriate doses.

MMR Vaccine

The simplest approach to resolving concerns about MMR vaccination is to revaccinate with 1 or 2 doses of MMR vaccine, depending on age. Serious adverse events after MMR vaccinations are rare (10). No evidence indicates that administering MMR vaccine increases the risk for adverse reactions among persons who are already immune to measles, mumps, or rubella as a result of previous vaccination or natural disease. Doses of measles-containing vaccine administered before the first birthday should not be counted as part of the series (10). Alternatively, serologic testing for IgG antibody to vaccine viruses indicated on the vaccination record can be considered. Serologic testing is widely available for measles and rubella IgG antibody. A person whose record indicates receipt of monovalent measles or measles-rubella vaccine on or after the first birthday and who has protective antibody against measles and rubella should receive 1 or 2 doses of MMR or MMRV as age appropriate to ensure protection against mumps and varicella (and rubella if measles vaccine alone had been administered). If a person whose record indicates receipt of MMR at age ≥ 12 months has a protective concentration of antibody to measles, no additional vaccination is needed unless a second dose is required for school entry.

Pneumococcal Vaccines

Many industrialized countries now routinely use pneumococcal vaccines. Although recommendations for pneumococcal polysaccharide vaccine also exist in many countries, the pneumococcal conjugate vaccine might not be routinely administered. PCV13 and PPSV23 should be administered according to age-appropriate vaccination schedules or as indicated by the presence of underlying medical conditions (43,60).

Poliovirus Vaccine

The simplest approach to vaccinating with poliovirus vaccine is to revaccinate persons aged <18 years with IPV according to the U.S. schedule. Adverse events after IPV are rare (42). Children appropriately vaccinated with 3 doses of OPV in economically developing countries might have suboptimal seroconversion, including to type 3 poliovirus (42).

Rotavirus Vaccine

Rotavirus vaccination should not be initiated for infants aged ≥ 15 weeks, 0 days. Infants who began the rotavirus vaccine series outside the United States but who did not complete the series and who are still aged ≤ 8 months, 0 days, should follow the routine schedule and receive doses to complete the series. If the brand of a previously administered dose is live, reassortment pentavalent rotavirus vaccine or is unknown, a total of 3 doses of rotavirus vaccine should be documented for series completion. All doses should be administered by age 8 months, 0 days.

Td and Tdap Vaccines

Children aged ≥ 7 years who are not considered fully vaccinated for pertussis should receive Tdap vaccine. “Fully vaccinated” means at least 5 doses of DTaP before the seventh birthday or at least 4 doses of DTaP before the seventh birthday if the fourth dose is given after the fourth birthday. One dose of Tdap is recommended after the

seventh birthday. If additional doses of vaccine are needed, Td should be administered as age appropriate.

Varicella Vaccine

Varicella vaccine is not available in most countries. A person who lacks evidence of varicella immunity should be vaccinated as age appropriate (3,59).

Zoster Vaccine

In the United States, zoster vaccination is recommended for all persons aged ≥ 60 years who have no contraindications, including persons who report a previous episode of zoster or who have chronic medical conditions. For persons who do not have documentation of receipt of zoster vaccine, the vaccine should be offered at the patient's first clinical encounter with the health care provider. The vaccine is administered as a single 0.65-mL subcutaneous dose. Zoster vaccination is not indicated to treat acute zoster, to prevent persons with acute zoster from developing postherpetic neuralgia, or to treat ongoing postherpetic neuralgia. Patients do not need to be asked about their history of varicella or to have serologic testing conducted to determine zoster immunity prior to administration of zoster vaccine.

Vaccinating Persons with Increased Bleeding Risk

Providers often avoid giving intramuscular injections or choose alternative routes for persons with bleeding disorders because of the risk for hematoma formation after injections. In one study, hepatitis B vaccine was administered intramuscularly to 153 persons with hemophilia. The vaccination was administered with a 23-gauge or smaller caliber needle, followed by application of steady pressure to the site for 1-2 minutes. The vaccinations resulted in a low (4%) bruising rate, and no patients required factor supplementation (61). Whether antigens that produce more local reactions (e.g., pertussis) would produce an equally low rate of bruising is unknown.

When hepatitis B or any other intramuscularly administered vaccine is indicated for a patient with a bleeding disorder, the vaccine should be administered intramuscularly if a physician familiar with the patient's bleeding risk determines that the vaccine can be administered by this route with reasonable safety. If the patient receives antihemophilia or similar therapy, intramuscularly administered vaccinations can be scheduled shortly after such therapy is administered. A fine-gauge needle (23-gauge or smaller caliber) should be used for the vaccination, followed by firm pressure on the site, without rubbing, for at least 2 minutes. The patient or family should be given information on the risk for hematoma from the injection. Patients receiving anticoagulation therapy presumably have the same bleeding risk as patients with clotting factor disorders and should follow the same guidelines for intramuscular administration. If possible, vaccination could be scheduled prior to the use of these medications, so that the patients' risk of bleeding is not increased by their therapeutic action.

^(a) Enzyme immunoassay tests are available. Physicians should contact the laboratory performing the test for interpretive standards and limitations. Protective concentrations for antibody to diphtheria and tetanus toxins are defined as >0.1 IU/mL.

TABLE 9-1. Approaches to evaluation and vaccination of persons vaccinated outside the United States who have no (or questionable) vaccination records

Vaccine	Recommended approach	Alternative approach^(a)
DTaP	Revaccination with DTaP, with serologic testing for specific IgG antibody to tetanus and diphtheria toxins in the event of a severe local reaction	Persons whose records indicate receipt of ≥ 3 doses: serologic testing for specific IgG antibody to diphtheria and tetanus toxins before administering additional doses (see text), or administer a single booster dose of DTaP, followed by serological testing after 1 month for specific IgG antibody to diphtheria and tetanus toxins with revaccination as appropriate (see text)
HepA	Age-appropriate revaccination	Serologic testing for IgG antibodies to hepatitis A
HepB	Age-appropriate revaccination and serologic testing for HBsAg ^(b)	—
Hib	Age-appropriate revaccination	—
HPV	Age-appropriate revaccination	—
Meningococcal conjugate (MenACWY)	Age-appropriate revaccination	—
MMR	Revaccination with MMR	Serologic testing for IgG antibodies to measles, mumps, and rubella
Pneumococcal conjugate (or in some cases, both PCV13 and PPSV23)	Age-appropriate revaccination	—

Poliovirus	Revaccination with inactivated poliovirus vaccine	—
Rotavirus	Age-appropriate revaccination	—
Tdap	Age-appropriate revaccination of persons who are candidates for Tdap vaccine	—
Varicella	Age-appropriate revaccination of persons who lack evidence of varicella immunity	—
Zoster	Age-appropriate revaccination	—

Abbreviations: DTaP = diphtheria and tetanus toxoids and acellular pertussis; HBsAg = hepatitis B surface antigen; HepA = hepatitis A; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; HPV = human papillomavirus; IgG = immune globulin G; MMR = measles, mumps, and rubella; PCV13 = pneumococcal conjugate vaccine; PPSV23= pneumococcal polysaccharide vaccine; Tdap = tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis.

^(a) There is a recommended approach for all vaccines and an alternative approach for some vaccines.

^(b) In rare instances, hepatitis B vaccine can give a false-positive HBsAg result up to 18 days after vaccination; therefore, blood should be drawn to test for HBsAg before vaccinating (20).

REFERENCES

1. Jackson BR, Iqbal S, Mahon B. Updated recommendations for the use of typhoid vaccine—Advisory Committee on Immunization Practices, United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2015;64(11):305-308.
2. Grohskopf LA, Shay DK, Shimabukuro TT, et al. Prevention and control of seasonal influenza with vaccines. Recommendations of the Advisory Committee on Immunization Practices—United States, 2013-2014. *MMWR Recomm Rep.* 2013;62(RR-7):1-43.
3. Marin M, Guris D, Chaves SS, Schmid S, Seward JF. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2007;56(RR-4):1-40.
4. Harpaz R, Ortega-Sanchez IR, Seward JF. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2008;57(RR-5):1-30; quiz CE32-34.
5. Starr S, Berkovich S. Effects of measles, gamma-globulin-modified measles and vaccine measles on the tuberculin test. *N Engl J Med.* 1964;270:386-391. DOI: 10.1056/nejm196402202700802
6. Brickman HF, Beaudry PH, Marks MI. The timing of tuberculin tests in relation to immunization with live viral vaccines. *Pediatrics.* 1975;55(3):392-396.
7. Berkovich S, Starr S. Effects of live type 1 poliovirus vaccine and other viruses on the tuberculin test. *N Engl J Med.* 1966;274(2):67-72. DOI: 10.1056/nejm196601132740203
8. Wharton M, Strikas RA, Harpaz R, et al. Recommendations for using smallpox vaccine in a pre-event vaccination program. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Healthcare Infection Control Practices Advisory Committee (HICPAC). *MMWR Recomm Rep.* 2003;52(RR-7):1-16.

9. Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K. Updated guidelines for using interferon gamma release assays to detect *Mycobacterium tuberculosis* infection - United States, 2010. *MMWR Recomm Rep.* 2010;59(RR-5):1-25.
10. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1998;47(RR-8):1-57.
11. Bernbaum JC, Daft A, Anolik R, et al. Response of preterm infants to diphtheria-tetanus-pertussis immunizations. *J Pediatr.* 1985;107(2):184-188. DOI: 10.1016/S0022-3476(85)80122-0
12. Koblin BA, Townsend TR, Munoz A, Onorato I, Wilson M, Polk BF. Response of preterm infants to diphtheria-tetanus-pertussis vaccine. *Pediatr Infect Dis J.* 1988;7(10):704-711.
13. Smolen P, Bland R, Heiligenstein E, Lawless MR, Dillard R, Abramson J. Antibody response to oral polio vaccine in premature infants. *J Pediatr.* 1983;103(6):917-919. DOI: 10.1016/S0022-3476(83)80714-8
14. Omenaca F, Garcia-Sicilia J, Garcia-Corbeira P, et al. Response of preterm newborns to immunization with a hexavalent diphtheria-tetanus-acellular pertussis-hepatitis B virus-inactivated polio and *Haemophilus influenzae* type b vaccine: first experiences and solutions to a serious and sensitive issue. *Pediatrics.* 2005;116(6):1292-1298. DOI: 10.1542/peds.2004-2336
15. Shinefield H, Black S, Ray P, Fireman B, Schwalbe J, Lewis E. Efficacy, immunogenicity and safety of heptavalent pneumococcal conjugate vaccine in low birth weight and preterm infants. *Pediatr Infect Dis J.* 2002;21(3):182-186. DOI: 10.1097/00006454-200203000-00003
16. Lau YL, Tam AY, Ng KW, et al. Response of preterm infants to hepatitis B vaccine. *J Pediatr.* 1992;121(6):962-965. DOI: 10.1016/S0022-3476(05)80352-X

17. Patel DM, Butler J, Feldman S, Graves GR, Rhodes PG. Immunogenicity of hepatitis B vaccine in healthy very low birth weight infants. *J Pediatr*. 1997;131(4):641-643. DOI: 10.1016/S0022-3476(97)70078-7
18. Kim SC, Chung EK, Hodinka RL, et al. Immunogenicity of hepatitis B vaccine in preterm infants. *Pediatrics*. 1997;99(4):534-536. DOI: 10.1542/peds.99.4.534
19. Losonsky GA, Wasserman SS, Stephens I, et al. Hepatitis B vaccination of premature infants: a reassessment of current recommendations for delayed immunization. *Pediatrics*. 1999;103(2):E14. DOI: 10.1542/peds.103.2.e14
20. Mast EE, Margolis HS, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children, and adolescents. *MMWR Recomm Rep*. 2005;54(RR-16):1-31.
21. Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2009;58(RR-2):1-25.
22. Bohlke K, Galil K, Jackson LA, et al. Postpartum varicella vaccination: is the vaccine virus excreted in breast milk? *Obstet Gynecol*. 2003;102(5 Pt 1):970-977. DOI: 10.1016/S0029-7844(03)00860-3
23. Krogh V, Duffy LC, Wong D, Rosenband M, Riddlesberger KR, Ogra PL. Postpartum immunization with rubella virus vaccine and antibody response in breast-feeding infants. *J Lab Clin Med*. 1989;113(6):695-699.
24. Staples JE, Gershman M, Fischer M. Yellow fever vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2010;59(RR-7):1-27.
25. Pickering LK, Granoff DM, Erickson JR, et al. Modulation of the immune system by human milk and infant formula containing nucleotides. *Pediatrics*. 1998;101(2):242-249. DOI: 10.1542/peds.101.2.242
26. Kim-Farley R, Brink E, Orenstein W, Bart K. Vaccination and breast feeding. *JAMA*. 1982;248(19):2451-2452. DOI: 10.1001/jama.1982.03330190021019

27. Patriarca PA, Wright PF, John TJ. Factors affecting the immunogenicity of oral poliovirus vaccine in developing countries: review. *Rev Infect Dis*. 1991;13(5):926-939.
28. Hahn-Zoric M, Fulconis F, Minoli I, et al. Antibody responses to parenteral and oral vaccines are impaired by conventional and low protein formulas as compared to breast-feeding. *Acta Paediatr Scand*. 1990;79(12):1137-1142. DOI: 10.1111/j.1651-2227.1990.tb11401.x
29. Koren G, Pastuszak A, Ito S. Drugs in pregnancy. *N Engl J Med*. 1998;338(16):1128-1137. DOI: 10.1056/nejm199804163381607
30. Grabenstein JD. Vaccines and antibodies in relation to pregnancy and lactation. *Hospital Pharmacy*. 1999;34:949-960.
31. CDC. Guiding principles for development of ACIP recommendations for vaccination during pregnancy and breastfeeding. *MMWR Morb Mortal Wkly Rep*. 2008;57(21):580.
32. Munoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. *JAMA*. 2014;311(17):1760-1769. DOI: 10.1001/jama.2014.3633
33. Wendelboe AM, Njamkepo E, Bourillon A, et al. Transmission of Bordetella pertussis to young infants. *Pediatr Infect Dis J*. 2007;26(4):293-299. DOI: 10.1097/01.inf.0000258699.64164.6d
34. Kretsinger K, Broder KR, Cortese MM, et al. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health care personnel. *MMWR Recomm Rep*. 2006;55(RR-17):1-37.
35. Neuzil KM, Reed GW, Mitchel EF, Simonsen L, Griffin MR. Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *Am J Epidemiol*. 1998;148(11):1094-1102. DOI: 10.1093/oxfordjournals.aje.a009587

36. Sumaya CV, Gibbs RS. Immunization of pregnant women with influenza A/New Jersey/76 virus vaccine: reactogenicity and immunogenicity in mother and infant. *J Infect Dis.* 1979;140(2):141-146. DOI: 10.1093/infdis/140.2.141
37. Munoz FM, Greisinger AJ, Wehmanen OA, et al. Safety of influenza vaccination during pregnancy. *Am J Obstet Gynecol.* 2005;192(4):1098-1106. DOI: 10.1016/j.ajog.2004.12.019
38. Englund JA, Mbawuike IN, Hammill H, Holleman MC, Baxter BD, Glezen WP. Maternal immunization with influenza or tetanus toxoid vaccine for passive antibody protection in young infants. *J Infect Dis.* 1993;168(3):647-656. DOI: 10.1093/infdis/168.3.647
39. Puck JM, Glezen WP, Frank AL, Six HR. Protection of infants from infection with influenza A virus by transplacentally acquired antibody. *J Infect Dis.* 1980;142(6):844-849. DOI: 10.1093/infdis/142.6.844
40. Reuman PD, Ayoub EM, Small PA. Effect of passive maternal antibody on influenza illness in children: a prospective study of influenza A in mother-infant pairs. *Pediatr Infect Dis J.* 1987;6(4):398-403. DOI: 10.1097/00006454-198704000-00011
41. Steinhoff MC, Omer SB, Roy E, et al. Influenza immunization in pregnancy—antibody responses in mothers and infants. *N Engl J Med.* 2010;362(17):1644-1646. DOI: 10.1056/NEJMc0912599
42. Prevots DR, Burr RK, Sutter RW, Murphy TV. Poliomyelitis prevention in the United States. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2000;49(RR-5):1-22; quiz CE21-27.
43. CDC. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1997;46(RR-8):1-24.
44. Bilukha OO, Rosenstein N. Prevention and control of meningococcal disease. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2005;54(RR-7):1-21.

45. Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-7):1-23.
46. Tsai TF, Paul R, Lynberg MC, Letson GW. Congenital yellow fever virus infection after immunization in pregnancy. *J Infect Dis*. 1993;168(6):1520-1523. DOI: 10.1093/infdis/168.6.1520
47. Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep*. 2006;55(RR-16):1-33; quiz CE31-34.
48. Wilson E, Goss MA, Marin M, et al. Varicella vaccine exposure during pregnancy: data from 10 years of the pregnancy registry. *J Infect Dis*. 2008;197 Suppl 2:S178-184. DOI: 10.1086/522136
49. CDC. Revised ACIP recommendation for avoiding pregnancy after receiving a rubella-containing vaccine. *MMWR Morb Mortal Wkly Rep*. 2001;50(49):1117.
50. CDC. Rubella vaccination during pregnancy—United States, 1971-1988. *MMWR Morb Mortal Wkly Rep*. 1989;38(17):289-293.
51. Black NA, Parsons A, Kurtz JB, McWhinney N, Lacey A, Mayon-White RT. Post-partum rubella immunisation: a controlled trial of two vaccines. *Lancet*. 1983;2(8357):990-992. DOI: 10.1016/S0140-6736(83)90979-0
52. CDC. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR Recomm Rep*. 2001;50(RR-12):1-23.
53. Murray TS, Groth ME, Weitzman C, Cappello M. Epidemiology and management of infectious diseases in international adoptees. *Clin Microbiol Rev*. 2005;18(3):510-520. DOI: 10.1128/cmr.18.3.510-520.2005
54. Hostetter MK. Infectious diseases in internationally adopted children: findings in children from China, Russia, and eastern Europe. *Adv Pediatr Infect Dis*. 1999;14:147-161.

55. Kriz B, Burian V, Sladky K, Burianova B, Mottlova O, Roth Z. Comparison of titration results of diphtheric antitoxic antibodies obtained by means of Jensen's method and the methods of tissue cultures and haemagglutination. *J Hyg Epidemiol Microbiol Immunol*. 1978;22(4):485-493.
56. CDC. Updated recommendations from the Advisory Committee on Immunization Practices (ACIP) for use of hepatitis A vaccine in close contacts of newly arriving international adoptees. *MMWR Morb Mortal Wkly Rep*. 2009;58(36):1006-1007.
57. CDC. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2000;49(RR-13):1-8.
58. Weinbaum CM, Williams I, Mast EE, et al. Recommendations for identification and public health management of persons with chronic hepatitis B virus infection. *MMWR Recomm Rep*. 2008;57(RR-8):1-20.
59. CDC. Recommended immunization schedules for persons aged 0 through 18 years—United States, 2011. *MMWR Morb Mortal Wkly Rep*. 2011;60(5):1-4.
60. Nuorti JP, Whitney CG. Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2010;59(RR-11):1-18.
61. Evans DI, Shaw A. Safety of intramuscular injection of hepatitis B vaccine in haemophiliacs. *BMJ*. 1990;300(6741):1694-1695. DOI: 10.1136/bmj.300.6741.1694-a

10. Vaccination Records

Records of Health Care Providers

Appropriate and timely vaccination documentation helps ensure not only that persons in need of recommended vaccine doses receive them but also that adequately vaccinated patients do not receive excess doses. Curtailing the number of excess doses administered to patients controls costs incurred by patients, providers, insurers, vaccination programs, and other stakeholders. In addition, avoidance of excess doses of vaccines should decrease the number of adverse reactions to vaccines. Health care providers who administer vaccines covered by the National Vaccine Injury Compensation Program (VICP) are required under the National Childhood Vaccine Injury Act (*1*) to ensure that the permanent medical record of the recipient (or a permanent office log or file) indicates the date the vaccine was administered, the vaccine manufacturer, the vaccine lot number, and the name, address, and title of the person administering the vaccine. This Act applies to any vaccine for which there is a routine recommendation for childhood vaccination, even if many or most doses of the vaccine are administered to adults (e.g., influenza vaccine). In addition, the provider is required to record the edition date of the VIS distributed and the date those materials were provided. The Act considers a health care provider to be any licensed health care professional, organization, or institution, whether private or public (including federal, state, and local departments and agencies), under whose authority a specified vaccine is administered. This information should be kept for all vaccines, not just for those required by the Act. Providers and staff members also should systematically update patients' permanent medical records to reflect any documented episodes of adverse events after vaccination and any serologic test results related to vaccine-preventable diseases (e.g., those for rubella screening and anti-HBs).

Personal Records of Patients

Official childhood vaccination records have been adopted by every state and territory and the District of Columbia to encourage uniformity of records and to facilitate assessment of vaccination status by schools and child-care centers. The records also are key tools in vaccination education programs aimed at increasing parental and patient awareness of the need for vaccines. This record can exist in electronic file format or in hardcopy format. A permanent vaccination record should be established for each newborn infant and maintained by the parent or guardian. The parent or guardian should be educated about the importance of keeping the record up-to-date and instructed to keep the record indefinitely. These records should be distributed to new parents and/or guardians before discharge from the hospital or birthing center. Using vaccination records for adolescents and adults also is encouraged. Standardized adult vaccination records are available at www.immunize.org.

Immunization Information Systems (IISs)

IISs (formerly referred to as immunization registries) are confidential, population-based, computerized information systems that collect and consolidate vaccination data from multiple health care providers within a geographic area. IISs are a critical tool that can increase and sustain vaccination coverage by consolidating vaccination records from multiple providers, generating reminder and recall vaccination notices for each person, and providing official vaccination forms and vaccination coverage assessments (2). Providers should be aware of state and/or regional IISs and requirements for reporting.

Changing vaccination providers during the course of an individual's vaccination series is common in the United States. In addition to changes in providers, the vaccination records of persons who have changed vaccination providers often are unavailable or incomplete or might not have been entered into an IIS (2). Missing or inaccurate information regarding vaccines received previously might preclude accurate determination of which vaccines are indicated at the time of a visit, resulting in administration of extra doses.

A fully operational IIS also can prevent duplicate vaccinations, forecast when the next dose is due, limit missed appointments, allow recall for those who missed appointments, determine when vaccines need to be repeated (the technical IIS term for this is “evaluation”), reduce vaccine waste, and reduce staff time required to produce or locate vaccination records or certificates. Most IISs have additional capabilities, such as measurement of vaccination update and coverage, aid in tracking vaccine inventory and placing vaccine orders, recall of vaccine by lot number, maintenance of lifetime vaccination histories, and interoperability with other health information systems. The National Vaccine Advisory Committee recommends that vaccination providers participate in these systems when possible. Electronic health records should maintain interoperability with IISs as part of an effort to improve the quality of care, reduce health disparities, engage patients and families in their health, improve the coordination of care, improve population health, and ensure adequate privacy and security protection for personal health information (see www.cdc.gov/ehrmeaningfuluse/introduction.html)

One of the national Healthy People objectives for 2020 is 95% participation of children aged <6 years in a fully operational population-based IIS (objective 20.1) (3,4). Participating in an IIS means having two or more vaccinations recorded in the IIS. 2012 IIS data indicate that approximately 86% of children aged <6 years with two or more vaccinations were participating in IISs (4,5).

The National Vaccine Advisory Committee recommends that public health departments work toward including adults in all state IISs, reduce barriers to including adult vaccination records in IISs, and ensure that IISs meet new standards of EHR interoperability to track and maintain adult vaccination records (6).

Nationally, 57.8 million U.S. adults aged 19 years or older participated in an IIS in 2012 (4). This number reflects adults who may have had childhood vaccines entered during childhood and now have aged to adults. In 2013, 32% of U.S. adults had a record in the IIS and at least one vaccination administered during adulthood.

REFERENCES

1. National Childhood Vaccine Injury Act, 42 U.S.C. Sect. 300aa-1 to 300aa-34 (1986).
2. CDC. Immunization information systems progress—United States, 2006. *MMWR Morb Mortal Wkly Rep.* 2008;57(11):289-291.
3. US Department of Health and Human Services. Immunization and infectious diseases. *Healthy people 2010*. Vol 1 (conference edition). 1st ed. Washington, DC: US Government Printing Office; 2000.
4. CDC. Progress in immunization information systems - United States, 2012. *MMWR Morb Mortal Wkly Rep.* 2013;62(49):1005-1008.
5. Mangione-Smith R, DeCristofaro AH, Setodji CM, et al. The quality of ambulatory care delivered to children in the United States. *N Engl J Med.* 2007;357(15):1515-1523. DOI: 10.1056/NEJMsa064637
6. National Vaccine Advisory Committee. Recommendations from the National Vaccine Advisory committee: standards for adult immunization practice. *Public Health Rep.* 2014;129(2):115-123.

11. Vaccination Programs

Updates

The major revision to this section is the addition of language related to Affordable Care Act (1) coverage of adult vaccination.

General Principles

Universal vaccination is a critical part of quality health care and should be accomplished through routine and catch-up vaccination provided in physicians' offices, public health clinics, and other appropriate settings. In the United States, vaccination is considered primarily the responsibility of individual health care providers and health care systems serving patients.

Certain programs and other efforts attempt to ensure all patients receive the full schedule of appropriate vaccinations by removing barriers posed by access to immunizations, cost, or other factors. Such efforts may include school-located clinics, school-based health centers, back-to-school immunization clinics, public health clinics for schoolchildren, periodic influenza vaccination clinics, public health nurse tracking of childhood immunizations, and government-sponsored financing of vaccines through the Vaccines for Children and Section 317 program (www.cdc.gov/vaccines/hcp/admin/vfc.html).

In the United States, vaccination programs have eliminated many vaccine-preventable diseases and markedly reduced the incidence of others (2). Because infants and young children were the principal recipients of most vaccines developed during the twentieth century (e.g., poliovirus vaccine), many persons in the United States might believe that vaccinations are solely for the young; however, vaccinations are recommended for persons of all ages (3,4). Improved vaccination coverage can result in additional reductions in the incidence of vaccine-preventable diseases that affect persons throughout the life span, and decrease associated morbidity and mortality.

Vaccination of Children and Adolescents

Physicians and other pediatric vaccination providers should adhere to the standards for child and adolescent vaccination practices (5). These standards are published by the National Vaccine Advisory Committee and define appropriate vaccination practices for both public and private sectors. The standards provide guidance on practices that eliminate barriers to vaccination, including eliminating unnecessary prerequisites for receiving vaccinations, eliminating missed opportunities to vaccinate, improving procedures to assess vaccination needs, enhancing knowledge about vaccinations among parents and providers, and improving management and reporting of adverse events. In addition, the standards address the importance of recall and reminder systems and using assessments to monitor clinic or office vaccination coverage levels. Health care providers should simultaneously administer as many vaccine doses as possible as indicated on the *Recommended Immunization Schedules for Persons Aged 0 Through 18 Years* (3).

While rates of childhood vaccination are generally higher than rates of adult vaccination, for some doses coverage rates are still low, like the birth dose of hepatitis B vaccine. Community health care providers, as well as state and local public health vaccination programs, should coordinate with partners to identify and maximize outreach to populations at risk for undervaccination and vaccine-preventable diseases. For example, the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) is a categorical federal grant program administered by the U.S. Department of Agriculture through state health departments. The program provides supplemental foods, health care referrals, and nutrition education to low-income pregnant, breastfeeding, or postpartum women, as well as to infants and children aged <5 years. Between 8.5 and 8.9 million people participated in this program in 2013 (www.fns.usda.gov/pd/wicmain.htm). In collaboration, WIC and state vaccination programs assess regularly the vaccination coverage levels of WIC participants and develop new strategies and aggressive outreach procedures in sites with coverage levels <90%. Vaccination programs and private providers are encouraged to refer eligible

children to obtain WIC nutritional services, at www.fns.usda.gov/wic/immunization-screening-and-referral-wic (6).

Adolescent-Specific Issues

Vaccinations are recommended throughout life, including during adolescence. The age range for adolescence is defined as 11-21 years by many professional associations, including the American Academy of Pediatrics and the American Medical Association (7,8). Definitions of these age cutoffs differ depending on the source of the definition and the source's purpose for creating a definition. Vaccination of adolescents is critical for preventing diseases for which adolescents are at particularly high or increasing risk, such as meningococcal disease and human papillomavirus infection. Three vaccines recommended for adolescents have been licensed since 2005: MenACWY and Tdap were licensed in 2005, and HPV was licensed in 2006. A second dose of varicella vaccine is recommended for persons who received 1 dose of varicella vaccine after age 12 months. In addition, annual seasonal influenza vaccination is recommended for persons aged >6 months who have no contraindications. To ensure vaccine coverage, clinicians and other health care providers who treat adolescents must review vaccination history on every occasion that an adolescent has an office visit.

National goals for vaccination coverage for adolescents aged 13-15 years were included in *Healthy People 2020*, at www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases. Targets of 80% coverage were specified for one dose of Tdap, one dose of meningococcal conjugate vaccine, and 3 doses of HPV vaccine. Results of the published 2014 National Immunization Survey—Teen indicate that coverage rates for 13-17 years olds is 87.6% for one dose of Tdap and 79.3% for one dose of meningococcal vaccine. Coverage rates for 13-17 years olds for HPV vaccine are considerably lower—39.7% for females and 21.6% for males (9,10).

Ensuring adolescents receive routine and catch-up vaccination and achieving high levels of vaccination coverage present challenges. In general, adolescents do not visit health care providers frequently. Health care providers should promote annual preventive

visits (11), including one specifically for adolescents aged 11 and 12 years. The annual visits should be used as opportunities to provide routinely recommended vaccine doses, additional catch-up doses needed for lapsed vaccine series, vaccines recommended for high-risk groups, additional doses that might have been recently recommended, and other recommended health care services. Additional strategies include adolescent immunizations at community-based venues such as pharmacies and schools.

All vaccine doses should be administered according to ACIP vaccine-specific statements and with the most recent schedules for both routine and catch-up vaccination. Before leaving any visit for medical care, adolescents should be encouraged to schedule return visits for any additional vaccine doses needed. During visits that occur outside of influenza season, providers should discuss and recommend seasonal influenza vaccination and make explicit plans for vaccination, including timing and anticipated setting (e.g., health care provider's office, school, or pharmacy). Catch-up vaccination with multidose adolescent vaccines generally can occur according to the routine dosing schedule for these vaccines, although in some circumstances the clinician or health care provider might use minimum intervals for vaccine doses. These circumstances include an outbreak that increases risk for disease or the likelihood that doses will be missed in the future (e.g., because of transportation challenges). Because of lack of efficacy data for HPV vaccine administration using minimum intervals, providers are encouraged, when possible, to use routine dosing intervals for females aged 11-26 years and males aged 11-21 years who have not yet received 3 HPV vaccine doses as recommended (3,4).

One of the challenges of adolescent vaccination is ensuring that current, complete vaccination histories are available. Insurers, covered services, or reimbursement levels can change, and these changes might affect reimbursement for vaccine doses and vaccination services directly while also causing disruptions in an adolescent's access to vaccination providers or venues. In circumstances in which a vaccination record is unavailable, vaccination providers should attempt to obtain this information from various sources (e.g., parent, previous providers, or school records). More detail about how to obtain these records is available from CDC at www.cdc.gov/vaccines/hcp/admin/immuniz-records.html. With the exception of

influenza and pneumococcal polysaccharide vaccines, if documentation of a vaccine dose is not available, the adolescent should be considered unvaccinated for that dose. Regardless of the venue in which an adolescent receives a dose of vaccine, that vaccine dose should be documented in the patient's chart or in an office log, and the information should be entered into an IIS. The adolescent also should be provided with a record that documents the vaccination history.

Adult Vaccination

In 2013, the National Vaccine Advisory Committee published updated standards for adult vaccination (12). These standards are targeted to distinct groups involved in adult vaccination, including immunizing providers, non-immunizing providers, professional health care organizations, and public health departments. All health care providers, whether they provide immunizations or not, should incorporate immunization needs assessment into every clinical encounter, strongly recommend needed vaccine(s) and either administer vaccine(s) or refer patients to a provider who can immunize, stay up-to-date on, and educate patients about vaccine recommendations, implement systems to incorporate vaccine assessment into routine clinical care, and understand how to access immunization information systems (i.e., immunization registries) (12).

Vaccination rates in adults are considered suboptimal (13,14). New *Healthy People 2020* goals include specific subsets of adults, including institutionalized adults aged ≥ 18 years (for pneumococcal vaccines) and noninstitutionalized adults at high risk aged >18 years (for pneumococcal vaccines) (9).

The most substantial barrier to vaccination coverage is lack of knowledge about these vaccines among adult patients and adult providers. Other barriers are cost (incomplete Medicare coverage for recommended vaccines) (15) and the lack of financing mechanisms for newly licensed and recommended vaccines. Effective for private health insurance plans drafted or updated after September 2010, coverage for all immunizations that are included on the immunization schedule(s) must be covered

without deductibles or co-pays, when delivered by an in-network provider. For this reason, cost may present less of a barrier to adult vaccination as time passes.

A common challenge for health care providers is vaccinating adults with unknown vaccination records. In general (except for influenza and pneumococcal polysaccharide vaccines), adults should receive a vaccine dose if the dose is recommended and no record of previous administration exists. If an adult has a record of military service and does not have records available, providers can assume that the person has received all vaccines recommended by the military at the time of service entry. Serologic testing might be helpful in clarifying immune status if questions remain, because at different times and depending on military assignments, there might be inter-service and individual differences.

Evidence-based Interventions to Increase Vaccination Coverage

The independent, nonfederal Task Force on Community Preventive Services, whose membership is appointed by CDC, provides public health decision-makers with recommendations on population-based interventions to promote health and prevent disease, injury, disability, and premature death. The recommendations are based on systematic reviews of the scientific literature about effectiveness and cost-effectiveness of these interventions. In addition, the task force identifies critical information about the other effects of these interventions, the applicability to specific populations and settings, and the potential barriers to implementation. Additional information, including updates of published reviews, is available from *The Community Guide* at <http://www.thecommunityguide.org>.

Beginning in 1996, the task force systematically reviewed published evidence on the effectiveness and cost-effectiveness of population-based interventions to increase coverage of vaccines recommended for routine use among children, adolescents, and adults. A total of 197 articles were identified that evaluated a relevant intervention, met inclusion criteria, and were published during 1980-1997. Reviews of 17 specific

interventions were published in 1999 (13,14,16,17). Using the results of their review, the task force made recommendations about the use of these interventions (15). Several interventions were identified and recommended on the basis of published evidence. Follow-up reviews were published in 2000, and a review of interventions to improve the coverage of adults at high risk was conducted in 2005 (15,17). The interventions and the recommendations are summarized in this section of this report (Table 11-1). Interventions designated for adults younger than 65 years at high risk for influenza, invasive pneumococcal disease, and hepatitis B, include provider reminder systems or a menu of items (combinations of strategies) (Table 11-2). In 1997, the task force categorized vaccination requirements for child care, school, and college as a recommended strategy (14).

A 2008 update of the original task force systematic review of the evidence on the effectiveness of provider assessment and feedback for increasing coverage rates found that this strategy remains an effective intervention (18). This later update reviewed 19 new studies published during 1997-2007. The updated review supports the original task force recommendation for use of assessment and feedback based on strong evidence of effectiveness. The task force reviewed studies of assessment and feedback as a strategy that were conducted in a range of settings, including private practice, managed care, public health, community health settings, and academic centers. Studies have assessed the effectiveness of this intervention to improve coverage with MMR, DTP, DTaP, Hib, influenza, pneumococcal, and Td vaccines (16). The most updated information on this review is available at www.thecommunityguide.org/findings/vaccination-programs-provider-assessment-and-feedback. As recognized by the task force, routine assessment and feedback of vaccination rates obtained at the provider site is one of the most effective strategies for achieving high, sustainable vaccine coverage. Since 1995, all states receiving federal funds for vaccination programs have been required to conduct annual assessments of vaccination rates both in public health clinics and in private provider offices. Primarily to aid local and state health departments in their efforts to conduct assessments and assist providers, CDC has developed numerous software applications to measure vaccination rates in provider practices.

Other General Programmatic Issues

Programmatic challenges, evolving issues, and effective interventions related to adult and adolescent vaccination programs have been described by other advisory groups and expert groups. Additional evidence-based approaches are being developed for certain issues (e.g., settings for adolescent vaccination delivery) through ongoing research and evaluation. Among current programmatic challenges, vaccine financing is especially difficult because certain problems and solutions differ markedly from one state to another. Practitioners interested in beginning or continuing to provide vaccinations to patients are encouraged to consult with local and state public health vaccination programs to learn about publicly funded programs that might be available in their areas for patients who need vaccination but have insufficient health insurance coverage and no financial resources. If not already participating, providers who care for adolescents and children aged <19 years should enroll in the Vaccines for Children Program (www.cdc.gov/vaccines/hcp/admin/vfc.html). Through this program's provision of ACIP-recommended, federally purchased vaccines, participating providers are able to fully vaccinate eligible children whose parents might not otherwise be able to afford the vaccinations. Interested providers are encouraged to work with insurers, state and specialty-specific medical organizations, vaccine manufacturers, and other stakeholders to address financial barriers to achieving high vaccination coverage. With availability of safe and effective vaccines for 18 vaccine-preventable diseases, the capacity for realizing the potential benefits of these products in the United States depends on reaching children, adolescents, and adults through dedicated, knowledgeable vaccination providers and efficient, strong vaccination programs at local, state, and federal levels.

TABLE 11-1. Recommendations regarding interventions to improve coverage of vaccines recommended for routine use among children, adolescents, and adults

Intervention	Recommendation
Increase community demand for vaccination	
Client reminder or recall systems	Recommended
Requirements for entry to schools, child-care facilities, and colleges	Recommended
Community education alone	Insufficient evidence
Community-based interventions implemented in combination	Recommended
Clinic-based education	Insufficient evidence
Patient or family incentives	Recommended
Patient or family monetary sanctions	Insufficient evidence
Client-held medical records	Insufficient evidence
Enhance access to vaccination services	
Reducing out-of-pocket costs	Recommended
Enhancing access through the U.S. Department of Agriculture's Women, Infants, and Children (WIC) program	Recommended
Home visits, outreach, and case management targeted to particularly hard-to-reach populations to increase vaccination rates	Recommended
Enhancing access at schools	Recommended
Expanding access in health care settings	Recommended as part of multicomponent interventions only
Enhancing access at organized child care centers	Recommended
Focus on providers	
Provider reminder or recall systems	Recommended

Provider assessment and feedback	Recommended
Standing orders	Recommended
Provider education alone	Insufficient evidence
Health care systems-based interventions integrated in combination	Recommended
Immunization information systems	Recommended
Source: www.thecommunityguide.org/topic/vaccination .	

TABLE 11-2. Strategies to improve influenza, pneumococcal polysaccharide, and hepatitis B vaccine coverage among high-risk adults younger than 65 years	
One or both of these interventions to improve access to vaccination services	<ol style="list-style-type: none"> 1. Expanded access in health care settings 2. Reducing client out-of-pocket costs
PLUS: One or more of these provider or system based interventions	<ol style="list-style-type: none"> 1. Standing orders 2. Provider reminder systems 3. Provider assessment or feedback
AND/OR: One or both of these interventions to increase client demand for vaccination services	<ol style="list-style-type: none"> 1. Client reminder systems 2. Client education

Source (15)

REFERENCES

1. The Patient Protection and Affordable Care Act, Pub. L. No. 111-148 (2010).
2. Roush SW, Murphy TV. Historical comparisons of morbidity and mortality for vaccine-preventable diseases in the United States. *JAMA*. 2007;298(18):2155-2163. DOI: 10.1001/jama.298.18.2155
3. Strikas RA. Advisory committee on immunization practices recommended immunization schedules for persons aged 0 through 18 years—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(4):93-94.
4. Kim DK, Bridges CB, Harriman KH. Advisory committee on immunization practices recommended immunization schedule for adults aged 19 years or older—United States, 2015. *MMWR Morb Mortal Wkly Rep*. 2015;64(4):91-92.
5. National Vaccine Advisory Committee. Standards for child and adolescent immunization practices. *Pediatrics*. 2003;112(4):958-963.
6. CDC. Recommendations of the Advisory Committee on Immunization Practices: programmatic strategies to increase vaccination coverage by age 2 years—linkage of vaccination and WIC services. *MMWR Morb Mortal Wkly Rep*. 1996;45(10):217-218.
7. Hagan J, Shaw J, Duncan P, eds. *Bright futures: guidelines for health supervision on infants, children and adolescents*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2008.
8. CDC. Immunization of adolescents. Recommendations of the Advisory Committee on Immunization Practices, the American Academy of Pediatrics, the American Academy of Family Physicians, and the American Medical Association. *MMWR Recomm Rep*. 1996;45(RR-13):1-16.
9. US Department of Health and Human Services. Immunization and infectious diseases. Healthy People 2020 website. <https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases>. Accessed 09 March, 2017.

10. CDC. U.S. vaccination coverage reported via NIS-Teen. 2016; <https://www.cdc.gov/vaccines/imz-managers/coverage/teenvaxview/index.html>. Accessed 09 March 2017.
11. Mangione-Smith R, DeCristofaro AH, Setodji CM, et al. The quality of ambulatory care delivered to children in the United States. *N Engl J Med*. 2007;357(15):1515-1523. DOI: 10.1056/NEJMsa064637
12. National Vaccine Advisory Committee. Recommendations from the National Vaccine Advisory committee: standards for adult immunization practice. *Public Health Rep*. 2014;129(2):115-123.
13. Shefer A, Briss P, Rodewald L, et al. Improving immunization coverage rates: an evidence-based review of the literature. *Epidemiol Rev*. 1999;21(1):96-142.
14. CDC. Vaccine-preventable diseases: improving vaccination coverage in children, adolescents, and adults. A report on recommendations from the Task Force on Community Preventive Services. *MMWR Recomm Rep*. 1999;48(RR-8):1-15.
15. Ndiaye SM, Hopkins DP, Shefer AM, et al. Interventions to improve influenza, pneumococcal polysaccharide, and hepatitis B vaccination coverage among high-risk adults: a systematic review. *Am J Prev Med*. 2005;28(5 Suppl):248-279. DOI: 10.1016/j.amepre.2005.02.016
16. Briss PA, Rodewald LE, Hinman AR, et al. Reviews of evidence regarding interventions to improve vaccination coverage in children, adolescents, and adults. The Task Force on Community Preventive Services. *Am J Prev Med*. 2000;18(1 Suppl):97-140. DOI: 10.1016/S0749-3797(99)00118-X
17. Task Force on Community Preventive S. Recommendations regarding interventions to improve vaccination coverage in children, adolescents, and adults¹². *Am J Prev Med*. 2000;18(1, Supplement 1):92-96. DOI: 10.1016/S0749-3797(99)00121-X
18. CDC. Vaccination programs: provider assessment and feedback. The Community Guide website. 2015; <https://www.thecommunityguide.org/findings/vaccination-programs-provider-assessment-and-feedback>. Accessed 09 March 2017.

12. Vaccine Information Sources

In addition to these general recommendations, the following sources contain specific and updated vaccine information.

CDC-INFO Contact Center

The CDC-INFO contact center is supported by CDC and provides public health-related information, including vaccination information, for health care providers and the public, 24 hours a day, 7 days a week. To contact CDC-INFO online at any time, visit wwwn.cdc.gov/dcs/RequestForm.aspx. To contact CDC-INFO by telephone, call between 8 am to 8 pm Eastern Time Monday through Friday at [English and Spanish]: 800-232-4636; telephone [TTY]: 800-232-6348.

CDC's National Center for Immunization and Respiratory Diseases

CDC's National Center for Immunization and Respiratory Diseases website provides direct access to ACIP's best practices for vaccination guidance, vaccination schedules, automated child schedulers, an adult immunization scheduler, vaccine safety information, publications, provider education and training, and links to other vaccination-related websites (www.cdc.gov/vaccines/hcp/admin/immuniz-records.html).

Morbidity and Mortality Weekly Report (MMWR)

Some ACIP guidance regarding vaccine use, statements of vaccine policy as they are developed, and reports of specific disease activity are published by CDC in the *MMWR* series and can be found at www.cdc.gov/vaccines/hcp/acip-recs/index.html. Electronic subscriptions are free (www.cdc.gov/mmwr/mmwrsubscribe.html). Subscriptions to print versions also are available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402-9235 (telephone: 202-512-1800).

American Academy of Family Physicians (AAFP)

Information from the professional organization of family physicians is available at www.aafp.org/home.html.

American Academy of Pediatrics (AAP)

Every 3 years, AAP issues the *Red Book: Report of the Committee on Infectious Diseases*, which contains a composite summary of AAP and ACIP recommendations concerning infectious diseases and vaccinations for infants, children, and adolescents (telephone: 888-227-1770; website: www.aap.org/en-us/Pages/Default.aspx).

American College of Physicians (ACP)

Produced by faculty of ACP's Quality Improvement Programs and members of the ACP Adult Immunization Advisory Board, the ACP Guide to Adult Immunization helps internists develop systematic processes for incorporating immunization in their day-to-day practice (see www.acponline.org/).

American Congress of Obstetricians and Gynecologists (ACOG)

The American Congress of Obstetricians and Gynecologists (ACOG), formerly the American College of Obstetricians and Gynecologists, is a professional association of physicians specializing in obstetrics and gynecology in the United States. Information about ACOG can be found at www.acog.org.

American Pharmacists Association (APhA)

Founded in 1852, APhA is the largest association of pharmacists in the United States, with more than 62,000 practicing pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians as members. Information about APhA educational activities can be found at www.pharmacist.com/immunization-center.

Group on Immunization Education of the Society of Teachers of Family Medicine

The Group on Immunization Education of the Society of Teachers of Family Medicine provides information for clinicians, including the free program Shots. Shots includes the childhood, adolescent, and adult schedules for iPhone, Palm, and Windows devices, as well as online versions (<http://www.immunized.org/>).

Immunization Action Coalition (IAC)

IAC provides child, teen, and adult immunization information for health care professionals and their patients at www.immunize.org. Free materials include CDC-reviewed technical pieces, patient handouts, VISs in multiple languages, and the weekly immunization news and information service “IAC Express,” available at www.immunize.org/express. Information for the general public about vaccines and vaccine-preventable diseases is available at www.vaccineinformation.org.

Institute for Vaccine Safety

Located at the Johns Hopkins University School of Public Health, the Institute for Vaccine Safety provides information about vaccine safety concerns and objective and timely information to physicians and health care providers and parents. The Institute for Vaccine Safety also includes links to tables that include all vaccine components (www.vaccinesafety.edu).

State and Local Health Departments

State and local health departments provide technical advice through hotlines, e-mail, and websites, including printed information regarding vaccines and immunization schedules, posters, and other educational materials

(see www.cdc.gov/vaccines/imz-managers/awardee-imz-websites.html and www.cdc.gov/mmwr/international/relres.html).

Vaccine Education Center

Located at the Children's Hospital of Philadelphia, the Vaccine Education Center provides patient and provider vaccine information (www.chop.edu/centers-programs/vaccine-education-center).

Appendix 1: Glossary

Adverse event. An untoward event that occurs after a vaccination that might be caused by the vaccine product or vaccination process. Adverse events include those that have the following characteristics: 1) vaccine induced (caused by the intrinsic characteristic of the vaccine preparation and the individual response of the vaccinee): these events would not have occurred without vaccination (e.g., vaccine-associated paralytic poliomyelitis); 2) vaccine potentiated: the events would have occurred anyway but were precipitated by the vaccination (e.g., first febrile seizure in a predisposed child); 3) programmatic error: the event was caused by technical errors in vaccine preparation, handling, or administration; and 4) coincidental: the event was associated temporally with vaccination by chance or caused by underlying illness. Special studies are needed to determine whether an adverse event is a reaction to the vaccine or the result of another cause. **Sources:** Chen RT. Special methodological issues in pharmacoepidemiology studies of vaccine safety. In: Strom BL, ed. *Pharmacoepidemiology*. 3rd ed. Sussex, England: John Wiley & Sons; 2000:707-732; and Fenichel GM, Lane DA, Livengood JR, Horwitz SJ, Menkes JH, Schwartz JF. Adverse events following immunization: assessing probability of causation. *Pediatr Neurol*. 1989;5:287--90.

Adverse reaction. An undesirable medical condition that has been demonstrated to be caused by a vaccine. Evidence for the causal relation is usually obtained through randomized clinical trials, controlled epidemiologic studies, isolation of the vaccine strain from the pathogenic site, or recurrence of the condition with repeated vaccination (i.e., rechallenge); synonyms include side effect and adverse effect.

Adjuvant. A vaccine component distinct from the antigen that enhances the immune response to the antigen.

Antitoxin. A solution of antibodies against a toxin. Antitoxin can be derived from either human (e.g., tetanus immune globulin) or animal (usually equine) sources (e.g.,

diphtheria and botulism antitoxin). Antitoxins are used to confer passive immunity and for treatment.

Hyperimmune globulin (specific). Special preparations obtained from blood plasma from donor pools preselected for a high antibody content against a specific antigen (e.g., hepatitis B immune globulin, varicella-zoster immune globulin, rabies immune globulin, tetanus immune globulin, vaccinia immune globulin, cytomegalovirus immune globulin, botulism immune globulin).

Immune globulin. A sterile solution containing antibodies, which are usually obtained from human blood. It is obtained by cold ethanol fractionation of large pools of blood plasma and contains 15%-18% protein. Intended for intramuscular administration, immune globulin is primarily indicated for routine maintenance of immunity among certain immunodeficient persons and for passive protection against measles and hepatitis A.

Immunobiologic. Antigenic substances (e.g., vaccines and toxoids) or antibody-containing preparations (e.g., globulins and antitoxins) from human or animal donors. These products are used for active or passive immunization or therapy. Examples of immunobiologics include antitoxin, immune globulin and hyperimmune globulin, monoclonal antibodies, toxoids, and vaccines.

Intravenous immune globulin. A product derived from blood plasma from a donor pool similar to the immune globulin pool, but prepared so that it is suitable for intravenous use. Intravenous immune globulin is used primarily for replacement therapy in primary antibody-deficiency disorders, for treatment of Kawasaki disease, immune thrombocytopenic purpura, hypogammaglobulinemia in chronic lymphocytic leukemia, and certain cases of human immunodeficiency virus infection ([Table 3-5](#)).

Monoclonal antibody. An antibody product prepared from a single lymphocyte clone, which contains only antibody against a single antigen.

Simultaneous. In the context of vaccine timing and spacing, occurring on the same clinic day, at different anatomic sites, and not combined in the same syringe.

Toxoid. A modified bacterial toxin that has been made nontoxic, but retains the ability to stimulate the formation of antibodies to the toxin.

Vaccination and immunization. The terms vaccine and vaccination are derived from *vacca*, the Latin term for cow. Vaccine was the term used by Edward Jenner to describe material used (i.e., cowpox virus) to produce immunity to smallpox. The term vaccination was used by Louis Pasteur in the 19th century to include the physical act of administering any vaccine or toxoid. Immunization is a more inclusive term, denoting the process of inducing or providing immunity by administering an immunobiologic. Immunization can be active or passive. Active immunization is the production of antibody or other immune responses through administration of a vaccine or toxoid. Passive immunization means the provision of temporary immunity by the administration of preformed antibodies. Although persons often use the terms vaccination and immunization interchangeably in reference to active immunization, the terms are not synonymous because the administration of an immunobiologic cannot be equated automatically with development of adequate immunity.

Vaccine. A suspension of live (usually attenuated) or inactivated microorganisms (e.g., bacteria or viruses) or fractions thereof administered to induce immunity and prevent infectious disease or its sequelae. Some vaccines contain highly defined antigens (e.g., the polysaccharide of *Haemophilus influenzae* type b or the surface antigen of hepatitis B); others have antigens that are complex or incompletely defined (e.g., *Bordetella pertussis* antigens or live, attenuated viruses).

Appendix 2: Membership

Advisory Committee on Immunization Practices

Membership List, October 2014

Chair: TEMTE, Jonathan L., MD, PhD, University of Wisconsin School of Medicine and Public Health Madison, WI

Executive Secretary: Larry Pickering, MD, National Center for Immunization and Respiratory Diseases, CDC, Atlanta, Georgia.

Members: BENNETT, Nancy, MD, MS, University of Rochester School of Medicine and Dentistry Rochester, NY

BELONGIA, Edward, MD, Marshfield Clinic Research Foundation Marshfield, WI

BOCCHINI, Joseph A., Jr., MD, Louisiana State University Health Sciences Center Shreveport, LA

CAMPOS-OUTCALT, Douglas, MD, MPA, Mercy Care Plan Phoenix, AZ

HARRIMAN, Kathleen, PhD, MPH, RN, California Department of Public Health Richmond, CA

HARRISON, Lee H., MD, University of Pittsburgh, Pittsburgh, PA

KARRON, Ruth A., MD, Johns Hopkins Bloomberg School of Public Health Baltimore, MD

KEMPE, Allison, MD, MPH, The Children's Hospital of Denver, Denver, CO

PELLEGRINI, Cynthia, March of Dimes Washington, DC

REINGOLD, Arthur L., MD, School of Public Health University of California Berkeley, CA

RILEY, Laura E., MD, Massachusetts General Hospital, Boston, MA

ROMERO, José R., MD, FAAP, Arkansas Children's Hospital Research Institute, Little Rock, AR

RUBIN, Lorry, MD, Hofstra-North Shore LIJ School of Medicine Hempstead, NY

VÁZQUEZ, Marietta, MD, Yale University School of Medicine New Haven, CT

Ex Officio Members: Amy Groom, MPH, Indian Health Service, Albuquerque, New Mexico; Jesse Geibe, MD, Department of Defense, CDC; Melissa Houston, MD, Health Resources and Services Administration, Rockville, Maryland; Bruce Gellin, MD, National Vaccine Program Office, Washington, District of Columbia; Mary Beth Hance,

Centers for Medicare and Medicaid Services, Baltimore, Maryland; Richard L. Gorman, MD, National Institutes of Health, Bethesda, Maryland; Wellington Sun, MD, Food and Drug Administration, Bethesda, Maryland; Linda Kinsinger, MD, Department of Veterans Affairs, Durham, North Carolina.

Liaison Representatives: American Academy of Family Physicians, Jamie Loehr, MD, Ithaca, New York; American Academy of Pediatrics, Carrie Byington, MD, Salt Lake City, Utah; David Kimberlin, MD, Birmingham, Alabama; American Academy of Physician Assistants, Marie-Michèle Léger MPH, Alexandria, Virginia; American College Health Association, Susan Even, MD, Columbia, Missouri; American College of Obstetricians and Gynecologists, Kevin Ault, MD, Kansas City, Kansas; American College of Physicians, Sandra Adamson Fryhofer, MD, Atlanta, Georgia; Gregory Poland, MD, Rochester, Minnesota; American Geriatrics Society, Kenneth Schmader, MD, Durham, North Carolina; America's Health Insurance Plans, Mark Netoskie, MD, MBA, Houston, Texas; American Medical Association, Sandra Adamson Fryhofer, MD, Atlanta, Georgia; American Nurses Association, Chad Rittle, DNP, Pittsburgh, Pennsylvania; Carol Hayes, CNM, Decatur, Georgia; American Osteopathic Association, Stanley Grogg, DO, Tulsa, Oklahoma; American Pharmacists Association, Stephan L. Foster, PharmD, Memphis, Tennessee; Association of Immunization Managers (AIM), Kelly Moore, MD, Nashville, Tennessee; Association for Prevention Teaching and Research, W. Paul McKinney, MD, Louisville, Kentucky; Association of State and Territorial Health Officials, Terry Dwelle, MD, Bismarck, North Dakota; Biotechnology Industry Organization, Clement Lewin, PhD, Cambridge, Massachusetts; Canadian National Advisory Committee on Immunization, Ian Gemmill, MD, Kingston, Ontario, Canada; Infectious Diseases Society of America, Kathleen Neuzil, MD, Seattle, Washington; Carol Baker, MD, Houston, Texas; National Association of County and City Health Officials, Matthew Zahn, MD, Santa Ana, California; National Association of Pediatric Nurse Practitioners, Patricia Stinchfield, MPH, St Paul, Minnesota; National Foundation for Infectious Diseases, William Schaffner, MD, Nashville, Tennessee; National Immunization Council and Child Health Program, Mexico, Ignacio Villaseñor Ruiz, Mexico; National Medical Association, Patricia Whitley-Williams, MD, New Brunswick, New Jersey; National Vaccine Advisory Committee, Walter Orenstein, MD, Atlanta, Georgia; Pediatric Infectious Diseases Society, Mark Sawyer, MD, San Diego, California; Janet Englund, MD, Seattle, Washington; Pharmaceutical Research and Manufacturers of America, Damian A. Braga, Swiftwater, Pennsylvania; Society for Adolescent Medicine, Amy Middleman, MD, Houston, Texas; Society for Healthcare Epidemiology of America, David Weber, MD, Chapel Hill, North Carolina.

Members of the General Recommendations on Immunization Working Group

Advisory Committee on Immunization Practices (ACIP), Marietta Vázquez, MD; Doug Campos-Outcalt, MD; Harriman, Kathleen, PhD, MPH, RN; Pellegrini, Cynthia; ACIP Liaison and *Ex-Officio* Members, Chris Barry, American Academy of Physician Assistants; Katie Brewer, MSN, RN, American Nurses Association; Stephan L. Foster, PharmD, American Pharmacists Association; Stanley E. Grogg, DO, American Osteopathic Association; Paul Hunter, MD, American Academy of Family Physicians;

Shainoor Ismail, Public Health Association of Canada; Walter Orenstein, MD, American Academy of Pediatrics; Mark Sawyer, MD, Pediatric Infectious Diseases Society; David Weber, MD, Society for Healthcare Epidemiology of America; CDC Staff Members, Angela Calugar, MD, Robin Curtis, MD, Sophia Greer, Theresa Harrington, MD, Andrew Kroger, MD, MPH, Jennifer Liang, DVM, MPH, Elaine Miller, Gina Mootrey, DO, Larry Pickering, MD, Jean Smith, MD, Raymond Strikas, MD, MPH, Donna Weaver, MSN, Jessie Wing, MD, MPH, Joellen Wolicki, RN, BSN, Skip Wolfe; other members and consultants, William Atkinson, MD, MPH, Immunization Action Coalition, Richard Clover, MD, University of Louisville School of Public Health, Jeffrey Duchin, MD, University of Washington, Susan Lett, MD, MPH, Massachusetts Department of Health, Kelly Moore, MD, MPH, Tennessee Department of Health, Deborah Wexler, MD, Immunization Action Coalition, Richard Zimmerman, MD, University of Pittsburgh.

Amendment and Compilation of Chapter 11-157
Hawaii Administrative Rules

September 5, 2018

1. Chapter 11-157, Hawaii Administrative Rules, entitled "Examination and Immunization", is amended and compiled to read as follows:

"HAWAII ADMINISTRATIVE RULES

TITLE 11

DEPARTMENT OF HEALTH

CHAPTER 157

EXAMINATION AND IMMUNIZATION

§11-157-1	Purpose
§11-157-2	Definitions
§11-157-3	Immunization
§11-157-3.05	Documentation of immunizations
§11-157-3.1	Responsibility
§11-157-3.2	Tuberculosis clearance requirements
§11-157-4	Performance of immunization; records
§11-157-4.1	Immunization of indigents and other persons
§11-157-5	Exemptions
§11-157-6	Repealed
§11-157-6.1	Health examination requirements
§11-157-6.2	Provisional attendance
§11-157-6.3	Notice of exclusion and exclusion
§11-157-6.4	School, post-secondary school, and child care facility reporting and records
§11-157-7	Penalties and remedies
§11-157-7.1	Suspension and revocation; exclusion
§11-157-8	Severability

§11-157-1 Purpose. The purpose of this chapter is to establish immunization requirements and immunization and examination requirements for school, post-secondary school, and child care facility attendance in the State of Hawaii and to provide for the immunization of indigents and other high risk individuals. [Eff 11/5/81; am and comp 6/17/93; am and comp 10/23/97; comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-2 Definitions. As used in this chapter: "Attend" or "attendance" means a student or child is physically present at school, post-secondary school, or child care facility after admission or enrollment.

~~["Certificate of TB examination" means a dated report of a tuberculosis examination including the information specified in subsections 11-157-3.2(c) to (e), on the stationery of a practitioner or the form of a health facility, health department, or school system, with the signature of a practitioner or a unique stamp of the practitioner, the licensed facility at which the practitioner practices, or the department.]~~

"Child" or "children" means a minor or minors who attend a child care facility in the State. Any child who attends a child care facility who is physically present for any amount of time at a child care facility shall comply with this chapter.

"Child care facility" has the same meaning as defined in section 346-151, HRS.

~~["Communicable tuberculosis" means tuberculosis in any form considered by the department to represent a risk of being transmitted to other individuals.]~~

"Department" means the department of health of the State of Hawaii, or any authorized officer or agent of the department~~[-]~~ of health.

"Director" means the director of health of the State of Hawaii or a duly authorized agent.

"Epidemic" means the occurrence in a community or region of an illness clearly in excess of normal expectancy, as determined by the department.

"Grace period" means the four day period prior to minimum required ages or intervals during which an immunization may still be considered valid.

"Immunization" means the process of administering a ~~[specific]~~ vaccine, toxoid, or other substance licensed by the United States Food and Drug Administration to promote an immune response, including antibody production~~[-]~~, in conformance with recognized standard medical practices.

"Immunizing agent" means a vaccine, toxoid, or other substance licensed by the United States Food and Drug Administration used to increase an individual's immunity to a disease.

~~["Mantoux tuberculin test" means an intradermal injection of five tuberculin units of Purified Protein Derivative in 0.1 cc of sterile diluent, followed within forty-eight to seventy-two hours by recording of the palpable induration, with a positive reaction being 10 mm or greater in its transverse diameter.]~~

"Outbreak" means the occurrence in a community or region of an illness clearly in excess of normal expectancy, as determined by the department.

"Physician" means a person licensed to practice medicine ~~[or]~~, osteopathic medicine, or naturopathic medicine in any of the states or territories of the United States. A person whose license is on inactive status or who is not actively practicing shall not be

deemed to be a physician for purposes of this chapter. Licensure or accreditation in chiropractic, homeopathy, acupuncture, or herbal healing ~~do~~ does not qualify a person as a physician in this chapter.

"Post-secondary school" means any ~~[adult education school, business school, trade school,]~~ community college, college ~~[or],~~ university, or any school enrolling or registering students above the age of compulsory school attendance.

"Practitioner" means a physician, advanced practice registered nurse, or physician assistant licensed to practice in any of the states or territories of the United States. A physician, advanced practice registered nurse, or physician assistant whose license is on inactive status or who is not actively practicing shall not be deemed to be a practitioner for the purposes of this chapter.

"Recognized standard medical practices" means in accordance with the United States Department of Health and Human Services', Advisory Committee on Immunization Practices (ACIP), General Best Practice Guidelines for Immunization, and future amendments that are adopted by the department.

"School" means ~~[any child care center, preschool, day care center, day nursery, Head Start program, group child care home, kindergarten, elementary, intermediate, middle, or secondary school, but excludes after-school programs, family child care, parent cooperatives, play groups, respite programs, and drop-in child care centers.]~~ a congregate setting for educational purposes, for example, kindergarten, elementary, intermediate, middle, or secondary school.

"Student" means any ~~[child]~~ minor or adult [enrolled in] attending any school or post-secondary school in the State. Any student who attends a school or post-secondary school who is required to be physically present for any amount of time at school or post-secondary school shall comply with this chapter.

[Eff 11/5/81; am and comp 6/17/93; am and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-3 Immunization. (a) Immunizations against certain [~~specified~~] vaccine preventable diseases, including minimum spacing between doses, and other conditions governing acceptability of immunizations, are required as set forth in the following exhibits:

Exhibit A, [~~"Guide to Hawaii Pediatric Immunization Requirements (July 1, 2002)"~~] "List of Required Vaccinations (July 1, 2020)."

Exhibit B, [~~"Guide to Hawaii Immunization & Examination Requirements for Schools (July 1, 2002)."~~] "General Best Practice Guidelines for Immunization; Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)."

[~~Exhibit C, "Guide to Hawaii Post-Secondary School Immunization & Tuberculosis Examination Requirements (July 1, 2002)."~~]

(b) The United States Department of Health and Human Services', General Best Practice Guidelines for Immunization; Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP), attached hereto as Exhibit B, are adopted as the requirements in the State of Hawaii for minimum age, required spacing between doses, and other conditions governing the acceptability of immunizations. Only those sections of Exhibit B that pertain to the requirements of this chapter, including the specific vaccinations listed in Exhibit A, shall apply.

(c) The Exhibits are located at the end of and are made a part of this chapter. If an exhibit conflicts with this chapter, this chapter shall prevail. Implementation of the amendments to this section shall occur on [~~July 1, 2002.~~] July 1, 2020.

(d) The director is authorized to suspend temporarily or amend any portion of the immunization requirements due to unforeseen circumstances. The director shall notify affected schools, post-secondary schools, or child care facilities in writing of any suspension or amendment. The notification shall include details of the suspension or amendment, including the suspended or amended requirements, the anticipated duration of the suspension or amendment, and policies to be implemented during the suspension or amendment. [Eff 11/5/81; am and comp 6/17/93; am and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-3.05 Documentation of immunizations.

(a) Documentation of immunizations shall indicate the department of health or the name of the practitioner responsible for administering or reviewing each immunization [and]. The documentation shall also bear the signature of [a] the practitioner or [a-unique] the stamp or imprinted name of the department, the practitioner, or the licensed facility at which the practitioner practices.

(b) Documentation of immunizations shall include the complete date (recorded as month/day/year) the vaccine was administered. [~~A record with only the month and year of immunization~~] An immunization record without complete dates may be accepted for school, post-secondary school, or child care facility attendance if it can be determined that each vaccination complied with the minimum interval and age requirements. A grace period applies to each minimum

age and interval. The grace period does not apply to the minimum interval between two doses of injectable or nasally administered live virus vaccines.

(c) Documentation of serologic evidence of immunity may be substituted for a record of immunizations for certain diseases as specified [~~in Exhibit B and Exhibit C.~~] by the United States Department of Health and Human Services', Advisory Committee on Immunization Practices in its General Best Practice Guidelines for Immunization, attached hereto as Exhibit B. The documentation shall include a laboratory report [and certification], signed by a practitioner, certifying that the [report provides evidence of immunity] student or child is immune to the named [~~disease.~~] diseases.

(d) [~~Documentation of a history of varicella (chicken pox) signed by a practitioner as specified in Exhibit B]~~ A signed, documented history of a diagnosis of varicella by a practitioner or a signed report by a practitioner that the practitioner has reviewed a reported history of varicella infection and has made a clinical judgment that the individual is immune to varicella may be substituted for a record of immunization with varicella vaccine.

(e) Electronic versions of the documentation of immunizations, documentation of serologic evidence of immunity, and documentation of a history of varicella (chicken pox), including records maintained in the Hawaii immunization registry, are acceptable provided all information required by this section is recorded.

~~[(e)]~~ (f) [~~Documentation of immunizations and evidence of immunity shall be kept with the student's health record.~~] Documentation of immunizations and evidence of immunity shall be maintained by schools, post-secondary schools, and child care facilities, either as a part of the student's health record, post-secondary school student's record, or child care

facility child's record, or as part of an electronic record that complies with this section. [Eff and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-1154 through 302A-1156, 321-1, 321-9, 321-11, 325-13, 325-32, 325-33, 325-37)

§11-157-3.1 Responsibility. (a) Each person is responsible for his or her own immunizations, except that each parent, guardian, or other person who has care, custody, or control of a minor, protected person, or dependent is responsible for the immunization and examination of his or her minor, protected person, or dependent.

(b) Each school ~~and~~, post-secondary school, and child care facility principal or administrator shall ensure that his or her school or facility only admits students or children who comply with this chapter. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 325-13) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38, 325-71 through 325-78)

§11-157-3.2 Tuberculosis ~~examination~~ clearance requirements. [~~a~~] Each student or child shall ~~be examined for infection with tuberculosis by a practitioner or the department within the twelve months prior to first attending school in Hawaii, except as noted in subsection (b). The tuberculosis examination requirements for attendance at post-secondary school are as provided in chapter 11-164.~~

~~—(b) A student first attending school before twelve months of age shall obtain and present a certificate of TB examination prior to age fourteen months or be excluded from school until a certificate of TB examination is obtained and presented.~~

~~(c) A certificate of TB examination shall report the results of a Mantoux tuberculin test, including the dates of administration and reading and the transverse diameter of induration in millimeters, and shall bear the signature or unique stamp of the practitioner, the facility at which the practitioner practices, or the department. If the transverse diameter is equal to or greater than 10 mm., the certificate shall also report the result of a chest x-ray, including the date and location the x-ray was obtained. If the reader of the x-ray or practitioner cannot determine that the student is free from communicable TB, then no certificate shall be issued and the case shall be immediately referred to the department of health.~~

~~(d) A person providing written documentation of a prior positive Mantoux tuberculin test result which includes the name of the practitioner or clinic administering the test, the dates of administration and reading and the diameter of induration in millimeters may have a certificate issued based on a chest x-ray without a repeat Mantoux tuberculin test, provided that the certificate shall contain the required information about the positive Mantoux tuberculin test.~~

~~(e) A person with a chest x-ray consistent with tuberculosis shall submit to further examination or treatment as deemed necessary by the department to exclude or treat a diagnosis of communicable tuberculosis before issuance of a valid TB certificate.~~

~~(f) A certificate of TB examination issued within 12 months before first attendance at school in Hawaii shall not expire for purposes of school attendance and may be used for transfer or attendance at all schools in Hawaii.~~

~~(g) A certificate of TB examination is required for school attendance. Every school shall maintain a copy of each student's certificate of TB examination~~

§11-157-3.2

~~while the student is enrolled, shall make that copy available for inspection by the department, and shall transmit a copy of the certificate together with the student's health record to the school to which a student transfers.]~~ comply with the department's tuberculosis rules as they apply to school, post-secondary school, and child care facility attendance. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-11, 325-71 through 325-78)

§11-157-4 Performance of immunization; records.

(a) Any immunization required by these rules shall be performed by a practitioner~~[or]~~, other medical personnel under the direction of a practitioner, or by the department. The manner and frequency of immunization administration shall conform with these rules and recognized standard medical practices.

(b) ~~[Records of any examination or immunization required by these rules shall be maintained by the practitioner or the department and shall be available for inspection and copying by the department.]~~ Records of any immunizations required by these rules that are not administered in the United States may be accepted if reviewed and signed or stamped by a practitioner.

(c) Documentation of any examination or immunization required by these rules shall be maintained by the practitioner or the department and shall be available for inspection and copying by the department. [Eff 11/5/81; am and comp 6/17/93; am and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11(22), 325-13, 325-32) (Imp: HRS §§302A-1154, 302A-1159, 302A-1160, 302A-1162, 302A-1163, 321-9, 321-11, 325-13, 325-32, 325-33, 325-35)

§11-157-4.1 Immunization of indigents and other persons. (a) The department shall provide for free immunization for the indigent and medically indigent for their protection against the diseases required by these rules. In this section, "indigent" and "medically indigent" have the meanings defined in ~~[HRS]~~ section 325-38~~[-]~~, HRS.

(b) The department may provide for free immunization of high risk individuals to interrupt transmission or limit morbidity from communicable diseases, or to protect employees of the department from communicable diseases which they may encounter in the performance of their duties. [Eff and comp 10/23/97; comp 8/27/01; am and comp]
(Auth: HRS §§302A-1162, 321-9, 321-11(22), 325-13, 325-32, 325-38) (Imp: HRS §§302A-1158, 325-38)

§11-157-5 Exemptions. (a) Medical exemptions from the requirements for specific immunizing agents shall be granted upon certification by a physician ~~[on the physician's professional stationery]~~ in a form or format specified by the department, that an immunization is medically contraindicated due to a stated cause, for a specific period of time~~[-]~~, in conformance with recognized standard medical practices. The ~~[original certificate]~~ form shall be provided to the exempt person or parent or guardian. ~~[A copy]~~ Copies of the ~~[certificate]~~ form shall be maintained in the student's school health record~~[-]~~, in the post-secondary school student's record, or in the child care facility child's record. Issuing physicians shall forward a copy of the form to the department. Reports of such ~~[certificates]~~ forms in a format specified by the department shall also be submitted to the department by each school~~[-]~~, post-secondary school, and child care facility.

(b) A religious exemption shall be granted to a student or child whose parent, custodian, guardian, or

other person in loco parentis certifies that the person's religious beliefs prohibit the practice of immunization. Requests for religious exemptions based on objections to specific immunizing agents will not be granted. Students who have reached the age of majority shall apply on their own behalf. The certification shall be retained in the student's health record~~[-]~~, in the post-secondary school student's record, or in the child care facility child's record. Reports of such exemptions in a format specified by the department shall be submitted to the department by each school~~[-]~~, post-secondary school, and child care facility.

(c) If at any time, the director determines that there is the danger or presence of an outbreak or epidemic from any of the communicable diseases for which immunization is required under this chapter, the exemption from immunization against such disease shall not be recognized, and inadequately immunized students or children shall be excluded from school, post-secondary school, or child care facilities until the director has determined that the presence or danger of the outbreak or epidemic no longer exists.

(d) After-school programs, family child care homes, parent cooperatives, play groups, respite programs, group child care homes, and drop-in child care centers are excluded from the requirements of this chapter. All schools and post-secondary schools that conduct classes and activities exclusively on-line or electronically via remote learning are excluded from the requirements of this chapter.

[Eff 11/5/81; am and comp 6/17/93; am and comp 10/23/97; am and comp 8/27/01; am and comp

] (Auth: HRS §§302A-1162, 321-9, 321-11(22), 325-13, 325-32) (Imp: HRS §§302A-1156, 302A-1157, 321-1, 321-9, 321-11, 325-13, 325-32, 325-34, 325-35)

§11-157-6 REPEALED. [R 10/23/97]

§11-157-6.1 Health examination requirements.

(a) Each student or child shall present a record of his or her physical examination by a practitioner as specified in subsection (b) before the student or child first attends school~~[-]~~ or a child care facility. The examination shall occur within 12 months before the date of first ~~[school]~~ attendance~~[-]~~ at school or child care facility in Hawaii. The record shall be transferred to subsequent schools attended by the student, and re-examination is not required.

(b) Pursuant section 302A-1159(b), HRS, every student entering seventh grade shall present a record of his or her physical examination (pre-seventh grade physical examination) by a practitioner performed within twelve months before the first date of attendance in the seventh grade.

~~[(b)]~~ (c) Results of the examination shall be reported to the school or child care facility on a form or in a format approved by the department. The report of physical examination shall be signed by the practitioner performing the examination.

~~[(c)]~~ (d) The report of physical examination shall be kept with the student's health record~~[-]~~ or child care facility child's record. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-6.2 Provisional attendance.

(a) A student or child who does not have evidence of all of the required immunizations ~~[or a report of physical examination]~~ may attend school, post-secondary school, or a child care facility provisionally upon submitting

written evidence from a practitioner or the department stating that the student or child is in the process of receiving required immunizations [~~or physical examination~~]. A student or child who does not have a report of physical examination may attend school or child care facility provisionally upon submitting written evidence from a practitioner stating that the student or child is in the process of receiving the physical examination. The failure to provide a report of the pre-seventh grade physical examination will not result in provisional attendance unless the student is first entering a Hawaii school in the seventh grade. A physical examination is not required for post-secondary school attendance. An appointment notice from a practitioner's office or the department shall be recognized as written evidence. A student or child without written evidence shall not be allowed to attend school, post-secondary school, or a child care facility.

(b) [~~If a preschool or K-12 student does not complete the required immunizations or examination within three months of the date of provisional entry, the school shall notify the parent by dated, written notice of exclusion that the student will be excluded from the school beginning 30 calendar days after the date of the notice.~~] The provisional attendance period shall be no longer than three calendar months after the date of provisional attendance to a school or child care facility and no longer than forty-five calendar days after the date of provisional attendance to a post-secondary school.

(c) [~~Beginning on the school day 30 calendar days after the date of notice of exclusion, the student shall be prohibited from attending school unless and until complete documentation covering the required immunizations and physical examination is provided to the school.~~] A student or child who fails to keep a scheduled appointment with their practitioner or the department during the provisional

attendance period may attend school, post-secondary school, or a child care facility only upon submitting a new appointment notice from a practitioner's office or the department. Failure to keep a scheduled appointment or transferring schools, post-secondary schools, or child care facilities during the provisional attendance period does not extend the provisional attendance period past the periods listed in subsection (b).

(d) If all of the required immunizations cannot be completed within [~~three months~~] the provisional attendance period due to the required minimum intervals between doses or other medical necessity, the school, post-secondary school, or child care facility may extend provisional attendance [~~may be extended~~] as long as evidence is provided that appointments have been made to complete the required immunizations. If a student or child whose provisional attendance period has been extended fails to keep a scheduled appointment, he or she shall be excluded from school, post-secondary school, or child care facilities until evidence that the required immunizations have been obtained is presented to the school[~~-~~], post-secondary school, or child care facility.

(e) [~~If a post-secondary school student does not complete the required immunizations within 45 days of the date of provisional entry, the school shall exclude the student from all school activities until documentation that the required immunizations have been obtained is provided to the school.~~] Provisional attendance may be suspended by the department when there is a danger or presence of an outbreak or epidemic from any of the communicable diseases for which immunization is required under this chapter until the director has determined that the presence or danger of the outbreak or epidemic no longer exists. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-1155

§11-157-6.2

through 302A-1157, 302A-1159, 302A-1160, 302A-1162, 321-1, 321-9, 321-11, 325-13, 325-32, 325-35, 325-36)

§11-157-6.3 [~~School reporting and records.~~]

Notice of exclusion and exclusion. (a) [~~Each school shall report to the department by October 10 and January 10 of each year the names of all students who have been provisionally admitted, have been excluded for failure to comply fully with the immunization or examination requirements in this chapter, and who have medical or religious exemptions. This report shall include the types of immunizations and dose numbers which are incomplete for each of these students and shall be in a format as specified by the department.]~~
If a student or child does not complete the required immunizations or examination within three months of the date of provisional attendance, the school or child care facility shall notify the parent or adult student by dated, written notice of exclusion that the student or child will be excluded from the school or child care facility beginning thirty calendar days after the date of the notice.

(b) [~~School and post-secondary school records documenting compliance with this chapter shall be made available for inspection and copying by the department upon request.]~~ Beginning on the school or business day thirty calendar days after the date of notice of exclusion, the school or child care facility shall prohibit the student or child from attending school or a child care facility until complete documentation covering the required immunizations and physical examination is provided to the school or child care facility.

(c) If a post-secondary school student does not complete the required immunizations within forty-five calendar days of the date of provisional attendance, the post-secondary school shall exclude the student from attending classes and all post-secondary school

activities until documentation that the required immunizations have been obtained is provided to the post-secondary school. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-1155, 302A-1157, 302A-1159, 302A-1160, 302A-1162, 321-1, 321-9, 321-11, 325-13, 325-32, 325-35, 325-36)

§11-157-6.4 School, post-secondary school, and child care facility reporting and records. (a) Each school and child care facility shall report to the department by October 10th and January 10th of each school year the names of all students or children who have been provisionally admitted, who have been excluded for failure to comply fully with the immunization or examination requirements in this chapter, or who have medical or religious exemptions. This report shall include the types of immunizations and dose numbers which are incomplete for each of these students or children and shall be in a format as specified by the department. Each school and child care facility is required to submit the report even if all students or children have met the immunization and examination requirements.

(b) School, post-secondary school, and child care facility records documenting compliance with this chapter shall be made available for inspection and copying by the department upon request. [Eff and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-7 Penalties and remedies. Penalties and remedies for failure to comply with these rules are provided in sections 321-18, 321-20, 325-14, and 325-

37, HRS. [Eff 11/5/81; am and comp 6/17/93; comp 10/23/97; comp 8/27/01; comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 321-18, 321-20, 325-13, 325-14, 325-32 through 325-38, 325-71 through 325-78)

§11-157-7.1 Suspension and revocation;

exclusion. (a) Valid [~~TB certificates,~~] certificates of TB clearance, immunization records, physical examination records, and certificates of medical or religious exemption (collectively "documents") may be suspended or revoked if a preponderance of the evidence shows that a document contains a material inaccuracy, misrepresentation, or is fraudulent.

(b) A [~~child or~~] student or child shall be excluded from school [~~or~~], post-secondary school, or child care facilities if any document required by this chapter is suspended or revoked. [Eff and comp 10/23/97; am and comp 8/27/01; am and comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38)

§11-157-8 Severability. If any provision of this chapter, or its application to any person or circumstance, is held invalid, the application of such provision to other persons or circumstances, and the remainder of this chapter, shall not be affected thereby." [Eff 11/5/81; comp 6/17/93; comp 10/23/97; comp 8/27/01; comp] (Auth: HRS §§302A-1162, 321-9, 321-11, 325-13, 325-32) (Imp: HRS §§302A-901, 302A-1154 through 302A-1163, 321-1, 321-9, 321-11, 325-13, 325-32 through 325-38, 325-71 through 325-78)

2. Material, except source notes and other notes, to be repealed is bracketed and stricken. New material, except source notes and other notes, is underscored.

3. Additions to update source notes and other notes to reflect these amendments and compilation are not underscored.

4. These amendments to and compilation of chapter 11-157, Hawaii Administrative Rules, shall take effect ten days after filing with the Office of the Lieutenant Governor; provided that the implementation of the amendments to section 11-157-3 shall occur on July 1, 2020.

I certify that the foregoing are copies of the rules, drafted in the Ramseyer format pursuant to the requirements of section 91-4.1, Hawaii Revised Statutes, which were adopted on _____ and filed with the Office of the Lieutenant Governor.

Bruce S. Anderson Ph.D.
Director of Health

APPROVED AS TO FORM:

Deputy Attorney General

Hawaii Revised Statutes 671-3 – Informed consent

Current as of: 2016 | Check for updates | Other versions

671-3 Informed consent. (a) The Hawaii medical board may establish standards for health care providers to follow in giving information to a patient, or to a patient's guardian or legal surrogate if the patient lacks the capacity to give an informed consent, to ensure that the patient's consent to treatment is an informed consent. The standards shall be consistent with subsection (b) and may include:

Terms Used In Hawaii Revised Statutes 671-3

Health care provider: means a physician, osteopathic physician, surgeon, or physician assistant licensed under chapter 453, a podiatrist licensed under chapter 463E, a health care facility as defined in section 323D-2, and the employees of any of them. See Hawaii Revised Statutes 671-1

- (1) The substantive content of the information to be given;
- (2) The manner in which the information is to be given by the health care provider; and
- (3) The manner in which consent is to be given by the patient or the patient's guardian or legal surrogate.

(b) The following information shall be supplied to the patient or the patient's guardian or legal surrogate prior to obtaining consent to a proposed medical or surgical treatment or a diagnostic or therapeutic procedure:

- (1) The condition to be treated;
- (2) A description of the proposed treatment or procedure;
- (3) The intended and anticipated results of the proposed treatment or procedure;
- (4) The recognized alternative treatments or procedures, including the option of not providing these treatments or procedures;
- (5) The recognized material risks of serious complications or mortality associated with:
 - (A) The proposed treatment or procedure;
 - (B) The recognized alternative treatments or procedures; and
 - (C) Not undergoing any treatment or procedure; and
- (6) The recognized benefits of the recognized alternative treatments or procedures.

AUTISM & ALUMINUM ADJUVANTS IN VACCINES

How Aluminum Adjuvants in Vaccines Can Cause Autism



Published: August 18, 2017 (Version 1.0)

The Centers for Disease Control (CDC) asserts that vaccines and vaccine ingredients have been disproven as potential causes of autism. Statements by the CDC are generic and encompass all vaccines and vaccine ingredients. For example, the CDC states:

*“Vaccines Do Not Cause Autism”
“There is no link between vaccines and autism.” “...no links have been found between any vaccine ingredients and autism spectrum disorder.” (CDC website, August 2017)*

These statements are not supported by available science. The CDC’s evidence supporting these statements is limited to the MMR vaccine (Taylor 2014), thimerosal preservative (Taylor 2014) and vaccine antigen exposure (DeStefano 2013).

Dr. Frank DeStefano of the CDC’s Immunization Safety Office is co-author of a paper (Glanz 2015) which states:

“To date, there have been no population-based studies specifically designed to evaluate associations between clinically meaningful outcomes and non-antigen ingredients, other than thimerosal.”

This statement applies to, among other vaccine ingredients, aluminum adjuvant. Studies of MMR vaccine cannot be used as evidence of safety for other vaccines, for example vaccines that contain aluminum adjuvant. The overly-broad, generic

assertions that no vaccines and no ingredients cause autism are thus not supported by scientific evidence. In fact, the CDC statements are contradicted by a large, consistent and growing body of scientific evidence, including:

1) studies showing neurotoxic and neuroinflammatory effects (e.g. microglial activation) from dosages of aluminum adjuvants lower than or approximately equal to dosages received by infants according to the CDC vaccine schedule (Crepeaux 2017, Petrik 2007, Shaw 2013, Shaw 2009);

2) studies linking vaccines to immune activation brain injury (Zerbo 2016, Li 2015);

3) studies showing that early-life immune activation is a causal factor in autism and other neurodevelopmental disorders and mental illnesses (e.g. schizophrenia) (Meyer 2009, Deverman 2009, Estes 2016, Kneusel 2014, Careaga 2017, Meyer 2014).

The accumulating evidence indicates that vaccine-induced immune activation, and aluminum adjuvants in particular, may cause mental illnesses and neurodevelopmental disorders, including autism.

In this paper, we present scientific evidence that aluminum adjuvants can cause autism and other brain injuries. Also, we explain why the studies allegedly supporting the safety of aluminum adjuvants do not show safety for adverse neurological outcomes.

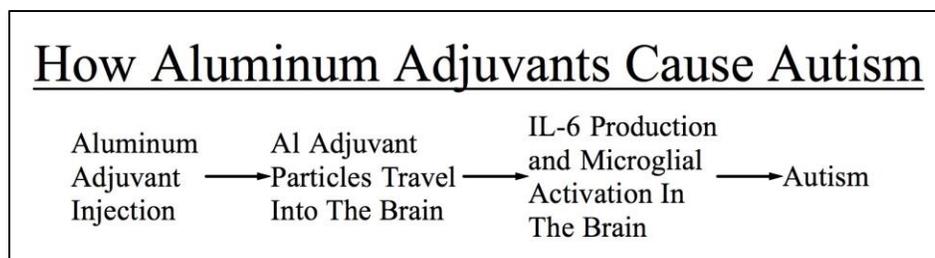


Fig 1: Proposed mechanism for how aluminum adjuvants cause autism. Each step is supported by replicated scientific studies.

Immune Activation: A Cause of Autism and Mental Illness

The term “immune activation” describes the activation of the cellular components of the immune system. The developing brain can be injured by immune activation, with life-long consequences (Meyer 2009, Deverman 2009, Estes 2016, Kneusel 2014, Careaga 2017, Meyer 2014). Immune activation injury is linked to autism, schizophrenia, depression and other mental illnesses or neurodevelopmental disorders. Immune activation effects on the brain are mediated by immune system signaling molecules, especially cytokines (Estes 2016, Meyer 2014, Smith 2007, Choi 2016, Pineda 2013).

It is generally accepted that immune activation (e.g., from infection) during pregnancy is a risk factor for autism and schizophrenia in the offspring (Ciaranello 1995, Atladottir 2010, Brown 2012). The intensity and duration of immune activation and cytokine expression appear to be important factors influencing autism risk (Meyer 2014). Intense immune activation is associated with greater risk of autism (Careaga 2017, Atladottir 2010). Chronic inflammation is associated with greater risk of autism (Jones 2016, Zerbo 2014). However, there is no evidence that short-duration, low-intensity

immune activation resulting from common childhood illnesses increase autism risk. Timing of immune activation in relation to stages of brain development is also an important factor (Meyer 2006, Meyer 2009).

Animal experiments have tested the effects of immune activation during pregnancy and postnatally on the development of offspring (Meyer 2009, Deverman 2009, Estes 2016, Kneusel 2014, Careaga 2017, Meyer 2014). In these experiments, pregnant animals (mice, rats and monkeys) or neonates are injected with a non-infectious immune activating substance such as “poly-IC” (which mimics a viral infection) or lipopolysaccharide (LPS, which mimics a bacterial infection). These substances cause immune system activation without infection. They induce fever and cytokine production and can have substantial effects on brain development if activation is sufficiently intense or prolonged and if exposure occurs during vulnerable developmental stages.

Immune activation has been demonstrated in mice to cause the three core behavioral symptoms of autism: decreased socialization and communication, and increased repetitive behaviors (Malkova 2012). Immune activation has also been shown to cause neuropathology (Weir 2015) and behavioral abnormalities in monkeys that resemble behaviors in human schizophrenia and autism (Bauman 2014, Machado 2015). See Fig. 2.

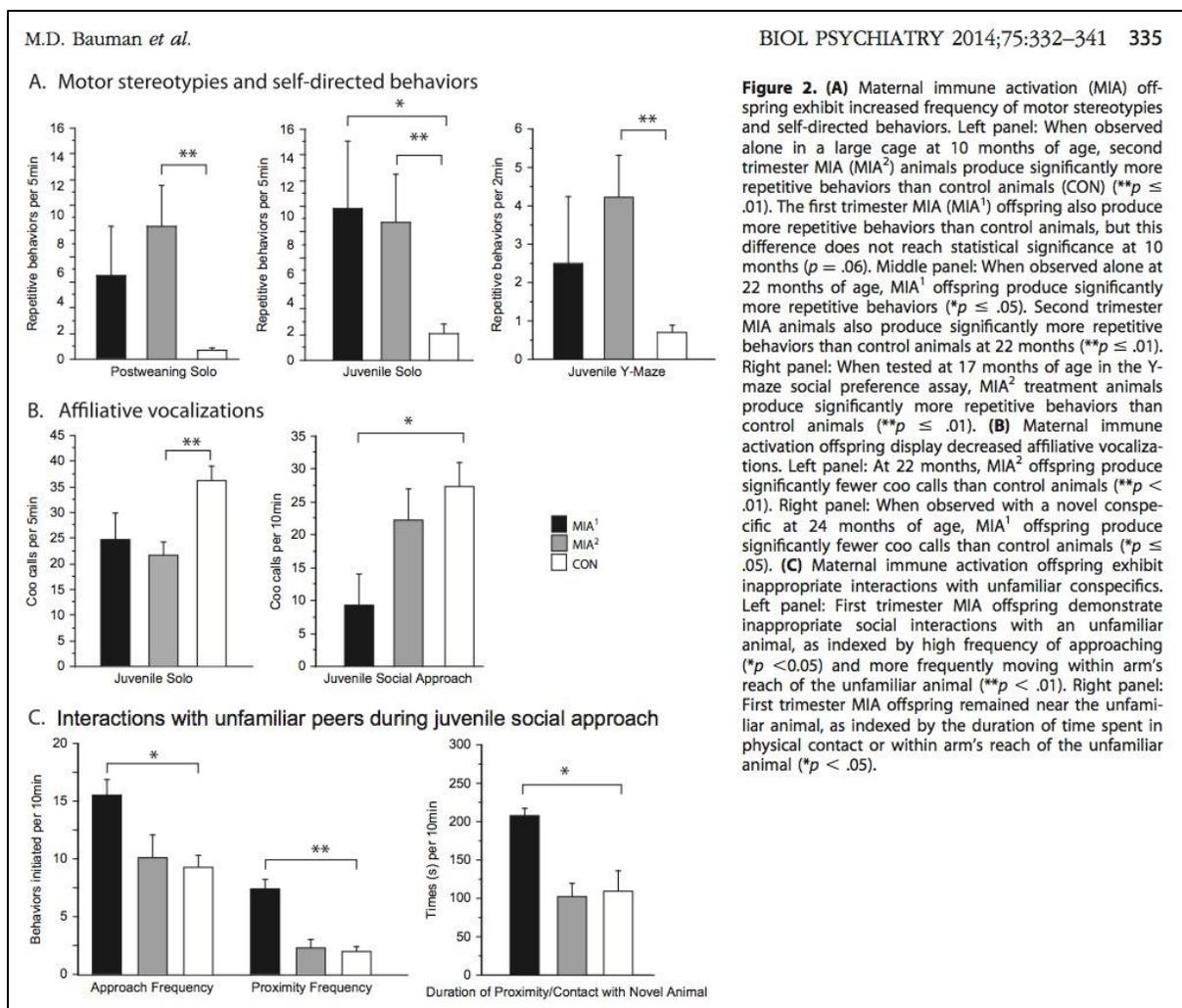


Fig 2: Maternal immune activation in monkeys caused behavioral abnormalities in juvenile offspring resembling behaviors in both autism and schizophrenia. MIA₁ (Black)= first trimester immune activation; MIA₂ (grey) 2nd trimester immune activation; CON (white) saline control. From Bauman et al. 2014

Immune activation also causes non-behavioral effects associated with human autism (citations here link immune activation with these effects):

- 1) reduction in Purkinje cells (Shi 2009);
- 2) mitochondrial dysfunction (Giulivi 2013);
- 3) increase in brain volume (from IL-6 exposure, Wei 2012(b)) and neuron density in the brain (Smith 2012);
- 4) long term chronic brain inflammation (Garay 2012); and
- 5) microbiome disruption (dysbiosis) (Hsiao 2013).

These non-behavioral similarities further support the relevance of the immune activation models to human autism. The non-behavioral (e.g., physiological) effects of immune activation have been reviewed (Labouesse 2015).

The cytokines interleukin-6 (IL-6) and interleukin-17a (IL-17) have been identified as mediating the behavioral effects of immune activation (Smith 2007, Malkova 2012, Choi 2016, Pineda 2013, Wei 2012(a), Wei 2013, Parker-Athill 2010, Wei 2016). The IL-6 findings have been replicated by different researchers using a variety of experimental methods. For example, in an experiment with

poly-IC, abnormal behavior is almost completely prevented by simultaneous administration of IL-6-blocking antibody (Smith 2007, Pineda 2013). Injection of IL-6 by itself causes abnormal behavior that closely matches behavior resulting from poly-IC immune activation (Smith 2007). Inhibition of IL-6 signaling in a genetic autism model (BTBR mice) normalized social and repetitive behavior (Wei 2016). These results demonstrate that IL-6 is responsible for causing abnormal autism-like behavior.

The Patterson laboratory at CalTech was the first to report that IL-6 is responsible for causing the autism-like behavioral effects of immune activation (Smith 2007). Two papers from this research group state:

“IL-6 is central to the process by which maternal immune activation causes long-term behavioral alterations in the offspring.” (Smith 2007)

“...blocking IL-6 prevents >90% of the changes seen in offspring of poly(I:C)-injected females, showing that gene expression changes, as well as behavioral changes, are normalized by eliminating IL-6 from the maternal immune response.” (Smith 2007)

“IL-6 is necessary and sufficient to mediate these effects since the effects...are prevented by injection of pregnant mice with poly-IC combined with an anti-IL-6 antibody, and are mimicked by a single maternal injection of IL-6.” (Garay 2013)

Brain exposure to elevated IL-6 by engineered virus showed that IL-6 exposure, initiated after birth, caused autism-like behaviors (Wei 2012(a)). The Wei 2012(a) paper states:

“We demonstrated that IL-6 is an important mediator of autism-like behaviors. Mice with an elevated IL-6 in brain developed autism-like behaviors, including impaired cognition ability, deficits in learning,

abnormal anxiety-like trait and habituation, as well as a decreased social interaction initiated at later stages. These findings suggest that an IL-6 elevation in the brain could modulate certain pathological alterations and contribute to the development of autism.” (Wei 2012(a))

More recent evidence shows that IL-17 acts downstream of IL-6 to cause autism-like behavioral abnormalities and atypical cortical development in mice (Choi 2016). Blocking either IL-6 or IL-17 prevents the autism-like behavior; an injection of IL-17 by itself causes the autism-like behavior (Choi 2016). IL-6 is known to induce IL-17 by promoting the development of Th17 cells which produce IL-17.

Immune activation animal models appear to be valid models for human neurological/psychiatric disorders, including autism (Estes 2016, Careaga 2017, Meyer 2014). The Estes 2016 review argues for the validity of the immune activation models to humans:

“These MIA (maternal immune activation) animal models meet all of the criteria required for validity for a disease model: They mimic a known disease-related risk factor (construct validity), they exhibit a wide range of disease-related symptoms (face validity), and they can be used to predict the efficacy of treatments (predictive validity).” (Estes 2016)

Evidence suggests a mediating role for IL-6 and IL-17 in human autism. For example, IL-6 is significantly elevated in the cerebellum in human autism (Wei 2011) and is highly elevated in some brain regions of some autistic individuals (Vargas 2005). Treatment of human autistics with the anti-inflammatory flavonoid luteolin improves autistic behaviors in the individuals that also experience a decline in IL-6 blood levels (Tsiloni 2015). This result is consistent with a causal role for IL-6 in human autism. Also, IL-17 is elevated in human autism (Akintunde 2015, Al-Ayadhi

2012, Suzuki 2011). Vitamin D reduces IL-17 production (Bruce 2011, Wobke 2014, Drozdenko 2014) and improves autistic behaviors in humans (Saad 2016, Jia 2015). The vitamin D findings are consistent with a causal role for IL-17 in human autism.

IL-6 functioning appears to be similar or identical in mice and humans. No mouse-human differences in IL-6 functioning are described in a 2004 review (Mestas 2004). IL-6 functioning is quite conserved across species (Brown 2014). Central nervous system development in rodents and humans is governed by the same principles (Brown 2014). Hence, the fact that IL-6 causes autism-like behavioral abnormalities in animal models deserves a presumption of validity to humans.

Immune activation is a risk factor for autism, schizophrenia and other neurological/psychiatric disorders. The cytokines IL-6 and IL-17 are responsible for mediating the autism-like behavioral effects of immune activation in the animal models. The available evidence supports a causal role for IL-6 and IL-17 in human autism.

Maternal vs. Postnatal Immune Activation

The timing of immune activation is an important factor influencing effects on the brain. The developing brain is vulnerable to immune activation injury; the mature, adult brain is apparently not nearly as vulnerable. Sensitivity to immune activation likely declines as the brain matures (Meyer 2014, Meyer 2007).

In most immune activation experiments, the offspring are exposed to immune activation during gestation (by stimulating the maternal immune system). In

contrast, most vaccines are administered postnatally. This raises the question of whether postnatal immune activation can have similar effects on the brain as maternal immune activation. Diverse evidence indicates that the brain can be adversely affected by postnatal immune activation. Postnatal immune activation experiments, human case reports, and consideration of brain development timelines suggest that the human brain is vulnerable to immune activation injury for years after birth.

In the maternal immune activation experiments, inflammatory signaling and some cytokines (e.g. IL-6) traverse the placenta into the fetus. Consequently, immune activation in the mother causes immune activation and elevated cytokines in the fetus, and in the fetal brain (Oskvig 2012, Ghiani 2011).

Postnatal immune activation can have adverse neurological effects, including increased seizure susceptibility (Chen 2013, Galic 2008), learning and memory deficits (Harre 2008), and an increase in excitatory synapse formation (Shen 2016). Seizure disorders, learning and memory dysfunction, and elevated excitatory signaling are associated with autism.

Elevated IL-6 in the brain in the postnatal period causes neuronal circuitry imbalance and mediates autism-like behaviors in mice (Wei 2012(a)). The circuitry imbalance observed in Wei 2012(a) was an excess of excitatory synapses and a deficit of inhibitory synapses. See Fig. 3. Excessive excitatory signaling is observed in human autism (Robertson 2016, Freyberg 2015). In fact, an imbalance between excitatory and inhibitory signaling (towards excess excitation) has been posited as a central characteristic of autism (Robertson 2016, Freyberg 2015).

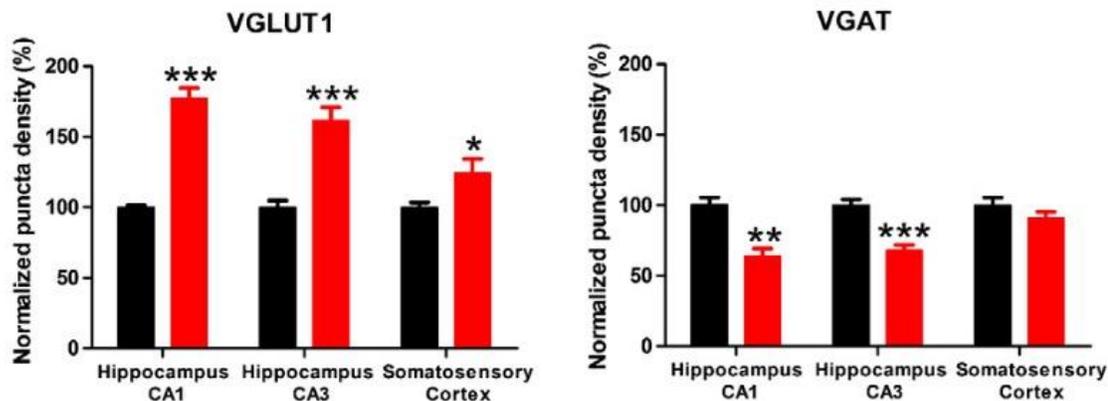


Fig 3: Elevation of IL-6 in the brains of mice (initiated shortly after birth) caused an increase in excitatory synapses (VGLUT1) and a decrease in inhibitory synapses (VGAT). Excessive excitatory signaling is observed in human autism. Red=Elevated IL-6; Black=Control. VGLUT1=excitatory synapses; VGAT=inhibitory synapses. *P<0.05, **P<0.01 and *P<0.001. Adapted from Wei et al 2012(a).**

In a maternal immune activation experiment with mice (Coiro 2015), autism-relevant behavior and dendritic spine abnormalities (relevant to autism and schizophrenia) were ameliorated by administering an anti-inflammatory drug postnatally. The drug was started at birth and continued for 2 weeks, which roughly corresponds to age 2 in humans (Semple 2013). This result indicates that brain development is affected by postnatal inflammation, at times corresponding to when vaccines are given to humans.

Several case reports describe previously-healthy children that displayed sudden-onset autistic behavior during or subsequent to infection in the brain. All the cases had signs of intense brain inflammation. Here are brief descriptions:

Delong 1981: describes 3 children, ages 5, 7 and 11 with full-blown autistic behavior associated with brain inflammation. Brain inflammation was presumed in two cases and confirmed in one. The 5 and 7 year olds recovered completely, and the 11-year recovered partially.

Marques 2014: describes a previously healthy 32-month-old girl that

suffered autistic regression from a viral central nervous system infection with associated brain inflammation.

Ghaziuddin 2002: describes a previously healthy 11-year-old boy that suffered permanent autistic regression after sudden onset herpes brain infection with associated brain inflammation.

Gillberg 1986: describes a previously healthy 14-year-old girl with permanent autistic regression from herpes brain infection with associated brain inflammation.

The most parsimonious explanation for these cases is that autistic behavior resulted from intense inflammation and cytokine production in the brain. Accordingly, these cases indicate that the human brain remains vulnerable to immune activation injury well into childhood, though the vulnerability almost certainly decreases with maturation. The susceptibility of older children to inflammation-induced autistic behavior strongly suggests that younger infants, of 0-2 years of age, are also vulnerable. It is not reasonable to claim, and there is no evidence to suggest, that the age range of 0-2 years (when most vaccines are given) is uniquely resistant to immune activation

injury. All the available evidence indicates the opposite.

The immune activation experiments and case reports are consistent and indicate that immune activation and elevated cytokines in the postnatal period can cause brain injury.

The next critical question to consider is whether vaccines can cause immune activation and elevated cytokines in the brain.

Postnatal Vaccination Affects Brain Development in Animal Model

The first study to test the effect of postnatal vaccination on brain development was published in 2015 (Li 2015). In this

experiment, neonatal rats were administered bacillus calmette-guerin (BCG) vaccine, hepatitis B (HBV) vaccine or a combination (BCG+HBV) timed to imitate human infant vaccination schedules. BCG and HBV vaccines produced opposite effects on the brain. Specifically, BCG enhanced synaptic plasticity and long-term potentiation (LTP, the basis for learning and memory); HBV inhibited synaptic plasticity and LTP. BCG and HBV vaccines also caused opposite changes in some synapse protein levels.

HBV vaccine (but not BCG vaccine) increased IL-6 gene expression in the brain; increased gene expression likely indicates an elevation in brain IL-6. The HBV vaccine contains aluminum adjuvant, and the BCG does not contain aluminum adjuvant. Hence, the aluminum adjuvant may be the ingredient responsible for the elevated IL-6 gene expression. See Fig. 4.

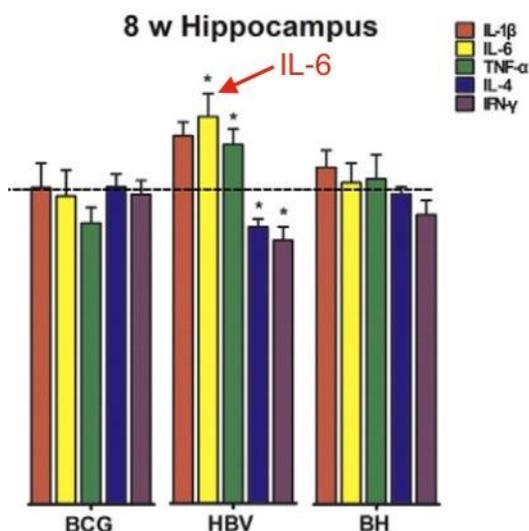


Fig. 4: Hepatitis B vaccine, but not BCG vaccine, increased IL-6 gene expression in the brain at 8 weeks after neonatal vaccination. Hepatitis B vaccine contains aluminum adjuvant; BCG vaccine does not. Elevated IL-6 causes autism-like behaviors in animal models. *P<0.05 Adapted from Li et al 2015.

The Li et al study showed that the vaccines caused other changes in the brain, including 1) changes in long-term potentiation (LTP) (Hep B decreased LTP), 2) changes in dendritic spines, and 3) changes in synapse protein expression. Changes in synapse

proteins and dendritic spines have been observed in human brain disorders.

Li et al. attribute the brain effects to changes in cytokine levels and immune polarization (Th1/Th2 polarization) induced by the vaccines. Aluminum adjuvants cause

Th2 polarization. Li et al. state that the results suggest vaccines can interact by way of immune activation effects:

“...our data suggested that combinations of different vaccines can mutually interact (enhance or counteract). The mechanism of synaptic plasticity modulation through neonatal BCG/HBV vaccination may be via systemic Th1/Th2 bias accompanied by a specific profile of cytokines and neurotrophins in the brain.” (Li 2015)

Li 2015 demonstrates that vaccines affect brain development by an immune activation mechanism. Further, since aluminum adjuvants induce Th2 activation and long term Th2 polarization, the Li 2015 results suggest that all aluminum-adjuvanted vaccines may cause adverse effects similar to the HBV vaccine. Accordingly, the Li 2015 results suggest that studies showing that immune activation causes neurological/psychiatric disorders are relevant to vaccine adverse effects.

Vaccines Are Given During Synaptogenesis

Another way to answer the question of brain vulnerability to immune activation is to consider the types of brain development processes occurring when vaccines are administered. Vaccines are given primarily in the first 18 months after birth. The human brain undergoes intense and rapid development during this period. Synaptogenesis (formation of synapse connections between neurons) is especially intense in this period.

The vulnerability of the developing brain to immune activation is apparently related to the specific types of brain development processes occurring (Tau 2010, Meyer 2006, Meyer 2007). Such processes include migration (movement of neurons to

final locations in the brain), adhesion (formation of chemical-mechanical attachments between brain cells), and synaptogenesis (formation of synapse connections between neurons), among others (neurogenesis, gliogenesis, myelination etc).

Cytokines affect brain development processes. For example, elevated IL-6 affects migration, adhesion and synaptogenesis (Wei 2011). Elevated IL-6 in the postnatal period promotes an excess of excitatory synapses and a deficit of inhibitory synapses, and mediates autism-like behaviors (Wei 2012(a)).

In humans, a dramatic increase in synaptogenesis begins around the time of birth, and continues until about age 3 (Huttenlocher 1997, Tau 2010, Stiles 2010, Semple 2013). Vaccines are administered during this intense synaptogenesis. See Figs. 5-6. Elevated brain IL-6 induced by vaccination during synaptogenesis may cause an excitatory-inhibitory imbalance, towards excitation. An excitatory imbalance has been observed in human autism (Robertson 2016, Freyberg 2015).

Synaptogenesis tapers off through childhood and adolescence. This fact may explain why some older children and teens can suffer autistic regression after intense brain inflammation, but apparently become less vulnerable to immune activation brain injury with age.

Intense synaptogenesis occurs at ages 0-18 months, when many vaccines are administered. Consequently, vaccines may adversely impact synaptogenesis if they induce inflammation or IL-6 in the brain.

The timing of brain development processes in humans supports the idea that the human brain is vulnerable to immune activation and cytokines in the first few years after birth, when vaccines are administered. Disruption of synaptogenesis by vaccine-induced immune activation is a particular concern.

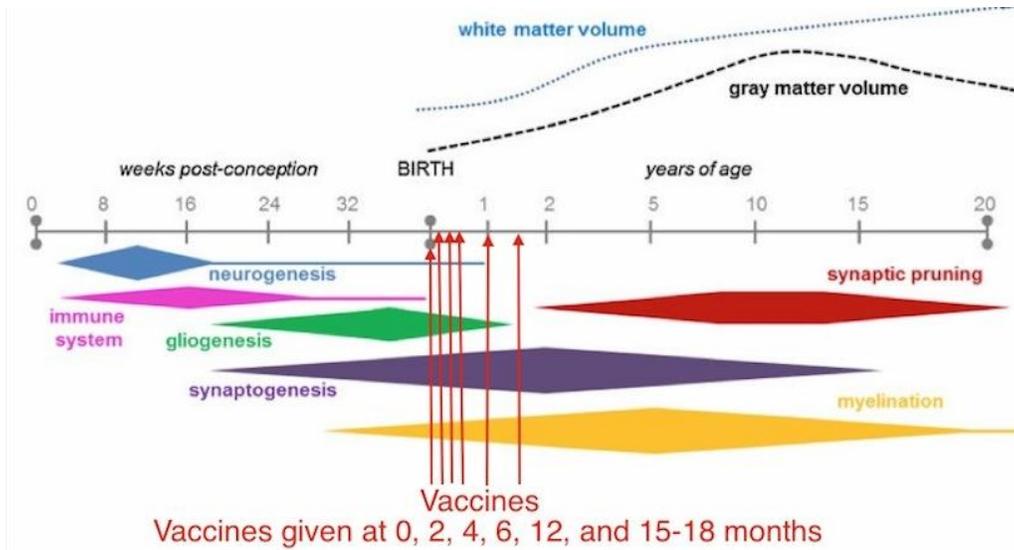


Fig. 5: Timeline of specific brain developmental processes in humans. Synaptogenesis is most intense during the first couple years of life, when vaccines are administered. Timing of vaccination according to the CDC vaccine schedule is shown. Elevated IL-6 during synaptogenesis may cause an excitatory-inhibitory synapse imbalance, towards excitation. Adapted from Semple 2013.

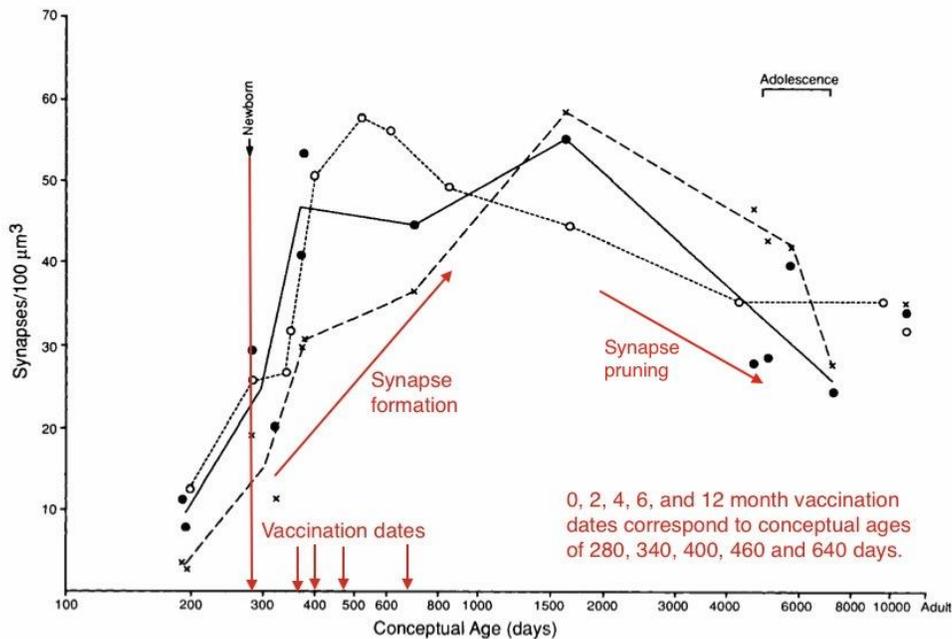


Fig. 2. Mean synaptic density in synapses/100 μm³ in auditory, calcarine, and prefrontal cortex at various ages. Open circles, visual cortex (area 17); filled circles, auditory cortex; x, prefrontal cortex (middle frontal gyrus).

Fig. 6: Measurements of synapse density in human cadavers of various ages indicate a dramatic increase in synapses in the first few years of life. Vaccines are administered during intense synapse formation. Elevated IL-6 during synaptogenesis may cause an excitatory-inhibitory synapse imbalance, towards excitation. Image adapted from Huttenlocher and Dabholkar 1997.

Aluminum Adjuvants: Neurotoxic At Vaccine Dosages

Aluminum (Al) adjuvants have an essential role in many vaccines: to stimulate immune activation. Without Al adjuvants, these vaccines would have greatly reduced efficacy.

Aluminum adjuvants comprise sub-micron particles (primary particles) of aluminum compounds, typically AlOH , AlPO_4 , AlSO_4 or mixtures. The primary particles are typically agglomerated into larger particles with sizes of about 2-20 microns (Harris 2012). The Al adjuvant materials have low solubility in water and body fluids. Al adjuvant particles are biopersistent and can remain in the body for months or years (Flarend 1997, Khan 2013, Gherardi 2001).

Aluminum ingested in the diet has low oral absorption (about 0.3%), is rapidly excreted by the kidneys, is (mostly) excluded from the brain by the blood-brain barrier, and is in a solubilized, Al^{3+} ionic form (not particulate). These defenses are adequate for protecting the brain from natural levels of aluminum exposure. These protective mechanisms are unable to protect the brain from injected aluminum adjuvant particles. Al adjuvant particles are too large to be removed by the kidneys, and are carried across the blood-brain barrier by macrophages.

Dosages of aluminum adjuvants received by infants according to the CDC vaccination schedule are:

Birth (Hep B):

74 mcg/kg (250 mcg for 3.4 kg infant)

2 month:

245 mcg/kg (1225 mcg for 5 kg infant)

4 month:

150 mcg/kg (975 mcg for 6.5 kg infant)

6 month:

153 mcg/kg (1225 mcg for 8 kg infant)

These are maximum-possible dosages (because different vaccine products have different amounts) for average-weight infants.

Accumulating evidence shows that aluminum adjuvants have adverse neurological effects at dosages lower than or approximately equal to dosages infants receive from vaccines. These effects appear to depend on the particulate nature and biopersistence of the aluminum adjuvant. Injected Al adjuvant has adverse effects that are apparently mediated by the particles and independent of solubilized Al^{3+} ions released by the slowly dissolving particles (Crepeaux 2017).

Al adjuvant injections in mice cause adverse effects at vaccine-relevant dosages of 100, 200, 300 and 550 mcg/Kg body weight (Crepeaux 2017, Shaw 2009, Petrik 2007, Shaw 2013). These include deficits in learning and memory (Shaw 2009), deficits in neuromuscular strength/function (Petrik 2007), and changes in locomotor activity and/or gait (Shaw 2009, Shaw 2013). Autism is associated with gait and movement abnormalities (Kindregan 2015) and memory dysfunction (Williams 2006).

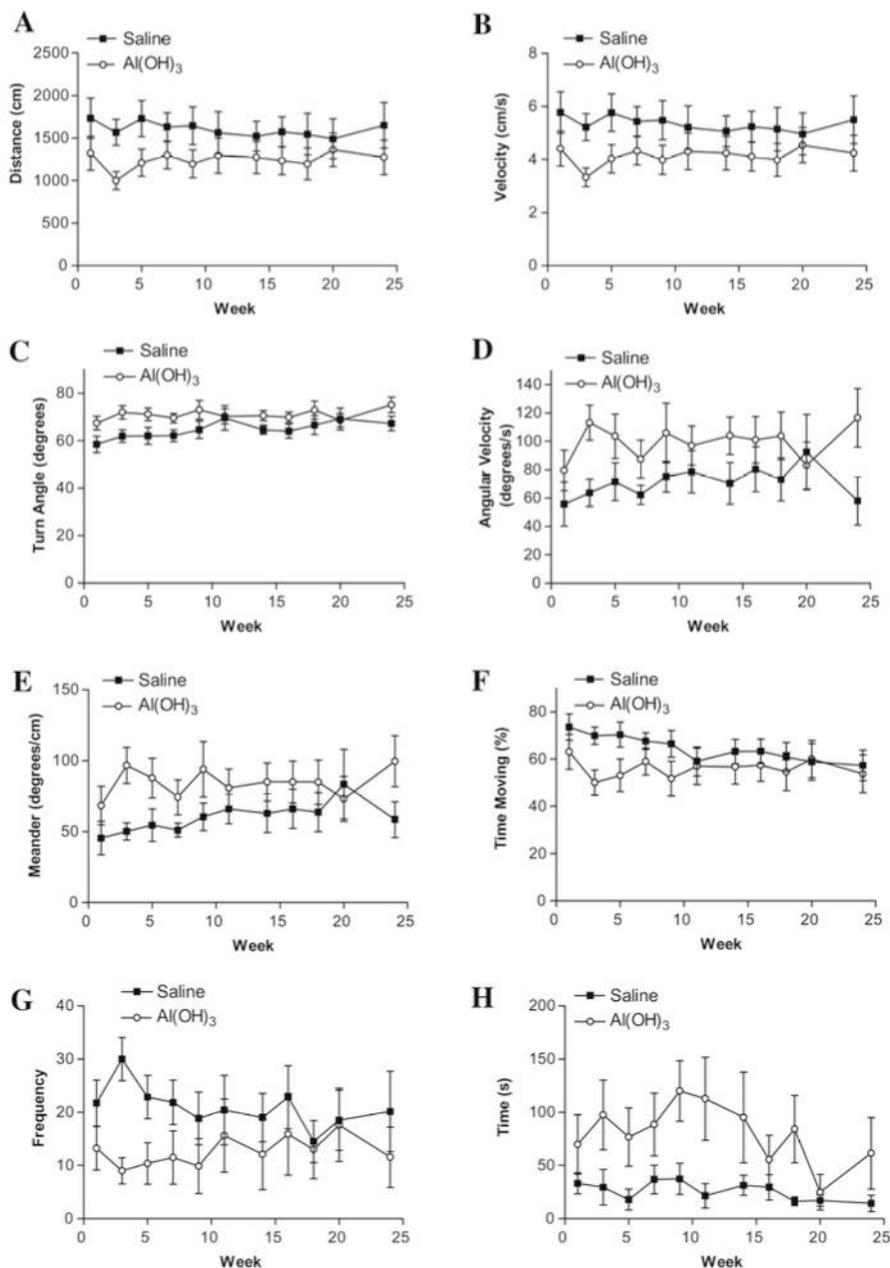


Fig. 4. Open field movement analysis as an assessment of spontaneous activity and anxiety in control mice vs. mice injected six times with aluminum hydroxide. Aluminum hydroxide injected mice showed the following behavioural changes: (A) Shorter distances moved ($***p < 0.0001$). (B) Slower movement ($***p < 0.0001$). (C) Greater mean turn angle ($***p < 0.0001$). (D) More rapid turning ($***p < 0.0001$). (E) Greater meander ($***p < 0.0001$). (F) Smaller percentage of time in overall movement ($**p = 0.0030$). (G) Fewer entries into the centre of the open field ($***p < 0.001$). Late entry into centre ($***p < 0.0001$). (All measures, two-way ANOVA).

Fig. 7: Dosage of 300mcg/Kg ALOH adjuvant caused large and persistent changes in exploratory behavior and movement in open field tests. This is an indicator of neurotoxicity. Human autistics also display abnormal movement and exploratory behavior. Adapted from Shaw and Petrik 2009.

Al adjuvant dosages of 200mcg/Kg (as 3 x 66mcg/Kg) (Crepeaux 2017) and 300mcg/Kg (as 6 x 50mcg/Kg) (Shaw 2009) increased microglial activation in the ventral forebrain and lumbar spinal cord, respectively. The elevated microglial activation was measured about 6 months after Al adjuvant injection, which suggests that the

microglial activation is chronic. Activated microglia indicate an ongoing inflammatory process and suggest the presence of elevated cytokines. Human autistics have activated microglia and elevated cytokines throughout the brain (Vargas 2005, Suzuki 2013, Li 2009).

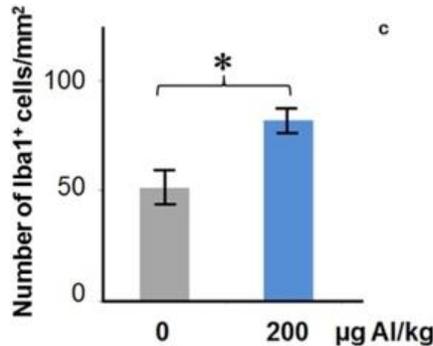


Fig. 8: Al adjuvant (200mcg/Kg) caused an increase in microglial activation in the brain of mice. The protein iba1 indicates activated microglia. Measurements were performed 6 months after Al adjuvant injection, indicating that the microglial activation is a chronic condition. * P<0.05. From Crepeaux et al., 2017.

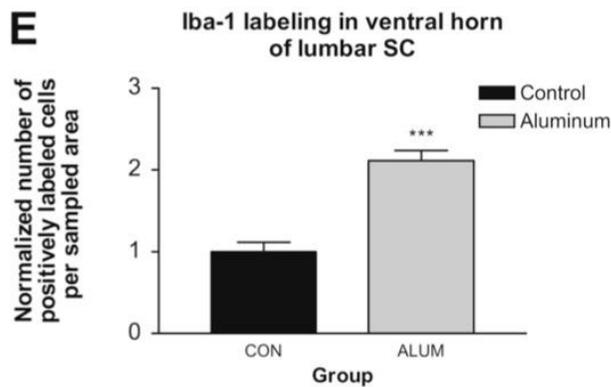


Fig. 9: Al adjuvant (300mcg/Kg) caused an increase in microglial activation in the lumbar spinal cord of mice. The protein iba1 indicates activated microglia. Measurements were performed 6 months after Al adjuvant injection, indicating that the microglial activation is a chronic condition. *p < 0.001, one-way ANOVA. From Shaw and Petrik 2009.**

Activated microglia are implicated as a causal factor in autism, because microglia mediate inflammation in the brain. Microglia can produce IL-6 when in an activated state. A recent review on microglia and autism (Takano 2015) states:

“...any factors that alter the number or activation state of microglia either in utero or during the early postnatal period can profoundly affect neural development, thus resulting in neurodevelopmental disorders, including autism.” (Takano 2015)

Microglia appear to play an important role in the causation of autism (Takano 2015, Kneusel 2014). Hence, the microglial activation caused by aluminum adjuvants suggests a role in autism.

Several studies show that Al adjuvants increase brain aluminum content (Crepeaux 2017, Flarend 1997, Shaw 2009, Khan 2013, Crepeaux 2015). A dosage of 200 mcg/Kg Al adjuvant caused a 50-fold increase in brain aluminum content in mice, from 0.02 ug/g to 1.00 ug/g dry weight of brain (Crepeaux 2017). These measurements were performed 6

months after the final injection, indicating that the Al persists in the brain long-term (Crepeaux 2017). See Fig. 10. Al adjuvants have been found to accumulate in the brain of mice up to one year after injection (Khan 2013). Crepeaux 2015 demonstrated persistence and increasing accumulation of Al adjuvant particles up to 270 days in spleen and lymph nodes of mice. Increasing accumulation of Al in distant organs over time suggests that toxic effects may increase with time, and may be delayed by months or years after exposure.

The 400 and 800 mcg/Kg doses used in the Crepeaux 2017 study did not cause adverse effects or elevated brain aluminum. The authors attribute this surprising inverted dose-response relationship to granulomas induced by the higher dosages. Granulomas trap the Al adjuvant at the injection site, thereby preventing its transport into the brain and other sensitive tissues. Granulomas occur after about 1% of vaccinations (Bergfors 2014). This is cause for concern because it indicates that, for 99% of vaccinations, the Al adjuvant can be transported around the body. It is not confined to a granuloma. See Fig. 11.

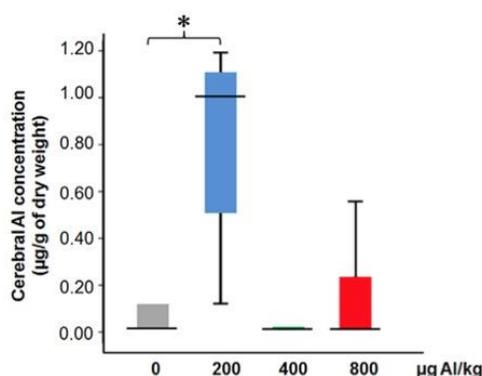


Fig. 10: Dosage of 200 mcg/Kg Al adjuvant caused a 50-fold increase in brain aluminum content, from 0.02 to 1.00 ug/g dry weight, in mice. Higher dosages (400 and 800 mcg/Kg) did not increase brain Al content, presumably because the higher dosages caused a granuloma at the injection site. A granuloma traps the Al adjuvant at the injection site, thereby preventing systemic dispersal and transport into the brain. These measurements were performed 6 months after the final injection, indicating that the Al persists in the brain long-term. *P<0.05. From Crepeaux et al., 2017.

Proposed Mechanism For Inverse Dose-Toxicity Relationship:

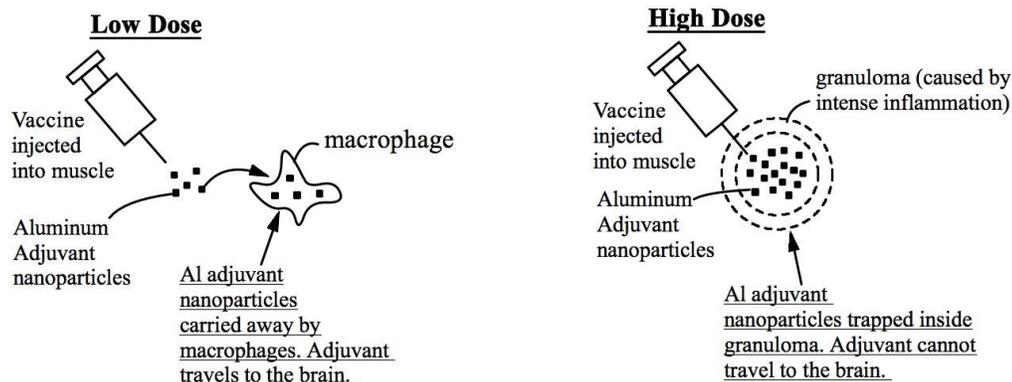


Fig. 11: High dose Al adjuvant injection into the muscle causes a granuloma, which traps the Al adjuvant and prevents it from traveling into the brain. Low dose does not form a granuloma. Hence, the lower dose is free to travel to the brain. Consequently, the lower dose is more toxic than the higher dose. This mechanism explains the surprising inverted dose-toxicity results of Crepeaux et al. 2017.

Particle Transport and Macrophage Chemotactic Protein (MCP-1)

Aluminum adjuvants travel into the brain (Khan 2013, Crepeaux 2015, Crepeaux 2017, Shaw 2009, Flarend 1997). Al adjuvant particles are carried through the blood-brain barrier and into the brain by macrophages (Khan 2013). Transport is promoted by macrophage chemotactic protein-1 (MCP-1) (Khan 2013). MCP-1 causes macrophages to travel around the body and into the brain. Particle transport into the brain by macrophages is well-established and has been investigated for therapeutic applications (Choi 2012, Pang 2016).

MCP-1 is elevated in the brains of human autistics (Vargas 2005) and is elevated in the blood of neonates later diagnosed with autism (Zerbo 2014). This suggests that neonates with high MCP-1 will experience elevated Al adjuvant transport into the brain when injected with Al adjuvanted vaccines. This is consistent with Al adjuvants causing autism by inducing immune activation and elevated cytokines in the brain.

Aluminum Induces IL-6 Expression In The Brain

Water-soluble aluminum salts (e.g. AlCl₃, Al lactate) induce elevated IL-6 in the brain and other tissues. In fact, aluminum appears to selectively induce IL-6 (Viezeliene 2013). Studies of aluminum exposure and IL-6 expression in the brain include:

Cao 2016: Ingestion of 30 or 90 mg/kg/day aluminum (as AlCl₃) for 90 days significantly increased gene expression of IL-6 and other cytokines in the brain (hippocampus).

Alawdi 2016: Ingestion of 3.4 mg/kg/day aluminum (as AlCl₃) for 6 weeks caused a 4-fold increase in IL-6 in the brain (hippocampus). This dosage is far lower than the outdated “no observed adverse effects level” (NOAEL) oral dosages (26 and 62 mg/kg/day) used as benchmarks for toxicity threshold (Mitkus 2011, Offit 2003).

In fact, other experiments show that oral dosages of 3.4, 4, 5.6, 6, and 20.2

mg/Kg/day aluminum cause numerous adverse effects in mice or rats and hence the NOAEL for orally ingested Al is currently unknown (Alawdi 2016, Dera 2016, Sethi 2008, Sethi 2009, Bilkei-Gorzo 1993).

The induction of IL-6 may occur because aluminum strongly induces oxidative stress (Exley 2003). Oxidative stress induces IL-6 expression (Viezeliene 2013).

CDC Website Cites Fatally Flawed Study Of Al Adjuvants (Mitkus 2011)

Dosages of Al adjuvants received by infants increased dramatically as the vaccine schedule was expanded in the 1980s and 1990s. However, as the vaccine schedule expanded, the increasing dosages of Al adjuvants were not tested for safety. Government agencies (HHS, NIH, CDC, FDA) have not pursued any new experimental work on Al adjuvant toxicity.

To support the safety of Al adjuvants at today's higher dosages, the CDC cites a 2011 FDA study of aluminum exposure from vaccines (Mitkus 2011). This study is the only scientific evidence cited by the CDC and FDA websites to support the safety of Al adjuvants.

The Mitkus 2011 study is a theoretical modeling study of Al adjuvant kinetics; it contains no new data concerning Al adjuvant toxicity (from animal models or epidemiology). Mitkus 2011 calculates a body burden of aluminum resulting from the slow dissolution of Al adjuvant particles, and compares the dissolved-aluminum body burden to a "minimal risk level" (MRL). The MRL is derived from a study of ingested Al toxicity in mice (Golub 2001). The Golub 2001 study provides the NOAEL (26 mg/kg/day ingested), which is converted into the MRL for human infants (based on 1mg/kg/day ingested) by using a safety factor of about 30.

The Mitkus study is fatally flawed for these reasons:

1) MITKUS ASSUMES AL ADJUVANT PARTICLES ARE HARMLESS

Mitkus makes an unstated assumption that Al adjuvants have zero toxicity while in particulate form. Mitkus only considers the potential toxicity of aluminum ions (Al³⁺) released by the slowly-dissolving Al adjuvant particles.

Al adjuvants comprise low-solubility and biologically-persistent microscopic particles. The Mitkus analysis assumes that the particles are absolutely nontoxic and perfectly harmless, even when present in the brain and other organs. Mitkus provides no justification for this unstated assumption. Further, the assumption is contradicted by recent findings on Al adjuvant toxicity (Crepeaux 2017) and particulate toxicity generally. Particles can have toxic effects mediated by surface chemistry (e.g. surface charge and surface catalytic activity) and particle shape, among other characteristics of solid particles (Sharifi 2012, Podila 2013).

Several studies show injected Al adjuvants cause behavioral abnormalities, abnormal weight gain, learning and memory impairment, motor neuron death/apoptosis, neuromuscular strength deficits, chronic microglial activation/brain inflammation, and large (e.g. 50X) increases in brain and spinal cord aluminum content (Petrik 2007, Shaw 2009, Shaw 2013, Crepeaux 2017). These adverse effects occur at dosages less than or approximately equal to dosages received by infants according to the CDC vaccine schedule.

2) NEW RESEARCH SHOWS INGESTED AL HARMFUL AT DOSAGES LOWER THAN 26 MG/KG/DAY

Mitkus assumes that Al adjuvant toxicity is mediated exclusively by solubilized Al (Al³⁺ ions) released by the slowly-dissolving Al adjuvant particles. To establish a threshold toxicity level from the solubilized Al, Mitkus relies on a mouse feeding study (Golub 2001) reporting a "no-observed adverse effects level" (NOAEL) oral dosage of 26 mg/Kg/day ingested aluminum. Mitkus

used a 30X safety factor for applying this dosage to humans, which is reasonable.

However, other experiments show that much lower oral dosages of 3.4, 4, 5.6, 6, and 20.2 mg/Kg/day aluminum cause adverse effects in mice or rats (Alawdi 2016, Dera 2016, Sethi 2008, Sethi 2009, Bilkei-Gorzo 1993). The adverse effects include chronic brain inflammation, learning and memory impairment, and kidney inflammation. So, the Mitkus analysis is wrong because 26 mg/kg/day is not a NOAEL. The “minimal risk level” (MRL) determined by Mitkus is too high by a factor of at least $26/3.4 = 7.6$. Using

a corrected NOAEL of 3.4 mg/Kg/day (based on Alawdi 2016) results in vaccine aluminum exposure exceeding the MRL for AlPO₄ adjuvant, and approximately matching the MRL for AlOH adjuvant. The new, corrected MRL lines indicate that Al phosphate adjuvant (Fig. 12) and Al hydroxide adjuvant (Fig. 13) from the CDC vaccine schedule may cause toxicity from the solubilized Al per se.

Since 3.4mg/Kg/day is not a NOAEL (adverse effects were observed at this dosage) the true NOAEL is less than 3.4/mg/Kg/day. See Figs. 12-13.

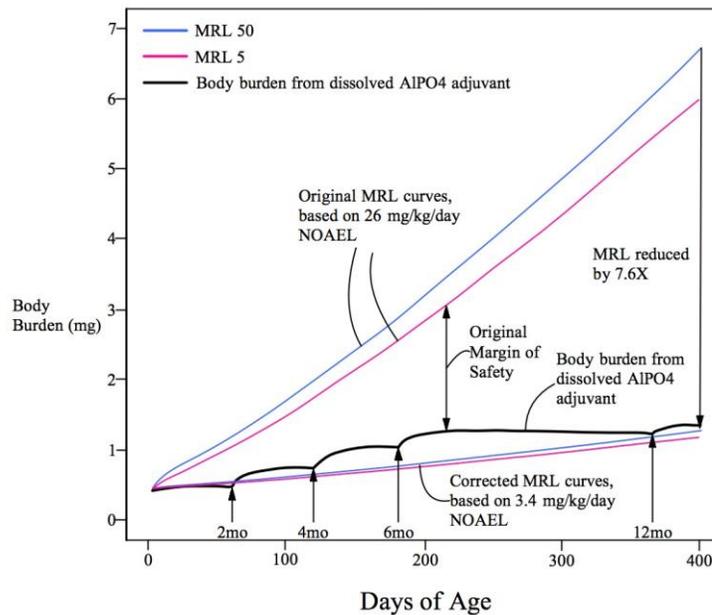


Fig. 12: Body burden vs. MRL comparison chart for Al phosphate adjuvant (AlPO₄) corrected in accordance with the new discovery (Alawdi 2016) that ingestion of 3.4 mg/kg/day Al causes adverse effects. The body burden exceeds the corrected MRL curve for almost the entire first year of life, indicating toxicity. The toxicity of Al adjuvant particles is a separate, additional issue. MRL 50 and MRL 5 refer to two different infant growth rates. Adapted from Mitkus et al., 2011.

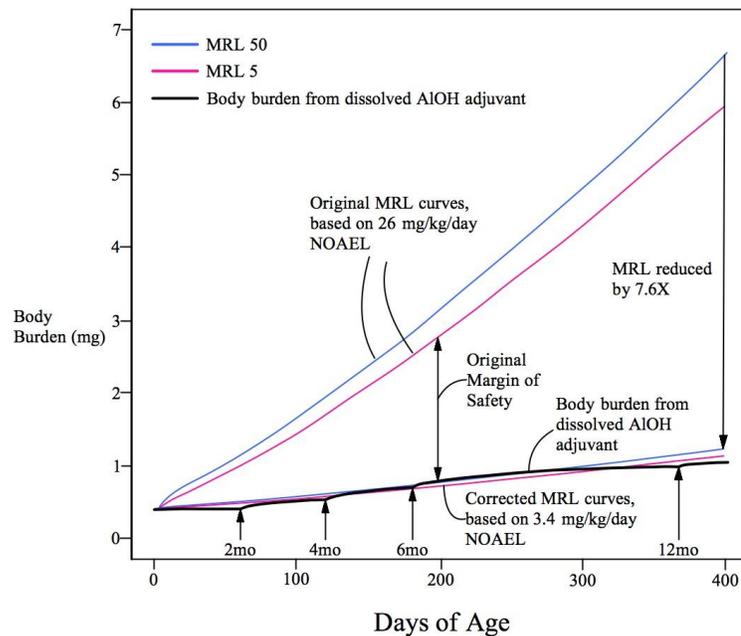


Fig. 13: Body burden vs. MRL comparison chart for Al hydroxide adjuvant (AlOH), corrected in accordance with the new discovery (Alawdi 2016) that ingestion of 3.4 mg/kg/day Al causes adverse effects. The body burden overlaps the new, corrected MRL, indicating borderline toxicity. The margin of safety is gone. MRL 50 and MRL 5 refer to two different infant growth rates. The toxicity of Al adjuvant particles is a separate, additional issue. Adapted from Mitkus et al., 2011.

3) NO AL ADJUVANT TOXICITY DATA CITED, DESPITE AVAILABILITY

Mitkus does not cite any toxicity data for injected Al adjuvants. Mitkus instead uses toxicity data for ingested, non-particulate, water-soluble Al (Golub 2001, which used Al lactate) to derive the MRL. This data comes from a single study (Golub 2001).

So, remarkably, Mitkus claims a safe level of injected Al adjuvant exposure, without citing any Al adjuvant toxicity data. The error is unnecessary and neglectful because at least two animal studies of injected Al adjuvant toxicity were available prior to the Mitkus publication in 2011 (Petrik 2007, Shaw 2009). These papers were not cited or mentioned by Mitkus 2011.

Each of these three flaws is fatal for the validity of the Mitkus study in establishing the safety of aluminum adjuvants. Hence, the CDC is completely lacking valid evidence for the

safety of Al adjuvants. This is especially true for safety regarding neurological and long-term outcomes, because other available studies of Al adjuvant safety (e.g., Jefferson 2004) do not consider (or are incapable of detecting) these outcomes.

CDC Fails To Investigate Toxicity of Al Adjuvants

The CDC has conducted no epidemiological studies on long term safety (e.g. considering neurological outcomes) of Al adjuvants. There is one ecological study of country-level data, which reported an association between Al adjuvant exposure and autism (Tomljenovic 2011). However, being an ecological study, it is highly susceptible to confounding and biases.

Dr Frank DeStefano of the CDC's Immunization Safety Office is co-author of a

feasibility study (Glanz 2015) on using the Vaccine Safety Datalink (VSD) to investigate the safety of individual vaccine ingredients. The paper focuses on Al adjuvants. It acknowledges that thimerosal is the only vaccine ingredient studied for autism or neurological safety, and that a possible association between Al adjuvants and autism has not been explored in epidemiological studies. Glanz 2015 states:

“To date, there have been no population-based studies specifically designed to evaluate associations between clinically meaningful outcomes and non-antigen ingredients, other than thimerosal.”

The CDC has not investigated Al adjuvant safety concerns, despite the accumulating scientific evidence of harm and evidence linking Al adjuvants to immune activation mechanisms of brain injury.¹

Conclusion

The science reviewed here tells a consistent and compelling story: that vaccines may cause autism by stimulating immune activation and elevated cytokines in the brain. Al adjuvants are implicated as a cause of autism because they can be transported into the brain, because they cause microglial activation at vaccine-relevant dosages, and because aluminum induces IL-6 in the brain.

In statements asserting no vaccine-autism link, the CDC cites scientific evidence that is not relevant to Al adjuvant safety or is incapable of disproving an Al adjuvant-autism link (Taylor 2014, DeStefano 2013, Mitkus 2011). In support of claims for Al adjuvant safety, the CDC relies on a profoundly flawed theoretical modelling study (Mitkus 2011). There is little scientific evidence supporting the safety of Al adjuvants, especially in relation to autism and other long term neurological outcomes.

¹ However, the Glanz paper notes that studies of aluminum adjuvants are problematic because of expected small differences in exposures in the low and high exposure groups. Glanz 2015 concludes: “...children below the 10th percentile would be exposed to between 0 mg and 3.1mg, while children above the 90th percentile would be exposed to between 4.8 mg and 5.3 mg of aluminum from vaccines. It is unclear if such differences in aluminum exposure would be biologically meaningful.” (Glanz 2015). So, epidemiological studies may not provide reliable evidence for safety or harm. Controlled, prospective human trials of aluminum adjuvant exposure from vaccines will likely be prohibited for ethical reasons. Also, Al adjuvants are essential ingredients for Al adjuvanted vaccines. Consequently, it will be

challenging to design studies of long term adverse effects of Al adjuvants in humans. Experiments in animal models can provide valuable information. Al adjuvants should be tested for effects on: 1) excitatory/inhibitory imbalance; 2) core symptoms of autism (social, communicative and repetitive/stereotyped behaviors); 3) IL-6, IL-17, and other cytokine levels in the brain; 4) other physiological abnormalities associated with autism (e.g. mitochondrial dysfunction, microbiome dysbiosis, Purkinje cell loss, cerebellum abnormalities etc); and 5) microglial activation and immune activity in the brain. Investigating these outcomes can provide valuable information concerning the safety of Al adjuvants.

References

- Akintunde et al., 2015 Increased production of IL-17 in children with autism spectrum disorders and co-morbid asthma, *Journal of Neuroimmunology* 286 (2015) 33-41.
- Al-Ayadhi et al., 2012 Elevated serum levels of interleukin-17A in children with autism, *Journal of Neuroinflammation* 2012, 9:158.
- Alawdi et al., Neuroprotective Effect of Nanodiamond in Alzheimer's Disease Rat Model: a Pivotal Role for Modulating NF- κ B and STAT3 Signaling, *Molecular Neurobiology*, 54 (3):1906-1918.
- Atladdottir et al., Maternal infection requiring hospitalization during pregnancy and autism spectrum disorders, *Journal of Autism and Developmental Disorders*, 2010 Dec;40(12):1423-1430.
- Bauman et al., 2014 Activation of the Maternal Immune System During Pregnancy Alters Behavioral Development of Rhesus Monkey Offspring, *Biological Psychiatry*, 2014;75: 332–341
- Bergfors et al., 2014 How common are long-lasting, intensely itching vaccination granulomas and contact allergy to aluminium induced by currently used pediatric vaccines? A prospective cohort study, *European Journal of Pediatrics*, 173:1297–1307.
- Bilkei-Gorzo, 1993, Neurotoxic effect of enteral aluminum, *Food and Chemical Toxicology*, 31(5):357-361.
- Brown et al., 2014 Metabolic consequences of interleukin-6 challenge in developing neurons and astroglia, *Journal of Neuroinflammation*, 11:183.
- Brown et al., Epidemiologic studies of exposure to prenatal infection and risk of schizophrenia and autism, *Developmental Neurobiology*, 2012 October ; 72(10): 1272–1276.
- Bruce et al., 2011 Converging pathways lead to overproduction of IL-17 in the absence of vitamin D signaling, 2011 Aug; 23(8): 519–528.
- Careaga et al 2017 Maternal Immune Activation and Autism Spectrum Disorder: From Rodents to Nonhuman and Human Primates, *Biological Psychiatry*, March 1, 2017; 81:391–401.
- Chen et al., Postnatal systemic inflammation exacerbates impairment of hippocampal synaptic plasticity in an animal seizure model, *Neuroimmunomodulation*, 2013;20(4):223-32.
- Choi et al., 2012, Delivery of nanoparticles to brain metastases of breast cancer using a cellular Trojan horse, *Cancer Nanotechnology*, 3:47–54.
- Choi et al., 2016 The maternal interleukin-17a pathway in mice promotes autismlike phenotypes in offspring, *Science*, 2016 Feb 26; 351(6276): 933–939.
- Ciaranello et al. The Neurobiology of Infantile Autism, *The Neuroscientist*, 1:361-367
- Coiro et al., Impaired synaptic development in a maternal immune activation mouse model of neurodevelopmental disorders, *Brain, Behavior, and Immunity*, Nov;50:249-258.
- Crepeaux et al., 2015 Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections, *Journal of Inorganic Biochemistry*, 152:199-205.
- Crepeaux et al., 2017 Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective low dose neurotoxicity, *Toxicology*, 375 (2017) 48–57.
- DeLong et al., 1981 Acquired reversible autistic syndrome in acute encephalopathic illness in children, *Archives of Neurology*, 36:191-194.
- Dera 2016, Protective effect of resveratrol against aluminum chloride induced nephrotoxicity in rats, *Saudi Medical Journal*, 37 (4).
- DeStefano et al., 2013 Increasing Exposure to Antibody-Stimulating Proteins and Polysaccharides in Vaccines Is Not Associated with Risk of Autism, *The Journal of Pediatrics*, 163 (2).
- Deverman and Patterson, 2009 Cytokines and CNS Development, *Neuron* 64:61-78.
- Drozdenko et al., 2014 Oral vitamin D increases the frequencies of CD38+ human B cells and ameliorates IL-17-producing T cells, *Experimental Dermatology*, 23: 107-112.

- Estes and McAllister, 2016 Maternal immune activation: implications for neuropsychiatric disorders, *Science*, 353 (6301) 772-777.
- Exley, 2003 The Pro-Oxidant Activity of Aluminum, *Free Radical Biology and Medicine*, 36(3): 380-387.
- Flarend et al., 1997 In vivo absorption of aluminum-containing vaccine adjuvants using ²⁶Al, *Vaccine*, 15(12/13):1314-1318.
- Freyberg et al., 2015 Reduced perceptual exclusivity during object and grating rivalry in autism, *Journal of Vision*, 15(13):11, 1–12.
- Galic et al., 2008 Postnatal Inflammation Increases Seizure Susceptibility in Adult Rats, *The Journal of Neuroscience*, 2008, 28 (27) 6904-6913.
- Garay et al., 2013 Maternal immune activation causes age- and region-specific changes in brain cytokines in offspring throughout development, *Brain, Behavior, and Immunity*, 31: 54-68.
- Ghaziuddin et al., 2002 Autistic symptoms following herpes encephalitis, *European Child and Adolescent Psychiatry*, Vol. 11, No. 3:142-146.
- Gherardi et al., 2001 Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle, *Brain*, 124:1821-1831.
- Ghiani et al., 2011 Early effects of lipopolysaccharide induced inflammation on foetal brain development in rat, *ASN Neuro*, 3 (4): 233-245.
- Gillberg 1986 Brief Report: Onset at Age 14 of a Typical Autistic Syndrome. A Case Report of a Girl with Herpes Simplex Encephalitis, *Journal of Autism and Developmental Disorders*, Vol 16, No. 3:369-375.
- Giulivi et al 2013 Gestational Exposure to a Viral Mimetic Poly(I:C) Results in Long-Lasting Changes in Mitochondrial Function by Leucocytes in the Adult Offspring, *Mediators of Inflammation*, Vol 2013:609602.
- Glanz et al., 2015, Cumulative and episodic vaccine aluminum exposure in a population-based cohort of young children, *Vaccine* 33:6736–6744.
- Golub et al., 2001 Long-term consequences of developmental exposure to aluminum in a suboptimal diet for growth and behavior of Swiss Webster mice, *Neurotoxicology and Teratology* 23 (2001) 365–372.
- Gupta et al., 1998 Th1- and Th2-like cytokines in CD4+ and CD8+ T cells in autism, *Journal of Neuroimmunology*, 85:106-109.
- Harre et al., 2008 Neonatal inflammation produces selective behavioural deficits and alters *N*-methyl-D-aspartate receptor subunit mRNA in the adult rat brain, *European Journal of Neuroscience*, 2008 Feb; 27(3): 644–653.
- Harris et al., 2012 Alhydrogel® adjuvant, ultrasonic dispersion and protein binding: A TEM and analytical study, *Micron*, 43:192-200.
- Hsiao et al., 2013 The microbiota modulates gut physiology and behavioral abnormalities associated with autism, *Cell*, 155(7): 1451-1463.
- Huttenlocher and Dabholkar, 1997 Regional Differences in Synaptogenesis in Human Cerebral Cortex, *Journal of Comparative Neurology*, 387:167–178 (1997).
- Jefferson 2004 Adverse events after immunisation with aluminium-containing DTP vaccines: systematic review of the evidence, *The Lancet* 4:84-90.
- Jones et al., 2016 Autism with Intellectual Disability is Associated with Increased Levels of Maternal Cytokines and Chemokines During Gestation, *Molecular Psychiatry*, 22(2):273-279.
- Khan et al., 2013 Slow CCL2-dependent translocation of biopersistent particles from muscle to brain, *BMC Medicine*, 11:99.
- Kindregan et al., 2015 Gait Deviations in Children with Autism Spectrum Disorders: A Review, *Autism Research and Treatment*, ID:741480.
- Knuesel et al., 2014, Maternal immune activation and abnormal brain development across CNS disorders, *Nature Reviews* 10:643-660.
- Labouesse et al., 2015, Long-term pathological consequences of prenatal infection: beyond brain disorders, *American Journal of Physiology*, 309:1.

Li et al. 2009 Elevated Immune Response in the Brain of Autistic Patients, *Journal of Neuroimmunology*, 207(1-2): 111–116.

Li et al., 2015 Neonatal vaccination with bacillus Calmette–Guérin and hepatitis B vaccines modulates hippocampal synaptic plasticity in rats, *Journal of Neuroimmunology*, 288 (2015) 1-12.

Machado et al., 2015 Maternal Immune Activation in Nonhuman Primates Alters Social Attention in Juvenile Offspring, *Biological Psychiatry*, 2015 May 1;77(9):823-32.

Malkova et al., 2012 Maternal immune activation yields offspring displaying mouse versions of the three core symptoms of autism, *Brain Behavior and Immunity*, 2012 May ; 26(4): 607–616.

Marques et al., 2014 Autism Spectrum Disorder Secondary to Enterovirus Encephalitis, *Journal of Child Neurology*, 2014, Vol. 29(5) 708-714.

Mestas et al., 2004 Of Mice and Not Men: Differences between Mouse and Human Immunology, *Journal of Immunology*, 0022-1767:2731-2738.

Meyer et al., 2006 The Time of Prenatal Immune Challenge Determines the Specificity of Inflammation-Mediated Brain and Behavioral Pathology, *The Journal of Neuroscience*, 26(18):4752– 4762.

Meyer et al., 2007 The neurodevelopmental impact of prenatal infections at different times of pregnancy: the earlier the worse?, *Neuroscientist*, Jun;13(3):241-56.

Meyer et al., 2009 In-vivo rodent models for the experimental investigation of prenatal immune activation effects in neurodevelopmental brain disorders, *Neuroscience and Biobehavioral Reviews*, 33 (2009) 1061–1079.

Meyer 2014, Prenatal Poly(I:C) Exposure and Other Developmental Immune Activation Models in Rodent Systems, *Biological Psychiatry*, 75:307-315.

Mitkus et al., 2011 Updated aluminum pharmacokinetics following infant exposures through diet and vaccination, *Vaccine* 29 (2011) 9538–9543.

Offit et al., 2003 Addressing Parents’ Concerns: Do Vaccines Contain Harmful Preservatives, Adjuvants, Additives, or Residuals? *Pediatrics*, 112(6): 1394-1401.

Oskvig et al., 2012 Maternal immune activation by LPS selectively alters specific gene expression profiles of interneuron migration and oxidative stress in the fetus without triggering a fetal immune response, *Brain Behavior and Immunity*, 2012 May ; 26(4): 623–634.

Pang et al., 2016 Exploiting macrophages as targeted carrier to guide nanoparticles into glioma, *Oncotarget* 7(24):37081.

Parker-Athill and Tan, 2010 Maternal Immune Activation and Autism Spectrum Disorder: Interleukin-6 Signaling as a Key Mechanistic Pathway, *NeuroSignals*, 2010;18:113–128.

Petrik et al., 2007 Aluminum Adjuvant Linked to Gulf War Illness Induces Motor Neuron Death in Mice, *NeuroMolecular Medicine*, Vol. 9, 83-100.

Pineda et al., 2013 Maternal immune activation promotes hippocampal kindling epileptogenesis in mice, *Annals of Neurology*, 2013 July ; 74(1): 11–19.

Podila et al., 2013 Toxicity of Engineered Nanomaterials: A Physicochemical Perspective, *Journal of Biochemical and Molecular Toxicology*, 2013 January ; 27(1): 50–55.

Robertson et al., 2016 Reduced GABAergic Action in the Autistic Brain, *Current Biology*, 26, 1-6.

Saad et al., 2016 Vitamin D status in autism spectrum disorders and the efficacy of vitamin D supplementation in autistic children, *Nutritional Neuroscience*, 19 (8) 346-351.

Semple et al., 2013 Brain development in rodents and humans: Identifying benchmarks of maturation and vulnerability to injury across species, *Progress in Neurobiology*, Jul-Aug;106-107:1-16.

Sethi et al., 2008 Aluminium-induced electrophysiological, biochemical and cognitive modifications in the hippocampus of aging rats, *Neurotoxicology* 29, 1069-1079.

Sethi et al., 2009 Curcumin attenuates aluminium-induced functional neurotoxicity in rats, *Pharmacology, Biochemistry, and Behavior* 93:31-39.

- Shen et al., 2016 Postnatal activation of TLR4 in astrocytes promotes excitatory synaptogenesis in hippocampal neurons, *Journal of Cell Biology*, 215(5):719-734.
- Sharifi et al., 2012 Toxicity of Nanomaterials, *Chemical Society Reviews*, 2012 Mar 21; 41(6): 2323–2343.
- Shaw and Petrik, 2009 Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration, *Journal of Inorganic Biochemistry* 103 (11).
- Shaw and Tomljenovic, 2013 Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes, *Journal of Inorganic Biochemistry*, 128 (2013) 237–244.
- Shi et al., 2009 Activation of the Maternal Immune System Alters Cerebellar Development in the Offspring, *Brain, Behavior, and Immunity*, January, 23(1): 116–123.
- Smith et al., 2007 Maternal Immune Activation Alters Fetal Brain Development through Interleukin-6, *Journal of Neuroscience*, 2007 October 3; 27(40).
- Smith et al., 2012, Maternal Immune Activation Increases Neonatal Mouse Cortex Thickness and Cell Density, *Journal of Neuroimmune Pharmacology*, 7(3):529-532.
- Stiles et al., 2010 The Basics of Brain Development, *Neuropsychology Reviews* (2010) 20:327–348.
- Suzuki et al., 2011 Plasma Cytokine Profiles in Subjects with High-Functioning Autism Spectrum Disorders, *PloS ONE* 6(5).
- Suzuki et al., 2013 Microglial Activation in Young Adults With Autism Spectrum Disorder, *JAMA Psychiatry* 70(1): 49-58.
- Takano 2015 Role of Microglia in Autism: Recent Advances, *Developmental Neuroscience*, 37:195-202.
- Tau and Peterson, 2010 Normal Development of Brain Circuits, *Neuropsychopharmacology*, (2010) 35:147–168.
- Taylor et al., 2014 Vaccines are not associated with autism: An evidence-based meta-analysis of case-control and cohort studies, *Vaccine*, 32:3623-3629.
- Tomljenovic and Shaw, 2011 Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? *Journal of Inorganic Biochemistry* 105.
- Tsilioni et al., 2015 Children with autism spectrum disorders, who improved with a luteolin-containing dietary formulation, show reduced serum levels of TNF and IL-6, *Translational Psychiatry*, 5, 647.
- Vargas et al., 2005 Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism, *Annals of Neurology*, 2005;57:67–81.
- Viezeliene et al., 2013 Selective induction of IL-6 by aluminum-induced oxidative stress can be prevented by selenium, *Journal of Trace Elements in Medicine and Biology*, 27:226-229.
- Wei et al., 2011 IL-6 is increased in the cerebellum of autistic brain and alters neural cell adhesion, migration and synaptic formation, *Journal of Neuroinflammation* 2011, 8:52.
- Wei et al., 2012 (a) Brain IL-6 elevation causes neuronal circuitry imbalances and mediates autism-like behaviors, *Biochimica et Biophysica Acta*, 1822 (2012) 831–842.
- Wei et al. 2012 (b) Alteration of brain volume in IL-6 overexpressing mice related to autism, *International Journal of Developmental Neuroscience*, 30:554-559.
- Wei et al., 2013 Brain IL-6 and autism, *Neuroscience* 252 (2013): 320–325.
- Wei et al., 2016 Inhibition of IL-6 trans-signaling in the brain increases sociability in the BTBR mouse model of autism, *Biochimica et Biophysica Acta*, 1862(10):1918-1925.
- Weir et al., 2015 Preliminary evidence of neuropathology in nonhuman primates prenatally exposed to maternal immune activation, *Brain, Behavior, and Immunity*, 48,139–146.
- Williams et al., 2006 The Profile of Memory Function in Children With Autism, *Neuropsychology*, 20(1): 21-29.
- Wobke et al., 2014 Vitamin D in inflammatory diseases, *Frontiers in Physiology*, 5: 244.
- Zerbo et al., 2014 Neonatal cytokines and chemokines and risk of Autism Spectrum Disorder: the Early Markers for Autism (EMA) study: a case-control study, *Journal of Neuroinflammation*, 11:113.

Zerbo et al., 2017 Association Between Influenza Infection and Vaccination During Pregnancy and Risk of Autism Spectrum Disorder, *JAMA Pediatrics*, 171(1).

Immunization Graphs:
Natural Infectious Disease Declines; Immunization
Effectiveness; and Immunization Dangers

Prepared by: Raymond Obomsawin Ph.D.
Senior Advisor – First Nations Centre

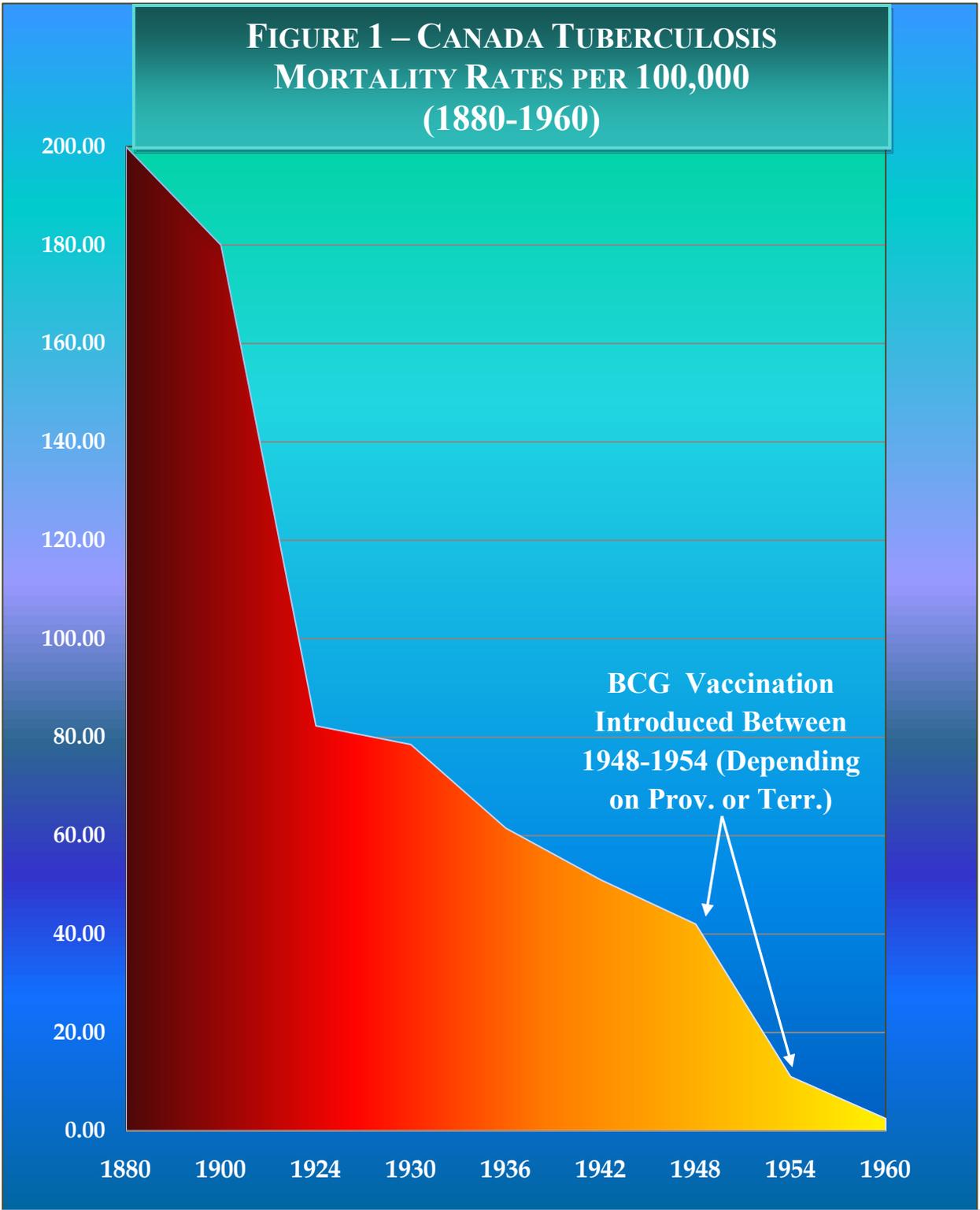
National Aboriginal Health Organization
October 2009

FIGURE SET I.

Natural Infectious Disease Declines Preceding Public Immunization Efforts

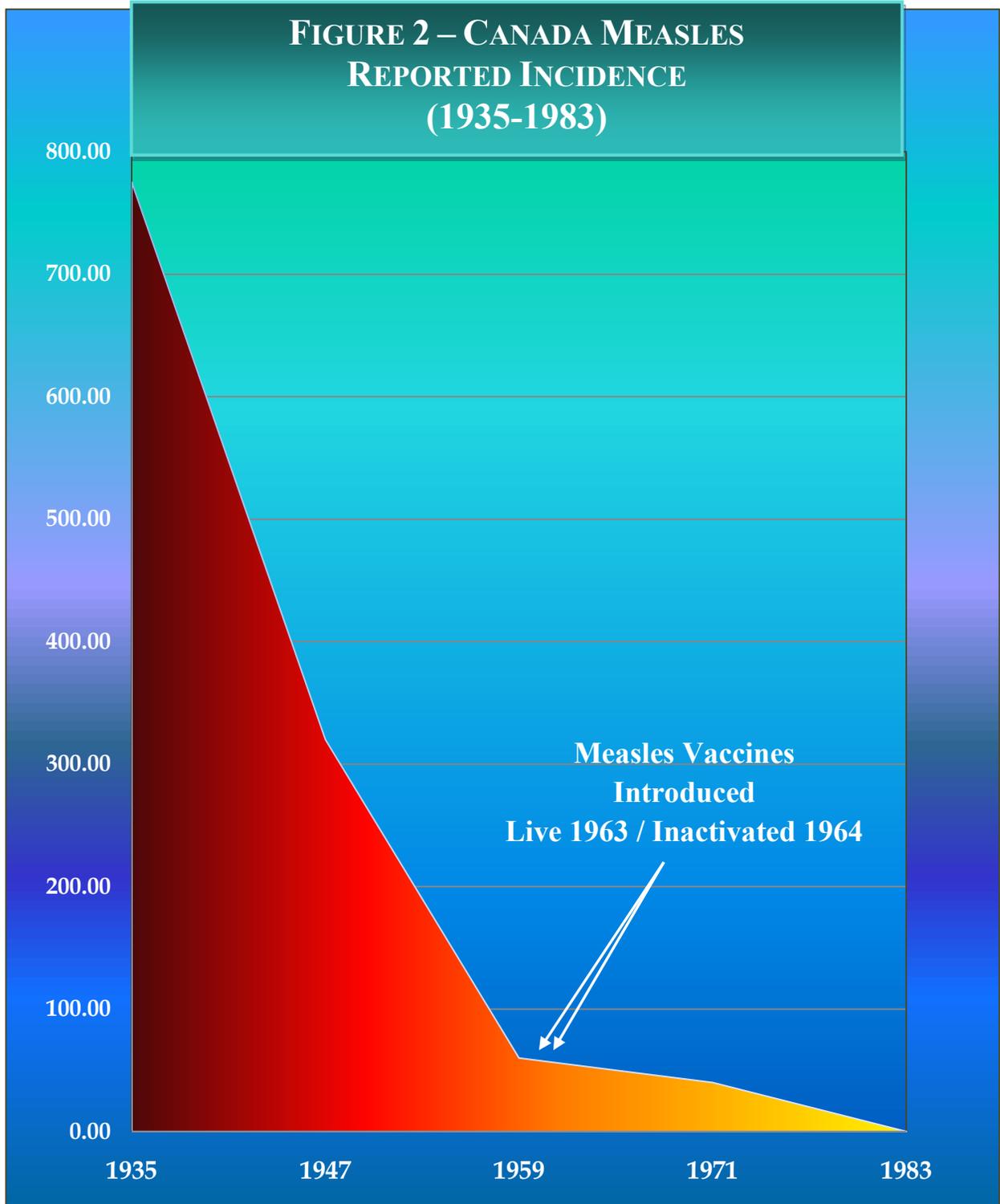
Figures one (1) through eleven (11) graphically illustrate that in North America, Europe, and the South Pacific , major declines in life-threatening infectious diseases occurred historically either without, or far in advance of public immunization efforts for specific diseases as listed. This provides irrefutable evidence that vaccines are not necessary for the effective elimination of a wide range of infectious diseases

FIGURE 1 – CANADA TUBERCULOSIS MORTALITY RATES PER 100,000 (1880-1960)



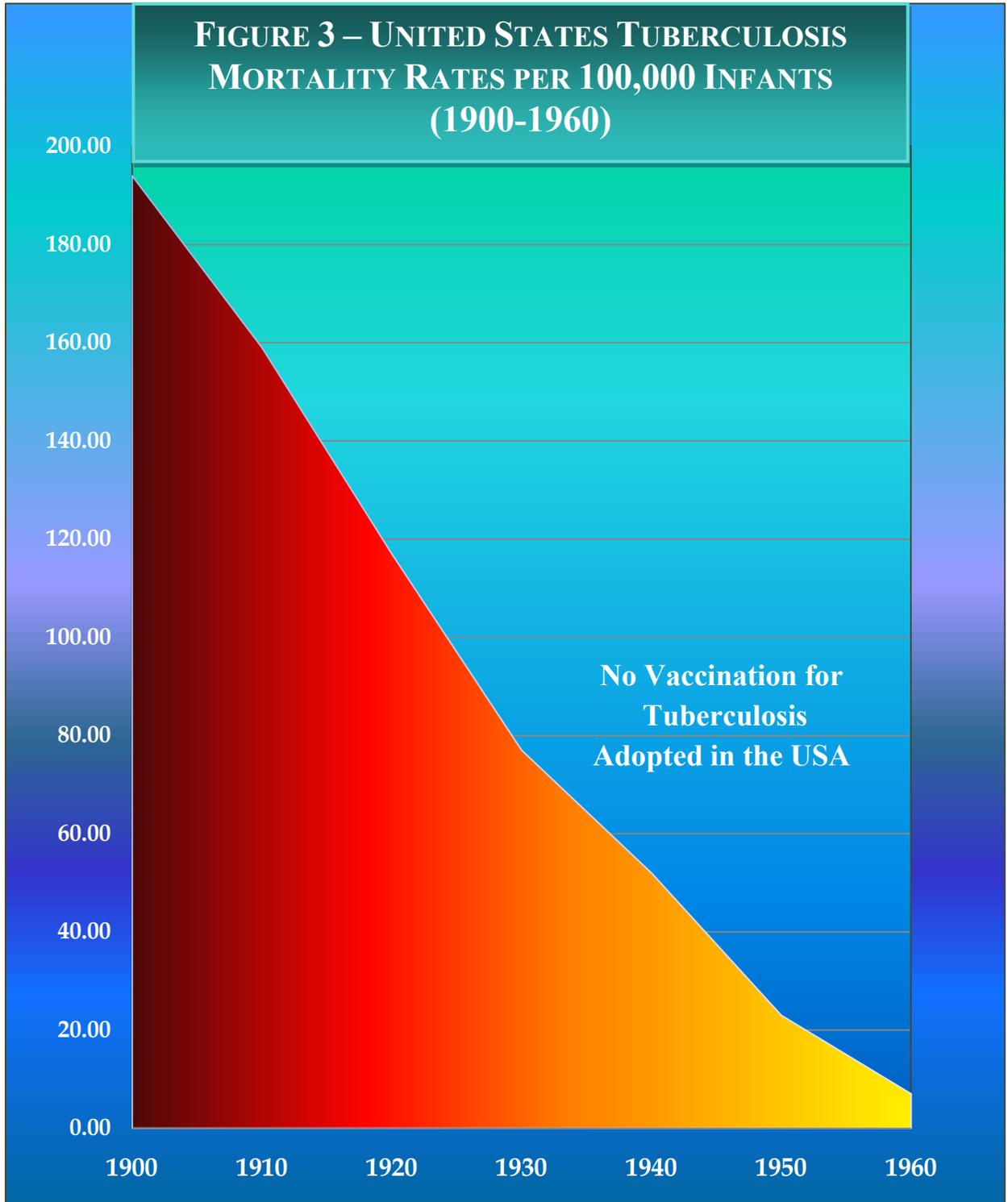
Source: Table based on data at: Timeline of TB in Canada <http://www.lung.ca/tb/tbhistory/timeline/>; <http://www.thecanadianencyclopedia.com/index.cfm?PgNm=TCE&Params=A1ARTA0008151>
Public Health Agency of Canada: <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-bcg-eng.php>; and
PHAC on BCG usage in Canada: http://www.phac-aspc.gc.ca/tbpc-latb/bcgvac_1206-eng.php

**FIGURE 2 – CANADA MEASLES
REPORTED INCIDENCE
(1935-1983)**



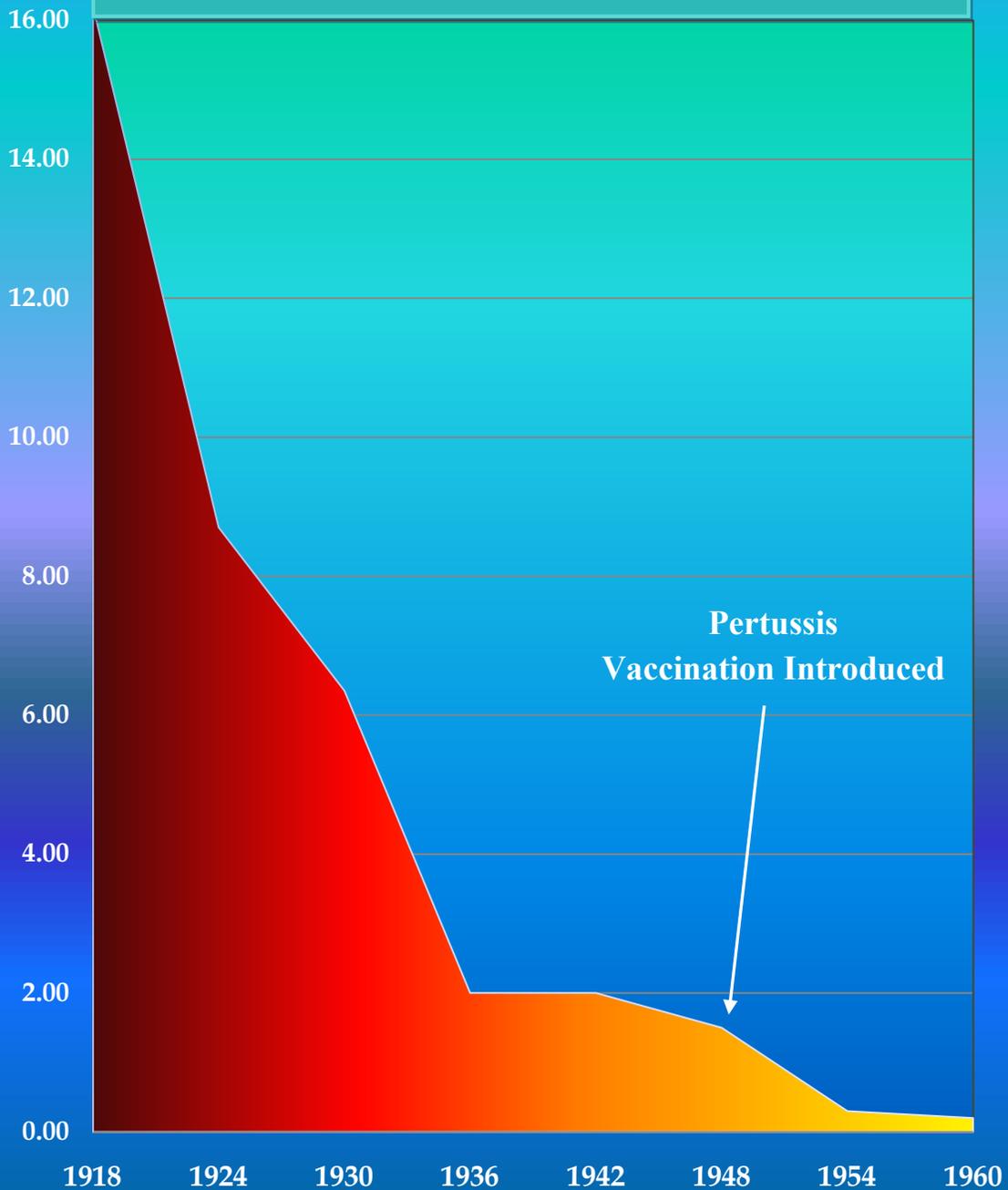
Source: Adapted from: Public Health Agency of Canada, Figure 8 – Measles Reported Incidence Canada. <http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-meas-roug-eng.php>

FIGURE 3 – UNITED STATES TUBERCULOSIS MORTALITY RATES PER 100,000 INFANTS (1900-1960)



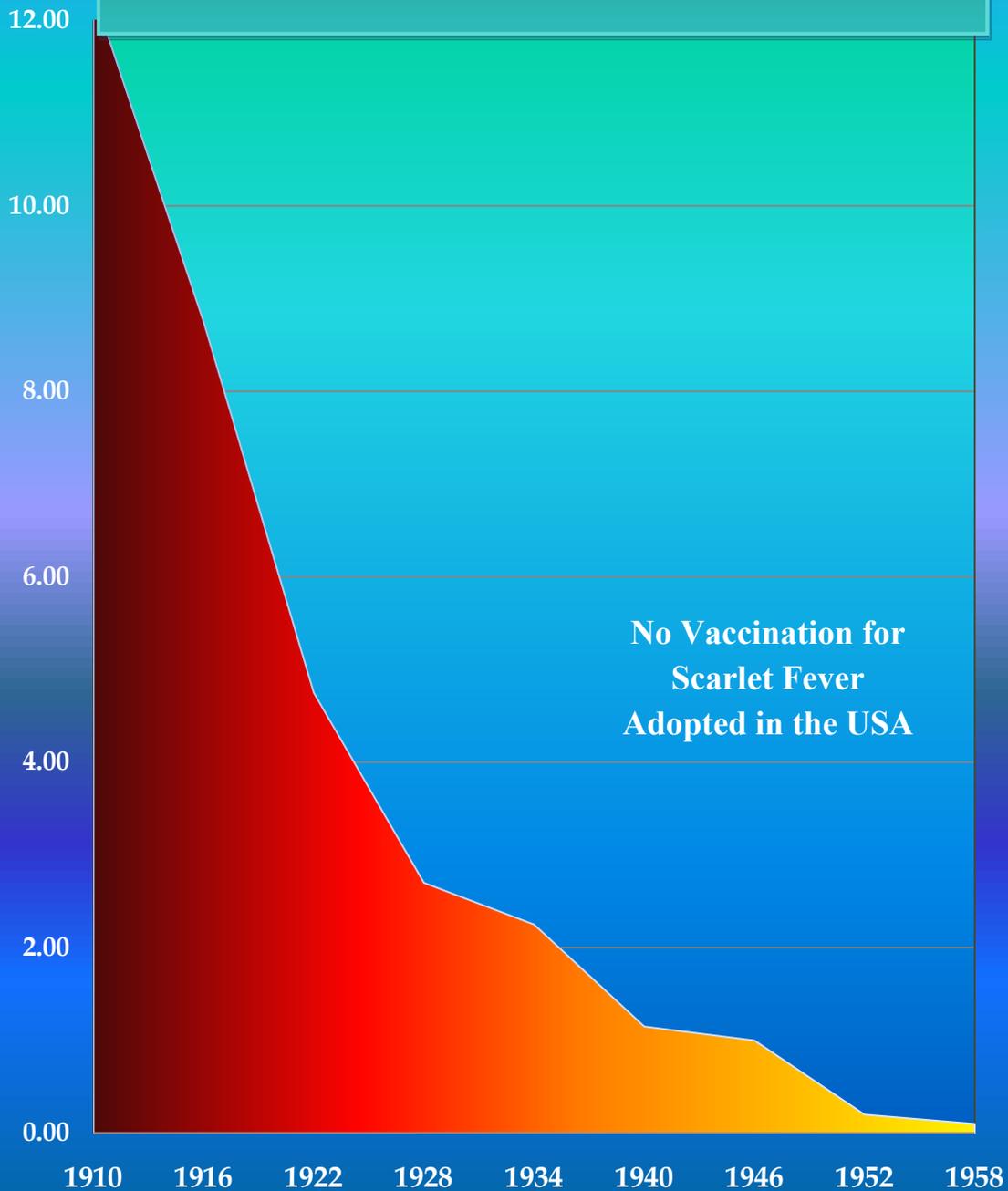
Source: John H. Dingle; Life and Death in Medicine; Scientific American; 1973; p. 56.

FIGURE 4 – USA MEAN ANNUAL PERTUSSIS MORTALITY RATES PER 100,000 (1918-1960)



Source: Data derived from: Vital Statistics of the United States 1937-1960; and Historical Statistics of the United States: Colonial Times to 1970 Part 1 Ch. B Vital Statistics and Health and Medical Care, pp. 44-86H.

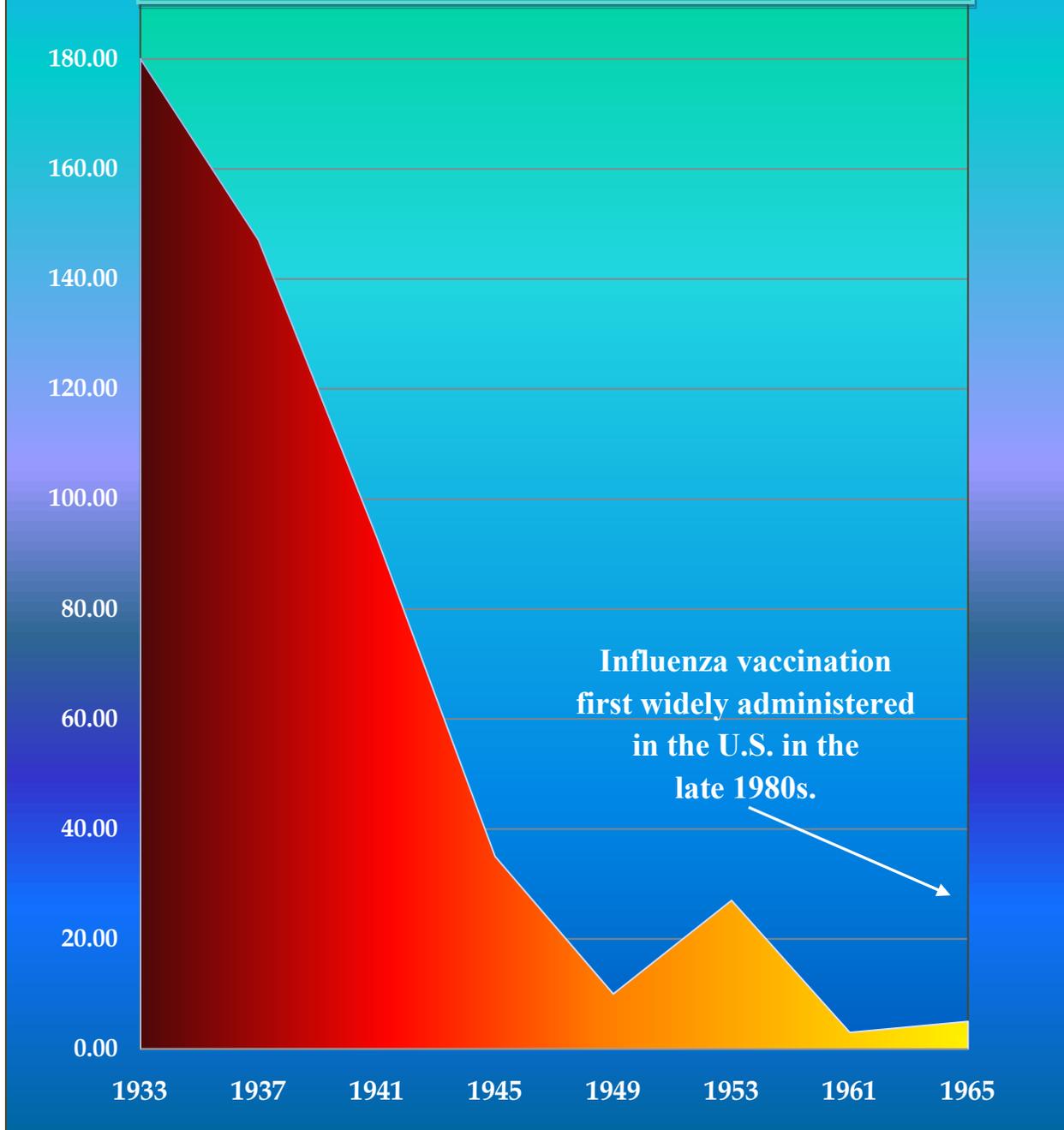
FIGURE 5 – USA MEAN ANNUAL SCARLET FEVER MORTALITY RATES PER 100,000 (1910-1958)



No Vaccination for
Scarlet Fever
Adopted in the USA

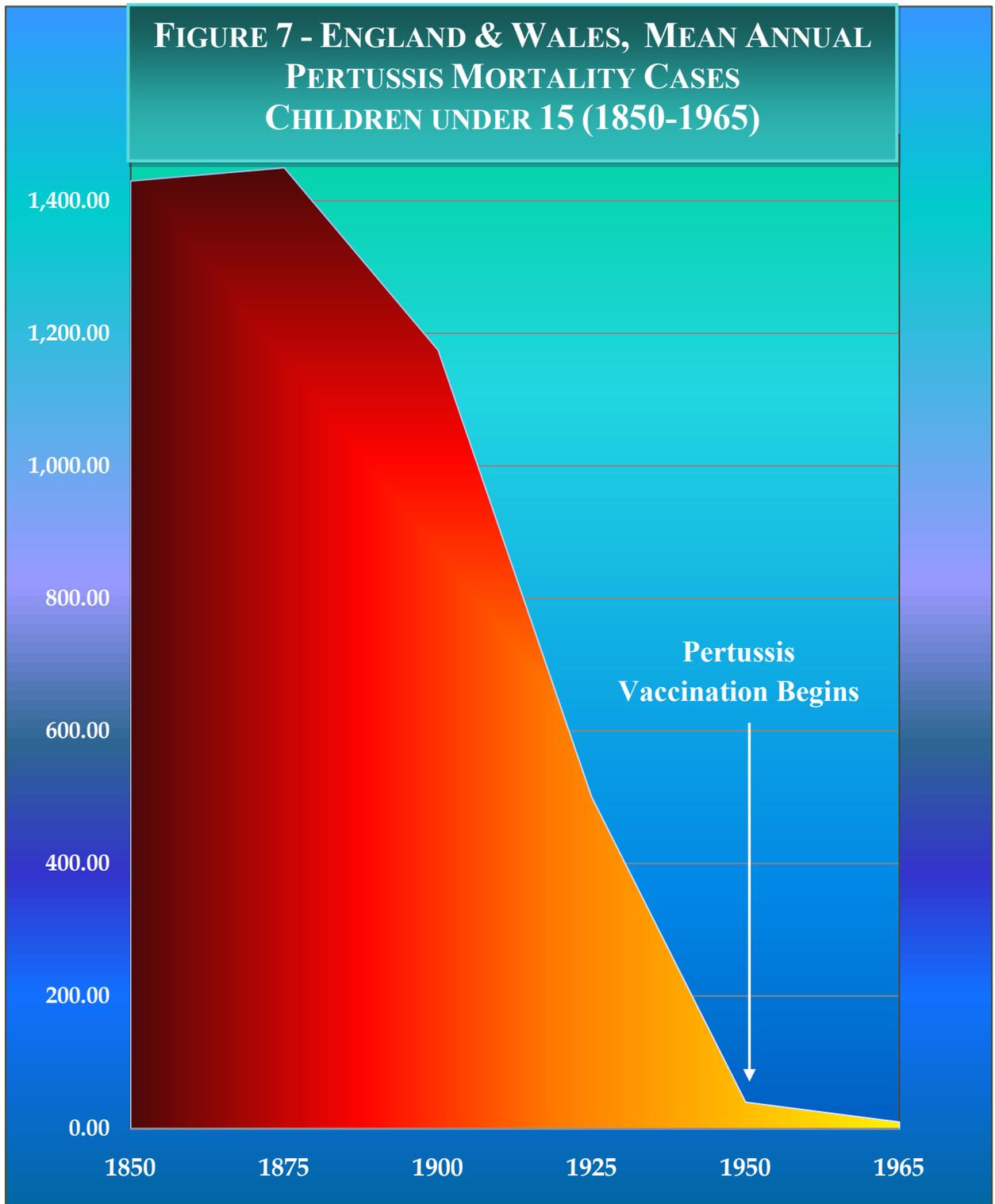
Source: Data derived from - Vital Statistics of the United States 1937-1960; and Historical Statistics of the United States: Colonial Times to 1970 Part 1 Ch. B Vital Statistics and Health and Medical Care, pp. 44-86H.

FIGURE 6 – USA ANNUAL INFLUENZA MORTALITY RATES PER 100,000 (1933-1965)

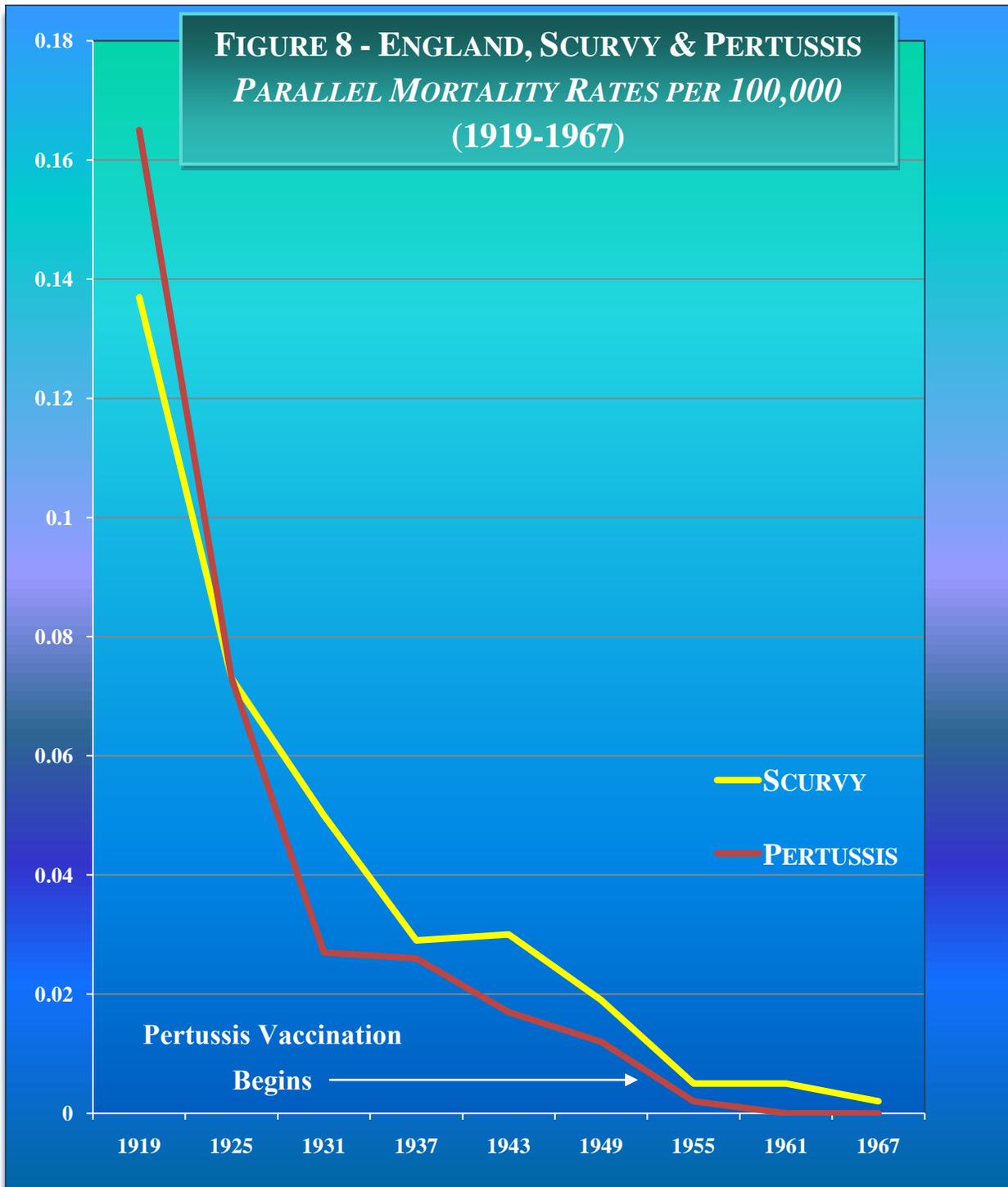


Source: Doshi, P., Trends in Recorded Influenza Mortality: United States 1900-2004, American Journal of Public Health, May 2008, vol. 98, no. 5, p. 941.

**FIGURE 7 - ENGLAND & WALES, MEAN ANNUAL
PERTUSSIS MORTALITY CASES
CHILDREN UNDER 15 (1850-1965)**

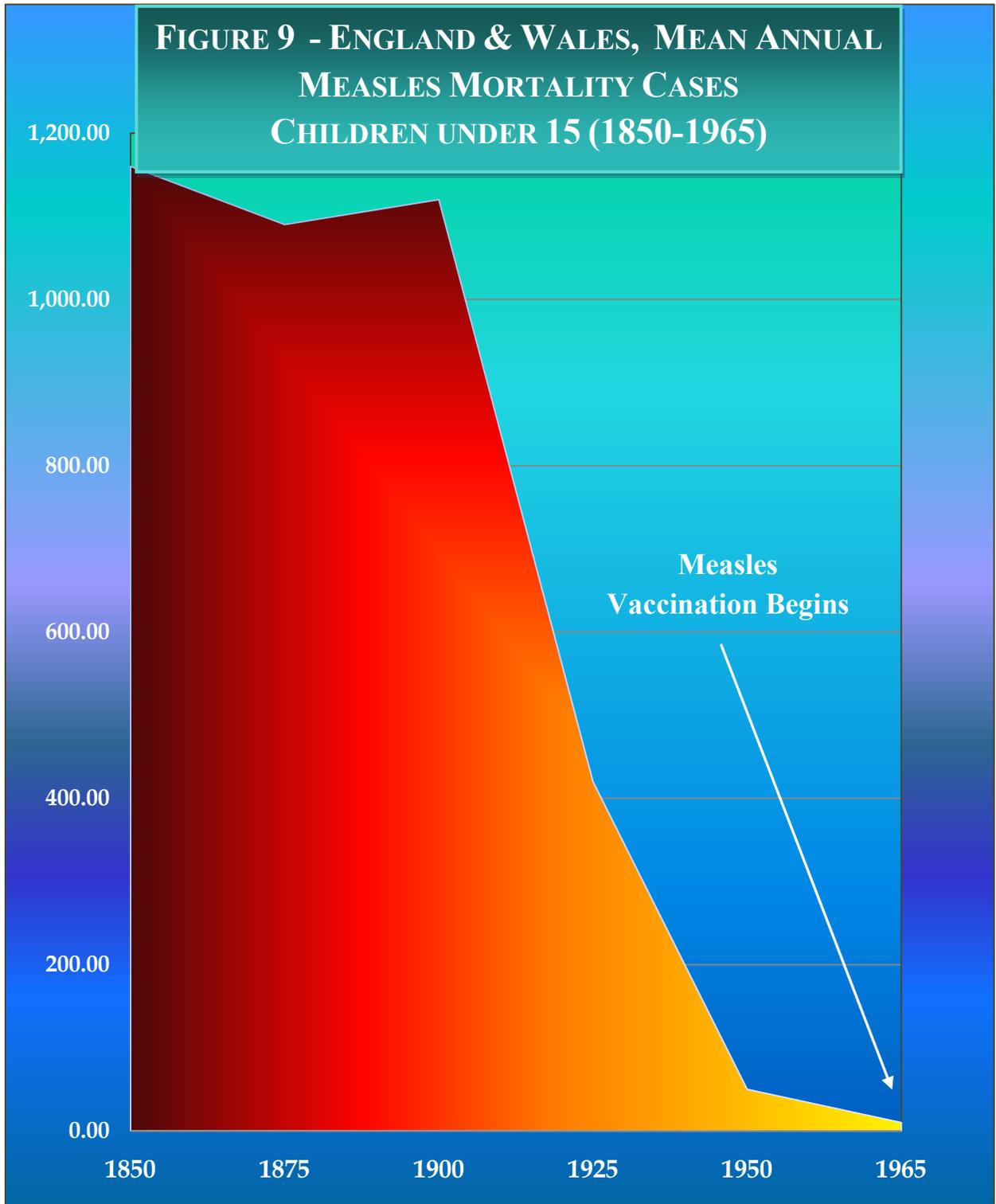


Source: Thomas McKeown, *The Role of Medicine: Dream, Mirage or Nemesis?*; Basil Blackwell; Oxford, UK; 1979; p. 103

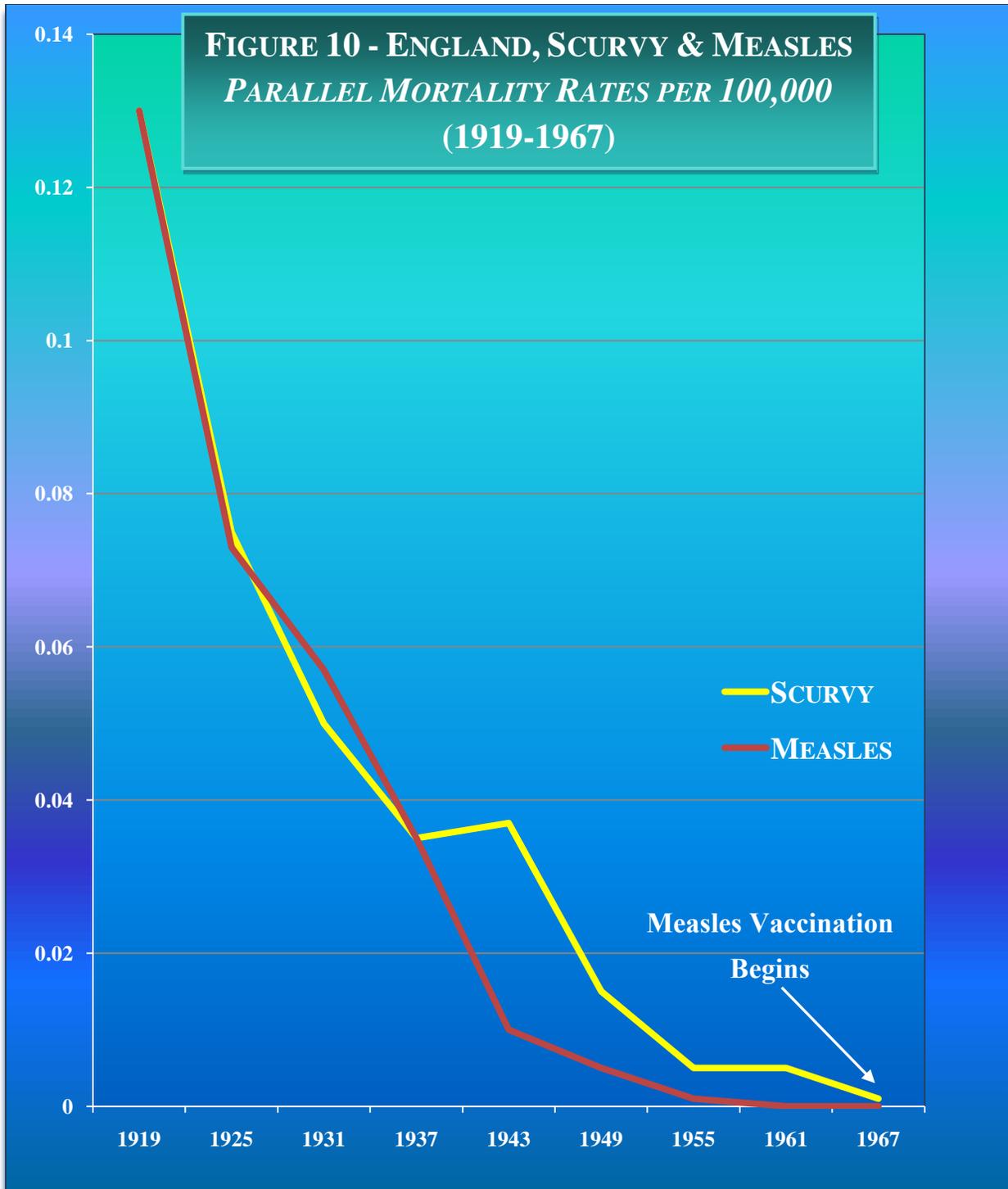


Sources: Data for years 1919-1967 Mortality Statistics: Deaths Registered in England & Wales; UK Office for National Statistics, 1997.

FIGURE 9 - ENGLAND & WALES, MEAN ANNUAL MEASLES MORTALITY CASES CHILDREN UNDER 15 (1850-1965)

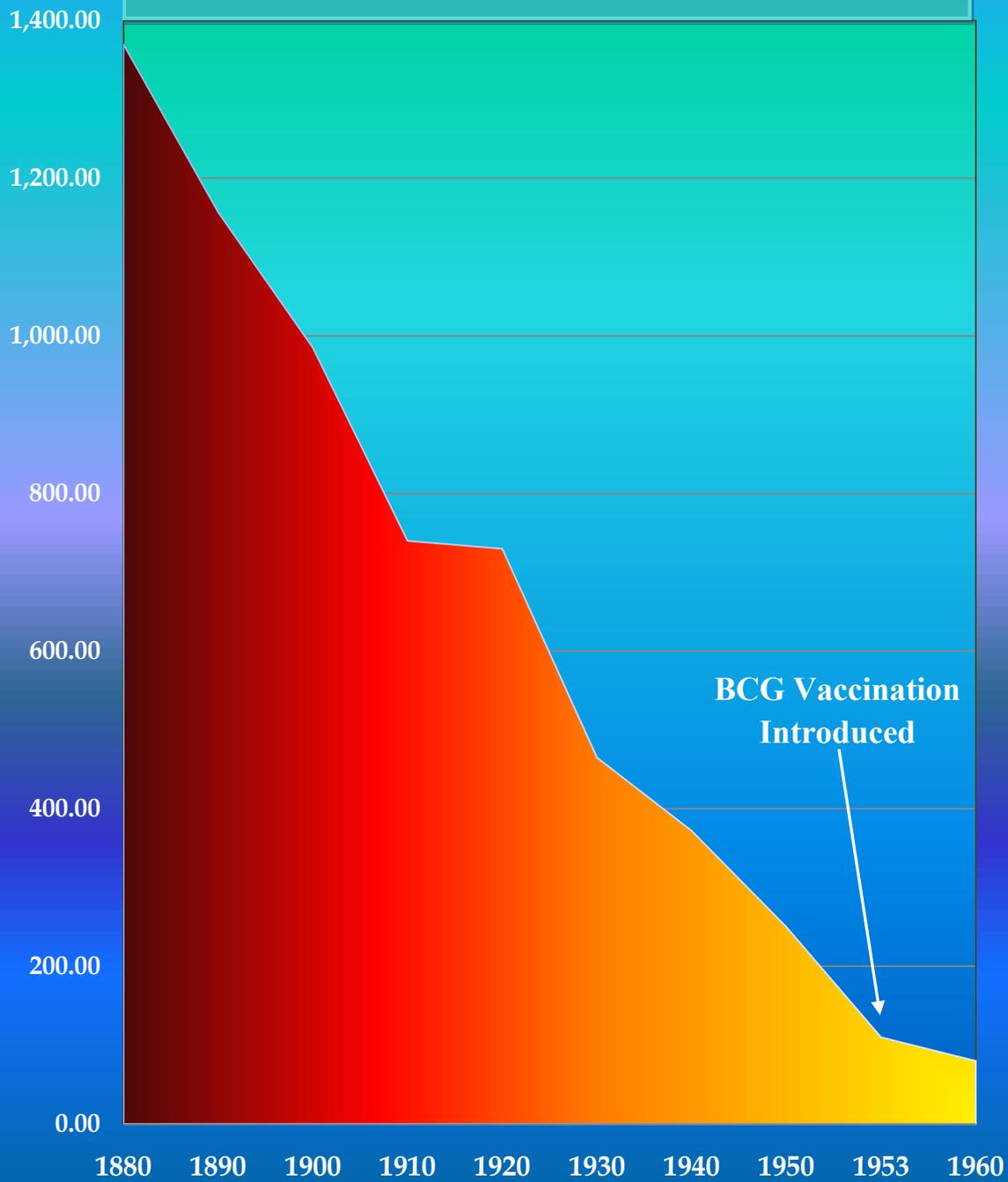


Source: McKeown, T., *The Role of Medicine: Dream, Mirage or Nemesis?*; Basil Blackwell; Oxford, UK; 1979; p. 105; & Waltzkin, H., in *The Relevance of Social Science for Medicine*; Springer; 1st edition, Dec. 31, 1980



Sources: Data for years 1919-1967 Mortality Statistics: Deaths Registered in England & Wales; UK Office for National Statistics, 1997.

**FIGURE 11 - NEW ZEALAND TUBERCULOSIS
DEATH RATES PER MILLION (1880-1960)**



Source: Director General Annual Mortality Reports Covering 1872-1960, New Zealand Parliamentary Journals for the Years Specified.

FIGURE SET II.

Immunization Effectiveness

Figures eleven (12) through twenty-four (24) graphically illustrate that immunization is not by any means a proven and foolproof measure for protection from various infectious disease conditions. It is often inconsequential epidemiologically, and in some cases it is shown to actually worsen health-care outcomes.

Figure 12

**Children Under 2 Yrs of Age
Inactivated Influenza Vaccine**



Source: Cochrane Collaboration Database of Systematic Reviews, (John Wiley & Sons, Ltd.) 2006 (1) Article No. CD004879 – Covers 51 Studies on 260,000 children

Figure 13

**Elderly Living in Communities
& Group Homes
Inactivated Influenza Vaccine**

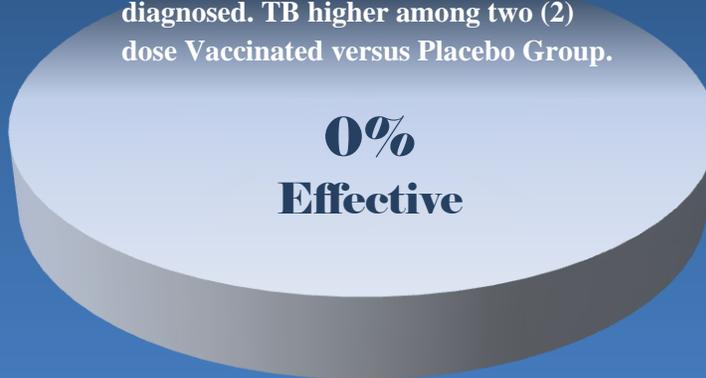


Source: Cochrane Collaboration Database of Systematic Reviews, (John Wiley & Sons, Ltd.) 2006 (3) Article No. CD004876 – Covers 64 Studies, over 40 years of influenza vaccination and see: <http://www.bmj.com/cgi/content/full/333/7574/912>

Figure 14

BCG for Tuberculosis

Note: Post-vaccination- 376 cases pulmonary TB & 31 cases glandular TB diagnosed. TB higher among two (2) dose Vaccinated versus Placebo Group.

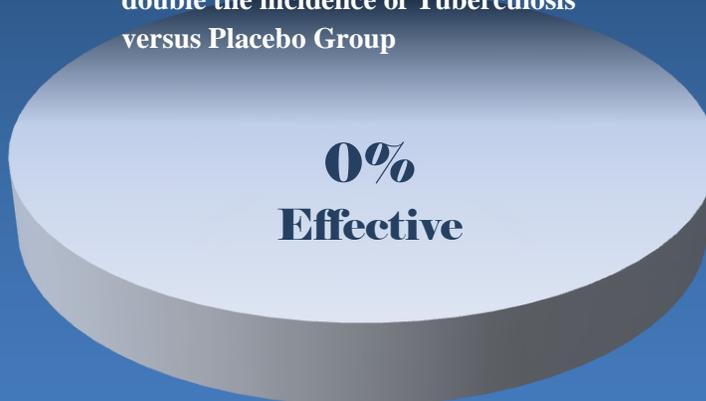


Source: Randomised controlled trial of single BCG, repeated BCG, or combined BCG and killed *Mycobacterium leprae* vaccine for prevention of leprosy and tuberculosis in Malawi; *The Lancet*, Volume 348, Issue 9019, Pages 17 - 24, 6 July 1996

Figure 15

BCG for Tuberculosis

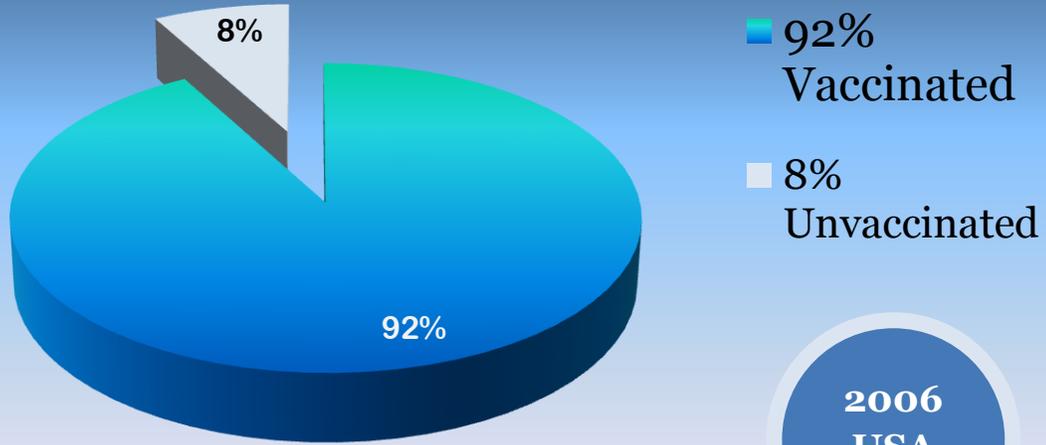
Note: In years 0-2.5 the vaccinated had double the incidence of Tuberculosis versus Placebo Group



Source: Double blind randomized controlled trial of BCG's effectiveness on 250,000 subjects Tuberculosis Research Centre (ICMR), Chennai, India: *Indian Journal of Medical Research*, 110, August 1999, pp. 56-69.

Figure 16

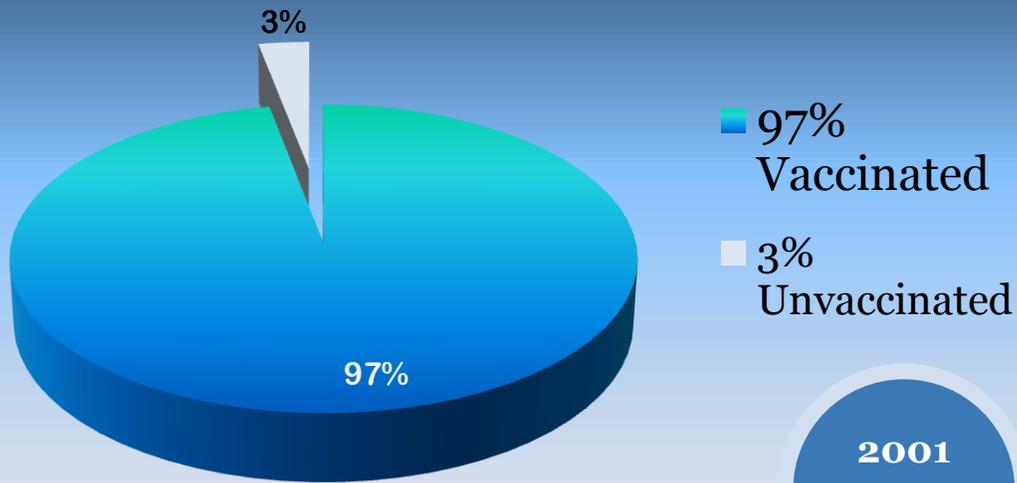
MUMPS OUTBREAK IN HIGHLY VACCINATED POPULATION



Source: Center for Disease Control , MMWR 55 (20); May 26, 2006; pp. 559-63.

Figure 17

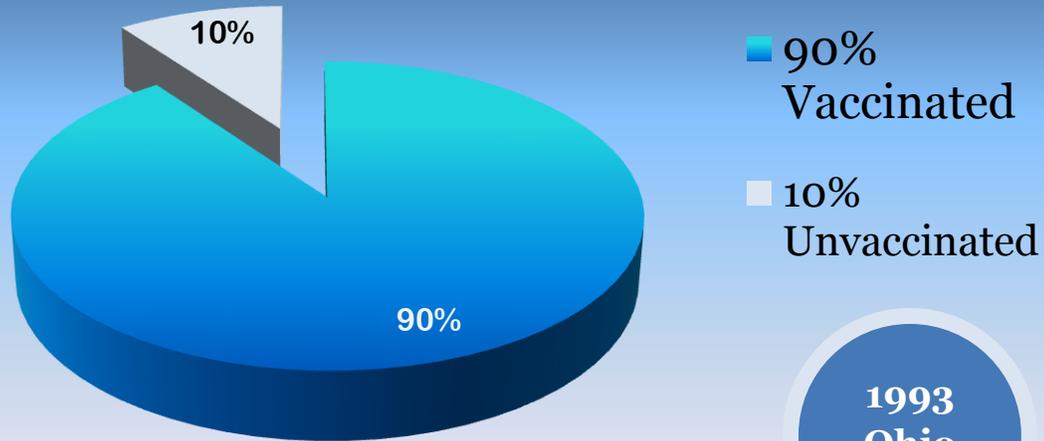
CHICKENPOX OUTBREAK IN HIGHLY VACCINATED POPULATION



Source: Pediatrics - Vol. 113; No. 3; pp. 455-459; (2004)

Figure 18

PERTUSSIS OUTBREAK IN HIGHLY VACCINATED POPULATION

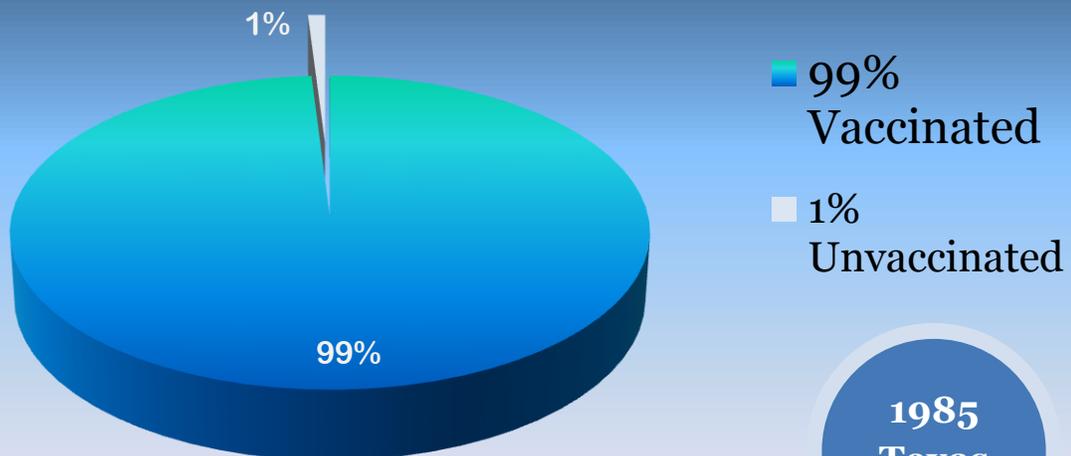


Source: N.Z. Miller; *Vaccine Safety Manual*,
N.A. Press, Sante Fe, New Mexico; p. 140; (2008)
(Refers to CDC & Official Surveillance data)



Figure 19

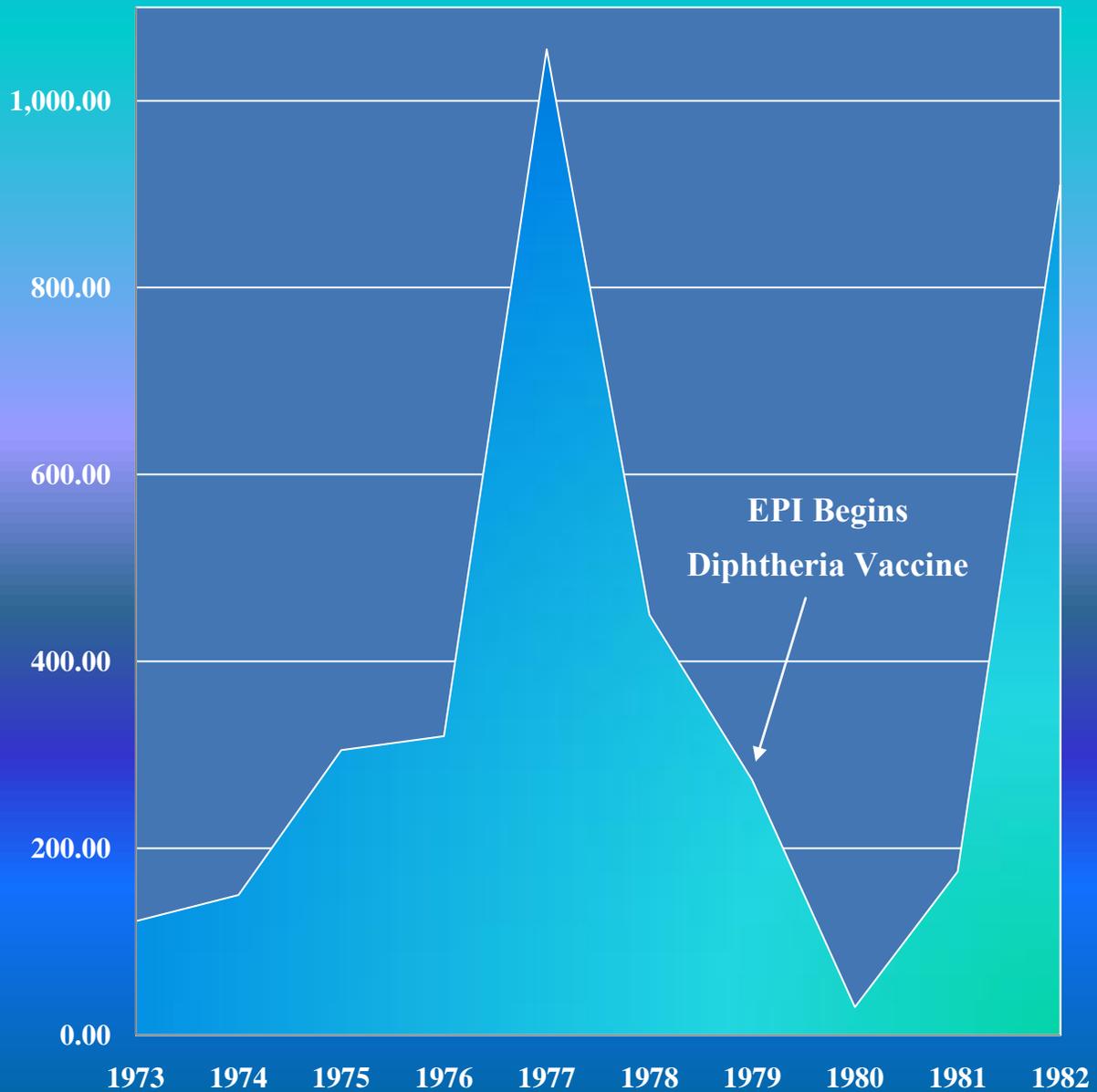
MEASLES OUTBREAK IN HIGHLY VACCINATED POPULATION



Source: *New England Journal of Medicine* -
Vol. 316; No. 13; pp. 771-774; (1987)

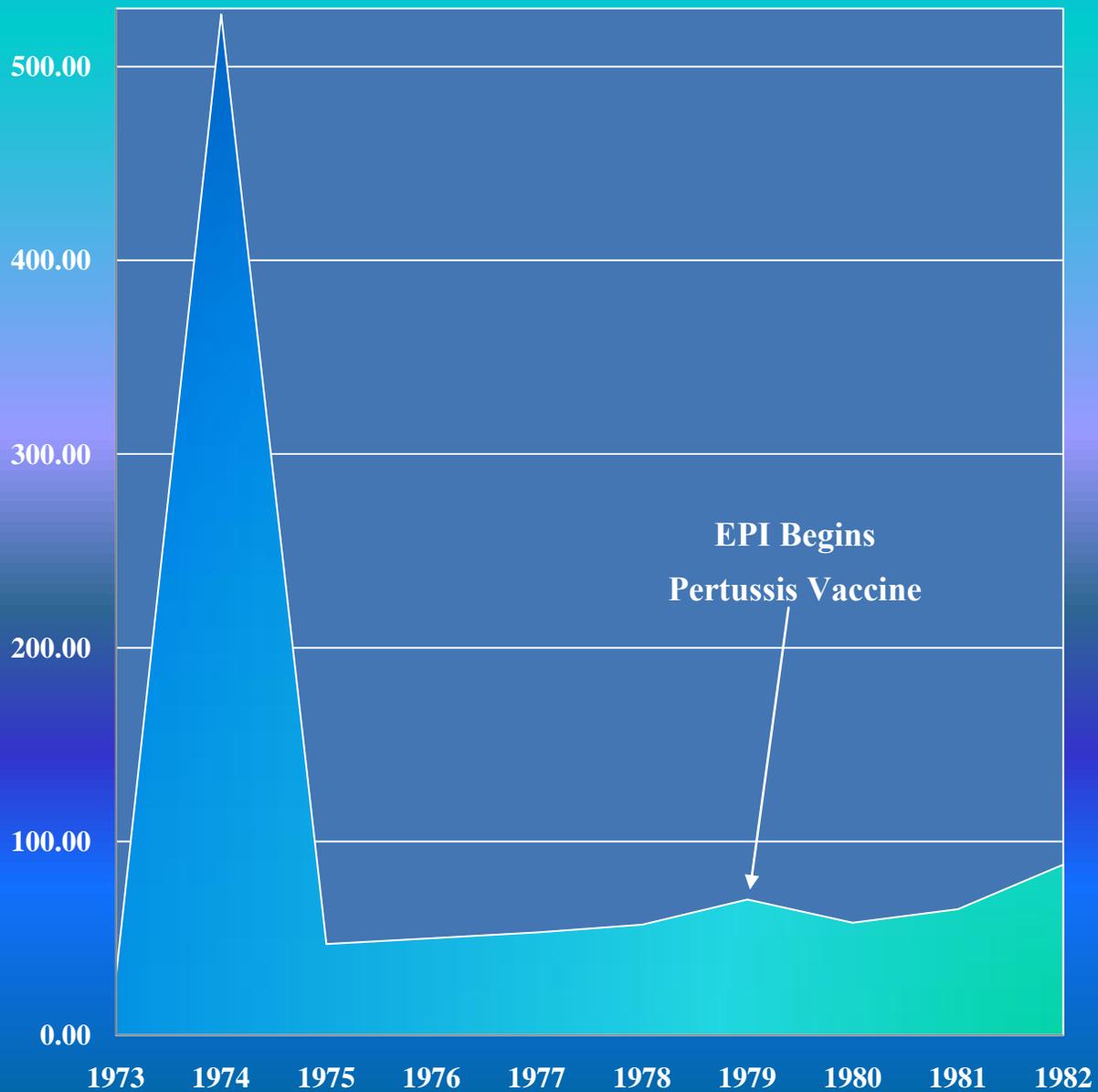


FIGURE 20 - NIGERIA
DIPHTHERIA REPORTED CASES
(1973-1982)



Source: E. Ekanem; A 10-Year Review of Morbidity from Childhood Preventable Diseases in Nigeria: How Successful is the Expanded Programme of Immunization (EPI)?; *Journal of Tropical Pediatrics*, Vol. 34; No. 6; UK; 1988; pp. 323-328.

FIGURE 21- NIGERIA
WHOOPIING COUGH CASE RATES PER 100,000
(1973-1982)



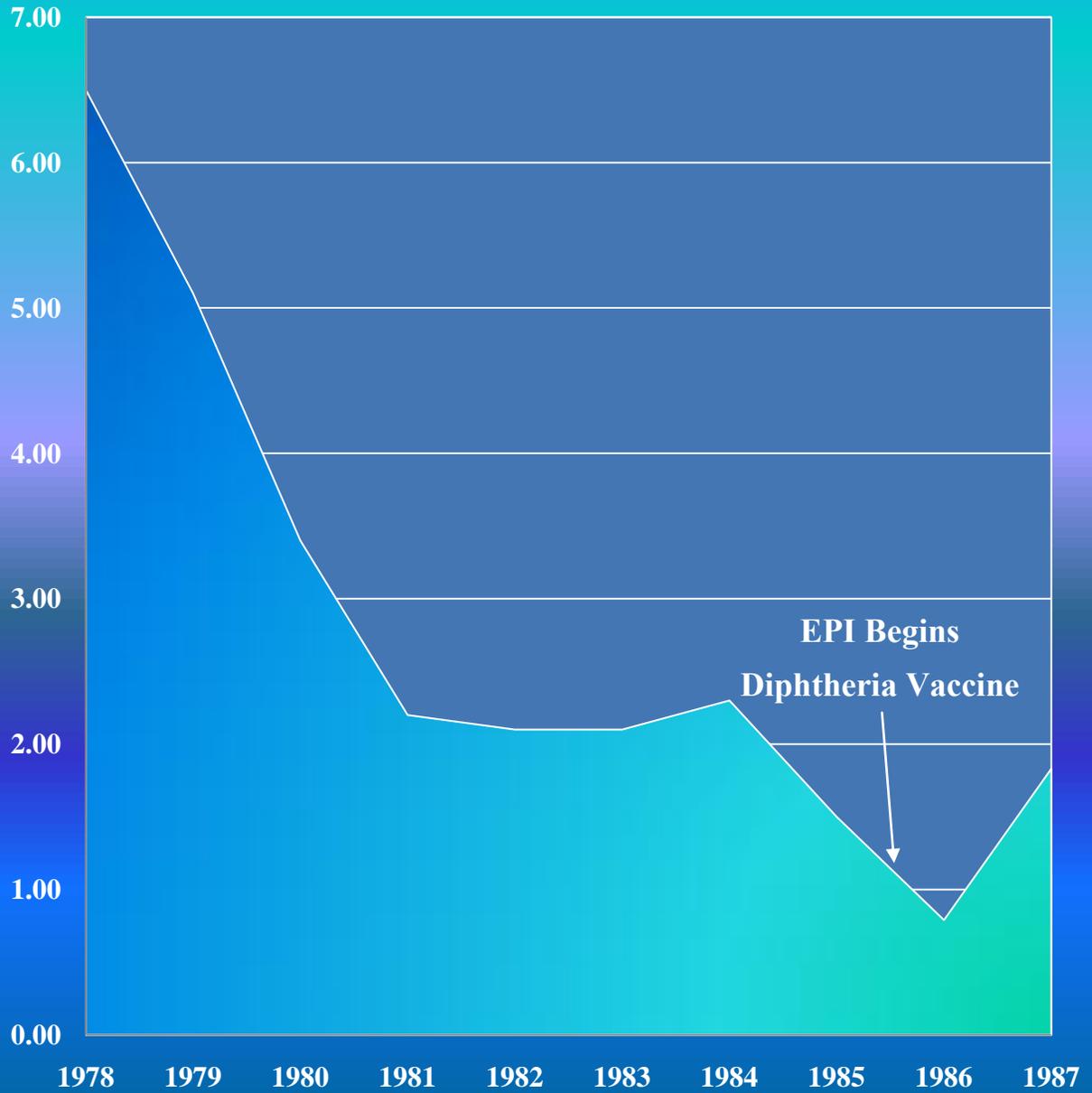
Source: E. Ekanem; A 10-Year Review of Morbidity from Childhood Preventable Diseases in Nigeria: How Successful is the Expanded Programme of Immunization (EPI)?; *Journal of Tropical Pediatrics*, Vol. 34; No. 6; UK; 1988; pp. 323-328.

**FIGURE 22 - DOMINICAN REPUBLIC
MEASLES CASE RATES PER 100,000
(1978-1989)**



Sources: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988; and Data for years 1988-1989 from personal communication from PAHO, EPI Unit, Aug. 21, 1990.

**FIGURE 23 - DOMINICAN REPUBLIC
DIPHTHERIA CASE RATES PER 100,000
(1978-1987)**



Source: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988.

**FIGURE 24 - DOMINICAN REPUBLIC
PERTUSSIS CASE RATES PER 100,000
(1978-1989)**



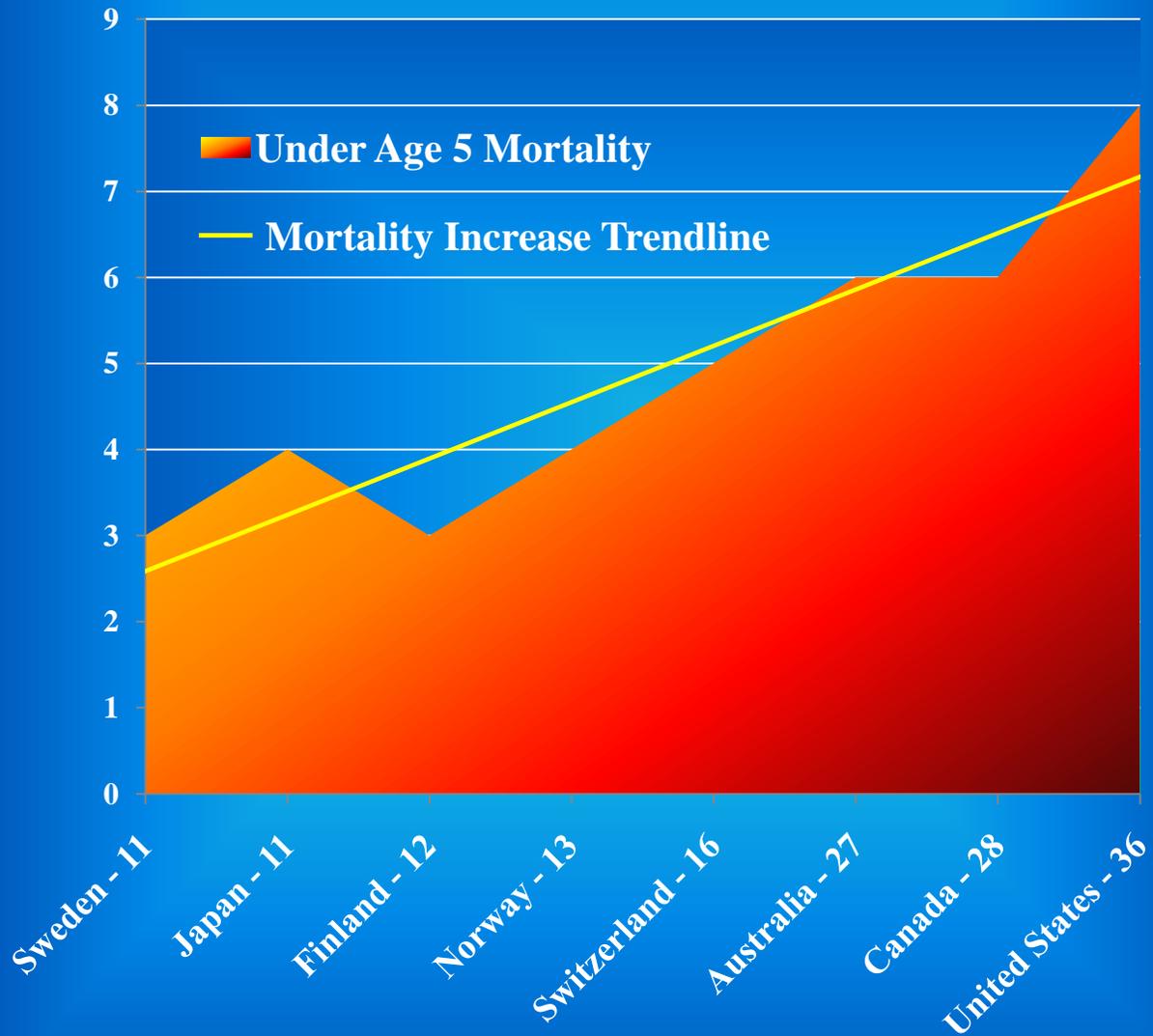
Sources: Data for years 1978-1987 Taken from UNICEF Evaluation Publication No. 6, Santo Domingo, Dominican Republic, May 27, 1988; and Data for years 1988-1989 from personal communication from PAHO, EPI Unit, Aug. 21, 1990.

FIGURE SET III.

Immunization Dangers

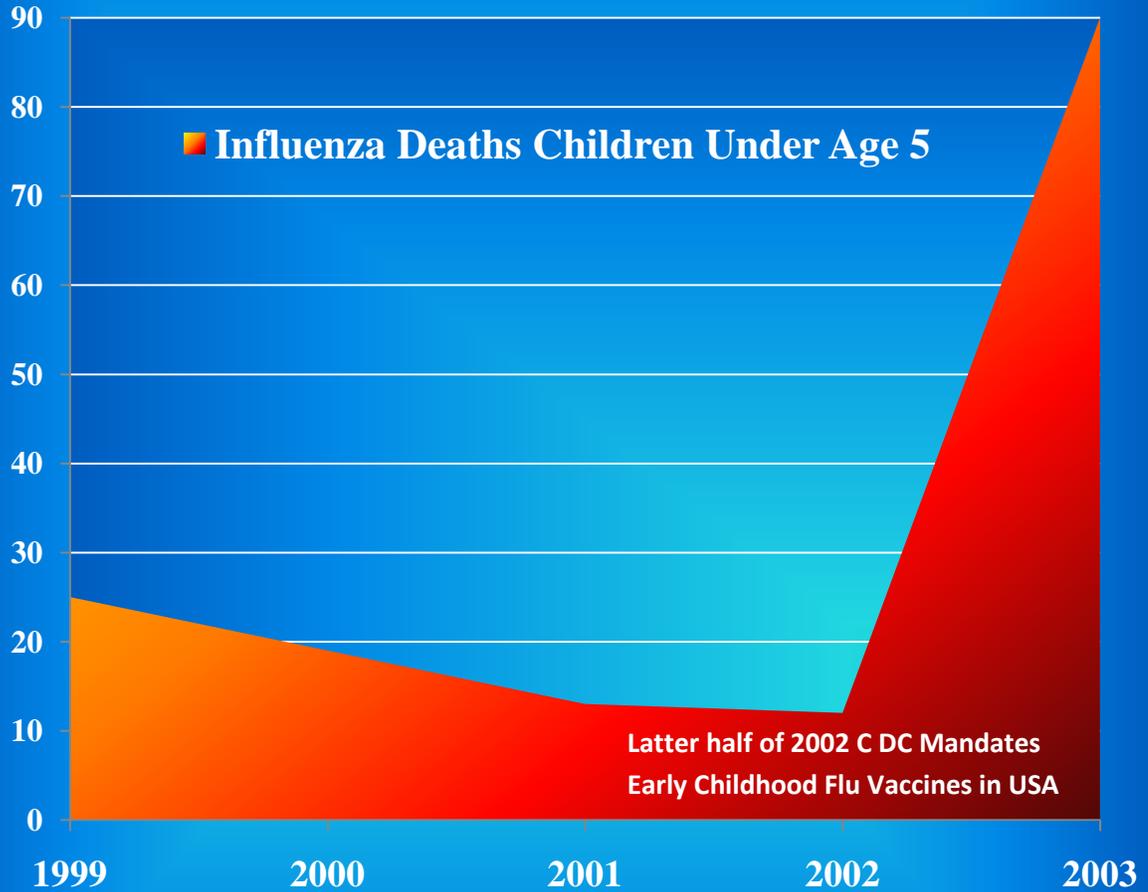
Figures twenty-five (25) through thirty three (33) graphically illustrate that increases in the number of governmental mandated vaccines correlates with significant increases in death rates for children under the age of five (5); and that the practice is linked to sudden infant death syndrome; various degenerative diseases, including diabetes; and appears to cause general immune system impairment in infants and children. Evidence also points to the practice of immunization as a principal factor in the recent massive increases in neurodegenerative conditions such as autism in children.

**FIGURE 25 - COUNTRIES & NUMBER
OF VACCINES MANDATED
UNDER AGE 5 MORTALITY RATES**



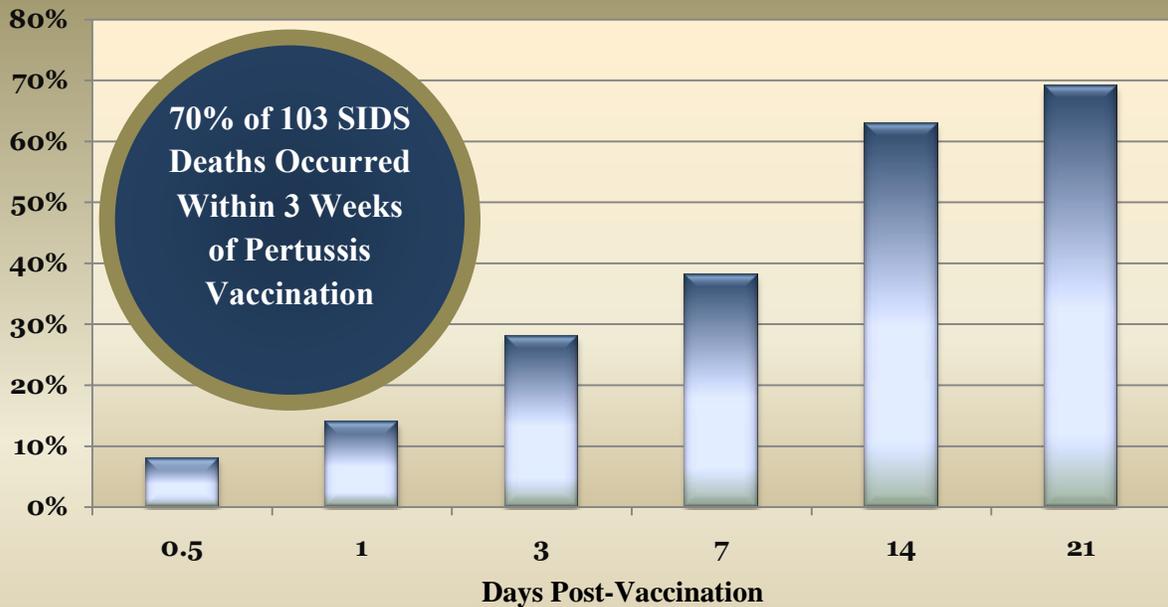
Under Age 5 Mortality statistics derived from: World Health Organization – World Health Statistics 2009 Report http://www.who.int/whosis/whostat/EN_WHS09_Table1.pdf
& Govt. Mandated Vaccines figures derived from: Generation Rescue Inc. 2009 <http://www.generationrescue.org/documents/SPECIAL%20REPORT%20AUTISM%202.pdf>

**FIGURE 26 - UNDER AGE 5 INFLUENZA DEATHS
BEFORE AND AFTER U.S. CDC MANDATES
FLU VACCINES IN EARLY CHILDHOOD**



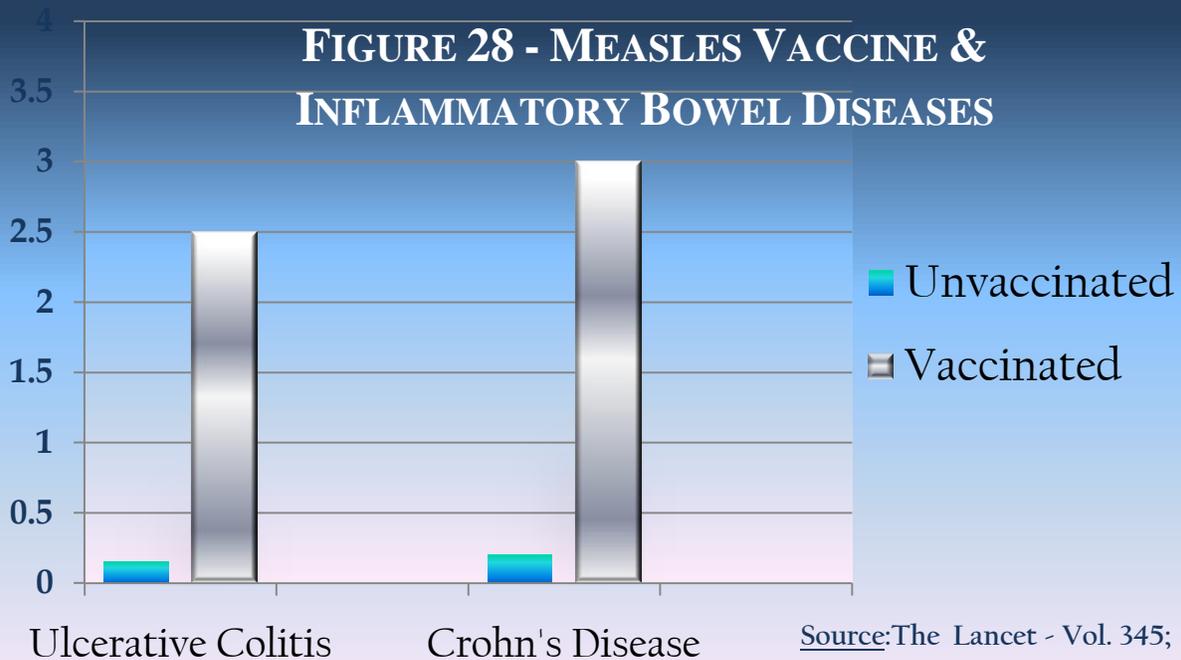
Under Age 5 Influenza Mortality statistics derived from: Center for Disease Control Vital Statistics Reports covering Years 1999-2003 reported in Miller, N.Z., Vaccine Safety Manual, New Atlantean Press, Sante Fe, New Mexico, 2008, p. 97.

FIGURE 27 - PERTUSSIS VACCINE & SUDDEN INFANT DEATH SYNDROME



2/3 of 103 infants had been vaccinated with pertussis prior to death which 6.5% within 12 hours; 13% within 24 hours; 26% within 3 days; 37%, 61% & 70% within 1, 2, & 3 weeks respectively. Source: Torch W., Neurology - 32 (4 - Pt. 2) A, 1982, pp. 169-170.

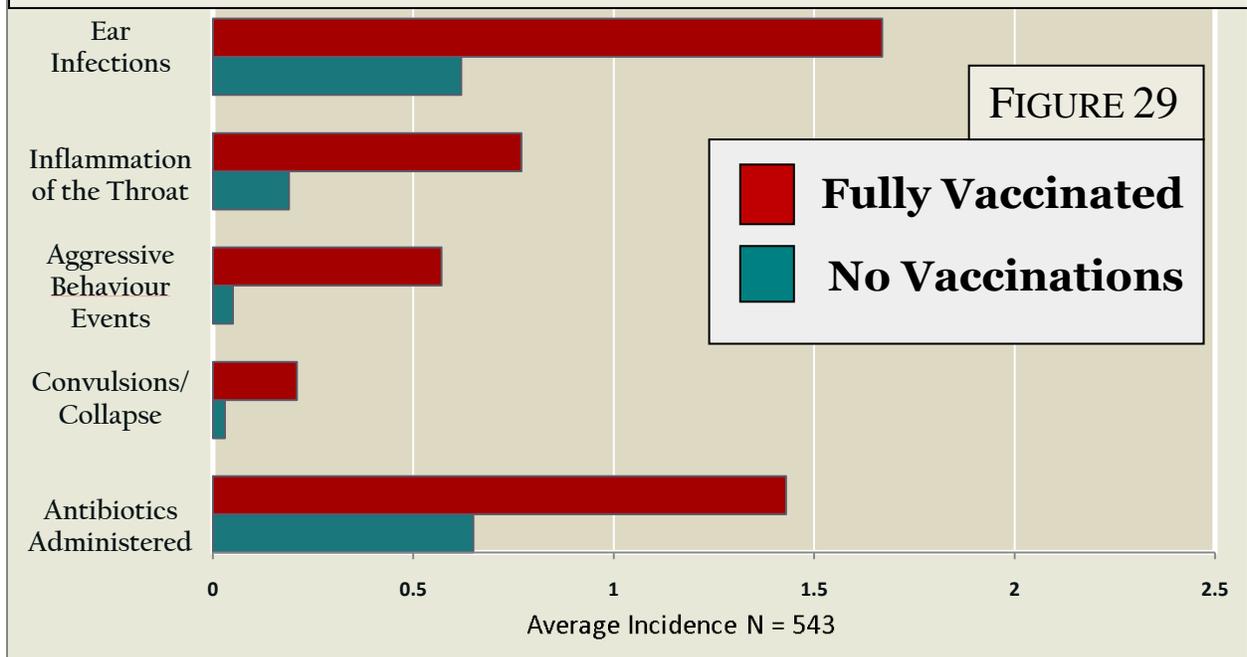
FIGURE 28 - MEASLES VACCINE & INFLAMMATORY BOWEL DISEASES



Source:The Lancet - Vol. 345; 8957; 1995, pp. 1062-1063.

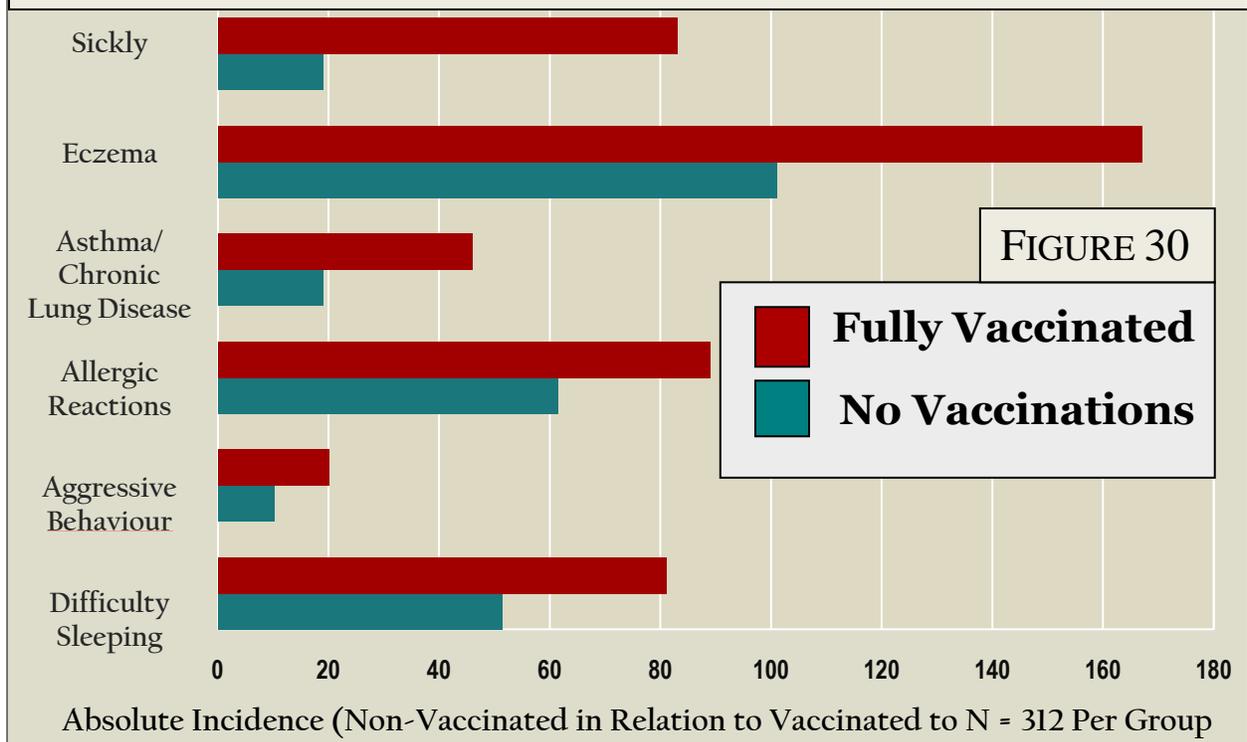
Average Incidence First Five (5) years of Life

Nederlands Vereniging Kritisch Prikken 2004 Survey Findings

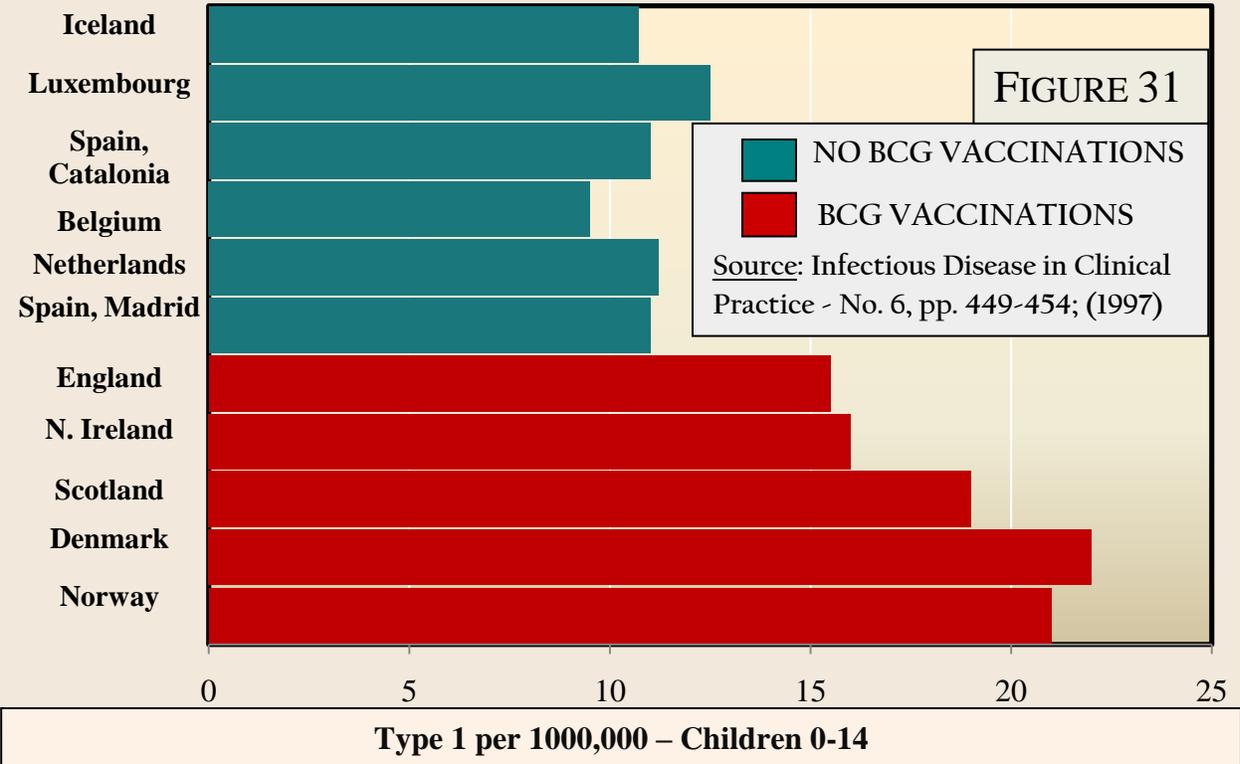


Absolute Incidence N=543

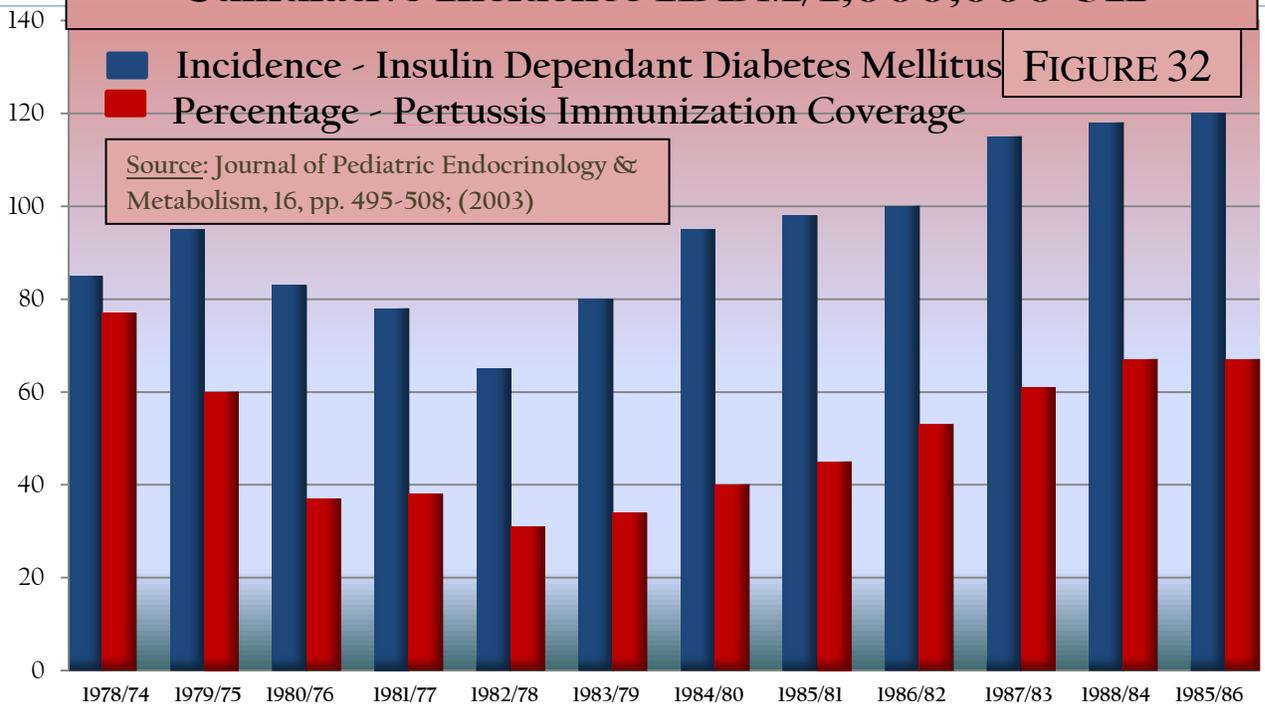
Nederlands Vereniging Kritisch Prikken 2004 Survey Findings



BCG Mandated in Schools & Diabetes Rates

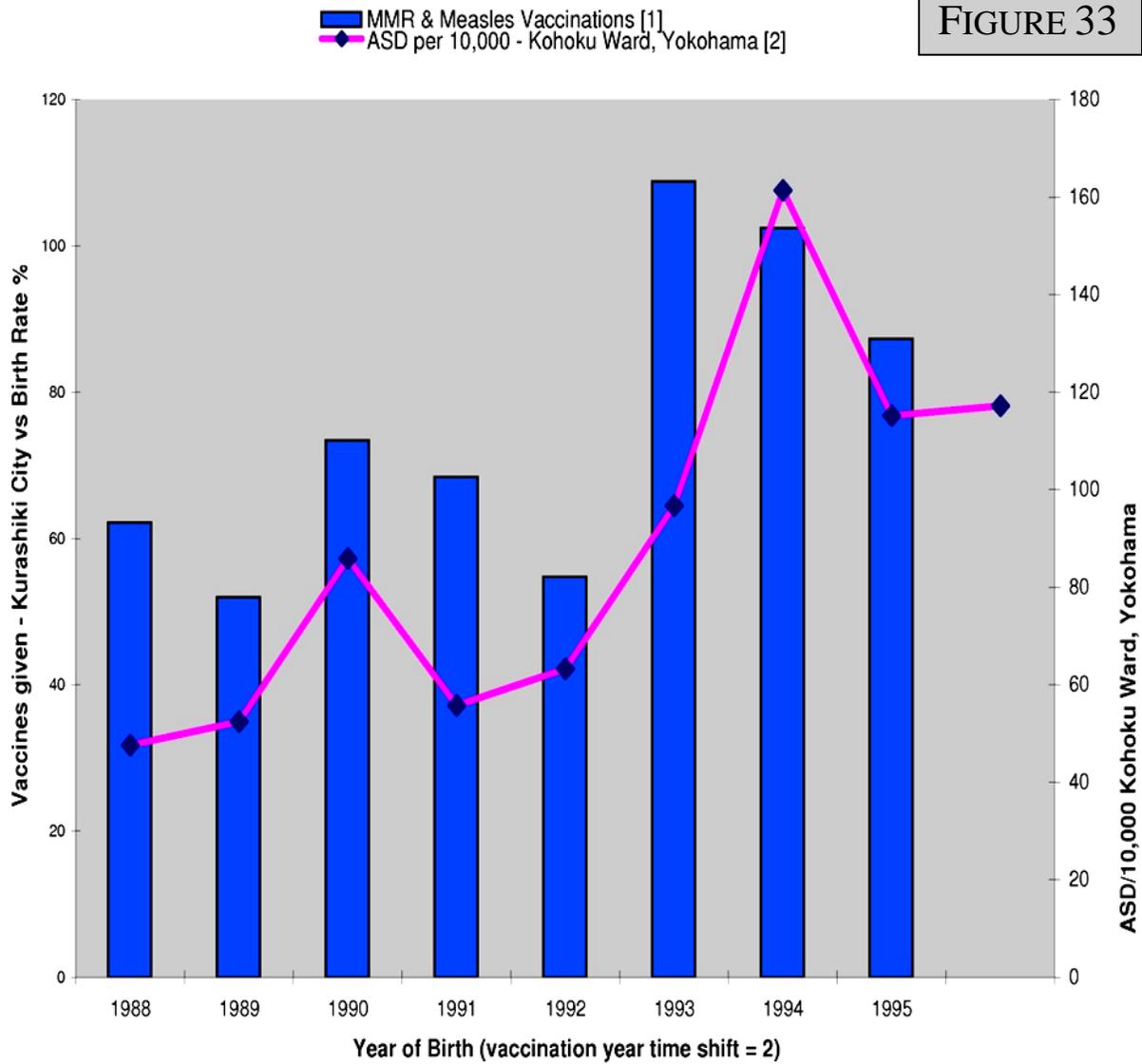


Cumulative Incidence IDDM/1,000,000 UK



Autism In Japan vs MMR & Measles Vaccination Uptake by birth cohort 1988 - 1996

FIGURE 33



<http://childhealthsafety.wordpress.com/2009/06/03/japvaxautism/> Figure based on: Kihei Terada et. al.; Alterations in epidemics and vaccination for measles during a 20 year period and a strategy for elimination in Kurashiki City, Japan; Kawasaki Medical School 2002 Mar; 76 (3):pp. 180-4. Correlated with: H. Honda et. al.; No effect of MMR withdrawal on the incidence of autism: a total population study; Journal of Child Psychology & Psychiatry; June 2005 (6); pp.572-579

Comparison of HPV prevalence between HPV-vaccinated and non-vaccinated young adult women (20–26 years)

Fangjian Guo, Jacqueline M Hirth, and Abbey B Berenson*

Department of Obstetrics & Gynecology; Center for Interdisciplinary Research in Women's Health; The University of Texas Medical Branch; Galveston, TX USA

Keywords: high-risk type, HPV vaccine, human papillomavirus (HPV), oncogenic virus, prevalence

Abbreviations: CDC, Centers for Disease Control and Prevention; CI, Confidence Interval; GED, General Education Development; HPV, Human Papillomavirus; MEC, Mobile Examination Center; NCHS, National Center for Health Statistics; NHANES, National Health and Nutrition Examination Survey.

There is some concern about the effectiveness of the HPV vaccine among young adult women due to the risk of prior HPV infection. This study used National Health and Nutrition Examination Survey (NHANES) 2007–2012 data to evaluate the effectiveness of HPV vaccination among women 20–26 years of age who were vaccinated after 12 years of age. This cross-sectional study examined 878 young adult women (20–26 years) with complete information on HPV prevalence and HPV vaccination status from NHANES 2007–2012. Vaginal swab specimens were analyzed for HPV DNA by L1 consensus polymerase chain reaction followed by type-specific hybridization. Multivariate logistic regression models controlling for sociodemographic characteristics and sexual behaviors were used to compare type-specific HPV prevalence between vaccinated and unvaccinated women. A total of 21.4% of young adult women surveyed through NHANES between 2007 and 2012 received the HPV vaccine. Vaccinated women had a lower prevalence of vaccine types than unvaccinated women (7.4% vs 17.1%, prevalence ratio 0.43, 95% CI 0.21–0.88). The prevalence of high-risk nonvaccine types was higher among vaccinated women than unvaccinated women (52.1% vs 40.4%, prevalence ratio 1.29, 95% CI 1.06–1.57), but this difference was attenuated after adjusting for sexual behavior variables (adjusted prevalence ratio 1.19, 95% CI 0.99–1.43). HPV vaccination was effective against all 4 vaccine types in young women vaccinated after age 12. However, vaccinated women had a higher prevalence of high-risk nonvaccine types, suggesting that they may benefit from newer vaccines covering additional types.

Introduction

It is estimated that over 80% of sexually active women in the US will acquire genital human papillomavirus (HPV) infection during their lifetime.¹ HPV is classified into low-risk types and high-risk types according to its oncogenic properties.^{2,3} In 2006, a quadrivalent vaccine, which prevents 2 low-risk (6, 11) and 2 high-risk (16, 18) types^{4–9} was approved for use in the US. Following its approval, the Advisory Committee on Immunization Practices recommended routine vaccination with 3 doses of this vaccine for all females aged 11 to 12 years, and catch-up vaccination up to age 26.¹⁰ To determine its effectiveness in a real world setting, however, post-licensure evaluation of the HPV vaccine is needed.¹¹

Although population studies have shown a decrease in vaccine-type HPV prevalence among young girls since the vaccine was introduced,¹² its effectiveness among women who received it after 12 years of age still needs to be determined. This is relevant because those vaccinated after the recommended age of 11–12 years may not have as strong of an immune response as

younger girls.¹³ Furthermore, women who have already engaged in sexual activity are more likely to have already been exposed to HPV,¹⁴ and the vaccine cannot eradicate prior infections.¹⁵ In fact, data from NHANES showed that 33% of 14–19 year olds and 60% of US women aged 20 to 24 years had current genital HPV infections.^{14,16} Finally, since the vaccine was initially targeted for 11–12 year old girls, the focus of surveillance efforts to date have been on younger adolescents, making it difficult to study its effectiveness among those who received the HPV vaccine as older adolescents or young adults in the general population. The purpose of this study was to compare type-specific HPV prevalence between vaccinated and unvaccinated young adult women using data from NHANES 2007–2012.

Results

A total of 177 vaccinated and 701 unvaccinated young women (20–26 years) were included in these analyses. Mean age was

*Correspondence to: Abbey B Berenson; Email: abberens@utmb.edu
Submitted: 04/22/2015; Revised: 06/05/2015; Accepted: 06/24/2015
<http://dx.doi.org/10.1080/21645515.2015.1066948>

22.4 years in vaccinated women and 23.1 years in unvaccinated women. Overall, 21.4% of the sample received at least one dose of the HPV vaccine (Table 1). HPV vaccination rate was lower in married women and those who did not finish high school. Vaccinated women and unvaccinated women had similar sexual behaviors, including ≥ 2 sexual partners in the past 12 months and ≥ 3 lifetime number of sexual partners, and sexually transmitted diseases.

Prevalence of individual human papillomavirus (HPV) types among young adult women (20–26 years) by vaccination status is presented in Figure 1. The prevalence of low-risk vaccine types (HPV 6 or 11) among vaccinated women was lower than unvaccinated women (0.3% vs 4.4%, $p < 0.001$; Table 2). The prevalence of high-risk (16 or 18) vaccine types was also lower among vaccinated women than unvaccinated women, although it did not reach statistical significance in the unadjusted model. After adjusting for sexual behavior variables (sexually transmitted diseases, number of lifetime sexual partners, and number of sexual partners in the past 12 months), the prevalence of high-risk vaccine types was lower in vaccinated women (adjusted prevalence ratio 0.46, 95% CI 0.22–0.98). Overall, vaccinated women had

a lower prevalence of vaccine types (HPV 6, 11, 16, or 18) than unvaccinated women (7.4% vs 17.1%, prevalence ratio 0.43, 95% CI 0.21–0.88).

In contrast, no difference was observed in the prevalence of low-risk nonvaccine types between vaccinated and unvaccinated women (38.8% vs 37.5%). However, vaccinated women had a markedly higher prevalence of high-risk nonvaccine types (52.1% vs 40.4, prevalence ratio 1.29, 95% CI 1.06–1.57). When further adjusted for sexual behavior variables in Model 2, the difference in prevalence of high-risk nonvaccine types between vaccinated and unvaccinated women was attenuated (adjusted prevalence ratio in Model 2 1.19, 95% CI 0.99–1.43).

When characteristics associated with HPV prevalence were examined, it was found that being unmarried, with a high school education, an income under the poverty level, a history of sexually transmitted infections, ≥ 3 lifetime sexual partners and ≥ 2 sexual partners in the past 12 months were associated with a lower prevalence of vaccine types among vaccinated women than unvaccinated women (Table 3). We also evaluated characteristics associated with high-risk nonvaccine HPV between vaccinated and unvaccinated women (Table 4). A difference in the

Table 1. Sociodemographic characteristics of US young adult women by vaccination status (N = 878)

	N (%) ^a		p Value ^b	Vaccination Rate % (95% CI)
	Vaccinated	Unvaccinated		
Total	177 (100)	701 (100)		21.4 (17.3–25.4)
Race/Ethnicity			0.007	
Non-Hispanic White	70 (66.0)	235 (55.6)		24.4 (18.4–30.4)
Non-Hispanic Black	48 (13.8)	169 (15.2)		19.7 (13.9–25.5)
Mexican American	12 (3.9)	149 (12.8)		7.7 (3.1–12.3)
Other	47 (16.3)	148 (16.3)		21.3 (14.4–28.2)
Marital Status			0.001	
Unmarried	144 (79.0)	432 (59.6)		26.5 (21.1–31.9)
Married	33 (21.0)	269 (40.4)		12.4 (7.5–17.3)
Education Level			0.005	
< High School	17 (6.7)	126 (14.2)		11.5 (5.1–17.8)
High School	25 (12.5)	171 (22.7)		13.0 (6.8–19.3)
> High School	135 (80.8)	404 (63.1)		25.8 (20.3–31.3)
Poverty Income Ratio			0.45	
≥ 1	109 (69.8)	398 (64.4)		22.7 (17.8–27.7)
< 1	56 (26.7)	244 (29.5)		19.7 (12.8–26.7)
Missing	12	59		
Smoking Status			0.47	
Never	134 (71.9)	495 (69.6)		21.9 (16.1–27.8)
Past	15 (11.3)	46 (8.2)		27.2 (14.3–40.2)
Current	28 (16.8)	160 (22.2)		17.0 (8.5–25.6)
Sexually Transmitted Infection		0.58		
No	141 (80.2)	560 (82.4)		20.9 (16.2–25.6)
Yes	36 (19.8)	141 (17.6)		23.5 (15.8–31.1)
Lifetime Sex Partners			0.39	
≤ 2	59 (30.9)	271 (35.4)		19.2 (13.3–25.0)
≥ 3	118 (69.1)	430 (64.6)		22.5 (17.3–27.7)
Sex Partners in the Past 12 Months		0.23		
≤ 1	118 (67.5)	518 (73.8)		19.9 (15.2–24.6)
≥ 2	59 (32.5)	183 (26.2)		25.2 (17.7–32.7)

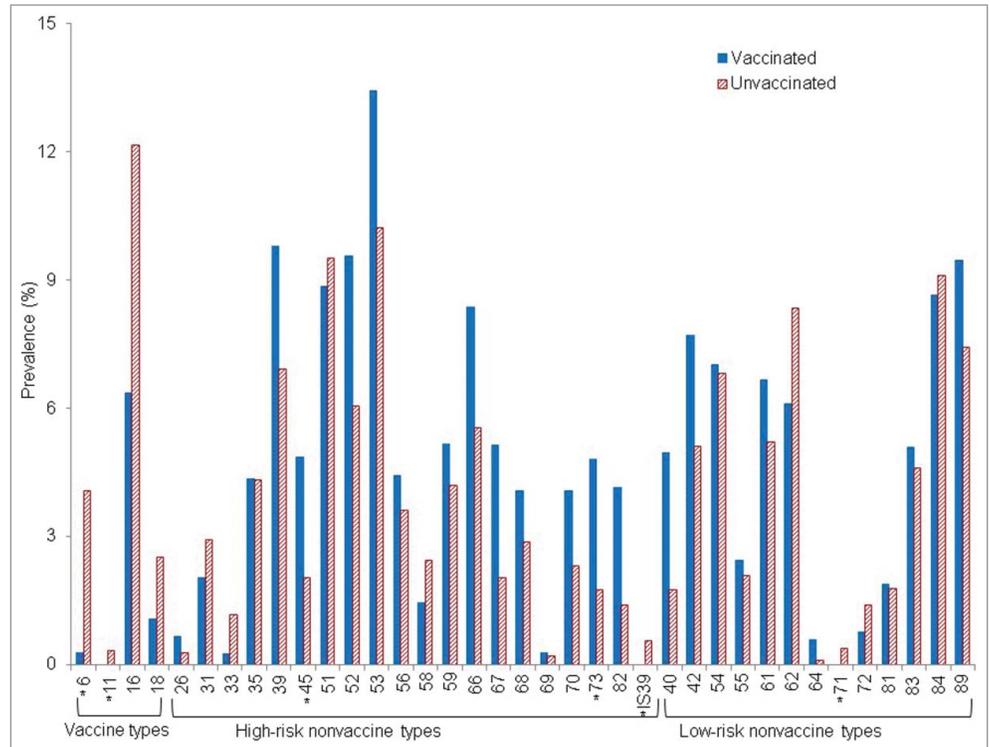
CI: confidence interval.

^aSample weights were used to calculate weighted percentages.

^bp value was derived from Wald χ^2 test.

prevalence of high-risk nonvaccine types was observed in non-Hispanic Whites, non-Hispanic Blacks, women with a college education, women living above the poverty level, past smokers, women with no prior sexually transmitted infections, and women with ≥ 3 lifetime sexual partners.

We found that among vaccinated women, 19.2% received one dose of the HPV vaccine, 25.1% received 2 doses, and 55.7% completed all 3 doses. Those who received ≥ 2 doses of the HPV vaccine had a lower, although not statistically significant, prevalence of vaccine type HPV compared to women who only received one dose (6.5% vs 11.3%, adjusted prevalence ratio 0.59, 95% CI 0.19–1.91).



Discussion

Using data from a nationally-representative survey conducted over 6 years, we found that young adult women who had received the vaccine after 12 years of age had a reduced prevalence of all 4 vaccine-type infections compared to their unvaccinated peers. This is consistent with data from clinical trials, which showed that the quadrivalent HPV vaccine has over 90% efficacy against vaccine type infections.^{4–8} These findings demonstrate that even though young girls may have a better immunological response to the HPV vaccine, it is still highly

effective when given at older ages. This may be because protection of the vaccine is provided through the production of serum neutralizing anti-HPV IgG antibodies binding to viral particles,^{17–19} which only requires small amounts of antibody to be present.^{20,21}

One interesting finding was that vaccinated young adult women had a higher prevalence than unvaccinated women of

Figure 1. Prevalence of individual human papillomavirus (HPV) types among young adult women (20–26 years) by vaccination status. Prevalence was weighted using sample weights. * Statistical significance for the comparison between vaccinated women and unvaccinated women, after adjusted for age, race/ethnicity, education, income, smoking status, sexually transmitted infections, number of lifetime sexual partners, and number of sexual partners in the past 12 months.

Table 2. Type-specific HPV prevalence among US adult women by HPV vaccination status

	Prevalence (95% CI) ^a			Adjusted Prevalence Ratio (95% CI) Vaccinated vs. Unvaccinated	
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Prevalence Ratio (95% CI)	Model 1 ^b	Model 2 ^c
Any HPV Type	63.3 (55.2–71.4)	54.9 (50.0–59.8)	1.15 (0.99–1.34)	1.15 (0.98–1.34)	1.11 (0.96–1.29)
Low-Risk Type	39.1 (31.1–47.2)	39.3 (33.7–45.0)	0.99 (0.78–1.27)	0.97 (0.76–1.24)	0.93 (0.74–1.18)
High-Risk Type	53.4 (43.8–63.0)	44.4 (39.6–49.1)	1.20 (0.99–1.46)	1.15 (0.95–1.40)	1.11 (0.93–1.33)
HPV 6, 11, 16 or 18	7.4 (2.1–12.7)	17.1 (13.9–20.3)	0.43 (0.21–0.88)	0.41 (0.21–0.84)	0.41 (0.20–0.82)
HPV 6 or 11	0.3 (0.0–0.8)	4.4 (2.8–6.0)	0.07 (0.01–0.45)	0.07 (0.01–0.55)	0.07 (0.01–0.54)
HPV 16 or 18	7.1 (1.7–12.5)	13.9 (10.9–17.0)	0.51 (0.24–1.10)	0.47 (0.22–1.00)	0.46 (0.22–0.98)
Nonvaccine Type	62.4 (54.3–70.5)	52.8 (47.8–57.8)	1.18 (1.02–1.37)	1.17 (1.00–1.37)	1.14 (0.99–1.31)
Nonvaccine Low-Risk Type	38.8 (30.8–46.9)	37.5 (31.8–43.2)	1.04 (0.80–1.34)	1.00 (0.77–1.30)	0.96 (0.75–1.23)
Nonvaccine High-Risk Type	52.1 (42.5–61.8)	40.4 (35.9–44.9)	1.29 (1.06–1.57)	1.23 (1.02–1.50)	1.19 (0.99–1.43)

CI: confidence interval.

^aPrevalence was weighted using sample weights.

^bModel 1 was adjusted for age, race/ethnicity, education, income, smoking status, and marital status.

^cModel 2 was adjusted for variables in Model 1 plus sexually transmitted diseases and number of lifetime sexual partners, and number of sexual partners in the past 12 months.

Table 3. Prevalence of HPV vaccine types among US adult women by HPV vaccination status and sociodemographic characteristics (N = 878)

	Prevalence (95% CI) ^a		Prevalence Ratio (95% CI)
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Vaccinated vs. Unvaccinated
Total	7.4 (2.1–12.7)	17.1 (13.9–20.3)	0.43(0.21–0.88)
Race/Ethnicity			
Non-Hispanic White	7.2 (0.0–15.0)	15.7 (11.4–20.0)	0.46(0.16–1.33)
Non-Hispanic Black	8.9 (0.5–17.3)	21.5 (14.0–29.0)	0.41(0.16–1.08)
Mexican American	4.5 (0.0–13.9)	10.8 (3.4–18.2)	0.42(0.05–3.46)
Other	7.5 (0.3–14.7)	22.5 (13.2–31.9)	0.33(0.12–0.95)
Marital Status			
Unmarried	8.0 (1.1–15.0)	20.1 (16.1–24.2)	0.40(0.17–0.94)
Married	4.9 (0.0–10.2)	12.6 (7.7–17.4)	0.39(0.13–1.19)
Education Level			
< High School	5.1 (0.0–15.4)	19.6 (10.9–28.2)	0.26(0.04–1.58)
High School	6.8 (0.0–14.7)	21.8 (12.6–31.0)	0.31(0.10–0.97)
> High School	7.7 (1.1–14.2)	14.8 (11.1–18.6)	0.52(0.21–1.27)
Poverty Income Ratio			
≥1	8.0 (0.7–15.2)	15.2 (10.7–19.6)	0.53(0.21–1.34)
<1	3.2 (0.0–7.2)	20.0 (13.7–26.2)	0.16(0.04–0.58)
Smoking Status			
Never	7.1 (1.0–13.2)	15.4 (11.5–19.2)	0.46(0.19–1.11)
Past	5.5 (0.0–13.0)	19.9 (5.3–34.4)	0.28(0.05–1.52)
Current	9.8 (0.0–27.3)	21.4 (14.5–28.3)	0.46(0.08–2.59)
Sexually Transmitted Infections			
No	8.8 (2.2–15.4)	15.4 (11.7–19.0)	0.57(0.27–1.21)
Yes	1.8 (0.0–5.3)	25.0 (17.4–32.6)	0.07(0.01–0.51)
Lifetime Sex Partners			
≤2	6.0 (0.0–13.4)	6.5 (3.2–9.7)	0.93(0.25–3.43)
≥3	8.0 (1.2–14.8)	22.9 (18.4–27.4)	0.35(0.15–0.82)
Sex Partners in the Past 12 Months			
≤1	7.3 (1.1–13.5)	11.7 (8.5–14.9)	0.63(0.27–1.47)
≥2	7.5 (0.0–17.3)	32.3 (24.8–39.8)	0.23(0.06–0.84)

CI: confidence interval.

^aPrevalence was estimated for the prevalence of vaccine types (HPV 6, 11, 16 or 18). Prevalence was weighted using sample weights.

high-risk types other than HPV 16 and 18, and thus are still at risk of cervical cancer and other HPV-related cancers. This is consistent with clinical trials on the quadrivalent vaccine which showed it provided some protection against HPV 31 and 59, but not other types.²² Thus, the limitations of the HPV vaccine should be discussed with all patients, so they understand the need to obtain regular cervical cancer screening after vaccination as recommended for their age group. The underlying causes for the increased prevalence of high-risk nonvaccine types we observed among vaccinated women cannot be determined from these data. However, we found that the association between vaccination and differences in prevalence of high-risk nonvaccine type infections was attenuated after adjusting for sexual behavior variables. Thus, it is possible that women who engaged in risky sexual behaviors were more likely to seek vaccination in the early years after its introduction. To reduce the increased prevalence of high-risk nonvaccine types, the 9-valent HPV vaccine may provide a practical solution. The 9-valent HPV vaccine which provides protection against the original 4 vaccine types (6, 11, 16, and 18) and 5 additional high-risk types (31, 33, 45, 52, and 58) has recently been approved by the Food and Drug Administration.²³ This new vaccine should help to reduce the increased

prevalence of several of the high-risk types we observed among women in the future.

Our results showed that young women who received one dose of the vaccine had a higher prevalence of vaccine type HPV infection compared to those who had at least 2 doses. This suggests that 1 dose may not be as protective in this age group. Our results for this finding were non-significant, but that may have been due to inadequate power. While it has been found that age impacts the type and level of the immune response to the HPV vaccine, it is generally agreed upon that at least 2 doses are needed to achieve a high level of immunity across time.^{13,24} In prior studies, young women who received 3 doses of the HPV vaccine (at 15 years of age or older) showed clinically significant levels of immunogenicity up to 6 years after administration.²⁵ Further, girls (9–13 years old) who received 3 doses were more likely to continue to have an immune response 36 months after vaccination compared to young women (16–26 years old) who received 3 doses, which may indicate that 3 doses is necessary among older adolescents and young adults. However, it is unknown what clinical threshold of immune response is needed to be effective. Therefore, the currently evolving guidelines issued by the World

Table 4. Prevalence of nonvaccine high-risk types among US adult women by characteristics and HPV vaccination status

	Prevalence (95% CI) ^a		Prevalence Ratio (95% CI)
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Vaccinated vs. Unvaccinated
All	52.1 (42.5–61.8)	40.4 (35.9–44.9)	1.29(1.06–1.57)
Race/Ethnicity			
Non-Hispanic White	55.2 (41.6–68.8)	39.4 (32.9–45.9)	1.40(1.05–1.86)
Non-Hispanic Black	67.6 (54.8–80.4)	50.5 (43.8–57.3)	1.34(1.10–1.63)
Mexican American	39.5 (8.8–70.1)	33.2 (26.0–40.4)	1.19(0.52–2.71)
Other	29.5 (16.2–42.7)	40.0 (30.7–49.4)	0.74(0.46–1.18)
Marital Status			
Unmarried	55.1 (46.1–64.2)	45.8 (40.3–51.4)	1.20(0.99–1.46)
Married	40.8 (20.9–60.7)	32.4 (25.4–39.3)	1.26(0.79–2.02)
Education Level			
< High School	62.3 (33.0–91.6)	46.0 (36.5–55.4)	1.36(0.85–2.17)
High School	36.2 (12.6–59.9)	43.1 (34.3–52.0)	0.84(0.43–1.66)
> High School	53.7 (42.3–65.2)	38.2 (31.6–44.7)	1.41(1.11–1.78)
Poverty Income Ratio			
≥1	49.4 (37.3–61.5)	37.2 (30.6–43.7)	1.33(1.00–1.76)
<1	56.4 (43.9–68.9)	46.4 (39.0–53.8)	1.22(0.95–1.56)
Smoking Status			
Never	45.4 (32.8–58.1)	36.2 (31.1–41.3)	1.26(0.95–1.67)
Past	83.8 (69.6–98.1)	43.4 (28.5–58.2)	1.93(1.29–2.90)
Current	59.4 (36.3–82.5)	52.6 (42.2–63.0)	1.13(0.73–1.75)
Sexually Transmitted Infections			
No	47.3 (37.2–57.4)	35.5 (31.1–39.8)	1.33(1.08–1.65)
Yes	71.6 (52.6–90.7)	63.6 (53.8–73.3)	1.13(0.82–1.54)
Lifetime Sex Partners			
≤2	25.8 (13.3–38.4)	22.4 (15.7–29.0)	1.15(0.68–1.96)
≥3	63.9 (51.9–75.8)	50.3 (44.9–55.7)	1.27(1.04–1.55)
Sex Partners in the Past 12 Months			
≤1	41.1 (30.2–52.1)	31.7 (26.7–36.7)	1.30(0.98–1.72)
≥2	74.9 (62.1–87.7)	64.9 (56.0–73.9)	1.15(0.93–1.43)

CI: confidence interval.

^aPrevalence was estimated for high-risk nonvaccine types. Prevalence was weighted using sample weights.

Health Organization (WHO) still recommend 3 doses of the HPV vaccine when administered to young adult women.²⁶

The strengths of our study included use of data from a large, nationally representative sample with high response rates. However, our study has several limitations. First, our sample size was not large enough to assess the efficacy of HPV vaccine in racial or sociodemographic subgroups. Second, the history of HPV vaccination was self-reported and may be subject to response bias. The possible overreporting or underreporting may bias our analyses and estimate of vaccine effectiveness. In addition, the information on the exact age at vaccination was not available in NHANES. However, we only included young women between 20 and 26 years of age from NHANES 2008–2012. Since the HPV vaccine was approved by the Food and Drug Administration (FDA) in the United States in 2006, it is unlikely that any of these women were vaccinated before 14 years of age. Although they may not have as high immunological response to the HPV vaccine as younger girls (11–12 years of age),¹³ women between 14 and 26 years still seroconvert at a high rate and are protected against vaccine type infections and related diseases.^{4–9} Finally, due to the cross-sectional nature of our study, we were not able to determine causation. NHANES is a cross sectional survey, so

the temporal relationship between HPV vaccination, HPV infection, and sexual behavior could not be determined.

In conclusion, HPV vaccination was protective against all 4 vaccine types even when vaccination occurred after the recommended age of 11–12 years. However, vaccinated young women had a higher prevalence of high-risk nonvaccine types. Thus, it is important to advise all women to undergo regular cervical cancer screening, as they may still be at risk of acquiring high-risk HPV infections.

Materials and Methods

NHANES is a cross-sectional survey conducted by the National Center for Health Statistics (NCHS), using a complex, stratified, multistage probability sample to represent the civilian, non-institutionalized, US population. The study was approved by the NCHS Institutional Review Board, and all adult participants provided written informed consent. Details about NHANES can be found elsewhere.²⁷ Our study included young adult women (20–26 years) with complete information on HPV vaccination status from NHANES 2007–2012. Since the vaccine

was first approved for use in 2006, all women in this age range would have received the vaccine after 12 years of age. This age group was selected because few data are available on those vaccinated after the recommended age of 11–12 years. Furthermore, this age group has a high prevalence of HPV infection.

In 2007–2012, 1061 young adult women were interviewed, of which 1030 had completed information on HPV vaccination status. Of those, 1004 received an examination in a mobile examination center (MEC) and 886 submitted a self-collected cervicovaginal swab specimen. A total of 878 specimens were adequate for HPV DNA typing. In our study, we excluded those without adequate cervicovaginal samples.

Demographic information was collected during the household interview. Race/ethnicity was self-reported and categorized as non-Hispanic White, non-Hispanic Black, Mexican Americans, and others. We collapsed marital status into the 2 categories of married (married, or living with partner) and unmarried (widowed/divorced/separated, and single), as it is documented that widowed/divorced/separated women and single women had a much higher prevalence of HPV infection than married women.¹⁶ Education level was categorized as less than high school (9–11th grade, includes 12th grade with no diploma), high school (high school graduate/General Education Development (GED) or equivalent), and greater than a high school education (college or above). Poverty income ratio was calculated by the NCHS according to the US Census definition by dividing total family income by the poverty threshold after adjusting for family size at the time of the interview. We classified poverty income ratio into 2 categories: ≤ 1 (under poverty) and > 1 (above poverty). Smoking status was classified into 3 categories: never (< 100 cigarettes in life), past (smoked at least 100 cigarettes in life, but not currently smoking cigarettes), and current (smoked at least 100 cigarettes in life and currently smoking cigarettes).

Sexual history was self-reported using an audio computer-assisted self-interview in MEC. Respondents who reported ever having sex (described as vaginal, oral, or anal) were asked additional questions, including lifetime number of partners and number of partners in the past 12 months. We classified number of sexual partners in their lifetime into 2 categories - ≥ 3 and ≤ 2 , and number of sexual partners in the past 12 months into 2 categories - ≥ 2 and ≤ 1 , as it has been reported that women with ≥ 3 lifetime sexual partners or ≥ 2 sexual partners in the past 12 months have a higher HPV prevalence than women with fewer sexual partners.¹⁶

Respondents who reported that a physician had ever told them they had a sexually transmitted infection were considered to have a history of a sexually transmitted infection. Reports of the following sexually transmitted infections were included: genital herpes, chlamydia, and gonorrhea. Young women who were tested positive for serum antibody to herpes simplex virus type 2, serum human immunodeficiency virus (HIV) antibody, or urine chlamydia were also considered to have a history of sexually transmitted infection. Cases of genital warts were not included because they are caused by HPV infection.

History of HPV vaccination was obtained by self-report. HPV infection was determined by the detection of HPV DNA in self-collected vaginal swabs. Extractions and testing on vaginal swab specimens were performed at the Centers for Disease Control and Prevention (CDC), with details described elsewhere.^{14,28} Briefly, vaginal swabs were analyzed for HPV DNA by L1 consensus polymerase chain reaction followed by type-specific hybridization. All specimens were hybridized to the typing strip that included probes for 37 HPV types, including high-risk types (16, 18, 31, 33, 35, 52, 58, 39, 45, 59, 68, 51, 56, 66, 26, 53, 67, 69, 70, 73, 82, and IS39) that can cause cancer and low-risk types (6, 11, 40, 42, 54, 55, 61, 62, 64, 71, 72, 81, 83, 84, and 89). The sample was considered inadequate if no β -globin was present in the sample and no HPV type was detected.

Statistical Analysis

Statistical analyses were carried out with SAS software version 9.3 (SAS Institute, Cary, NC) and STATA 13 (STATA Corporation, College Station, TX USA). $P < 0.05$ was considered statistically significant. Prevalence of HPV infections was estimated for any HPV type, low-risk types, high-risk types, vaccine types (6, 11, 16 and 18), nonvaccine types, low-risk nonvaccine types, and high-risk nonvaccine types. All analyses for NHANES data took into account differential probabilities of selection and the complex sample design by using sample weights,²⁹ following NHANES Analytic and Reporting Guidelines. Standard errors were calculated using Taylor series linearization.³⁰

Multivariate logistic regression models controlling for socio-demographic characteristics and sexual behaviors were used to compare differences in HPV prevalence between vaccinated and unvaccinated young women. We also compared the prevalence of vaccine type HPV infection among young women who reported one dose compared to ≥ 2 doses of the HPV vaccine. Adjusted prevalence ratios were obtained from average marginal predictions in the fitted logistic regression model.^{31,32} We constructed 2 models with additional variables included in the subsequent model. Model 1 was adjusted for sociodemographic variables including age, race/ethnicity, education, income, smoking status, and marital status. Model 2 was further adjusted for sexually transmitted infections, number of lifetime sexual partners, and number of sexual partners in the past 12 months in addition to the variables in Model 1. We included sexual behavior variables in the model because this affects the risk of acquiring HPV infections.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Funding

Dr. Guo is currently a postdoctoral fellow supported by an institutional training grant (National Research Service Award

T32HD055163, Berenson, Principal Investigator) from the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD) at the National Institutes of Health (NIH). Dr. Hirth, is supported by a research career development award (Building Interdisciplinary Research Careers in Women's Health Program -BIRCWH K12HD052023, Berenson, Principal Investigator) from the Office of Research on Women's Health (ORWH), the Office of the Director (OD), the National Institute of Allergy and Infectious Diseases (NIAID), the Eunice Kennedy Shriver National Institute of Child Health and Human Development at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or the NIH.

Authors' Contributions

Initial concept: FG. Study design: FG, JMH, ABB. Data collection and data preparation: FG. Analysis: FG. Interpretation of results: FG, JMH, ABB. Wrote the manuscript: FG. Critically reviewed and edited the manuscript: FG, JMH, ABB.

Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of CDC/NCHS. Part of the results has been presented as a poster at the AACR (American Association for Cancer Research) Annual Meeting 2015. April 18–22, 2015. Philadelphia, Pennsylvania.

References

- Chesson HW, Dunne EF, Hariri S, Markowitz LE. The estimated lifetime probability of acquiring human papillomavirus in the United States. *Sex Transm Dis*. 2014;41(11):660-4; PMID:25299412; <http://dx.doi.org/10.1097/OLQ.0000000000000193>
- Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, et al. A review of human carcinogens—Part B: biological agents. *Lancet Oncol*. 2009;10(4):321-2; PMID:19350698; [http://dx.doi.org/10.1016/S1470-2045\(09\)70096-8](http://dx.doi.org/10.1016/S1470-2045(09)70096-8)
- de Sanjose S, Quint WG, Alemany L, Geraets DT, Klaustermeier JE, Lloveras B, Tous S, Felix A, Bravo LE, Shin HR, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol*. 2010;11(11):1048-56; PMID:20952254; [http://dx.doi.org/10.1016/S1470-2045\(10\)70230-8](http://dx.doi.org/10.1016/S1470-2045(10)70230-8)
- Villa LL, Costa RL, Petta CA, Andrade RP, Ault KA, Giuliano AR, Wheeler CM, Koutsky LA, Malm C, Lehtinen M, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. *Lancet Oncol*. 2005;6(5):271-8; PMID:15863374; [http://dx.doi.org/10.1016/S1470-2045\(05\)70101-7](http://dx.doi.org/10.1016/S1470-2045(05)70101-7)
- Group FIS. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med*. 2007;356(19):1915-27; PMID:17494925; <http://dx.doi.org/10.1056/NEJMoa061741>
- Joura EA, Leodolter S, Hernandez-Avila M, Wheeler CM, Perez G, Koutsky LA, Garland SM, Harper DM, Tang GW, Ferris DG, et al. Efficacy of a quadrivalent prophylactic human papillomavirus (types 6, 11, 16, and 18) L1 virus-like-particle vaccine against high-grade vulvar and vaginal lesions: a combined analysis of three randomised clinical trials. *Lancet*. 2007;369(9574):1693-1702; PMID:17512854; [http://dx.doi.org/10.1016/S0140-6736\(07\)60777-6](http://dx.doi.org/10.1016/S0140-6736(07)60777-6)
- Dillner J, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen OE, Hernandez-Avila M, Perez G, Brown DR, Koutsky LA, Tay EH, et al. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *BMJ*. 2010; 341:c3493; PMID:20647284; <http://dx.doi.org/10.1136/bmj.c5128>
- Palefsky JM, Giuliano AR, Goldstone S, Moreira ED Jr, Aranda C, Jessen H, Hillman R, Ferris D, Coutlee F, Stoler MH, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. *N Engl J Med*. 2011;365(17):1576-85; PMID:22029979; <http://dx.doi.org/10.1056/NEJMoa1010971>
- Powell SE, Hariri S, Steinau M, Bauer HM, Bennett NM, Bloch KC, Nicolai LM, Schafer S, Unger ER, Markowitz LE. Impact of human papillomavirus (HPV) vaccination on HPV 16/18-related prevalence in precancerous cervical lesions. *Vaccine*. 2012;31(1):109-13; PMID:23137842; <http://dx.doi.org/10.1016/j.vaccine.2012.10.092>
- Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Quadrivalent human papillomavirus vaccine: recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep*. 2007; 56(RR-2):1-24; PMID:17380109
- Markowitz LE, Hariri S, Unger ER, Saraiya M, Datta SD, Dunne EF. Post-licensure monitoring of HPV vaccine in the United States. *Vaccine*. 2010;28(30):4731-7; PMID:20188681; <http://dx.doi.org/10.1016/j.vaccine.2010.02.019>
- Drolet M, Bénard É, Boily MC, Ali H, Baandrup L, Bauer H, Beddows S, Brisson J, Brotherton JM, Cummings T, et al. Population-level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infect Dis*. 2015; 15(5):565-80; PMID:25744474
- Dobson SR, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, Sauvageau C, Scheifele DW, Kollmann TR, Halperin SA, et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. *JAMA*. 2013;309(17):1793-802; PMID:23632723; <http://dx.doi.org/10.1001/jama.2013.1625>
- Markowitz LE, Hariri S, Lin C, Dunne EF, Steinau M, McQuillan G, Unger ER. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. *J Infect Dis*. 2013;208(3):385-93; PMID:23785124; <http://dx.doi.org/10.1093/infdis/jit192>
- Hildesheim A, Herrero R, Wacholder S, Rodriguez AC, Solomon D, Bratti MC, Schiller JT, Gonzalez P, Dubin G, Porras C, et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA*. 2007;298(7):743-53; PMID:17699008; <http://dx.doi.org/10.1001/jama.298.7.743>
- Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, Markowitz LE. Prevalence of HPV infection among females in the United States. *JAMA*. 2007;297(8):813-9; PMID:17327523; <http://dx.doi.org/10.1001/jama.297.8.813>
- Stanley M, Lowy DR, Frazer I. Chapter 12: Prophylactic HPV vaccines: underlying mechanisms. *Vaccine*. 2006; 24 Suppl 3:S3/106-113; PMID:16949996
- Block SL, Nolan T, Sattler C, Barr E, Giacoletti KE, Marchant CD, Castellsagué X, Rusche SA, Lukac S, Bryan JT, et al. Comparison of the immunogenicity and reactogenicity of a prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in male and female adolescents and young adult women. *Pediatrics*. 2006;118(5):2135-45; PMID:17079588; <http://dx.doi.org/10.1542/peds.2006-0461>
- Romanowski B, Schwarz TF, Ferguson LM, Peters K, Dionne M, Schulze K, Ramjattan B, Hillemanns P, Catteau G, Dobbelaere K, et al. Immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose schedule compared with the licensed 3-dose schedule: results from a randomized study. *Hum Vaccin*. 2011;7(12):1374-86; PMID:22048171; <http://dx.doi.org/10.4161/hv.7.12.18322>
- Day PM, Kines RC, Thompson CD, Jagu S, Roden RB, Lowy DR, Schiller JT. In vivo mechanisms of vaccine-induced protection against HPV infection. *Cell Host Microbe*. 2010;8(3):260-70; PMID:20833377; <http://dx.doi.org/10.1016/j.chom.2010.08.003>
- Longet S, Schiller JT, Bobst M, Jichlinski P, Nardelli-Haeffiger D. A murine genital-challenge model is a sensitive measure of protective antibodies against human papillomavirus infection. *J Virol*. 2011;85(24):13253-9; PMID:21976653; <http://dx.doi.org/10.1128/JVI.06093-11>
- Wheeler CM, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Perez G, Brown DR, Koutsky LA, Tay EH, García P, et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in sexually active women aged 16-26 years. *J Infect Dis*. 2009;199(7):936-44; PMID:19236277; <http://dx.doi.org/10.1086/597309>
- Joura EA, Ault KA, Bosch FX, Brown D, Cuzick J, Ferris D, Garland SM, Giuliano AR, Hernandez-Avila M, Huh W, et al. Attribution of 12 high-risk human papillomavirus genotypes to infection and cervical disease. *Cancer Epidemiol Biomarkers Prev*. 2014;23(10):1997-2008; PMID:25274978; <http://dx.doi.org/10.1158/1055-9965.EPI-14-0410>
- Smolen KK, Gelinas L, Franzen L, Dobson S, Dawar M, Ogilvie G, Krajden M, Fortuno ES 3rd, Kollmann TR. Age of recipient and number of doses differentially impact human B and T cell immune memory responses to HPV vaccination. *Vaccine*. 2012;30(24):3572-3579; PMID:22469863; <http://dx.doi.org/10.1016/j.vaccine.2012.03.051>
- Schwarz T, Spaczynski M, Kaufmann A, Wysocki J, Galaj A, Schulze K, Suryakiran P, Thomas F, Descamps D. Persistence of immune responses to the HPV-16/18 AS04-adjuvanted vaccine in women aged 15-55 years and first-time modelling of antibody responses in mature women: results from an open-label 6-year follow-up study. *BJOG*. 2015;122(1):107-18;

- PMID:25208608; <http://dx.doi.org/10.1111/1471-0528.13070>
26. Human papillomavirus vaccines: WHO position paper, October 2014. *Wkly Epidemiol Rec.* 2014;89(43):465-91; PMID:25346960
 27. National Health and Nutrition Examination Survey: Questionnaires, datasets, and related documentation. http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm. Accessed November 20, 2014.
 28. Hariri S, Unger ER, Sternberg M, Dunne EF, Swan D, Patel S, Markowitz LE. Prevalence of genital human papillomavirus among females in the United States, the National Health And Nutrition Examination Survey, 2003-2006. *J Infect Dis.* 2011;204(4):566-73; PMID:21791659; <http://dx.doi.org/10.1093/infdis/jir341>
 29. Design and estimation for the National Health Interview Survey, 1995-2004. *Vital Health Stat 2.* 2000(130):1-31; PMID:AMBIGUOUS
 30. Korn EL, Graubard BI. Epidemiologic studies utilizing surveys: accounting for the sampling design. *Am J Public Health.* 1991;81(9):1166-73; PMID:1951829; <http://dx.doi.org/10.2105/AJPH.81.9.1166>
 31. Bieler GS, Brown GG, Williams RL, Brogan DJ. Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. *Am J Epidemiol.* 2010;171(5):618-23; PMID:20133516; <http://dx.doi.org/10.1093/aje/kwp440>
 32. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. *Stata Journal.* 2013;13(3):492-509

Comparison of HPV prevalence between HPV-vaccinated and non-vaccinated young adult women (20–26 years)

Fangjian Guo, Jacqueline M Hirth, and Abbey B Berenson*

Department of Obstetrics & Gynecology; Center for Interdisciplinary Research in Women's Health; The University of Texas Medical Branch; Galveston, TX USA

Keywords: high-risk type, HPV vaccine, human papillomavirus (HPV), oncogenic virus, prevalence

Abbreviations: CDC, Centers for Disease Control and Prevention; CI, Confidence Interval; GED, General Education Development; HPV, Human Papillomavirus; MEC, Mobile Examination Center; NCHS, National Center for Health Statistics; NHANES, National Health and Nutrition Examination Survey.

There is some concern about the effectiveness of the HPV vaccine among young adult women due to the risk of prior HPV infection. This study used National Health and Nutrition Examination Survey (NHANES) 2007–2012 data to evaluate the effectiveness of HPV vaccination among women 20–26 years of age who were vaccinated after 12 years of age. This cross-sectional study examined 878 young adult women (20–26 years) with complete information on HPV prevalence and HPV vaccination status from NHANES 2007–2012. Vaginal swab specimens were analyzed for HPV DNA by L1 consensus polymerase chain reaction followed by type-specific hybridization. Multivariate logistic regression models controlling for sociodemographic characteristics and sexual behaviors were used to compare type-specific HPV prevalence between vaccinated and unvaccinated women. A total of 21.4% of young adult women surveyed through NHANES between 2007 and 2012 received the HPV vaccine. Vaccinated women had a lower prevalence of vaccine types than unvaccinated women (7.4% vs 17.1%, prevalence ratio 0.43, 95% CI 0.21–0.88). The prevalence of high-risk nonvaccine types was higher among vaccinated women than unvaccinated women (52.1% vs 40.4%, prevalence ratio 1.29, 95% CI 1.06–1.57), but this difference was attenuated after adjusting for sexual behavior variables (adjusted prevalence ratio 1.19, 95% CI 0.99–1.43). HPV vaccination was effective against all 4 vaccine types in young women vaccinated after age 12. However, vaccinated women had a higher prevalence of high-risk nonvaccine types, suggesting that they may benefit from newer vaccines covering additional types.

Introduction

It is estimated that over 80% of sexually active women in the US will acquire genital human papillomavirus (HPV) infection during their lifetime.¹ HPV is classified into low-risk types and high-risk types according to its oncogenic properties.^{2,3} In 2006, a quadrivalent vaccine, which prevents 2 low-risk (6, 11) and 2 high-risk (16, 18) types^{4–9} was approved for use in the US. Following its approval, the Advisory Committee on Immunization Practices recommended routine vaccination with 3 doses of this vaccine for all females aged 11 to 12 years, and catch-up vaccination up to age 26.¹⁰ To determine its effectiveness in a real world setting, however, post-licensure evaluation of the HPV vaccine is needed.¹¹

Although population studies have shown a decrease in vaccine-type HPV prevalence among young girls since the vaccine was introduced,¹² its effectiveness among women who received it after 12 years of age still needs to be determined. This is relevant because those vaccinated after the recommended age of 11–12 years may not have as strong of an immune response as

younger girls.¹³ Furthermore, women who have already engaged in sexual activity are more likely to have already been exposed to HPV,¹⁴ and the vaccine cannot eradicate prior infections.¹⁵ In fact, data from NHANES showed that 33% of 14–19 year olds and 60% of US women aged 20 to 24 years had current genital HPV infections.^{14,16} Finally, since the vaccine was initially targeted for 11–12 year old girls, the focus of surveillance efforts to date have been on younger adolescents, making it difficult to study its effectiveness among those who received the HPV vaccine as older adolescents or young adults in the general population. The purpose of this study was to compare type-specific HPV prevalence between vaccinated and unvaccinated young adult women using data from NHANES 2007–2012.

Results

A total of 177 vaccinated and 701 unvaccinated young women (20–26 years) were included in these analyses. Mean age was

*Correspondence to: Abbey B Berenson; Email: abberens@utmb.edu
Submitted: 04/22/2015; Revised: 06/05/2015; Accepted: 06/24/2015
<http://dx.doi.org/10.1080/21645515.2015.1066948>

22.4 years in vaccinated women and 23.1 years in unvaccinated women. Overall, 21.4% of the sample received at least one dose of the HPV vaccine (Table 1). HPV vaccination rate was lower in married women and those who did not finish high school. Vaccinated women and unvaccinated women had similar sexual behaviors, including ≥ 2 sexual partners in the past 12 months and ≥ 3 lifetime number of sexual partners, and sexually transmitted diseases.

Prevalence of individual human papillomavirus (HPV) types among young adult women (20–26 years) by vaccination status is presented in Figure 1. The prevalence of low-risk vaccine types (HPV 6 or 11) among vaccinated women was lower than unvaccinated women (0.3% vs 4.4%, $p < 0.001$; Table 2). The prevalence of high-risk (16 or 18) vaccine types was also lower among vaccinated women than unvaccinated women, although it did not reach statistical significance in the unadjusted model. After adjusting for sexual behavior variables (sexually transmitted diseases, number of lifetime sexual partners, and number of sexual partners in the past 12 months), the prevalence of high-risk vaccine types was lower in vaccinated women (adjusted prevalence ratio 0.46, 95% CI 0.22–0.98). Overall, vaccinated women had

a lower prevalence of vaccine types (HPV 6, 11, 16, or 18) than unvaccinated women (7.4% vs 17.1%, prevalence ratio 0.43, 95% CI 0.21–0.88).

In contrast, no difference was observed in the prevalence of low-risk nonvaccine types between vaccinated and unvaccinated women (38.8% vs 37.5%). However, vaccinated women had a markedly higher prevalence of high-risk nonvaccine types (52.1% vs 40.4, prevalence ratio 1.29, 95% CI 1.06–1.57). When further adjusted for sexual behavior variables in Model 2, the difference in prevalence of high-risk nonvaccine types between vaccinated and unvaccinated women was attenuated (adjusted prevalence ratio in Model 2 1.19, 95% CI 0.99–1.43).

When characteristics associated with HPV prevalence were examined, it was found that being unmarried, with a high school education, an income under the poverty level, a history of sexually transmitted infections, ≥ 3 lifetime sexual partners and ≥ 2 sexual partners in the past 12 months were associated with a lower prevalence of vaccine types among vaccinated women than unvaccinated women (Table 3). We also evaluated characteristics associated with high-risk nonvaccine HPV between vaccinated and unvaccinated women (Table 4). A difference in the

Table 1. Sociodemographic characteristics of US young adult women by vaccination status (N = 878)

	N (%) ^a		p Value ^b	Vaccination Rate % (95% CI)
	Vaccinated	Unvaccinated		
Total	177 (100)	701 (100)		21.4 (17.3–25.4)
Race/Ethnicity			0.007	
Non-Hispanic White	70 (66.0)	235 (55.6)		24.4 (18.4–30.4)
Non-Hispanic Black	48 (13.8)	169 (15.2)		19.7 (13.9–25.5)
Mexican American	12 (3.9)	149 (12.8)		7.7 (3.1–12.3)
Other	47 (16.3)	148 (16.3)		21.3 (14.4–28.2)
Marital Status			0.001	
Unmarried	144 (79.0)	432 (59.6)		26.5 (21.1–31.9)
Married	33 (21.0)	269 (40.4)		12.4 (7.5–17.3)
Education Level			0.005	
< High School	17 (6.7)	126 (14.2)		11.5 (5.1–17.8)
High School	25 (12.5)	171 (22.7)		13.0 (6.8–19.3)
> High School	135 (80.8)	404 (63.1)		25.8 (20.3–31.3)
Poverty Income Ratio			0.45	
≥ 1	109 (69.8)	398 (64.4)		22.7 (17.8–27.7)
< 1	56 (26.7)	244 (29.5)		19.7 (12.8–26.7)
Missing	12	59		
Smoking Status			0.47	
Never	134 (71.9)	495 (69.6)		21.9 (16.1–27.8)
Past	15 (11.3)	46 (8.2)		27.2 (14.3–40.2)
Current	28 (16.8)	160 (22.2)		17.0 (8.5–25.6)
Sexually Transmitted Infection		0.58		
No	141 (80.2)	560 (82.4)		20.9 (16.2–25.6)
Yes	36 (19.8)	141 (17.6)		23.5 (15.8–31.1)
Lifetime Sex Partners			0.39	
≤ 2	59 (30.9)	271 (35.4)		19.2 (13.3–25.0)
≥ 3	118 (69.1)	430 (64.6)		22.5 (17.3–27.7)
Sex Partners in the Past 12 Months		0.23		
≤ 1	118 (67.5)	518 (73.8)		19.9 (15.2–24.6)
≥ 2	59 (32.5)	183 (26.2)		25.2 (17.7–32.7)

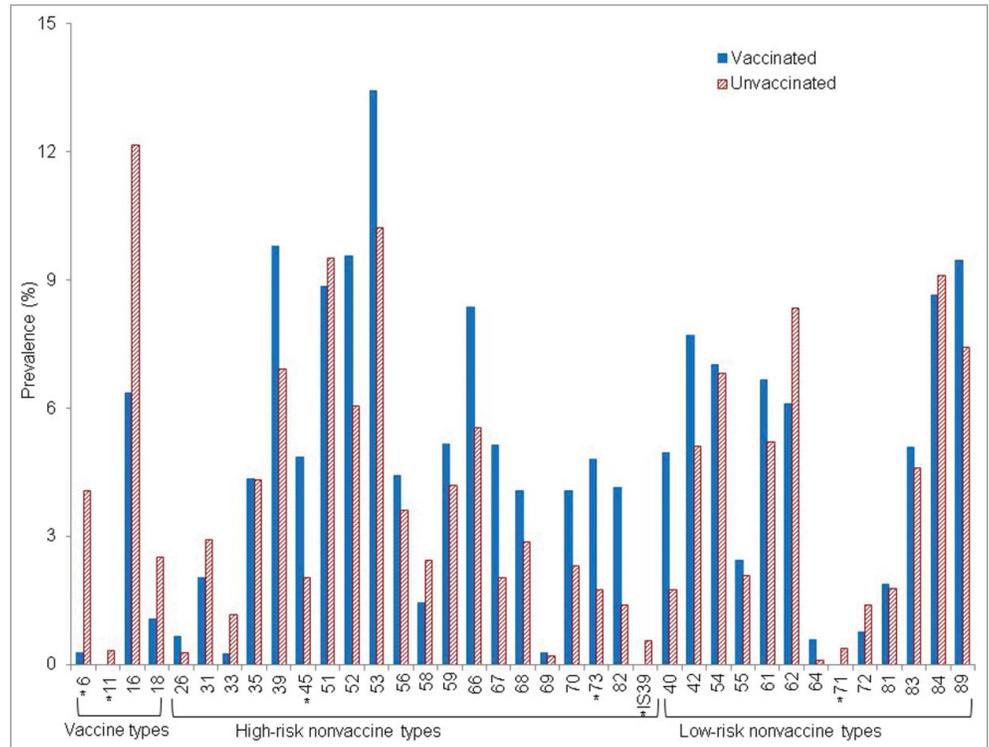
CI: confidence interval.

^aSample weights were used to calculate weighted percentages.

^bp value was derived from Wald χ^2 test.

prevalence of high-risk nonvaccine types was observed in non-Hispanic Whites, non-Hispanic Blacks, women with a college education, women living above the poverty level, past smokers, women with no prior sexually transmitted infections, and women with ≥ 3 lifetime sexual partners.

We found that among vaccinated women, 19.2% received one dose of the HPV vaccine, 25.1% received 2 doses, and 55.7% completed all 3 doses. Those who received ≥ 2 doses of the HPV vaccine had a lower, although not statistically significant, prevalence of vaccine type HPV compared to women who only received one dose (6.5% vs 11.3%, adjusted prevalence ratio 0.59, 95% CI 0.19–1.91).



Discussion

Using data from a nationally-representative survey conducted over 6 years, we found that young adult women who had received the vaccine after 12 years of age had a reduced prevalence of all 4 vaccine-type infections compared to their unvaccinated peers. This is consistent with data from clinical trials, which showed that the quadrivalent HPV vaccine has over 90% efficacy against vaccine type infections.^{4–8} These findings demonstrate that even though young girls may have a better immunological response to the HPV vaccine, it is still highly

effective when given at older ages. This may be because protection of the vaccine is provided through the production of serum neutralizing anti-HPV IgG antibodies binding to viral particles,^{17–19} which only requires small amounts of antibody to be present.^{20,21}

One interesting finding was that vaccinated young adult women had a higher prevalence than unvaccinated women of

Figure 1. Prevalence of individual human papillomavirus (HPV) types among young adult women (20–26 years) by vaccination status. Prevalence was weighted using sample weights. * Statistical significance for the comparison between vaccinated women and unvaccinated women, after adjusted for age, race/ethnicity, education, income, smoking status, sexually transmitted infections, number of lifetime sexual partners, and number of sexual partners in the past 12 months.

Table 2. Type-specific HPV prevalence among US adult women by HPV vaccination status

	Prevalence (95% CI) ^a			Adjusted Prevalence Ratio (95% CI) Vaccinated vs. Unvaccinated	
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Prevalence Ratio (95% CI)	Model 1 ^b	Model 2 ^c
Any HPV Type	63.3 (55.2–71.4)	54.9 (50.0–59.8)	1.15 (0.99–1.34)	1.15 (0.98–1.34)	1.11 (0.96–1.29)
Low-Risk Type	39.1 (31.1–47.2)	39.3 (33.7–45.0)	0.99 (0.78–1.27)	0.97 (0.76–1.24)	0.93 (0.74–1.18)
High-Risk Type	53.4 (43.8–63.0)	44.4 (39.6–49.1)	1.20 (0.99–1.46)	1.15 (0.95–1.40)	1.11 (0.93–1.33)
HPV 6, 11, 16 or 18	7.4 (2.1–12.7)	17.1 (13.9–20.3)	0.43 (0.21–0.88)	0.41 (0.21–0.84)	0.41 (0.20–0.82)
HPV 6 or 11	0.3 (0.0–0.8)	4.4 (2.8–6.0)	0.07 (0.01–0.45)	0.07 (0.01–0.55)	0.07 (0.01–0.54)
HPV 16 or 18	7.1 (1.7–12.5)	13.9 (10.9–17.0)	0.51 (0.24–1.10)	0.47 (0.22–1.00)	0.46 (0.22–0.98)
Nonvaccine Type	62.4 (54.3–70.5)	52.8 (47.8–57.8)	1.18 (1.02–1.37)	1.17 (1.00–1.37)	1.14 (0.99–1.31)
Nonvaccine Low-Risk Type	38.8 (30.8–46.9)	37.5 (31.8–43.2)	1.04 (0.80–1.34)	1.00 (0.77–1.30)	0.96 (0.75–1.23)
Nonvaccine High-Risk Type	52.1 (42.5–61.8)	40.4 (35.9–44.9)	1.29 (1.06–1.57)	1.23 (1.02–1.50)	1.19 (0.99–1.43)

CI: confidence interval.

^aPrevalence was weighted using sample weights.

^bModel 1 was adjusted for age, race/ethnicity, education, income, smoking status, and marital status.

^cModel 2 was adjusted for variables in Model 1 plus sexually transmitted diseases and number of lifetime sexual partners, and number of sexual partners in the past 12 months.

Table 3. Prevalence of HPV vaccine types among US adult women by HPV vaccination status and sociodemographic characteristics (N = 878)

	Prevalence (95% CI) ^a		Prevalence Ratio (95% CI)
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Vaccinated vs. Unvaccinated
Total	7.4 (2.1–12.7)	17.1 (13.9–20.3)	0.43(0.21–0.88)
Race/Ethnicity			
Non-Hispanic White	7.2 (0.0–15.0)	15.7 (11.4–20.0)	0.46(0.16–1.33)
Non-Hispanic Black	8.9 (0.5–17.3)	21.5 (14.0–29.0)	0.41(0.16–1.08)
Mexican American	4.5 (0.0–13.9)	10.8 (3.4–18.2)	0.42(0.05–3.46)
Other	7.5 (0.3–14.7)	22.5 (13.2–31.9)	0.33(0.12–0.95)
Marital Status			
Unmarried	8.0 (1.1–15.0)	20.1 (16.1–24.2)	0.40(0.17–0.94)
Married	4.9 (0.0–10.2)	12.6 (7.7–17.4)	0.39(0.13–1.19)
Education Level			
< High School	5.1 (0.0–15.4)	19.6 (10.9–28.2)	0.26(0.04–1.58)
High School	6.8 (0.0–14.7)	21.8 (12.6–31.0)	0.31(0.10–0.97)
> High School	7.7 (1.1–14.2)	14.8 (11.1–18.6)	0.52(0.21–1.27)
Poverty Income Ratio			
≥1	8.0 (0.7–15.2)	15.2 (10.7–19.6)	0.53(0.21–1.34)
<1	3.2 (0.0–7.2)	20.0 (13.7–26.2)	0.16(0.04–0.58)
Smoking Status			
Never	7.1 (1.0–13.2)	15.4 (11.5–19.2)	0.46(0.19–1.11)
Past	5.5 (0.0–13.0)	19.9 (5.3–34.4)	0.28(0.05–1.52)
Current	9.8 (0.0–27.3)	21.4 (14.5–28.3)	0.46(0.08–2.59)
Sexually Transmitted Infections			
No	8.8 (2.2–15.4)	15.4 (11.7–19.0)	0.57(0.27–1.21)
Yes	1.8 (0.0–5.3)	25.0 (17.4–32.6)	0.07(0.01–0.51)
Lifetime Sex Partners			
≤2	6.0 (0.0–13.4)	6.5 (3.2–9.7)	0.93(0.25–3.43)
≥3	8.0 (1.2–14.8)	22.9 (18.4–27.4)	0.35(0.15–0.82)
Sex Partners in the Past 12 Months			
≤1	7.3 (1.1–13.5)	11.7 (8.5–14.9)	0.63(0.27–1.47)
≥2	7.5 (0.0–17.3)	32.3 (24.8–39.8)	0.23(0.06–0.84)

CI: confidence interval.

^aPrevalence was estimated for the prevalence of vaccine types (HPV 6, 11, 16 or 18). Prevalence was weighted using sample weights.

high-risk types other than HPV 16 and 18, and thus are still at risk of cervical cancer and other HPV-related cancers. This is consistent with clinical trials on the quadrivalent vaccine which showed it provided some protection against HPV 31 and 59, but not other types.²² Thus, the limitations of the HPV vaccine should be discussed with all patients, so they understand the need to obtain regular cervical cancer screening after vaccination as recommended for their age group. The underlying causes for the increased prevalence of high-risk nonvaccine types we observed among vaccinated women cannot be determined from these data. However, we found that the association between vaccination and differences in prevalence of high-risk nonvaccine type infections was attenuated after adjusting for sexual behavior variables. Thus, it is possible that women who engaged in risky sexual behaviors were more likely to seek vaccination in the early years after its introduction. To reduce the increased prevalence of high-risk nonvaccine types, the 9-valent HPV vaccine may provide a practical solution. The 9-valent HPV vaccine which provides protection against the original 4 vaccine types (6, 11, 16, and 18) and 5 additional high-risk types (31, 33, 45, 52, and 58) has recently been approved by the Food and Drug Administration.²³ This new vaccine should help to reduce the increased

prevalence of several of the high-risk types we observed among women in the future.

Our results showed that young women who received one dose of the vaccine had a higher prevalence of vaccine type HPV infection compared to those who had at least 2 doses. This suggests that 1 dose may not be as protective in this age group. Our results for this finding were non-significant, but that may have been due to inadequate power. While it has been found that age impacts the type and level of the immune response to the HPV vaccine, it is generally agreed upon that at least 2 doses are needed to achieve a high level of immunity across time.^{13,24} In prior studies, young women who received 3 doses of the HPV vaccine (at 15 years of age or older) showed clinically significant levels of immunogenicity up to 6 years after administration.²⁵ Further, girls (9–13 years old) who received 3 doses were more likely to continue to have an immune response 36 months after vaccination compared to young women (16–26 years old) who received 3 doses, which may indicate that 3 doses is necessary among older adolescents and young adults. However, it is unknown what clinical threshold of immune response is needed to be effective. Therefore, the currently evolving guidelines issued by the World

Table 4. Prevalence of nonvaccine high-risk types among US adult women by characteristics and HPV vaccination status

	Prevalence (95% CI) ^a		Prevalence Ratio (95% CI)
	Vaccinated (n = 177)	Unvaccinated (n = 701)	Vaccinated vs. Unvaccinated
All	52.1 (42.5–61.8)	40.4 (35.9–44.9)	1.29(1.06–1.57)
Race/Ethnicity			
Non-Hispanic White	55.2 (41.6–68.8)	39.4 (32.9–45.9)	1.40(1.05–1.86)
Non-Hispanic Black	67.6 (54.8–80.4)	50.5 (43.8–57.3)	1.34(1.10–1.63)
Mexican American	39.5 (8.8–70.1)	33.2 (26.0–40.4)	1.19(0.52–2.71)
Other	29.5 (16.2–42.7)	40.0 (30.7–49.4)	0.74(0.46–1.18)
Marital Status			
Unmarried	55.1 (46.1–64.2)	45.8 (40.3–51.4)	1.20(0.99–1.46)
Married	40.8 (20.9–60.7)	32.4 (25.4–39.3)	1.26(0.79–2.02)
Education Level			
< High School	62.3 (33.0–91.6)	46.0 (36.5–55.4)	1.36(0.85–2.17)
High School	36.2 (12.6–59.9)	43.1 (34.3–52.0)	0.84(0.43–1.66)
> High School	53.7 (42.3–65.2)	38.2 (31.6–44.7)	1.41(1.11–1.78)
Poverty Income Ratio			
≥1	49.4 (37.3–61.5)	37.2 (30.6–43.7)	1.33(1.00–1.76)
<1	56.4 (43.9–68.9)	46.4 (39.0–53.8)	1.22(0.95–1.56)
Smoking Status			
Never	45.4 (32.8–58.1)	36.2 (31.1–41.3)	1.26(0.95–1.67)
Past	83.8 (69.6–98.1)	43.4 (28.5–58.2)	1.93(1.29–2.90)
Current	59.4 (36.3–82.5)	52.6 (42.2–63.0)	1.13(0.73–1.75)
Sexually Transmitted Infections			
No	47.3 (37.2–57.4)	35.5 (31.1–39.8)	1.33(1.08–1.65)
Yes	71.6 (52.6–90.7)	63.6 (53.8–73.3)	1.13(0.82–1.54)
Lifetime Sex Partners			
≤2	25.8 (13.3–38.4)	22.4 (15.7–29.0)	1.15(0.68–1.96)
≥3	63.9 (51.9–75.8)	50.3 (44.9–55.7)	1.27(1.04–1.55)
Sex Partners in the Past 12 Months			
≤1	41.1 (30.2–52.1)	31.7 (26.7–36.7)	1.30(0.98–1.72)
≥2	74.9 (62.1–87.7)	64.9 (56.0–73.9)	1.15(0.93–1.43)

CI: confidence interval.

^aPrevalence was estimated for high-risk nonvaccine types. Prevalence was weighted using sample weights.

Health Organization (WHO) still recommend 3 doses of the HPV vaccine when administered to young adult women.²⁶

The strengths of our study included use of data from a large, nationally representative sample with high response rates. However, our study has several limitations. First, our sample size was not large enough to assess the efficacy of HPV vaccine in racial or sociodemographic subgroups. Second, the history of HPV vaccination was self-reported and may be subject to response bias. The possible overreporting or underreporting may bias our analyses and estimate of vaccine effectiveness. In addition, the information on the exact age at vaccination was not available in NHANES. However, we only included young women between 20 and 26 years of age from NHANES 2008–2012. Since the HPV vaccine was approved by the Food and Drug Administration (FDA) in the United States in 2006, it is unlikely that any of these women were vaccinated before 14 years of age. Although they may not have as high immunological response to the HPV vaccine as younger girls (11–12 years of age),¹³ women between 14 and 26 years still seroconvert at a high rate and are protected against vaccine type infections and related diseases.^{4–9} Finally, due to the cross-sectional nature of our study, we were not able to determine causation. NHANES is a cross sectional survey, so

the temporal relationship between HPV vaccination, HPV infection, and sexual behavior could not be determined.

In conclusion, HPV vaccination was protective against all 4 vaccine types even when vaccination occurred after the recommended age of 11–12 years. However, vaccinated young women had a higher prevalence of high-risk nonvaccine types. Thus, it is important to advise all women to undergo regular cervical cancer screening, as they may still be at risk of acquiring high-risk HPV infections.

Materials and Methods

NHANES is a cross-sectional survey conducted by the National Center for Health Statistics (NCHS), using a complex, stratified, multistage probability sample to represent the civilian, non-institutionalized, US population. The study was approved by the NCHS Institutional Review Board, and all adult participants provided written informed consent. Details about NHANES can be found elsewhere.²⁷ Our study included young adult women (20–26 years) with complete information on HPV vaccination status from NHANES 2007–2012. Since the vaccine

was first approved for use in 2006, all women in this age range would have received the vaccine after 12 years of age. This age group was selected because few data are available on those vaccinated after the recommended age of 11–12 years. Furthermore, this age group has a high prevalence of HPV infection.

In 2007–2012, 1061 young adult women were interviewed, of which 1030 had completed information on HPV vaccination status. Of those, 1004 received an examination in a mobile examination center (MEC) and 886 submitted a self-collected cervicovaginal swab specimen. A total of 878 specimens were adequate for HPV DNA typing. In our study, we excluded those without adequate cervicovaginal samples.

Demographic information was collected during the household interview. Race/ethnicity was self-reported and categorized as non-Hispanic White, non-Hispanic Black, Mexican Americans, and others. We collapsed marital status into the 2 categories of married (married, or living with partner) and unmarried (widowed/divorced/separated, and single), as it is documented that widowed/divorced/separated women and single women had a much higher prevalence of HPV infection than married women.¹⁶ Education level was categorized as less than high school (9–11th grade, includes 12th grade with no diploma), high school (high school graduate/General Education Development (GED) or equivalent), and greater than a high school education (college or above). Poverty income ratio was calculated by the NCHS according to the US. Census definition by dividing total family income by the poverty threshold after adjusting for family size at the time of the interview. We classified poverty income ratio into 2 categories: ≤ 1 (under poverty) and > 1 (above poverty). Smoking status was classified into 3 categories: never (< 100 cigarettes in life), past (smoked at least 100 cigarettes in life, but not currently smoking cigarettes), and current (smoked at least 100 cigarettes in life and currently smoking cigarettes).

Sexual history was self-reported using an audio computer-assisted self-interview in MEC. Respondents who reported ever having sex (described as vaginal, oral, or anal) were asked additional questions, including lifetime number of partners and number of partners in the past 12 months. We classified number of sexual partners in their lifetime into 2 categories - ≥ 3 and ≤ 2 , and number of sexual partners in the past 12 months into 2 categories - ≥ 2 and ≤ 1 , as it has been reported that women with ≥ 3 lifetime sexual partners or ≥ 2 sexual partners in the past 12 months have a higher HPV prevalence than women with fewer sexual partners.¹⁶

Respondents who reported that a physician had ever told them they had a sexually transmitted infection were considered to have a history of a sexually transmitted infection. Reports of the following sexually transmitted infections were included: genital herpes, chlamydia, and gonorrhea. Young women who were tested positive for serum antibody to herpes simplex virus type 2, serum human immunodeficiency virus (HIV) antibody, or urine chlamydia were also considered to have a history of sexually transmitted infection. Cases of genital warts were not included because they are caused by HPV infection.

History of HPV vaccination was obtained by self-report. HPV infection was determined by the detection of HPV DNA in self-collected vaginal swabs. Extractions and testing on vaginal swab specimens were performed at the Centers for Disease Control and Prevention (CDC), with details described elsewhere.^{14,28} Briefly, vaginal swabs were analyzed for HPV DNA by L1 consensus polymerase chain reaction followed by type-specific hybridization. All specimens were hybridized to the typing strip that included probes for 37 HPV types, including high-risk types (16, 18, 31, 33, 35, 52, 58, 39, 45, 59, 68, 51, 56, 66, 26, 53, 67, 69, 70, 73, 82, and IS39) that can cause cancer and low-risk types (6, 11, 40, 42, 54, 55, 61, 62, 64, 71, 72, 81, 83, 84, and 89). The sample was considered inadequate if no β -globin was present in the sample and no HPV type was detected.

Statistical Analysis

Statistical analyses were carried out with SAS software version 9.3 (SAS Institute, Cary, NC) and STATA 13 (STATA Corporation, College Station, TX USA). $P < 0.05$ was considered statistically significant. Prevalence of HPV infections was estimated for any HPV type, low-risk types, high-risk types, vaccine types (6, 11, 16 and 18), nonvaccine types, low-risk nonvaccine types, and high-risk nonvaccine types. All analyses for NHANES data took into account differential probabilities of selection and the complex sample design by using sample weights,²⁹ following NHANES Analytic and Reporting Guidelines. Standard errors were calculated using Taylor series linearization.³⁰

Multivariate logistic regression models controlling for socio-demographic characteristics and sexual behaviors were used to compare differences in HPV prevalence between vaccinated and unvaccinated young women. We also compared the prevalence of vaccine type HPV infection among young women who reported one dose compared to ≥ 2 doses of the HPV vaccine. Adjusted prevalence ratios were obtained from average marginal predictions in the fitted logistic regression model.^{31,32} We constructed 2 models with additional variables included in the subsequent model. Model 1 was adjusted for sociodemographic variables including age, race/ethnicity, education, income, smoking status, and marital status. Model 2 was further adjusted for sexually transmitted infections, number of lifetime sexual partners, and number of sexual partners in the past 12 months in addition to the variables in Model 1. We included sexual behavior variables in the model because this affects the risk of acquiring HPV infections.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Funding

Dr. Guo is currently a postdoctoral fellow supported by an institutional training grant (National Research Service Award

T32HD055163, Berenson, Principal Investigator) from the Eunice Kennedy Shriver National Institute of Child Health & Human Development (NICHD) at the National Institutes of Health (NIH). Dr. Hirth, is supported by a research career development award (Building Interdisciplinary Research Careers in Women's Health Program -BIRCWH K12HD052023, Berenson, Principal Investigator) from the Office of Research on Women's Health (ORWH), the Office of the Director (OD), the National Institute of Allergy and Infectious Diseases (NIAID), the Eunice Kennedy Shriver National Institute of Child Health and Human Development at the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or the NIH.

Authors' Contributions

Initial concept: FG. Study design: FG, JMH, ABB. Data collection and data preparation: FG. Analysis: FG. Interpretation of results: FG, JMH, ABB. Wrote the manuscript: FG. Critically reviewed and edited the manuscript: FG, JMH, ABB.

Disclaimer

The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of CDC/NCHS. Part of the results has been presented as a poster at the AACR (American Association for Cancer Research) Annual Meeting 2015. April 18–22, 2015. Philadelphia, Pennsylvania.

References

- Chesson HW, Dunne EF, Hariri S, Markowitz LE. The estimated lifetime probability of acquiring human papillomavirus in the United States. *Sex Transm Dis*. 2014;41(11):660-4; PMID:25299412; <http://dx.doi.org/10.1097/OLQ.0000000000000193>
- Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, Benbrahim-Tallaa L, Guha N, Freeman C, Galichet L, et al. A review of human carcinogens—Part B: biological agents. *Lancet Oncol*. 2009;10(4):321-2; PMID:19350698; [http://dx.doi.org/10.1016/S1470-2045\(09\)70096-8](http://dx.doi.org/10.1016/S1470-2045(09)70096-8)
- de Sanjose S, Quint WG, Alemany L, Geraets DT, Klaustermeier JE, Lloveras B, Tous S, Felix A, Bravo LE, Shin HR, et al. Human papillomavirus genotype attribution in invasive cervical cancer: a retrospective cross-sectional worldwide study. *Lancet Oncol*. 2010;11(11):1048-56; PMID:20952254; [http://dx.doi.org/10.1016/S1470-2045\(10\)70230-8](http://dx.doi.org/10.1016/S1470-2045(10)70230-8)
- Villa LL, Costa RL, Petta CA, Andrade RP, Ault KA, Giuliano AR, Wheeler CM, Koutsky LA, Malm C, Lehtinen M, et al. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. *Lancet Oncol*. 2005;6(5):271-8; PMID:15863374; [http://dx.doi.org/10.1016/S1470-2045\(05\)70101-7](http://dx.doi.org/10.1016/S1470-2045(05)70101-7)
- Group FIS. Quadrivalent vaccine against human papillomavirus to prevent high-grade cervical lesions. *N Engl J Med*. 2007;356(19):1915-27; PMID:17494925; <http://dx.doi.org/10.1056/NEJMoa061741>
- Joura EA, Leodolter S, Hernandez-Avila M, Wheeler CM, Perez G, Koutsky LA, Garland SM, Harper DM, Tang GW, Ferris DG, et al. Efficacy of a quadrivalent prophylactic human papillomavirus (types 6, 11, 16, and 18) L1 virus-like-particle vaccine against high-grade vulvar and vaginal lesions: a combined analysis of three randomised clinical trials. *Lancet*. 2007;369(9574):1693-1702; PMID:17512854; [http://dx.doi.org/10.1016/S0140-6736\(07\)60777-6](http://dx.doi.org/10.1016/S0140-6736(07)60777-6)
- Dillner J, Kjaer SK, Wheeler CM, Sigurdsson K, Iversen OE, Hernandez-Avila M, Perez G, Brown DR, Koutsky LA, Tay EH, et al. Four year efficacy of prophylactic human papillomavirus quadrivalent vaccine against low grade cervical, vulvar, and vaginal intraepithelial neoplasia and anogenital warts: randomised controlled trial. *BMJ*. 2010; 341:c3493; PMID:20647284; <http://dx.doi.org/10.1136/bmj.c5128>
- Palefsky JM, Giuliano AR, Goldstone S, Moreira ED Jr, Aranda C, Jessen H, Hillman R, Ferris D, Coutlee F, Stoler MH, et al. HPV vaccine against anal HPV infection and anal intraepithelial neoplasia. *N Engl J Med*. 2011;365(17):1576-85; PMID:22029979; <http://dx.doi.org/10.1056/NEJMoa1010971>
- Powell SE, Hariri S, Steinau M, Bauer HM, Bennett NM, Bloch KC, Nicolai LM, Schafer S, Unger ER, Markowitz LE. Impact of human papillomavirus (HPV) vaccination on HPV 16/18-related prevalence in precancerous cervical lesions. *Vaccine*. 2012;31(1):109-13; PMID:23137842; <http://dx.doi.org/10.1016/j.vaccine.2012.10.092>
- Markowitz LE, Dunne EF, Saraiya M, Lawson HW, Chesson H, Unger ER; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP). Quadrivalent human papillomavirus vaccine: recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep*. 2007; 56(RR-2):1-24; PMID:17380109
- Markowitz LE, Hariri S, Unger ER, Saraiya M, Datta SD, Dunne EF. Post-licensure monitoring of HPV vaccine in the United States. *Vaccine*. 2010;28(30):4731-7; PMID:20188681; <http://dx.doi.org/10.1016/j.vaccine.2010.02.019>
- Drolet M, Bénard É, Boily MC, Ali H, Baandrup L, Bauer H, Beddows S, Brisson J, Brotherton JM, Cummings T, et al. Population-level impact and herd effects following human papillomavirus vaccination programmes: a systematic review and meta-analysis. *Lancet Infect Dis*. 2015; 15(5):565-80; PMID:25744474
- Dobson SR, McNeil S, Dionne M, Dawar M, Ogilvie G, Krajden M, Sauvageau C, Scheifele DW, Kollmann TR, Halperin SA, et al. Immunogenicity of 2 doses of HPV vaccine in younger adolescents vs 3 doses in young women: a randomized clinical trial. *JAMA*. 2013;309(17):1793-802; PMID:23632723; <http://dx.doi.org/10.1001/jama.2013.1625>
- Markowitz LE, Hariri S, Lin C, Dunne EF, Steinau M, McQuillan G, Unger ER. Reduction in human papillomavirus (HPV) prevalence among young women following HPV vaccine introduction in the United States, National Health and Nutrition Examination Surveys, 2003-2010. *J Infect Dis*. 2013;208(3):385-93; PMID:23785124; <http://dx.doi.org/10.1093/infdis/jit192>
- Hildesheim A, Herrero R, Wacholder S, Rodriguez AC, Solomon D, Bratti MC, Schiller JT, Gonzalez P, Dubin G, Porras C, et al. Effect of human papillomavirus 16/18 L1 viruslike particle vaccine among young women with preexisting infection: a randomized trial. *JAMA*. 2007;298(7):743-53; PMID:17699008; <http://dx.doi.org/10.1001/jama.298.7.743>
- Dunne EF, Unger ER, Sternberg M, McQuillan G, Swan DC, Patel SS, Markowitz LE. Prevalence of HPV infection among females in the United States. *JAMA*. 2007;297(8):813-9; PMID:17327523; <http://dx.doi.org/10.1001/jama.297.8.813>
- Stanley M, Lowy DR, Frazer I. Chapter 12: Prophylactic HPV vaccines: underlying mechanisms. *Vaccine*. 2006; 24 Suppl 3:S3/106-113; PMID:16949996
- Block SL, Nolan T, Sattler C, Barr E, Giacoletti KE, Marchant CD, Castellsagué X, Rusche SA, Lukac S, Bryan JT, et al. Comparison of the immunogenicity and reactogenicity of a prophylactic quadrivalent human papillomavirus (types 6, 11, 16, and 18) L1 virus-like particle vaccine in male and female adolescents and young adult women. *Pediatrics*. 2006;118(5):2135-45; PMID:17079588; <http://dx.doi.org/10.1542/peds.2006-0461>
- Romanowski B, Schwarz TF, Ferguson LM, Peters K, Dionne M, Schulze K, Ramjattan B, Hillemanns P, Catteau G, Dobbelaere K, et al. Immunogenicity and safety of the HPV-16/18 AS04-adjuvanted vaccine administered as a 2-dose schedule compared with the licensed 3-dose schedule: results from a randomized study. *Hum Vaccin*. 2011;7(12):1374-86; PMID:22048171; <http://dx.doi.org/10.4161/hv.7.12.18322>
- Day PM, Kines RC, Thompson CD, Jagu S, Roden RB, Lowy DR, Schiller JT. In vivo mechanisms of vaccine-induced protection against HPV infection. *Cell Host Microbe*. 2010;8(3):260-70; PMID:20833377; <http://dx.doi.org/10.1016/j.chom.2010.08.003>
- Longet S, Schiller JT, Bobst M, Jichlinski P, Nardelli-Haeffiger D. A murine genital-challenge model is a sensitive measure of protective antibodies against human papillomavirus infection. *J Virol*. 2011;85(24):13253-9; PMID:21976653; <http://dx.doi.org/10.1128/JVI.06093-11>
- Wheeler CM, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Perez G, Brown DR, Koutsky LA, Tay EH, García P, et al. The impact of quadrivalent human papillomavirus (HPV; types 6, 11, 16, and 18) L1 virus-like particle vaccine on infection and disease due to oncogenic nonvaccine HPV types in sexually active women aged 16-26 years. *J Infect Dis*. 2009;199(7):936-44; PMID:19236277; <http://dx.doi.org/10.1086/597309>
- Joura EA, Ault KA, Bosch FX, Brown D, Cuzick J, Ferris D, Garland SM, Giuliano AR, Hernandez-Avila M, Huh W, et al. Attribution of 12 high-risk human papillomavirus genotypes to infection and cervical disease. *Cancer Epidemiol Biomarkers Prev*. 2014;23(10):1997-2008; PMID:25274978; <http://dx.doi.org/10.1158/1055-9965.EPI-14-0410>
- Smolen KK, Gelinas L, Franzen L, Dobson S, Dawar M, Ogilvie G, Krajden M, Fortuno ES 3rd, Kollmann TR. Age of recipient and number of doses differentially impact human B and T cell immune memory responses to HPV vaccination. *Vaccine*. 2012;30(24):3572-3579; PMID:22469863; <http://dx.doi.org/10.1016/j.vaccine.2012.03.051>
- Schwarz T, Spaczynski M, Kaufmann A, Wysocki J, Galaj A, Schulze K, Suryakiran P, Thomas F, Descamps D. Persistence of immune responses to the HPV-16/18 AS04-adjuvanted vaccine in women aged 15-55 years and first-time modelling of antibody responses in mature women: results from an open-label 6-year follow-up study. *BJOG*. 2015;122(1):107-18;

- PMID:25208608; <http://dx.doi.org/10.1111/1471-0528.13070>
26. Human papillomavirus vaccines: WHO position paper, October 2014. *Wkly Epidemiol Rec.* 2014;89(43):465-91; PMID:25346960
 27. National Health and Nutrition Examination Survey: Questionnaires, datasets, and related documentation. http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm. Accessed November 20, 2014.
 28. Hariri S, Unger ER, Sternberg M, Dunne EF, Swan D, Patel S, Markowitz LE. Prevalence of genital human papillomavirus among females in the United States, the National Health And Nutrition Examination Survey, 2003-2006. *J Infect Dis.* 2011;204(4):566-73; PMID:21791659; <http://dx.doi.org/10.1093/infdis/jir341>
 29. Design and estimation for the National Health Interview Survey, 1995-2004. *Vital Health Stat 2.* 2000(130):1-31; PMID:AMBIGUOUS
 30. Korn EL, Graubard BI. Epidemiologic studies utilizing surveys: accounting for the sampling design. *Am J Public Health.* 1991;81(9):1166-73; PMID:1951829; <http://dx.doi.org/10.2105/AJPH.81.9.1166>
 31. Bieler GS, Brown GG, Williams RL, Brogan DJ. Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. *Am J Epidemiol.* 2010;171(5):618-23; PMID:20133516; <http://dx.doi.org/10.1093/aje/kwp440>
 32. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. *Stata Journal.* 2013;13(3):492-509

List of Added Vaccines

1. **Hepatitis A**

HARVIX – MRC-5 human diploid cells, 250mcg of aluminum hydroxide (pediatric dose), polysorbate 20, formalin, neomycin sulfate

HAVRIX has NOT been evaluated for its carcinogenic potential, mutagenic potential, or potential for impairment of fertility.

VAQTA – Whole live virus from human MRC-5 diploid fibroblasts, formalin, 225mcg of aluminum hydroxyphosphate sulfate, neomycin.

2. **Influenza**

FLULAVAL – egg protein, formaldehyde, 50mcg of thimerosal in multidose vial (no thimerosal in single vial), polysorbate 80

3. **Pneumococcal Conjugate Vaccine (PCV)**

PREVNAR 13 – Soy, yeast, polysorbate 80, aluminum phosphate 125mcg
Serious adverse events reported following vaccination in infants and toddlers occurred in 8.2% among Prevnar 13 recipients and 7.2% among Prevnar recipients.

4. **Rotavirus**

ROTARIX

The lyophilized vaccine contains amino acids, dextran, Dulbecco's Modified Eagle Medium (DMEM), sorbitol, and sucrose. DMEM contains the following ingredients: sodium chloride, potassium chloride, magnesium sulfate, ferric (III) nitrate, sodium phosphate, sodium pyruvate, D-glucose, concentrated vitamin solution, L-cystine, L-tyrosine, amino acids solution, L-glutamine, calcium chloride, sodium hydrogenocarbonate, and phenol red.

In the manufacturing process, porcine-derived materials are used. Porcine (pig) circovirus type 1 (PCV-1) is present in ROTARIX (THIS IS A PIG VIRAL DNA COMPONENT)

ROTATEQ

The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, and trace amounts of fetal bovine serum. RotaTeq contains no preservatives. In the manufacturing process for RotaTeq, a porcine-derived material is used. DNA from porcine circoviruses (PCV) 1 and 2 has been detected in RotaTeq. PCV-1 and PCV-2 are not known to cause disease in humans.

Shedding of vaccine virus was evaluated among a subset of subjects in the Rotavirus Efficacy and Safety Trial (REST) 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission of vaccine virus was not evaluated in phase 3 studies. Transmission of vaccine virus strains from vaccinees to non-vaccinated contacts has been observed post-marketing.

5. **HPV (Human Papillomavirus Vaccine)**

GARDASIL 9

GARDASIL 9 is a sterile suspension for intramuscular administration. Each 0.5-mL dose contains approximately 30 mcg of HPV Type 6 L1 protein, 40 mcg of HPV Type 11 L1 protein, 60 mcg of HPV Type 16 L1 protein, 40 mcg of HPV Type 18 L1 protein, 20 mcg of HPV Type 31 L1 protein, 20 mcg of HPV Type 33 L1 protein, 20 mcg of HPV Type 45 L1 protein, 20 mcg of HPV Type 52 L1 protein, and 20 mcg of HPV Type 58 L1 protein.

Each 0.5-mL dose of the vaccine also contains approximately 500 mcg of aluminum (provided as AAHS), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, <7 mcg yeast protein, and water for injection. The product does not contain a preservative or antibiotics.

Using the MedAlerts search engine, as of April 30, 2018, the federal Vaccine Adverse Events Reporting System (VAERS) contains more than [58,992](#) reports of HPV vaccine reactions, hospitalizations, injuries and deaths and, includes 430 related deaths, 794 hospitalizations, and 2,773 disabling conditions. Over 45 percent of the reported serious adverse events occurred in children and teens 12-17 years of age.

As of [June 29, 2018](#), 387 claims were filed with the federal Vaccine Injury Compensation Program (VICP) for injuries and deaths following HPV vaccination, which included 14 deaths and 376 serious injuries. Less than a third of claims received compensation.

After the original Gardasil vaccine was licensed for 11-12 year old girls and young women, thousands of adverse reaction reports were filed for: sudden collapse with unconsciousness within 24 hours, seizures, muscle pain and

weakness, disabling fatigue, Guillain Barre Syndrome (GBS), facial paralysis brain inflammation, rheumatoid arthritis, lupus, blood clots, premature ovarian failure, optic neuritis, multiple sclerosis, strokes, heart and other serious health problems, including death.²³ Similar reports have been filed for the Gardasil 9 vaccine,²⁴ even though the recommended number of doses was reduced from three to two.

6. MCV (Meningococcal Conjugate Vaccine)

MENOMUNE – 25mcg of Thimerosal, Latex, Aluminum, Sucrose, Antibiotics, Polysorbate 80

DRUG INTERACTIONS: No safety and immunogenicity data are available on the concomitant administration of Menomune _ A/C/Y/W-135 vaccine with other US licensed vaccines (Vaccine Insert).



Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective low dose neurotoxicity



Guillemette Crépeaux^{a,b,*}, Housam Eidi^{a,c}, Marie-Odile David^c, Yasmine Baba-Amer^a, Eleni Tzavara^d, Bruno Giros^d, François-Jérôme Authier^a, Christopher Exley^e, Christopher A. Shaw^f, Josette Cadusseau^{a,g,1}, Romain K. Gherardi^{a,1}

^a Inserm U955 E10, Université Paris Est Créteil (UPEC), Créteil, France

^b Ecole Nationale Vétérinaire d'Alfort, Maisons-Alfort, France

^c Inserm U1204, Université Evry Val d'Essonne (UEVE), Evry, France

^d Inserm U1130, CNRS UMR 8246, UPMC UM CR18, Paris, France

^e Birchall Centre, Keele University, Staffordshire, UK

^f Department of Ophthalmology, University of British Columbia, Vancouver, BC, Canada

^g Faculté des Sciences & Technologies UPEC, Créteil, France

ARTICLE INFO

Article history:

Received 10 November 2016

Received in revised form 26 November 2016

Accepted 28 November 2016

Available online 28 November 2016

Keywords:

Aluminium oxyhydroxide

Adjuvant

Particle

Neurotoxicity

Non-monotonous dose response

Macrophagic myofasciitis

ABSTRACT

Aluminium (Al) oxyhydroxide (Alhydrogel[®]), the main adjuvant licensed for human and animal vaccines, consists of primary nanoparticles that spontaneously agglomerate. Concerns about its safety emerged following recognition of its unexpectedly long-lasting biopersistence within immune cells in some individuals, and reports of chronic fatigue syndrome, cognitive dysfunction, myalgia, dysautonomia and autoimmune/inflammatory features temporally linked to multiple Al-containing vaccine administrations. Mouse experiments have documented its capture and slow transportation by monocyte-lineage cells from the injected muscle to lymphoid organs and eventually the brain. The present study aimed at evaluating mouse brain function and Al concentration 180 days after injection of various doses of Alhydrogel[®] (200, 400 and 800 µg Al/kg of body weight) in the *tibialis anterior* muscle in adult female CD1 mice. Cognitive and motor performances were assessed by 8 validated tests, microglial activation by Iba-1 immunohistochemistry, and Al level by graphite furnace atomic absorption spectroscopy.

An unusual neuro-toxicological pattern limited to a low dose of Alhydrogel[®] was observed. Neurobehavioural changes, including decreased activity levels and altered anxiety-like behaviour, were observed compared to controls in animals exposed to 200 µg Al/kg but not at 400 and 800 µg Al/kg. Consistently, microglial number appeared increased in the ventral forebrain of the 200 µg Al/kg group. Cerebral Al levels were selectively increased in animals exposed to the lowest dose, while muscle granulomas had almost completely disappeared at 6 months in these animals.

We conclude that Alhydrogel[®] injected at low dose in mouse muscle may selectively induce long-term Al cerebral accumulation and neurotoxic effects. To explain this unexpected result, an avenue that could be explored in the future relates to the adjuvant size since the injected suspensions corresponding to the lowest dose, but not to the highest doses, exclusively contained small agglomerates in the bacteria-size range known to favour capture and, presumably, transportation by monocyte-lineage cells. In any event, the view that Alhydrogel[®] neurotoxicity obeys “the dose makes the poison” rule of classical chemical toxicity appears overly simplistic.

© 2016 Elsevier Ireland Ltd. All rights reserved.

Abbreviations: Al, aluminium; dLNs, draining lymph nodes; im, intra-muscular; MME, macrophagic myofasciitis; NOR, novel object recognition test; PFA, paraformaldehyde.

* Corresponding author at: Inserm U955 E10, Faculté de médecine, 8 rue du général Sarrail, 94010, Créteil, France.

E-mail address: guillemette.crepeaux@vet-alfort.fr (G. Crépeaux).

¹ These authors contributed equally to this work.

² www.imrb.inserm.fr/en/.

1. Introduction

Many severe infectious diseases can be prevented and some of them have been eradicated by vaccines. Commonly used vaccines are generally well tolerated and considered safe by regulatory agencies. However, as other effective medical compounds, vaccines may occasionally cause adverse effects. In particular, a condition

manifesting by the combination of myalgia, arthralgia, chronic fatigue, cognitive dysfunction, dysautonomia and autoimmunity has been temporally linked to aluminium adjuvant-containing vaccine administration, called Macrophagic Myofasciitis (MMF) (Gherardi and Authier, 2003; Authier et al., 2003; Exley et al., 2009; Rosenblum et al., 2011; Santiago et al., 2014; Brinth et al., 2015; Palmieri et al., 2016).

Although no consensus has been reached so far on a cause-to-effect relationship, environmental aluminium has long been suspected to act as a co-factor of several chronic neurological diseases (Van Rensburg et al., 2001; De Sole et al., 2013; Exley 2013, 2014) and the idea has emerged that aluminium adjuvants may be insidiously unsafe over the long-term in some predisposed individuals (reviewed in Tomljenovic and Shaw, 2011; Gherardi et al., 2015). Among aluminium salts used in vaccines, crystalline Al hydroxide or oxyhydroxide (Alhydrogel[®]) is the more widely used and is found in vaccines against tetanus, hepatitis A, hepatitis B, *Haemophilus influenzae* B, pneumococcal and meningococcal infections, and anthrax (Gherardi et al., 2015). This adjuvant consists of primary particles in the nano-sized range spontaneously forming micron-sized agglomerates (Eidi et al., 2015).

Although aluminium salts have been added to vaccines since 1926 (Glenny et al., 1926), exact mechanisms underlying their immuno-potentiating effects remain incompletely understood (Exley et al., 2010). Previous studies from our laboratory have shown that alum particles, as other poorly degradable particles, may not stay entirely localized in the injected tissue in mice, but can disseminate within phagocytic cells to regional lymph nodes and then to more distant sites and to the brain (Khan et al., 2013; Crépeaux et al., 2015; Eidi et al., 2015). In contrast to a previous belief, alum is characterized by striking biopersistence within immune cells in both the injected muscle, and the draining lymph nodes (dLNs) and spleen, where it may be found in conspicuous quantities 9 months after injection (Crépeaux et al., 2015). In humans, long term biopersistence of aluminium hydroxide within innate immune cells causes a specific lesion at site of previous immunization, called MMF, that may be detected up to >12 years after the last vaccine injection (Gherardi et al., 2001) in patients with a clinical condition now designated as ASIA 'Autoimmune/inflammatory syndrome induced by adjuvants' (Shoenfeld and Agmon-Levin, 2011).

The potential impact of aluminium adjuvant on the nervous system has been studied in mouse models. Alhydrogel[®] adjuvant, dosed at 100 µg Al/kg and subcutaneously injected in CD1 mice induced motor deficits and cognitive alterations associated with motor neuron death and a significant increase (350%) of reactive astrocytes indicative of an inflammatory process (Petrik et al., 2007). Although no motor neuron death was observed at the dose of 300 µg Al/kg, both microglial and astroglial reactions were observed in the spinal cord and were associated with altered motor and cognitive functions in CD1 mice (Shaw and Petrik, 2009).

In the same way, a neuro-inflammatory/degenerative syndrome has been described in sheep after repeated administrations of alum-containing vaccines (Luján et al., 2013), and impairment of neurocognitive functions and brain gliosis were reported in a murine model of systemic lupus erythematosus-like disease following intramuscular injection of Al hydroxide or vaccine against the hepatitis B virus (Agmon-Levin et al., 2014).

Previous in vivo aluminium adjuvant neurotoxicological studies did not include dose-response analyses. However, several reports studying neurotoxicity of soluble aluminium compounds administered by the oral route (Al chloride, Al nitrate, Al ammonium sulfate) to rodents showed a non-linear biphasic response on acetyl-cholinesterase activity (Kumar, 1998), dopamine turnover (Tsunoda and Sharma, 1999), nitric oxide synthase expression (Kim, 2003), and behavioural performances (Roig et al., 2006).

Poorly understood biphasic Al effects were also observed in vitro: cell cultures showing increased cell growth at low concentrations and diminished cell growth at high concentrations (Exley and Birchall, 1992). Similar unusual observations were made in studies of hippocampal long-term potentiation (Platt et al., 1995), and neuronal cell death in NSC-34 neuron-like cells (Eidi et al., 2015).

The present dose-response study was designed to evaluate long-term aluminium hydroxide neurotoxicity by assessing mouse behaviour, aluminium cerebral concentrations and microglial changes in CD1 mice 180 days after intramuscular injections of Alhydrogel[®]. Strikingly, the lower dose selectively induced neurobehavioural changes, cerebral aluminium level increases and microglial activation.

2. Materials and methods

2.1. Alhydrogel[®] doses

Animals were injected with Alhydrogel[®] adjuvant (InvivoGen), the characteristics of which have been previously determined in terms of size and positive zeta potential (Eidi et al., 2015). Doses were calculated by reference to medical histories of MMF patients who received a median of 4 doses of an Al-containing vaccine within the 10 years prior to their diagnosis (Gherardi et al., 2001). A 60-kg woman (MMF affects mainly women) injected with 1 dose of HBV ENGERIX[®] vaccine (GSK laboratories, France) receives 500 µg of Al, i.e. 8.3 µg Al/kg of body weight. Extrapolating mouse to human dosage is a challenging issue. Although a firm scientific basis for allometric conversion is still lacking, we used an allometry calculation based on body surface area that reflects the metabolic rate to determine the human equivalent dose per Kg. This $\times 12.3$ allometric conversion factor from human to mouse (Sharma and McNeill, 2009) is easy to apply, and has been recommended to us by toxicologists of the French drug agency (AFFSAPS). Conversion resulted in an approximate of 100 µg Al/kg mouse body weight for one human dose. Four groups were used: control group (phosphate buffered saline (PBS) vehicle: Phosphate 0.1 M; NaCl 0.9%; pH 7.4); Alhydrogel[®] groups at the doses of 200, 400 or 800 µg Al/kg, in 3 injections of Alhydrogel in 20 µL PBS with a four-day interval. The animals thus received the mouse equivalent of 2, 4 and 8 human doses of Al-containing vaccine.

2.2. Animals

40 female CD1 mice, weighing 25–30 g (7 week old), were obtained from Charles Rivers Laboratories (France). Upon arrival, the females were housed at 5 animals per cage. Animals were maintained under a 12 h light cycle (8.00: 20.00), at a constant temperature (22 ± 2 °C) and a relative humidity of $55 \pm 10\%$. Mice were given ad libitum access to food and water. After a 1-week period for acclimatization, 8-week old females were separated in 4 experimental groups of 10 animals, and 20 µL im injections were made in the left *tibialis anterior*, with a 4-day interval between each injection.

At the end of the behavioural tests, 5 animals per group were sacrificed with an overdose of pentobarbital and transcardially perfused with PBS followed by ice-cold 4% paraformaldehyde (PFA) in PBS. Brains were collected for histological examination, post-fixed in PFA for 4 h at 4 °C and immersed overnight in a 30% sucrose/PBS solution, then frozen and stored at -80 °C until sectioning. Whole brains were serially cut into 40 µm-thick coronal cryosections stored at -20 °C until use.

The other 5 animals per group were sacrificed with an overdose of pentobarbital. Brains were retrieved, quickly frozen in isopentane and kept at -80 °C for subsequent determination of Al levels.

All the experiments on animals were performed in respect to the guidelines provided by the European Union (Directive 2010/63/EU).

2.3. Behavioural and motor testing

A battery of 8 behavioural or physical tests was performed in the 4 experimental groups (n = 10 mice/group) 180 days after the third injection. Tests were chosen in order to assess locomotor activity in the open-field (Walsh and Cummins, 1976), level of anxiety in the O-maze (Shepherd et al., 1994; Coutellier et al., 2009), short-term memory in the novel object recognition test (Ennaceur and Delacour, 1988; Dudchenko, 2004; Ennaceur, 2010; Moore et al., 2013), muscular strength in the wire mesh hang (Kondziela, 1964) and the grip strength tests (Maurissen et al., 2003), locomotor coordination in the rotarod test (Pratte et al., 2011), depression in the tail suspension test (Steru et al., 1985), and pain sensitivity in the hot plate test (Espejo and Mir, 1993).

All the tests were performed under white light <100 Lux between 9 a.m. and 1 p.m. They were video-recorded and all the variables were analyzed by the same experimenter, using ViewPoint Life Sciences Inc software (Canada).

The animals were transferred to the behavioural testing room 30 min prior to beginning of test in order to let the animal adapt to the test room conditions. Between each animal, the apparatus was cleaned with a 30% ethanol solution. At the end of a whole testing session, mice were sacrificed and samples were retrieved.

2.3.1. Open-field

The general locomotor activity was assessed by the open-field test (Walsh and Cummins, 1976). The apparatus was made of a square open-field arena (42 cm side × 25 cm high walls) with the floor divided into 3 distinct areas: the peripheral, the medium and the central areas. At the beginning of the test, the mouse was placed in the center of the central area, and was let free to explore for 5 min. During this period the total distance and the distance and time spent in each of the three areas and the number of rearing, were recorded.

2.3.2. Elevated O-maze

The level of animal anxiety was assessed by the elevated O-maze test (Shepherd et al., 1994), with the advantage of the lack of the ambiguous central square compared to the traditional plus-maze (Coutellier et al., 2009). The maze was elevated to a 70 cm height, with 2 open (50 × 10 cm) and 2 closed (50 × 10 × 40 cm) arms. Arms of the same type were opposite to each other. Each mouse was tested within a 5-min test session. At the beginning, a mouse was placed individually in one of the closed arms, and was allowed to freely explore the maze. The time spent in closed and open arms, latency time to exit the closed arm for the first time, and the number of head-dippings and rearings were recorded.

2.3.3. Novel object recognition test

The novel object recognition test (NOR) was first proposed by Ennaceur and Delacour in 1988. This test is based on the spontaneous behaviour of rodents to interact more with a novel object than with a familiar one because of their inherent preference for novelty. Thus, in this test, rodents must be able to remember the previously encountered familiar object to determine which object is “novel” during the test trial (Moore et al., 2013).

The NOR task can be configured to cover various aspects and types of memory, including working memory (Dudchenko, 2004; Ennaceur, 2010).

The apparatus consisted of a square chamber (40 × 40 × 25 cm) and a digital camera was used to record behaviour videos. Videos

were analyzed and the time spent by mice exploring each object was measured. The test consisted of four sessions: habituation to the field (10 min, day 1), habituation to objects (5 min, day 1), familiarization phase with 2 identical objects (5 min, day 2), test 1 h later (5 min, day 2), with one familiar and one novel object. The novel objects were different in shape and colour but similar in size. The interaction of mouse with both objects (familiar and novel) was recorded for 5 min and percent discrimination index was calculated to determine memory performance as follow:

Discrimination index = exploration time with novel object / (exploration time with familiar object + novel object) × 100.

Exploration of an object is defined as the orientation of animal's snout toward the object, sniffing or touching with snout, while running around the object, sitting or climbing on it was not recorded as exploration (Antunes and Biala, 2012).

2.3.4. Wire mesh hang test

The hang wire mesh test was designed to test muscle strength using all four limbs (Kondziela, 1964). The inverted screen is a 43 cm square of wire mesh consisting of 12 mm squares of 1 mm diameter wire. The time during which the animals were able to sustain their weight holding onto the metal rail suspended in midair above the surface of soft bedding material was recorded for a 5 min-maximum time. Each mouse was subjected to three trials and the best performance was retained. Mouse body weight was considered, because this variable can influence performance.

2.3.5. Grip strength test

The rodent grip strength test was developed to measure muscular strength (Maurissen et al., 2003). The apparatus (Bio-GS3, Bioseb, France) consists of a grasping device or platform (i.e. grid and T-bar) that is connected to a load cell. The test measurement is conducted by allowing the animal to grasp the device and then having the experimenter pull it away until its grip is broken. The maximal force achieved by the animal was recorded for two types of measurements: forelimb measurement and forelimb and hindlimb measurement. Five such trials for the forelimbs and five others for the four limbs were performed and both best performances were kept.

2.3.6. Accelerating rotarod

Motor coordination and balance were tested using an accelerating rotarod (LE8200, Bioseb, France) consisting of a 3 cm diameter drum (15 cm above the base), divided with flanges into five lanes (Pratte et al., 2011). The apparatus is electronically controlled and evenly increases the speed of the bar from 4 to 40 rpm over a 5-min session. The mice were placed on the rod body orientation opposite to beam movement in the longitudinal axis, so that forward locomotion was necessary to avoid a fall. The mice were acclimated and trained on a morning session, and then they were given five successive trials on the afternoon. The best trial (longest latency to fall) for each mouse was retained. Since body weight may affect performance, mouse weight was considered in the score determination.

2.3.7. Tail suspension test

The method is based on the observation that a mouse suspended by the tail shows alternate periods of agitation characterized by intense motor activity and expense of energy, and waiting-behaviour with immobility and energy saving (Steru et al., 1985).

For these experiments, the mouse was hung on a hook by an adhesive tape placed 20 mm from the extremity of its tail. Mice were both acoustically and visually isolated. Each mouse was

suspended by its tail for 5 min, allowing the ventral surface and front and hind limbs to be video-recorded using a digital camera facing the test box. Total immobility time and latency time to be immobile were measured during the entire 5 min test period. Immobility was defined as the absence of initiated movements, and included passive waving of the body. Times were scored manually by observer watching the video. Each mouse was tested only once. Mouse body weight was considered in the score determination.

2.3.8. Hot plate test

The hot plate test is a behavioural model of nociception in which mice display several noxious-evoked patterns as well as exploratory and self-care responses (Espejo and Mir, 1993). The animals were individually placed on a preheated 50 °C hotplate (LE7406 Bioseb, France). An open-ended cylindrical Plexiglas tube with a 20 cm diameter and a 25 cm height was placed on top of the hot plate to prevent the mice from escaping but leaving their paws exposed to the hot plate. The time from placing the animals on the hot plate to the time of the first paw lick, the first rearing and the first jump were measured with a stopwatch. To prevent tissue damage, the mice were removed from the hot plate after 3 min regardless of their response. Mice were observed only once.

2.4. Microglia immunohistochemistry

Analyses were carried out on 3 brains per group. Brain sections were incubated with primary antibody Anti-Iba1 (goat ab5076, AbCam Paris, France, 1/2000 in PBS with 1% BSA) overnight at 4 °C. Then sections were incubated with secondary biotinylated rabbit anti-goat antibody (1/200, Vector Laboratories, Paris, France) for 2 h at room temperature. Labeling was determined using the chromogenic diaminobenzidine (DAB) method.

Microscopy: Brain sections were viewed with a Zeiss AxioPlan (Carl ZeissCanada Limited, Toronto, ON, Canada) microscope at 20× magnification. Images were captured using Zen2012 software. Microglia cell density and cell body area were measured in 4 regions mapped by reference to the Paxinos mouse brain atlas (Paxinos and Franklin, 2001): ventral forebrain, inferior colliculus and visual and motor cortex. Determinations were done on selected areas (mean area of 175,000 μm²) in 3 animals per group, by at least 2 of us, blinded for the identity of the group.

2.5. Brain Al analysis

Analyses were carried out on 5 brains per group (groups PBS, Alhydrogel[®] 200, 400, 800 μg Al/kg) 180 days following injection, according to the published method of House et al. (2012) and as described in our previous study (Crépeaux et al., 2015). Briefly, Al concentrations were determined by TH GFAAS in half brains dried to a constant weight at 37 °C and digested in a microwave (MARS

Xpress CEM Microwave Technology Ltd) in a mixture of 1 mL 15.8 M HNO₃ (Fischer Analytical Grade) and 1 mL of 30% w/v H₂O₂ (BDH Aristar Grade). Digests were clear and colourless or light yellow with no visible precipitate or fatty residue. Upon cooling each digest was diluted to a total volume of 5 mL with ultrapure water. Total Al was measured immediately post digestion using an AAnalyst 600 atomic absorption spectrometer with a transversely heated graphite atomizer (THGA) and longitudinal Zeeman-effect background corrector and an AS-800 autosampler with WinLab32 software (Perkin Elmer, UK). Standard THGA pyrolytically-coated graphite tubes with integrated L'Vovplatform (Perkin Elmer, UK) were used. The Zeeman background corrected peak area of the atomic absorption signal was used for the determinations.

Results were expressed as μg Al/g tissue dry weight. Each determination was the arithmetic mean of a triplicate analysis.

2.6. Muscle analysis

Analyses were carried out on 3 muscles per group (groups PBS, Alhydrogel[®] 200, 400, 800 μg Al/kg) 180 days following injection. Serial muscle tissue sections of 10 μm were successively deposited on 30 different Superfrost[®]-plus slides in order to obtain 30 identical series. For each animal one slide containing 20 representative longitudinal sections was used for haematoxylin-eosin staining, and two alternate slides were treated for Morin staining and CD11b immunostaining respectively.

- Immunostaining was done using commercial primary antibody routinely used in the lab, raised against CD11b (1/50, AbD Serotec, MCA711, Oxford, UK). The labeling was made with Cyanine 3 AffiniPure F(ab')₂ Fragment Donkey Anti-Rat (1/200, Jackson ImmunoResearch laboratory INC, Suffolk, UK).
- Al was stained with Morin (M4008-2 G, Sigma-Aldrich, Saint-Quentin-Fallavier, France) that was dissolved in a solution consisting of 0.5% acetic acid in 85% ethanol. Formation of a fluorescent complex with Al was detected under a 420 nm excitation wavelength as an intense green fluorescence with a characteristic 520 nm emission.
- Conventional microscopy was done using Carl Zeiss photonic and fluorescence microscopes.
- The presence of a muscle granuloma was semi-quantitatively assessed at magnification ×20, and quoted as: 0 (no or virtually no inflammatory cell), + (1 to 3 small granulomas), ++ (>3 small granulomas), +++ (>3 large granulomas).

2.7. Statistical analysis

Normality distribution of data was first analyzed by Shapiro-Wilk test, and then parametric or non-parametric tests were decided according to p values of Shapiro-Wilk test, i.e. parametric

Table 1
Effects of different doses of Alhydrogel[®] on motor activity and anxiety assessed in the open-field.

Open field	Control			Alhydrogel [®] 200 μg/kg			Alhydrogel [®] 400 μg/kg			Alhydrogel [®] 800 μg/kg			ANOVA	
	mean	±	sem	mean	±	sem	mean	±	sem	mean	±	sem	F _(3,39)	p
Total distance (cm)	2401.01	±	300.62	1303.48	±	213.04 *	2181.90	±	166.76	2622.46	±	205.96	4.220	p < 0.05
Distance in central area (cm)	236.34	±	35.96	228.01	±	44.92	163.33	±	31.02	238.50	±	38.89	0.831	n.s.
Distance in intermediate area (cm)	677.41	±	108.29	431.85	±	86.21	459.20	±	64.02	811.68	±	76.32	3.205	p < 0.05
Distance in peripheral area (cm)	1487.26	±	173.89	643.61	±	142.06 *	1530.20	±	106.15	1572.29	±	200.96	6.025	p < 0.01
Time spent in central area (s)	25.30	±	5.17	62.34	±	21.22 *	17.67	±	3.678	19.89	±	2.92	4.157	p < 0.05
Time spent in intermediate area (s)	77.99	±	6.80	93.03	±	13.28	60.68	±	7.60	73.33	±	8.24	2.100	n.s.
Time spent in peripheral area (s)	196.68	±	9.94	144.43	±	22.43 *	228.93	±	8.48	206.83	±	10.14	5.571	p < 0.01

Results are expressed as mean ± S.E.M. of n = 10 mice/group. Bonferroni's *t*-test was used for multiple comparisons.

im, intra-muscular; n.s., not significant.

* p < 0.05, statistical significant difference from controls.

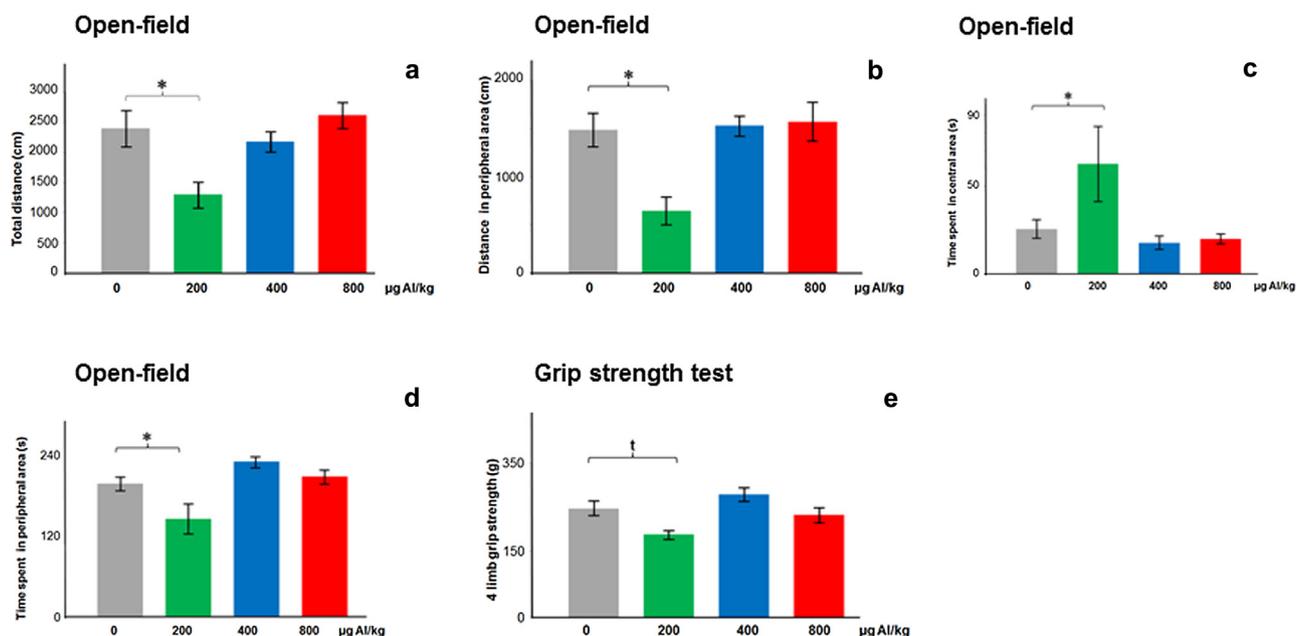


Fig. 1. Effects of different doses of Alhydrogel[®] on mouse behaviour. Altered scores were selectively observed with low Alhydrogel[®] doses. (a) Total distance in the open field; (b) distance in the peripheral area in the open field; (c) time spent in the central area in the open field; (d) time spent in the peripheral area in the open-field; (e) 4 limbs grip strength; 10 mice/group, results expressed as mean \pm S.E.M, ANOVA test with post-hoc Bonferroni's test. * $p < 0.05$, statistical significant difference from controls; † $p < 0.10$, statistical tendency difference from controls.

tests (ANOVA or Student's *t*-test) can be used when normality distribution is assumed $p > 0.05$, whereas we used non-parametric test (Kruskal-Wallis test) when normality distribution is not assumed ($p < 0.05$). Data from behavioural tests were analyzed using a one-way analysis of variance (one-way ANOVA). Post hoc comparisons have been performed using the Bonferroni's test when Anova was significant. Data from microglia IHC were analyzed using a Student's *t*-test. Data from Al concentration measurement were analyzed using a non-parametric Kruskal-Wallis test followed by a Mann-Whitney procedure modified for multiple comparisons when appropriate. Significance was set at $p < 0.05$. All statistical analyses were carried out using SPSS 16.0 software (SPSS INC., Chicago, IL, USA).

3. Results

3.1. Body weight

The initial body weight was 30 g. Animals were weighed once a week during the whole procedure. No effects of treatment were observed on body weight (data not shown).

3.2. Behavioural tests

3.2.1. Open-field

In the open-field (Table 1), a one-way ANOVA showed a significant difference of the total distance walked ($p = 0.012$), the distance in peripheral area ($p = 0.002$), and time spent in both

central ($p = 0.013$) and peripheral ($p = 0.003$) areas (Fig. 1a–d). Bonferroni's post hoc analysis showed that mice from the group Alhydrogel[®] 200 $\mu\text{g Al/kg}$ crossed a significantly smaller total distance ($p = 0.026$) and distance in the peripheral area ($p = 0.005$) (1303.48 ± 213.04 cm and 643.61 ± 142.06 cm respectively) than controls (2401.01 ± 300.62 cm). Furthermore, animals injected with Alhydrogel[®] 200 $\mu\text{g Al/kg}$ spent more time ($p = 0.047$) in the central (62.34 ± 21.22 s) and less ($p = 0.044$) in the peripheral areas (144.43 ± 22.43 s), as compared to controls (respectively 25.30 ± 5.17 s and 196.68 ± 9.94 s).

3.2.2. Elevated o-maze

In the elevated O-maze (Table S1 in the Supplemental data section) no significant differences between groups were observed across all measured variables.

3.2.3. Novel object recognition test

On the novel object recognition test (Table S2 in the Supplemental data section), one-way ANOVA did not reveal any statistical significant difference between groups across all studied variables.

3.2.4. Grip strength test

In the grip strength test (Table 2), significant difference ($p = 0.011$) between groups was observed for the 4-limb grip strength (Fig. 1e). Animals injected with Alhydrogel[®] at 200 $\mu\text{g Al/kg}$ tended ($p = 0.076$) to have less strength (187.24 ± 9.84 g) compared to controls (246.76 ± 16.46 g).

Table 2

Effects of different doses of Alhydrogel[®] on muscular performances assessed in the grip strength test.

Grip strength test	Control			Alhydrogel [®] 200 $\mu\text{g/kg}$			Alhydrogel [®] 400 $\mu\text{g/kg}$			Alhydrogel [®] 800 $\mu\text{g/kg}$			ANOVA	
	mean	\pm	sem	mean	\pm	sem	mean	\pm	sem	mean	\pm	sem	$F_{(3,39)}$	<i>p</i>
Fore limbs (g)	171.69	\pm	6.36	162.85	\pm	10.68	157.33	\pm	7.14	160.20	\pm	6.61	0.788	n.s.
4 limbs (g)	246.76	\pm	16.46	187.24	\pm	9.84[†]	278.59	\pm	15.95	231.97	\pm	17.32	4.188	$p < 0.05$

Results are expressed as mean \pm S.E.M. of $n = 10$ mice/group. Bonferroni's *t*-test was used for multiple comparisons.

im, intra-muscular; n.s., not significant.

[†] $p < 0.10$, statistical tendency from controls.

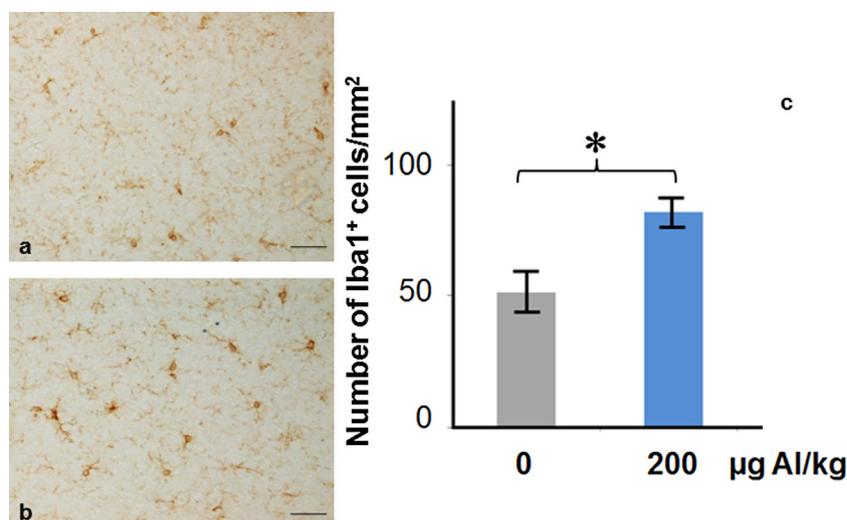


Fig. 2. Iba1⁺ microglial cell density in the ventral forebrain. Iba-1 immunostaining showed a slight increase of the microglial cell density in the group of mice injected with Alhydrogel[®] 200 µg Al/kg; (a) control mice injected with PBS; (b) mice injected with Alhydrogel[®] 200 µg Al/kg; (c) quantification of the microglial cell density. 3 mice/group; results expressed as means ± S.E.M, ANOVA test with post-hoc Bonferroni's test * $p < 0.05$; scale bars: 50 µm.

Table 3

Aluminum cerebral concentration measured by furnace atomic absorption spectrometry (µg/g of dry weight).

Cerebral Al concentration	Control	Alhydrogel [®] 200 µg/kg	Alhydrogel [®] 400 µg/kg	Alhydrogel [®] 800 µg/kg	Kruskal-Wallis
	0.0200 (0.0152–0.2088)	1.0027 (0.3368–1.1493)	0.0143 (0.0127–0.0200)	0.0156 (0.0137–0.3970)	0.017

Results are expressed as median and quartiles (in brackets) of $n = 5$ brains/group. Non parametric Kruskal-Wallis test followed by a Mann-Whitney procedure was used for multiple comparisons.

3.2.5. Wire-mesh hang test, accelerating rotarod, hot plate test and tail suspension test

No statistical differences were observed between the 4 experimental groups for these 4 tests (Tables S3–S6 in the Supplemental data section).

3.3. Microglia immunohistochemistry

As shown in Fig. 2, Alhydrogel[®] injections at doses of 200 µg Al/kg induced a significant increase ($p = 0.033$) in the number of Iba-1⁺ microglial cells in the ventral forebrain (81.90 ± 5.30 cells/mm²) compared to controls (51.43 ± 7.87 cells/mm²). Microglial density was similar to controls in visual and motor cortex and inferior colliculus in all groups. Microglial cell body size was similar in all groups (data not shown).

3.4. Cerebral Al level

The measurement of cerebral Al levels (Table 3) revealed a significantly ($p = 0.011$) higher Al level in brains from animals injected with 200 µg Al/kg (median value 1.00 µg/g of dry weight) than in brains from control group (0.02 µg/g of dry weight). No significant increase was observed in animals injected with 400 or 800 µg Al/kg (Fig. 3).

3.5. Muscle analysis

Granulomas with aluminium accumulations within macrophages were detected by Morin stain in the injected muscle of 6 animals (Fig. 4). As shown in Table 4, granulomas were found in 3/3 mice injected with 800 µg Al/kg, 3/3 mice injected with 400 µg Al/kg, and 0/3 mice injected with 200 µg Al/kg. The highest granuloma size was detected in mice injected with 800 µg Al/kg

(Fig. 4). An unusual aspect reminiscent of aluminium adjuvant-induced pseudo-lymphoma (Maubec et al., 2005) was observed in one case of the 800 µg Al/kg group and in another one of the 400 µg Al/kg group. The lesion appeared as a dense central area filled with monocyte-like and small lymphocytic cells and a rim of large macrophages with clear cytoplasm (Fig. 4a), in which aluminium was accumulated (Fig. 4b, c). Medium-sized CD11b-expressing monocyte lineage cells were found throughout the dense area of the lesion (Fig. 4d, e) often mixed with abundant nuclei of other mononuclear cell types as assessed by DAPI staining (Fig. 4d). Multinucleated giant cells were not found.

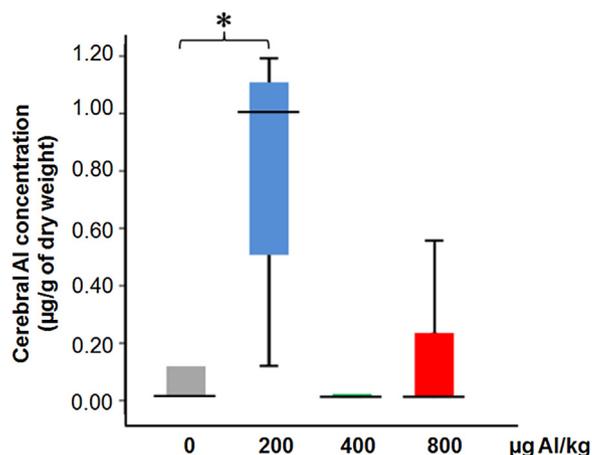


Fig. 3. Aluminium level determination in brain (µg/g of dry weight). Increased cerebral concentrations of aluminium were selectively observed with 200 µg/kg low Alhydrogel[®] dose. 5 mice/group; results expressed as median and range values, with quartiles boxes; non parametric Kruskal-Wallis test followed by Mann-Whitney test. * $p < 0.05$.

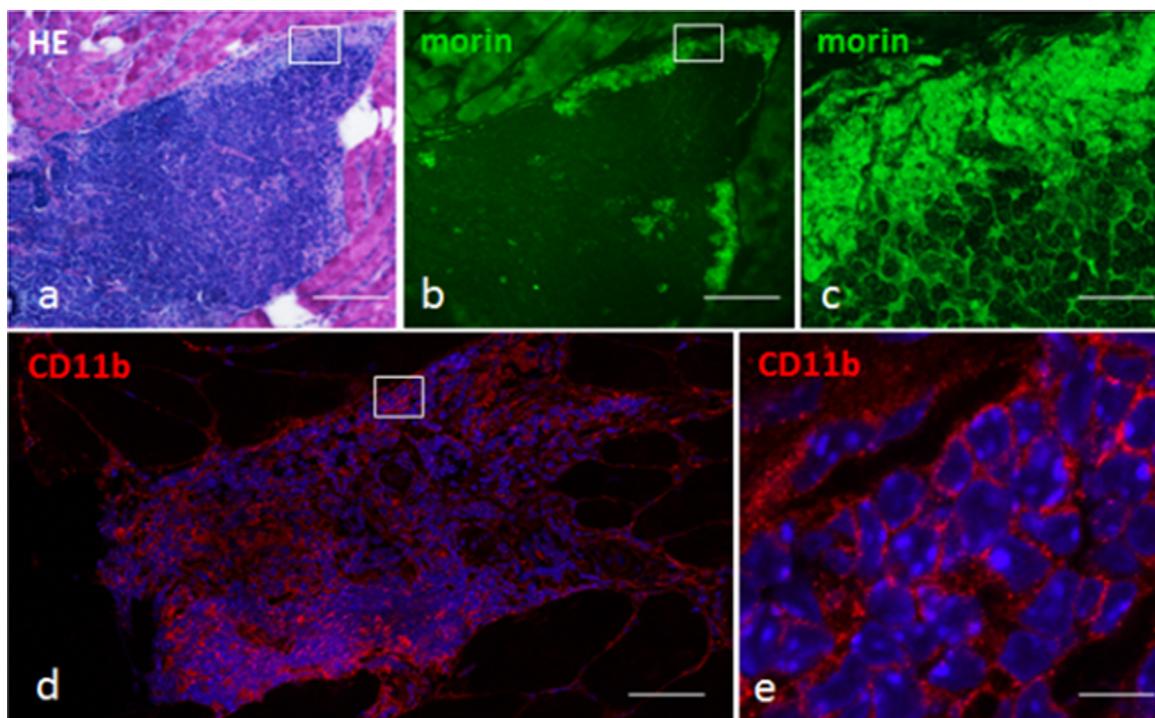


Fig. 4. Muscle sections 6 months after Alhydrogel[®] injections (800 µg Al/kg).

(a) Pseudolymphomatous lesion including a dense central area filled with mononuclear cells and a rim of macrophages with clear cytoplasm (HE: haematoxyline eosin, scale bar: 40 µm); (b,c) the rim of macrophages is selectively associated with aluminium accumulation stained in green (Morin stain, scale bars: 40 µm and 100 µm respectively); (d) CD11b-expressing monocyte lineage cells are present throughout the dense area of the pseudolymphomatous lesion, mixed with abundant DAPI⁺ nuclei of other mononuclear cell types (scale bar: 10 µm); (e) CD11b-expressing cells in an area prominently composed of medium-sized monocyte-lineage cells (scale bar: 20 µm).

Table 4

A semi-quantitative study of the granuloma size in injected muscle with Alhydrogel[®].

Alhydrogel [®] group	No granuloma (0)	1 to 3 small granuloma (+)	>3 small granuloma (++)	>3 large granuloma (+++)
200 µg Al/kg	3	0	0	0
400 µg Al/kg	0	0	3	0
800 µg Al/kg	0	1	1	1

According to their size, observed granulomas were divided to four types: without granuloma (0), 1 to 3 small (+), >3 small (++) and >3 large (+++) granuloma. Then, number of animals of each criteria was determined, for n=3 animals per group.

4. Discussion

In the present study, 8 widely used behavioural tests performed 180 days after im injections of 200, 400, or 800 µg Al/kg in form of Alhydrogel[®], in adult female CD1 mice, showed significant effects restricted to animals exposed to the lowest dose. Animals injected with 200 µg Al/kg showed decreased locomotor activity levels assessed by lower total distance crossed in the open-field, as reported previously after subcutaneous injection of 100 and 300 µg Al/kg of Alhydrogel[®] (Petrik et al., 2007; Shaw and Petrik, 2009), with concomitant decrease of the grip strength test suggestive of moderate motor weakness. In addition, increase of time spent in central area concomitantly with a decrease of both walked distance and time spent in peripheral area pointed to a behavioural change impacting the protective aversion of rodents for open spaces (Bourin et al., 2007), whereas other studies have reported increased anxiety levels (Petrik et al., 2007; Agmon-Levin et al., 2014). In sharp contrast, the highest doses of 400 and 800 µg Al/kg did not cause such changes. Consistently with the altered behavioural tests, microglial cell density appeared significantly increased in animals exposed to 200 µg Al/kg. This mild cerebral innate immune activation was selectively observed in ventral forebrain including the amygdaloid nuclei, which are implicated in

aversion/anxiety-like behaviours (LeDoux, 2007). Moreover, Al cerebral levels were significantly increased in animals injected with 200 µg Al/kg, but not in those injected with 400 and 800 µg Al/kg doses which showed neither neurobehavioural changes nor microglial reaction. The increased level of aluminium in brain was associated with an almost complete disappearance of aluminium-induced granuloma in mice injected with 200 µg Al/kg, while granulomas were constantly detected in the muscles injected with 400 or 800 µg Al/kg. In addition to conspicuous granuloma formation, 2/6 of these animals exhibited a pseudo-lymphomatous aspect suggesting an unusually strong local immune reaction to the foreign material.

In the present study we did not assess the concentration of Al in other tissues such as blood. Indeed, by using isotopic ²⁶Al, it was previously shown that the maximal increase in the plasma Al within 28 days after Al hydroxide im injection in the rabbit was about 2 ng/mL. Since the normal Al concentration was about 30 ng/mL in the animal, it was said that such a small increase would have been masked by the Al background if ²⁶Al-labelled adjuvants were not used (Flarend et al., 1997). Thus, Al plasma level determination on the long term, i.e. 6 months after im injection, cannot provide information in our mice. Furthermore in the present study the proposed method whereby Al is transported to organs and tissues

which are distant from the injection site does not actually involve the dissolution of the Al adjuvant into the muscle interstitial fluid and thereafter the blood but we are proposing that the transport of significant amounts of Al takes place in those cells which have infiltrated the injection site and taken up Al by endocytosis. Considering measurements of Al in muscle biopsies, we thought that they would not discriminate between extracellular and intracellular Al.

Evidence of a non-linear dose response curve of the neurotoxic effects of Alhydrogel[®], with selective toxicity of the lowest dose used in the study challenges the classic toxicology paradigm “the dose makes the poison”. Non-monotonic dose-response curves have been previously reported in the field of aluminium toxicology. Non-monotonic biphasic neurotoxic effects have been observed both in vitro (see for review [Exley and Birchall, 1992](#); [Platt et al., 1995](#); [Eidi et al., 2015](#)) and in vivo ([Kumar, 1998](#); [Tsunoda and Sharma, 1999](#); [Kim, 2003](#); [Roig et al., 2006](#)) after oral Al administration. However, the dose-response curve of the present study was not biphasic. Moreover, since cerebral aluminium level was not increased in mice injected with 400 or 800 µg Al/kg, the lack of neurotoxicity observed with these high doses was likely due to limited Al cerebral translocation, rather than to its paradoxical cytotoxic effects on neural cells. This puzzling result is challenging in the absence of solid knowledge on Alhydrogel[®] pharmacokinetics. We previously studied the fate of aluminium particles following im injections. Aluminium hydroxide is a highly hydrated crystalline compound composed of elementary nano-needles of approximately 2.2 nm × 4.5 nm × 10 nm ([Mao et al., 2013](#)) and displays a fibrous morphology at transmission electron microscopy ([Shirodkar et al., 1990](#); [Eidi et al., 2015](#)). This compound spontaneously forms micron-sized agglomerates ([Johnston et al., 2002](#)), subjected to slight size variations after antigen adsorption ([Eidi et al., 2015](#)) and in vivo interactions with phosphate, organic acid and proteinaceous environments. A series of recent reports from our laboratory have shown that translocation of aluminium hydroxide may be specifically related to monocyte lineage cell uptake of this poorly biodegradable compound ([Khan et al., 2013](#); [Crépeaux et al., 2015](#); [Eidi et al., 2015](#)), likely resulting from phagocytosis or macropinocytosis ([Mao et al., 2013](#)).

Recent studies suggest that the adjuvant effect requires uptake by dendritic cells ([Morefield et al., 2005](#)) and combines i) local up-regulation of chemokines, including CCL2 (MCP-1) and CCL3 (MIP-1α), that increase the recruitment of immune cells into the injection site; ii) increase of antigen uptake by innate immune cells; iii) induction of monocyte differentiation into dendritic cells, and iv) facilitation of migration of dendritic cells towards the dLNs to prime adaptive immune responses ([Seubert et al., 2008](#)). Macrophages capture bacteria which are usually in the 1–4 µm size range ([Kowalski et al., 1999](#)). A previous report showed in vitro exposure of monocyte lineage THP1 cells to Alhydrogel[®] 200 µg Al/mL resulted in cellular incorporation of Alhydrogel[®] agglomerates, the size of which was 1.20 µm as measured by transmission electron microscopy after 24h ([Mold et al., 2014, 2016](#)). Consistently, this size range was shown to be optimal for particle uptake by mouse peritoneal macrophages (1–2 µm) ([Tabata and Ikada, 1988](#)) and for particle attachment and subsequent internalization by mouse alveolar macrophages (2–3 µm), whereas internalization markedly drops when the size exceeds 4.2 µm ([Champion et al., 2008](#)).

Alhydrogel[®] biopersistence was confirmed in a variety of laboratory animal models up to 6–12 months post-injection, in both the injected muscle ([Verdier et al., 2005](#); [Authier et al., 2006](#); [Khan et al., 2013](#); [Eidi et al., 2015](#)) and distant lymphoid organs ([Crépeaux et al., 2015](#)). Particles traffic from an injected tissue to the dLNs is size-dependent, smaller particles (20–200 nm) being able to drain in a free form whereas medium-sized particles (0.5–

2 µm) are exclusively subjected to cell transportation ([Manolova et al., 2008](#)). Although the point has not been precisely addressed in the literature for particles >2 µm, it seems possible that rapid cellular uptake of limited size particles is associated with quicker cell transportation to dLNs compared to large particles subjected to slow cell uptake, showing that, in this period of time, lower doses of adjuvant can diffuse in the body and reach the brain whereas higher ones do not, for a considered time point ([Crépeaux et al., 2015](#)).

On these grounds, we performed an exploratory evaluation of the size of agglomerates, a parameter that could be modified when concentration of the colloid suspension is increased to adjust doses (0.1, 0.2, 0.4 g Al/L in PBS 1X corresponding to 200, 400, and 800 µg Al/kg respectively). Dynamic light scattering showed that the colloid suspensions in PBS at pH 7.2 corresponding to the neurotoxic 200 µg Al/kg condition was exclusively composed of small bacteria-size agglomerates (mean = 1750 ± 100 nm), easily captured by innate immune cells. In contrast, suspensions corresponding to higher doses showed 2 size peaks, including one peak corresponding to very large agglomerates (about 35,000 nm) and another one corresponding to either small agglomerates (mean = 1500 ± 400 nm in the 400 µg Al/kg condition) or medium-sized agglomerates (mean = 4800 ± 500 nm in the 800 µg Al/kg condition).

Although further studies are clearly required to document the influence of Alhydrogel[®] agglomeration state on in vivo neurotoxic effects, such a finding would not be unprecedented in the field of particle toxicology since both cellular uptake and distribution in the body of other types of particles are influenced by the particle size ([Buzea et al., 2007](#); [Reddy et al., 2007](#); [Landsiedel et al., 2012](#)), and aggregation rate ([Mühlfeld et al., 2008](#)), two parameters that strongly determine particle toxicity ([Bell et al., 2014](#); [Leclerc et al., 2012](#); [Nascarella and Calabrese, 2012](#); [Mold et al., 2016](#)).

In conclusion, the non-linear dose-response profile documented herein, in which the lowest dose but not the highest doses is neurotoxic in mice, is a novel insight in the field of aluminium adjuvant safety. It may suggest that Alhydrogel[®] toxicity obeys the specific rules of particle toxicology rather than any simplistic dose-response relationship. As a possible consequence, comparing vaccine adjuvant exposure to other non-relevant aluminium exposures, e.g. soluble aluminium and other routes of exposure, may not represent valid approaches. For example, aluminium retention rate observed after intravenous injections of traceable soluble aluminium citrate ([Priest, 2004](#)) has been used to set up the reassuring infant retention model of aluminium adjuvants ([Mitkus et al., 2011](#)). This model was based on the hypothesis that aluminium adjuvants are solubilized by citrate ions in muscle interstitial fluid ([Flarend et al., 1997](#)), without any consideration of quick adjuvant cellular uptake and systemic long term diffusion of adjuvant agglomerates ([Khan et al., 2013](#); [Eidi et al., 2015](#)). In the context of massive development of vaccine-based strategies worldwide, the present study may suggest that aluminium adjuvant toxicokinetics and safety require reevaluation.

Competing interests

The authors declare that there are no conflicts of interest.

Acknowledgements

This study was supported by grants from ANSM, CMSRI and University of British Columbia in Vancouver (Luther Allyn Dean Shourds Estate).

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at <http://dx.doi.org/10.1016/j.tox.2016.11.018>.

References

- Agmon-Levin, N., Arango, M.T., Kivity, S., Katzav, A., Gilburd, B., Blank, M., et al., 2014. Immunization with hepatitis B vaccine accelerates SLE-like disease in a murine model. *J. Autoimmun.* 54, 21–32.
- Antunes, M., Biala, G., 2012. The novel object recognition memory: neurobiology, test procedure, and its modifications. *Cogn. Process.* 13, 93–110.
- Authier, F.J., Sauvat, S., Champey, J., Drogou, I., Coquet, M., Gherardi, R.K., 2003. Chronic fatigue syndrome in patients with macrophagic myofasciitis. *Arthritis Rheum.* 48 (2), 569–570.
- Authier, F.J., Sauvat, S., Christov, C., Chariot, P., Raisbeck, G., Poron, M.F., et al., 2006. AIOH3-adjuvanted vaccine-induced macrophagic myofasciitis in rats is influenced by the genetic background. *Neuromuscul. Disord.* 16, 347–352.
- Bell, I.R., Ives, J.A., Jonas, W.B., 2014. Nonlinear effects of nanoparticles: biological variability from hormetic doses, small particle sizes, and dynamic adaptive interactions. *Dose-Response* 12, 202–232.
- Bourin, M., Petit-Demoulière, B., Dhonnchadha, B.N., Hascöet, M., 2007. Animal models of anxiety in mice. *Fundam. Clin. Pharmacol.* 21 (6), 567–574.
- Brinth, L., Pors, K., Grube Hoppe, A.A., Badreldin, I., Mehlsen, J., 2015. Is chronic fatigue syndrome/myalgic encephalomyelitis a relevant diagnosis in patients with suspected side effects to human papilloma virus vaccine? *Int. J. Vaccines Vaccin.* 1 (1), 00003.
- Buzea, C., Pacheco, I.L., Robbie, K., 2007. Nanomaterials and nanoparticles: sources and toxicity. *Biointerphases* 2 (4), MR17–MR71.
- Champion, J.A., Walker, A., Mitragotri, S., 2008. Role of particle size in phagocytosis of polymeric microspheres. *Pharm. Res.* 25 (8), 1815–1821.
- Coutellier, C., Friedrich, A.C., Failing, K., Marashi, V., Würbel, H., 2009. Effects of foraging demand on maternal behaviour and adult offspring anxiety and stress response in C57BL/6 mice. *Behav. Brain Res.* 196, 192–199.
- Crépeaux, G., Eidi, H., David, M.O., Tzavara, E., Giros, B., Exley, C., Curmi, P.A., Shaw, C.A., Gherardi, R.K., Cadusseau, J., 2015. Highly delayed systemic translocation of aluminum-based adjuvant in CD1 mice following intramuscular injections. *J. Inorg. Biochem.* 152, 199–205.
- De Sole, P., Rossi, C., Chiarpotto, M., Ciasca, G., Bocca, B., Alimonti, A., et al., 2013. Possible relationship between Al/ferritin complex and Alzheimer's disease. *Clin. Biochem.* 46, 89–93.
- Dudchenko, P.A., 2004. An overview of the tasks used to test working memory in rodents. *Neurosci. Biobehav. Rev.* 28, 699–709.
- Eidi, H., David, M.O., Crépeaux, G., Henry, L., Joshi, V., Berger, M.H., Sennour, M., Cadusseau, J., Gherardi, R.K., Curmi, P.A., 2015. Fluorescent nanodiamonds as a relevant tag for the assessment of alum adjuvant particle biodisposition. *BMC Med.* 13, 144.
- Ennaceur, A., Delacour, J., 1988. A new one-trial test for neurobiological studies of memory in rats. 1: behavioural data. *Behav. Brain Res.* 31, 47–59.
- Ennaceur, A., 2010. One-trial object recognition in rats and mice: methodological and theoretical issues. *Behav. Brain Res.* 215, 244–254.
- Espejo, E.F., Mir, D., 1993. Structure of the rat's behaviour in the hot plate test. *Behav. Brain Res.* 56, 171–176.
- European Union Directive, European Union Directive, 2010/63/EU of 22 September 2010 on the Approximation of Laws, Regulations and Administrative Provisions of the Member States Regarding the Protection of Animals Used for Experimental and Other Scientific Purposes.
- Exley, C., Birchall, J.D., 1992. The cellular toxicity of aluminium. *J. Theor. Biol.* 159, 83–98.
- Exley, C., Swarbrick, L., Gherardi, R.K., Authier, F.J., 2009. A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome. *Med. Hypotheses* 72, 135–139.
- Exley, C., Siesjö, P., Eriksson, H., 2010. The immunobiology of aluminium adjuvants: how do they really work? *Trends Immunol.* 31, 103–109.
- Exley, C., 2013. Human exposure to aluminium. *Environ. Sci. Process. Impacts* 15, 1807–1816.
- Exley, C., 2014. What is the risk of aluminium as a neurotoxin? *Expert Rev. Neurother.* 14, 589–591.
- Flarend, R.E., Hem, S.L., White, J.L., Elmore, D., Suckow, M.A., Rudy, A.C., Dandashli, E.A., 1997. In vivo absorption of aluminium containing vaccine adjuvants using 26 Al. *Vaccine* 15 (12113), 1314–1318.
- Gherardi, R.K., Authier, F.J., 2003. Aluminium inclusion macrophagic myofasciitis: a recently identified condition. *Immunol. Allergy Clin. North Am.* 23, 699–712.
- Gherardi, R.K., Coquet, M., Cherin, P., Belec, L., Moretto, P., Dreyfus, P.A., Pellissier, J.F., Chariot, P., Authier, F.J., 2001. Macrophagic myofasciitis lesions assess long-term persistence of vaccine-derived aluminium hydroxide in muscle. *Brain J. Neurol.* 124, 1821–1831.
- Gherardi, R.K., Eidi, H., Crépeaux, G., Authier, F.J., Cadusseau, J., 2015. Bipersistence and brain translocation of aluminium adjuvants of vaccines. *Front. Neurosci.* 6, 4.
- Glenny, A.T., Pope, C.G., Waddington, H., Wallace, U., 1926. XXIII—the antigenic value of toxoid precipitated by potassium alum. *J. Pathol. Bacteriol.* 29, 38–39.
- House, E., Esiri, M., Forster, G., Ince, P.G., Exley, C., 2012. Aluminium, iron and copper in human brain tissues donated to the Medical Research Council's Cognitive Function and Ageing Study. *Metallomics* 4, 56–65.
- Johnston, C.T., Wang, S.L., Hem, S.L., 2002. Measuring the surface area of aluminum hydroxide adjuvant. *J. Pharm. Sci.* 91 (7), 1702–1706.
- Khan, Z., Combadière, C., Authier, F.J., Itier, V., Lux, F., Exley, C., et al., 2013. Slow CCL2-dependent translocation of biopersistent particles from muscle to brain. *BMC Med.* 11, 99.
- Kim, K., 2003. Perinatal exposure to aluminum alters neuronal nitric oxide synthase expression in the frontal cortex of rat offspring. *Brain Res. Bull.* 61, 437–441.
- Kondziela, W., 1964. Eine neue method zur messung der muskulären relaxation bei weissen mausen. *Arch. Int. Pharmacodyn.* 152, 277–284.
- Kowalski, W.J., Bahnfleth, W., Withem, T.S., 1999. Filtration of airborne microorganisms: modeling and prediction. *ASHRAE Trans.* 105 (2), 4–17.
- Kumar, S., 1998. Biphasic effect of aluminium on cholinergic enzyme of rat brain. *Neurosci. Lett.* 248, 121–123.
- Landsiedel, R., Fabian, E., Ma-Hock, L., van Ravenzwaay, B., Wohlleben, W., Wiench, K., Oesch, F., 2012. Toxicokinetics of nanomaterials. *Arch. Toxicol.* 86, 1021–1060.
- LeDoux, J., 2007. The amygdala. *Curr. Biol.* 17, R868–R874.
- Leclerc, L., Rima, W., Boudard, D., Pourchez, J., Forest, V., Bin, V., Mowat, P., Perriat, P., Tillement, O., Grosseau, P., Bernache-Assollant, D., Cottier, M., 2012. Size of submicrometric and nanometric particles affect cellular uptake and biological activity of macrophages in vitro. *Inhal. Toxicol.* 24 (9), 580–588.
- Luján, L., Pérez, M., Salazar, E., Álvarez, N., Gimeno, M., Pinczowski, P., et al., 2013. Autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) in commercial sheep. *Immunol. Res.* 56, 317–324.
- Mühlfeld, C., Gehr, P., Rothen-Rutishauser, B., 2008. Translocation and cellular entering mechanisms of nanoparticles in the respiratory tract. *Swiss Med. Wkly.* 138 (July (27–28)), 387–391.
- Manolova, V., Flace, A., Bauer, M., Schwarz, K., Saudan, P., Bachmann, M.F., 2008. Nanoparticles target distinct dendritic cell populations according to their size. *Eur. J. Immunol.* 38 (5), 1404–1413.
- Mao, Z., Zhou, X., Gao, C., 2013. Influence of structure and properties of colloidal biomaterials on cellular uptake and cell functions. *Biomater. Sci.* 1, 896–911.
- Maubec, E., Pinquier, L., Viguier, M., Caux, F., Amsler, E., Aractingi, S., Chafi, H., Janin, A., Cayuela, J.M., Dubertret, L., Authier, F.J., Bachelez, H., 2005. Vaccination-induced cutaneous pseudolymphoma. *J. Am. Acad. Dermatol.* 52 (4), 623–629.
- Maurissen, J.P., Marable, B.R., Andrus, A.K., Stebbins, K.E., 2003. Factors affecting grip strength testing. *Neurotoxicol. Teratol.* 25, 543–553.
- Mitkus, R.J., King, D.B., Hess, M.A., Forshee, R.A., Walderhaug, M.O., 2011. Updated aluminum pharmacokinetics following infant exposures through diet and vaccination. *Vaccine* 29 (51), 9538–9543.
- Mold, M., Eriksson, H., Siesjö, P., Darabi, A., Shardlow, E., Exley, C., 2014. Unequivocal identification of intracellular aluminium adjuvant in a monocytic THP-1 cell line. *Sci. Rep.* 4, 6287.
- Mold, M., Shardlow, E., Exley, C., 2016. Insight into the cellular fate and toxicity of aluminium adjuvants used in clinically approved human vaccinations. *Sci. Rep.* 6, 31578.
- Moore, S.J., Deshpande, K., Stinnett, G.S., Seasholtz, A.F., Murphy, G.G., 2013. Conversion of short-term to long-term memory in the novel object recognition paradigm. *Neurobiol. Learn. Mem.* 105, 174–185.
- Morefield, G.L., Sokolovska, A., Jiang, D., HogenEsch, H., Robinson, J.P., Hem, S.L., 2005. Role of aluminium-containing adjuvants in antigen internalization by dendritic cells in vitro. *Vaccine* 23 (13), 1588–1595.
- Nascarella, M.A., Calabrese, E.J., 2012. A method to evaluate hormesis in nanoparticle dose-responses. *Dose-Response* 10, 344–354.
- Palmieri, B., Poddighe, D., Vadalà, M., Laurino, C., Carnovale, C., Clementi, E., 2016. Severe somatoform and dysautonomic syndromes after HPV vaccination: case series and review of literature. *Immunol. Res.* (in press).
- Paxinos, Franklin, 2001. The mouse brain in stereotaxic coordinates, second ed.
- Petrik, M.S., Wong, M.C., Tabata, R.C., Garry, R.F., Shaw, C.A., 2007. Aluminium adjuvant linked to Gulf War illness induces motor neuron death in mice. *Neuromolecular Med.* 9, 83–100.
- Platt, B., Carpenter, D.O., Büsselberg, D., Reyman, K.G., Riedel, G., 1995. Aluminium impairs hippocampal long-term potentiation in rats in vitro and in vivo. *Exp. Neurol.* 134, 73–86.
- Pratte, M., Panayotis, N., Ghata, A., Villard, L., Roux, J.C., 2011. Progressive motor and respiratory metabolism deficits in post-weaning Mecp2-null male mice. *Behav. Brain Res.* 216, 313–320.
- Priest, N.D., 2004. The biological behaviour and bioavailability of aluminium in man, with special reference to studies employing aluminium-26 as a tracer: review and study update. *J. Environ. Monit.* 6 (5), 375–403.
- Reddy, S.T., van der Vlies, A.J., Simeoni, E., Angeli, V., Randolph, G.J., O'Neil, C.P., Lee, L.K., Swartz, M.A., Hubbell, J.A., 2007. Exploiting lymphatic transport and complement activation in nanoparticle vaccines. *Nat. Biotechnol.* 25 (10), 1159–1164.
- Roig, J.L., Fuentes, S., Teresa Colomina, M., Vicens, P., Domingo, J.L., 2006. Aluminium, restraint stress and aging: behavioural effects in rats after 1 and 2 years of aluminium exposure. *Toxicology* 218, 112–124.
- Rosenblum, H., Shoenfeld, Y., Amital, H., 2011. The common immunogenic etiology of chronic fatigue syndrome: from infections to vaccines via adjuvants to the ASIA syndrome. *Infect. Dis. Clin. North Am.* 25 (4), 851–863.
- Santiago, T., Rebelo, O., Negrão, L., Matos, A., 2014. Macrophagic myofasciitis and vaccination: consequence or coincidence? *Rheumatol. Int.* 35, 189–192.
- Seubert, A., Monaci, E., Pizza, M., O'Hagan, D.T., Wack, A., 2008. The adjuvants aluminium hydroxide and MF59 induce monocyte and granulocyte chemoattractants and enhance monocyte differentiation toward dendritic cells. *J. Immunol.* 180 (8), 5402–5412 Erratum in: *J. Immunol.* 2009;182(1):726.

- Sharma, V., McNeill, J.H., 2009. To scale or not to scale: the principles of dose extrapolation. *Br. J. Pharmacol.* 157, 907–921.
- Shaw, C.A., Petrik, M.S., 2009. Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration. *J. Inorg. Biochem.* 103, 1555–1562.
- Shepherd, J.K., Grewal, S.S., Fletcher, A., Bill, D.J., Dourish, C.T., 1994. Behavioural and pharmacological characterisation of the elevated zero-maze as an animal model of anxiety. *Psychopharmacology (Berl.)* 116, 56–64.
- Shirodkar, S., Hutchinson, R.L., Perry, D.L., White, J.L., Hem, S.L., 1990. Aluminum compounds used as adjuvants in vaccines. *Pharm. Res.* 7 (12), 1282–1288.
- Shoenfeld, Y., Agmon-Levin, N., 2011. ASIA- autoimmune/inflammatory syndrome induced by adjuvants. *J. Autoimmun.* 36 (1), 4–8.
- Steru, L., Chermat, R., Thierry, B., Simon, P., 1985. The tail suspension test: a new method for screening antidepressants in mice. *Psychopharmacology (Berl.)* 85, 367–370.
- Tabata, Y., Ikada, Y., 1988. Effect of the size and surface-charge of polymer microspheres on their phagocytosis by macrophage. *Biomaterials* 9, 356–362.
- Tomljenovic, L., Shaw, C.A., 2011. Do aluminum vaccine adjuvants contribute to the rising prevalence of autism? *J. Inorg. Biochem.* 105, 1489–1499.
- Tsunoda, M., Sharma, R.P., 1999. Altered dopamine turnover in murine hypothalamus after low-dose continuous oral administration of aluminum. *J. Trace Elem. Med. Biol.* 13, 224–231.
- Van Rensburg, S.J., Potocnik, F.C., Kiss, T., Hugo, F., van Zijl, P., Mansvelt, E., et al., 2001. Serum concentrations of some metals and steroids in patients with chronic fatigue syndrome with reference to neurological and cognitive abnormalities. *Brain Res. Bull.* 55, 319–325.
- Verdier, F., Burnett, R., Michelet-Habchi, C., Moretto, P., Fievet-Groyne, F., Sauzeat, E., 2005. Aluminium assay and evaluation of the local reaction at several time points after intramuscular administration of aluminium containing vaccines in the cynomolgus monkey. *Vaccine* 23, 1359–1367.
- Walsh, R.N., Cummins, R.A., 1976. The open-field test: a critical review. *Psychol. Bull.* 83, 482–504.

Research Citations Linking Vaccines To Disease

Bichel, "Post-vaccinial Lymphadenitis Developing into Hodgkin's Disease", Acta Med Scand, 1976, Vol 199, p523-525.

Stewart, AM, et al, "Aetiology of Childhood Leukaemia", Lancet, 16 Oct, 1965, 2:789-790. [Listed under Vaccine Adverse Reactions.]

Glathe, H et al, "Evidence of Tumorigenic Activity of Candidate Cell Substrate in Vaccine Production by the Use of Anti-Lymphocyte Serum", Development Biol Std, 1977, 34:145-148.

Bolognesi, DP, "Potential Leukemia Virus Subunit Vaccines: Discussion", Can Research, Feb 1976, 36(2 pt 2):655-656.

Colon, VF, et al, "Vaccinia Necrosum as a Clue to Lymphatic Lymphoma", Geriatrics, Dec 1968, 23:81-82.

Park-Dincsoy, H et al, "Lymphoid Depletion in a case of Vaccinia Gangrenosa", Laval Med, Jan 1968, 39:24-26.

Hugoson, G et al, "The Occurrence of Bovine Leukosis Following the Introduction of Babesiosis Vaccination", Bibl Haemat, 1968, 30:157-161.

Hartstock, , ""Post-vaccinial Lymphadenitis: Hyperplasia of Lymphoid Tissue That Simulates Malignant Lymphomas", Apr 1968, Cancer, 21(4):632-649.

Allerberger, F, "An Outbreak of Suppurative Lymphadenitis Connected with BCG Vaccination in Austria- 1990/1991," Am Rev Respir Disorder, Aug 1991, 144(2) 469.

Omokoku B, Castells S, "Post-DPT inoculation cervical lymphadenitis in children." N Y State J Med 1981 Oct;81(11):1667-1668. Vaccines and Chromosome Changes Leading to Mutations:

Knuutila, S et al, "An Increased Frequency of Chromosomal Changes and SCE's in Cultured Lymphocytes of 12 Subjects Vaccinated Against Smallpox," Hum Genet, 1978 Feb 23; 41(1):89-96.

Cherkeziiia, SE, et al, "Disorders in the Murine Chromosome Apparatus Induced By Immunization with a Complex of Anti-viral Vaccines," Vopr Virusol, 1979 Sept Oct, (5):547-550.

[Note: SCE means sister chromatid exchange and is an indication that genetic mutations are occurring, which could possibly lead to cancer-causing mutations. Vaccines and Auto-immunity Citations:

Romanov, V A, et al, "Role of Auto-immune Processes in the Pathogenesis of Post-Vaccinal Lesions of the Nervous System", Oct 1977, Zh Mikrobiol Epidemiol Immunobiol, 10:80-83.

Grachev, V P, et al, "Formation of Auto-antibodies in Laboratory Animals After Inoculation of Viruses With Different Virulence. I. Results of Studies ..., July 1973, Acta Virol (Praha), 17:319-326.

Movsesiants, AA, et al, "Experimental Study of the Ability of Different Strains of Vaccinia Virus to Induce Auto-Antibody Formation", *Vopr Virusol*, May-Jun 1975; (3):297-302.

Negina, IuP, "Comparative Study of Auto-antibody Formation Following Immunization With Different Types of Typhoid Vaccines", *Zh Mikrobiol Epidemiol Immunobiol*, May 1980; (5):69-72. Vaccinations and Diabetes Citations:

Sinaniotis, et al, "Diabetes Mellitus after Mumps Vaccination", *Arc Dis Child*, 1975, 50:749.66

Polster, H, "Diabetes insipidus after Smallpox vaccination", *Z Aerztl Fortbild (Jena)*, 1 Apr 1966, 60:429-432.

Patan, "Postvaccinal Severe Diabetes Mellitus", *Ter Arkh*, Jul 1968, 40:117-118.

Classen, JB, MD, "The Timing of Immunization Affects The Development of Diabetes in Rodents", *Autoimmunity*, 1996, 24:137-145.

Classen JB, "The diabetes epidemic and the hepatitis B vaccines," *N Z Med J*, 109(1030):366 1996 Sep 27. [letter]

Classen JB, "Childhood immunisation and diabetes mellitus," *N Z Med J*, 109(1022):195 1996 May 24 [letter]

Poutasi K, " Immunisation and diabetes," *N Z Med J* 1996 Jul 26;109(1026):283. [letter; comment]

Other Articles Linking Diabetes to Vaccines:

Dokheel, T M, "An Epidemic of Childhood Diabetes in the United States? Evidence from", *Diabetes Care*, 1993, 16:1606-1611.

Parent ME, et al, "Bacille Calmette-Guerin vaccination and incidence of IDDM in Montreal, Canada," *Diabetes Care* 1997 May; 20(5):767-772.

House DV, Winter WE, "Autoimmune diabetes. The role of auto-antibody markers in the prediction and prevention of insulin-dependent diabetes mellitus," *Clin Lab Med* 1997 Sep; 17(3):499-545.

Zeigler, M et al , "[Autoantibodies in type 1 diabetes mellitus]" *Z Arztl Fortbild (Jena)*. 1994 Aug; 88(7-8):561-5 Vaccines and Nervous System Changes:

Bondarev, VN et al, "The Changes of the Nervous System in Children After Vaccination", *Pediatrics*, Jun 1969; 48:20-24.

Ehrengut W, "Central nervous sequelae of vaccinations," *Lancet* 1986 May 31;1(8492):1275-1276.

Provvidenza, G et al, [On a Case of Benign Acute Cerebellar Ataxia in Childhood], *Arch Ital Sci Med Trop*, 43:189-194, Apr 1962.

Katsilambros, L, "[The Phenomenom of Apathy in Man and Animals After the Injection of Viruses in Very High Doses. Clinical Data]", *Rev Med Moyen Orient*, 20:539-546, Nov – Dec 1963. Vaccinations and Autism Citations:

Eggers, C, "Autistic Syndrome (Kanner) And Vaccinations against Smallpox", *Klin Paediatr*, Mar 1976, 188(2):172-180.

Kiln MR, "Autism, inflammatory bowel disease, and MMR vaccine." *Lancet* 1998 May 2;351(9112):1358.

Selway, "MMR vaccination and autism 1998. Medical practitioners need to give more than reassurance." *BMJ* 1998 Jun 13;316(7147):1824.

Nicoll A, Elliman D, Ross E, "MMR vaccination and autism 1998," *MJ* 1998 Mar 7;316(7133):715-716.

Lindley K J, Milla PJ, "Autism, inflammatory bowel disease, and MMR vaccine." *Lancet* 1998 Mar 21;351(9106):907-908.

Bedford H, et al, "Autism, inflammatory bowel disease, and MMR vaccine." *Lancet* 1998 Mar 21;351(9106):907.

Vijendra K. Singh, Sheren X. Lin, and Victor C. Yang, "Serological Association of Measles Virus and Human Herpesvirus-6 with Brain Autoantibodies in Autism," *Clinical Immunology and Immunopathology*, Oct 1998, Vol. 89, No. 1, p 105-108. ["None of the autistic children in the study had measles in the past, but all had the MMR" stated David Whalgren. Vaccines and Demyelination Citations:

Herroelen, L et al, "Central-Nervous-System Demyelination After Immunization with Recombinant Hepatitis B Vaccine", *Lancet*, Nov 9, 1991, 338(8776):1174-1175.

Kaplanski G, Retornaz F, Durand J, Soubeyrand J, "Central nervous system demyelination after vaccination against hepatitis B and HLA haplotype." *J Neurol Neurosurg Psychiatry* 1995 Jun; 58(6):758-759.

Matyszak MK, Perry VH, "Demyelination in the central nervous system following a delayed-type hypersensitivity response to bacillus Calmette-Guerin." *Neuroscience* 1995 Feb;64(4):967-977.

Tornatore CS, Richert JR, "CNS demyelination associated with diploid cell rabies vaccine." *Lancet* 1990 Jun 2;335(8701):1346-1347.

Adams, JM et al, "Neuromyelitis Optica: Severe Demyelination Occurring Years After Primary Smallpox Vaccinations", *Rev Roum Neurol*, 1973, 10:227-231.

In 1988, Dietrich used MRI to show that developmentally delayed children had alterations in their myelin. Coulter described that central nervous system damage can be exhibited as abnormal behavior of the child. In 1935, Thomas Rivers, experimental allergic encephalitis (EAE) can be the result of a viral or bacterial infection of the nervous system. "The fact of the matter is that it is a matter of record that it was known that vaccination produced encephalitis since 1926." The authors stated, "In regions in which there is no organized vaccination of the population, general paralysis is rare. ... It is impossible to deny a connection between vaccinations and the encephalitis (brain damage) which follows it." Vaccines have been linked to seizures, convulsions and epilepsy. Vaccinations and Seizures:

Hirtz DG, Nelson KB, Ellenberg J H, "Seizures following childhood immunizations", *Pediatr* 1983 Jan; 102(1):14-18.

Cherry JD, Holtzman AE, Shields WD, Buch D, Nielsen, "Pertussis immunization and characteristics related to first seizures in infants and children," *J Pediatr* 1993 Jun;122(6):900-903.

Coplan J, "Seizures following immunizations," *J Pediatr* 1983 Sep;103(3):496.

Barkin RM, Jabhour JT, Samuelson J S, "Immunizations, seizures, and subsequent evaluation," *JAMA* 1987 Jul 10;258(2):201.

Griffin MR, et al, "Risk of seizures after measles-mumps-rubella immunization," *Pediatrics* 1991 Nov;88(5):881-885.

Griffin MR, et al, "Risk of seizures and encephalopathy after immunization with the diphtheria-tetanus-pertussis vaccine," *JAMA* 1990 Mar 23-30;263(12):1641-1645.

Cizewska S, Huber Z, Sluzewski W, "[Prophylactic inoculations and seizure activity in the EEG]," *Neurol Neurochir Pol* 1981 Sep-Dec;15(5-6):553-557. [Article in Polish]

Huttenlocher PR, Hapke RJ, "A follow-up study of intractable seizures in childhood." *Ann Neurol* 1990 Nov; 28(5):699-705.

Blumberg DA, "Severe reactions associated with diphtheria-tetanus-pertussis vaccine: detailed study of children with seizures, hypotonic-hypo-responsive episodes, high fevers, and persistent crying." *Pediatrics* 1993 Jun; 91(6):1158-1165. Vaccinations and Convulsions Citations:

Prensky AL, et al, "History of convulsions and use of pertussis vaccine," *J Pediatr* 1985 Aug; 107(2):244-255.

Baraff LJ, "Infants and children with convulsions and hypotonic-hypo-responsive episodes following diphtheria-tetanus-pertussis immunization: follow-up evaluation," *Pediatrics* 1988 Jun; 81(6):789-794.

Jacobson V, "Relationship of pertussis immunization to the onset of epilepsy, febrile convulsions and central nervous system infections: a retrospective epidemiologic study," *Tokai J Exp Clin Med* 1988;13 Suppl: 137-142.

Cupic V, et al, "[Role of DTP vaccine in the convulsive syndromes in children]," *Lijec Vjesn* 1978 Jun; 100(6):345-348. [Article in Serbo-Croatian (Roman)]

Pokrovskaja Ia, "[Convulsive syndrome in DPT vaccination (a clinico-experimental study)]," *Pediatriia* 1983 May;(5):37-39. [Article in Russian] Vaccinations and Epilepsy Citations:

Ballerini, Ricci, B, et al, "On Neurological Complications of Vaccination, With Special Reference to Epileptic Syndromes," *Riv Neurol*, Jul-Aug 1973, 43:254-258.

Wolf SM, Forsythe A, "Epilepsy and mental retardation following febrile seizures in childhood," *Acta Paediatr Scand* 1989 Mar;78(2):291-295. _____ Vaccines and Brain Swelling:

Iwasa, S et al, "Swelling of the Brain in Mice Caused by Pertussis ... Quantitative Determination and the Responsibility of the Vaccine", *Jpn J Med Sci Biol*, 1985 , 38(2):53-65.

Mathur R, Kumari S, "Bulging fontanel following triple vaccine." *Indian Pediatr* 1981 Jun;18(6):417-418.

Barry W, Lenney W, Hatcher G, "Bulging fontanelles in infants without meningitis." *Arch Dis Child* 1989 Apr;64(4):635-636.

Shendurnikar N, "Bulging fontanel following DPT" *Indian Pediatr* 1986 Nov;23(11):960.

Gross TP, Milstien JB, Kuritsky JN, "Bulging fontanelle after immunization with diphtheria-tetanus-pertussis vaccine and diphtheria-tetanus vaccine." *J Pediatr* 1989 Mar;114(3):423-425.

Jacob J, Mannino F, "Increased intracranial pressure after diphtheria, tetanus, and pertussis immunization." *Am J Dis Child* 1979 Feb;133(2):217-218.

Dugmore, WN, "Bilateral Oedema at the Posterior Pole. Hypersensitivity Reaction to Alavac P injection." *Br J Ophthalmol*, Dec 1972, 55:848-849. Vaccines and Neurological Damage

Nedar P R, and Warren, R J, "Reported Neurological Disorders Following Live Measles Vaccine", 1968, *Ped*, 41:997-1001.

Paradiso, G et al, "Multifocal Demyelinating Neuropathy after Tetanus Vaccine", *Medicina (B Aires)*, 1990, 50(1):52-54.

Landrigan, PJ, Whitte, J, "Neurologic Disorders Following Live Measles-virus Vaccination", *JAMA*, Mar 26, 1973, v223(13):1459-1462.

Turnbull, H M, "Encephalomyelitis Following Vaccination", *Brit Jour Exper Path*, 7:181, 1926.

Kulenkampff, M et al, "Neurological Complications of Pertussis Inoculation", *Arch Dis Child*, 1974, 49:46.

Strom, J, "Further Experience of Reactions, Especially of a Cerebral Nature in Conjunction with Triple Vaccination", Brit Med Jour, 1967, 4:320-323.

Berg, J M, "Neurological Complications of Pertussis Immunization," Brit Med Jour, July 5,1958; p 24.

Bondarev, VN et al, "The Changes of the Nervous System in Children After Vaccination", Peditria, Jun 1969; 48:20-24.

Badalian, LO, "Vaccinal Lesions of the Nervous System in Children," Vop Okhr Materin Dets, Dec 1959, 13:54-59

Lorentz, IT, et al, "Post-Vaccinal Sensory Polyneuropathy with Myoclonus", Proc Aust Ass Neurol, 1969, 6:81-86.

Trump, R C, White, T R, "Cerebellar Ataxia Presumed Due To Live Attenuated Measles Virus Vaccine," JAMA, 1967, 199:165-166.

Allerdist, H, "Neurological Complications Following Measles Vaccination", Inter Symp, Brussels, 1978, Development Biol Std, Vol 43, 259-264.

Finley, K H, "Pathogenesis of Encephalitis Occurring With Vaccination, Variola and Measles, Arch Neur and Psychologist, 1938; 39:1047-1054.

Froissart, M et al, "Acute Meningoencephalitis Immediately after an Influenza Vaccination", Lille Med, Oct 1978, 23(8):548-551.

Pokrovskaja, Nia, et al, "Neurological Complications in Children From Smallpox Vaccination", Peditriia, Dec 1978, (12):45-49.

Allerdist, H, "Neurological Complications Following Measles Virus Vaccination. Evaluation of the Cases seen Between 1971-1977", Monatsschr Kinderheilkd, Jan 1979, 127(1): 23-28.

Ehregut, W et al, "On Convulsive Reactions Following Oral vaccination Against Polio", Klin Paediatr, May 1979, 191(3):261-270.

Naumova, R P, et al, "Encephalitis Developing After Vaccination without a Local Skin Reaction", Vrach Delo, Jul 1979, (7):114-115.

Goswamy, BM, "Neurological Complications After Smallpox Vaccination", J Ass Phys India, Jan 1969, 17:41-43.

Schchelkunov, SN et al, "The Role of Viruses in the Induction of Allergic Encephalomyelitis," Dokl Akad Nauk SSSR, 1990,315(1):252-255. [Vaccines contain viruses, too]

Walker AM, "Neurologic events following diphtheria-tetanus-pertussis immunization," Pediatrics 1988 Mar;81(3):345-349.

Shields WD, et al, "Relationship of pertussis immunization to the onset of neurologic disorders: a retrospective epidemiologic study," J Pediatr 1988 Nov; 113(5):801-805.

Wilson J, "Proceedings: Neurological complications of DPT inoculation in infancy," Arch Dis Child 1973 Oct; 48(10):829-830.

Iakunin IaA, "[Nervous system complications in children after preventive vaccinations]," Pediatriia 1968 Nov; 47(11):19-26. [Article in Russian]

Greco D, et al, "Case-control study on encephalopathy associated with diphtheria-tetanus immunization in Campania, Italy," Bull World Health Organ 1985;63(5):919-925.

Ehregut W at Institute of Vaccinology and Virology, Hamburg, Germany states, "Bias in the evaluation of CNS complications following pertussis immunization are the following: 1) Notifications of post-immunization adverse events, 2) Publications by vaccine producers on the frequency of adverse reactions, 3) Comparison of permanent brain damage after DPT and DT immunization, 4) Pro-immunization, 5) Immunization associated viral encephalitis, 6) Accuracy of statistics, 7) Personal. A review of these points indicates an underestimation of CNS complications after pertussis immunization."

Reference: Ehregut W, "Bias in evaluating CNS complications following pertussis immunization." Acta Paediatr Jpn, 1991 Aug; 33(4):421-427. Vaccinations and Unexplained Diseases:

Hiner, E E, Frasc, C E, "Spectrum of Disease Due to Haemophilus Influenza Type B Occurring in Vaccinated Children", J Infect Disorder, 1988 Aug; 158(2): 343-348.

Olin P, Romanus, V, Storsaeter, J, "Invasive Bacterial Infections During an Efficacy Trial of Acellular Pertussis Vaccines — Implications For Future Surveillance In Pertussis Vaccine Programmes", Tokai J Exp Clin Med, 1988; 13 Suppl: 143-144.

Storsaeter, J, et al, "Mortality and Morbidity From Invasive Bacterial Infections During a Clinical Trial of Acellular Pertussis Vaccines in Sweden", Pediatr Infect Disorder J, 1988 Sept; 7(9):637-645.

Vadheim, CM, et al, "Effectiveness and Safety of an Haemophilus Influenzae type b Conjugate Vaccine (PRP-T) in Young Infants. Kaiser-UCLA Vaccine Study Group," Pediatrics, 1993 Aug; 92(2):272-279. [The vaccines caused fevers, irritability, crying, and seizures, but were declared to be "safe and ... effective ... ".]

Stickl, H, "Estimation of Vaccination Damage", Med Welt, Oct 14, 1972, 23:1495-1497.

Waters, VV, et al, "Risk Factors for Measles in a Vaccinated Population", JAMA, Mar 27, 1991, 265(12): 1527.

Stickl, H, "Iatrogenic Immuno-suppression as a Result of Vaccination", Fortschr Med, Mar 5, 1981, 99(9);289-292. Vaccine Citations Linking the Vaccine to the "prevented" Disease:

Nkowane, et al, "Vaccine-Associated Paralytic Poliomyelitis, US 1973 through 1984, JAMA, 1987, Vol 257:1335-1340.

Quast, et al, "Vaccine Induced Mumps-like Diseases", nd, Int Symp on Immun, Development Bio Stand, Vol 43, p269-272.

Green, C et al, "A Case of Hepatitis Related to Etretinate Therapy and Hepatitis B Vaccine", Dermatologica, 1991, 182(2):119-120.

Shasby, DM, et al, "Epidemic Measles in Highly Vaccinated Population", NEJM, Mar 1977, 296(11): 585-589.

Tesovic, G et al, "Aseptic Meningitis after Measles, Mumps and Rubella Vaccine", Lancet, Jun 12, 1993, 341(8859):1541.

Johnson, RH, et al, "Nosocomial Vaccinia Infection", West J Med, Oct 1976, 125(4):266-270.

Malengreau, M, "Reappearance of Post-Vaccination Infection of Measles, Rubella, and Mumps. Should Adolescents be re-vaccinated?" Pedaitric, 1992;47(9):597-601 (25 ref)

Basa, SN, "Paralytic Poliomyelitis Following Inoculation With Combined DTP Prophylactic. A review of Sixteen cases with Special Reference to Immunization Schedules in Infancy", J Indian Med Assoc, Feb 1, 1973, 60:97-99.

Landrigan, PJ et al, "Measles in Previously Vaccinated Children in Illinois", Ill Med J, Apr 1974, 141:367-372.

NA, "Vaccine-Associated Poliomyelitis", Med J Aust, Oct 1973, 2:795-796. Vaccine Failures Citations:

Hardy, GE, Jr, et al, "The Failure of a School Immunization Campaign to Terminate an Urban Epidemic of Measles," Amer J Epidem, Mar 1970; 91:286-293.

Cherry, JD, et al, "A Clinical and Serologic Study of 103 Children With Measles Vaccine Failure", J Pediatr, May 1973; 82:801-808.

Jilg, W, et al, "Inoculation Failure Following Hepatitis B Vaccination", Dtsch Med wochenschr, 1990 Oct 12; 115(41):1514-1548.

Plotkin, SA, "Failures of Protection by Measles Vaccine," J Pediatr, May 1973; 82:798-801.

Bolotovskii, V, et al, "Measles Incidence Among Children Properly Vaccinated Against This Infection", ZH Mikrobiol Epidemiol Immunobiol, 1974; 00(5):32-35.

Landrigan, PJ, et al, "Measles in Previously Vaccinated Children in Illinois", Ill Med J, Apr 1974; 141:367-372.

Strebel, P et al, "An Outbreak of Whooping Cough in a Highly Vaccinated Urban Community", *J Trop Pediatr*, Mar 1991, 37(2): 71-76.

Forrest, JM, et al, "Failure of Rubella Vaccination to Prevent Congenital Rubella," *Med J Aust*, 1977 Jan 15; 1(3): 77.

Jilg, W, "Unsuccessful Vaccination against Hepatitis B", *Dtsch Med Wochenschr*, Nov 16, 1990, 115(46):1773.

Coles, FB, et al, "An Outbreak of Influenza A (H3N2) in a Well-Immunized Nursing home Population," *J Am ger Sociologist*, Jun 1992, 40(6):589-592.

Jilg, W, et al, "Inoculation Failure following Hepatitis B Vaccination," *Dtsch Med Wochenschr*, Oct 12, 1990, 115(41):1545-1548.

Hartmann, G et al, "Unsuccessful Inoculation against Hepatitis B," *Dtsch Med Wochenschr*, May 17, 1991, 116(20): 797.

Buddle, BM et al, "Contagious Ecthyma Virus-Vaccination Failures", *Am J Vet Research*, Feb 1984, 45(2):263-266.

Mathias, R G, "Whooping Cough In Spite of Immunization", *Can J Pub Health*, 1978 Mar/Apr; 69(2):130-132.

Osterholm, MT, et al, "Lack of Efficacy of Haemophilus b Polysaccharide Vaccine in Minnesota", *JAMA*, 1988 Sept 9; 260(10):1423-1428.

Johnson, RH, et al, "Nosocomial Vaccinia Infection", *West J Med*, Oct 1976, 125(4):266-270. Vaccines Causing Another Vaccinal Disease:

Basa, SN, "Paralytic Poliomyelitis Following Inoculation With Combined DTP Prophylactic. A review of Sixteen cases with Special Reference to Immunization Schedules in Infancy", *J Indian Med Assoc*, Feb 1, 1973, 60:97-99.

Pathel, JC, et al, "Tetanus Following Vaccination Against Small-pox", *J Pediatr*, Jul 1960; 27:251-263.

Favez, G, "Tuberculous Superinfection Following a Smallpox Re-Vaccination", *Praxis*, July 21, 1960; 49:698-699.

Quast, Ute, and Hennesen, "Vaccine-Induced Mumps-like Diseases", *Intern Symp on Immunizations , Development Bio Stand*, Vol 43, p 269-272.

Forrest, J M, et al, "Clinical Rubella Eleven months after Vaccination," *Lancet*, Aug 26, 1972, 2:399-400.

Dittman, S, "Atypical Measles after Vaccination", *Beitr Hyg Epidemiol*, 1989, 25:1-274 (939 ref)

Sen S, et al, "Poliomyelitis in Vaccinated Children", *Indian Pediatr*, May 1989, 26(5): 423-429.

Arya, SC, "Putative Failure of Recombinant DNA Hepatitis B Vaccines", *Vaccine*, Apr 1989, 7(2): 164-165.

Lawrence, R et al, "The Risk of Zoster after Varicella Vaccination in Children with Leukemia", *NEJM*, Mar 3, 1988, 318(9): 543-548. Vaccination Citations and Death

Na, "DPT Vaccination and Sudden Infant Death – Tennessee, US Dept HEW, *MMWR Report*, Mar 23, 1979, vol 28(11): 132.

Arevalo, "Vaccinia Necrosum. Report on a Fatal Case", *Bol Ofoc Sanit Panamer*, Aug 1967, 63:106-110.

Connolly, J H, Dick, G W, Field, CM, "A Case of Fatal Progressive Vaccinia", *Brit Med Jour*, 12 May 1962; 5288:1315-1317.

Aragona, F, "Fatal Acute Adrenal Insufficiency Caused by Bilateral Apoplexy of the Adrenal Glands (WFS) following Anti-poliomyelitis Vaccination", *Minerva Medicolegale*, Aug 1960; 80:167-173.

Mobius, G et al, "Pathological-Anatomical Findings in Cases of Death Following Poliomyelitis and DPT Vaccination", *Dtsch Gesundheitsw*, Jul 20, 1972, 27:1382-1386.

NA, "Immunizations and Cot Deaths", *Lancet*, Sept 25, 1982, np.

Goetzeler, A, "Fatal Encephalitis after Poliomyelitis Vaccination", 22 Jun 1961, *Muenchen Med Wschr*, 102:1419-1422.

Fulginiti, V, "Sudden Infant Death Syndrome, Diphtheria-Tetanus Toxoid-Pertussis Vaccination and Visits to the Doctor: Chance Association or Cause and Effect?", *Pediatr Infect Disorder*, Jan-Feb 1983, 2(1): 7-11.

Baraff, LJ, et al, "Possible Temporal Association Between Diphtheria-tetanus toxoid-Pertussis Vaccination and Sudden Infant Death Syndrome", *Pediatr Infect Disorder*, Jan-Feb 1983, 2(1): 5-6.

Reynolds, E, "Fatal Outcome of a Case of Eczema Vaccinatum", *Lancet*, 24 Sept 1960, 2:684-686.

Apostolov. et al, "Death of an Infant in Hyperthermia After Vaccination", *J Clin Path*, Mar 1961, 14:196-197.

Bouvier-Colle, MH, "Sex-Specific Differences in Mortality After High-Titre Measles Vaccination", *Rev Epidemiol Sante Publique*, 1995; 43(1): 97.

Stewart GT, "Deaths of infants after triple vaccine.", *Lancet* 1979 Aug 18;2(8138):354-355.

Flahault A, "Sudden infant death syndrome and diphtheria/tetanus toxoid/pertussis/poliomyelitis immunisation.", *Lancet* 1988 Mar 12;1(8585):582-583.

Larbre, F et al, "Fatal Acute Myocarditis After Smallpox Vaccination", *Pediatric*, Apr-May 1966, 21:345-350.

Mortimer EA Jr, "DTP and SIDS: when data differ", Am J Public Health 1987 Aug; 77(8):925-926.
Vaccines and Metabolism Citations:

Deutsch J, " [Temperature changes after triple-immunization in infant age]," Padiatr Grenzgeb 1976;15(1):3-6. [Article in German]

NA, "[Temperature changes after triple immunization in childhood]," Padiatr Grenzgeb 1976;15(1):7-10. [Article in German]

[Considering that the thyroid controls our Basal Metabolism, it would appear that vaccines altered (depressed) thyroid activity.] Vaccines Altering Resistance to Disease:

Burmistrova AL, "[Change in the non-specific resistance of the body to influenza and acute respiratory diseases following immunization diphtheria-tetanus vaccine]," Zh Mikrobiol Epidemiol Immunobiol 1976; (3):89-91. [Article in Russian] Vaccinations and Deafness Citations: So I did a background check to see if there was any scientific evidence linking vaccines to deafness and hearing loss. Here are some of the articles I found:

Kaga, "Unilateral Total Loss of Auditory and Vestibular Function as a Complication of Mumps Vaccination", Int J Ped Oto, Feb 1998, 43(1):73-73

Nabe-Nielsen, Walter, "Unilateral Total Deafness as a Complication of the Measles- Mumps- Rubella Vaccination", Scan Audio Suppl, 1988, 30:69-70

Hulbert, et al, "Bilateral Hearing Loss after Measles and Rubella Vaccination in an Adult", NEJM, 1991 July, 11;325(2):134

Healy, "Mumps Vaccine and Nerve Deafness", Am J Disorder Child, 1972 Jun; 123(6):612

Jayarajan, Sedler, "Hearing Loss Following Measles Vaccination", J Infect, 1995 Mar; 30(2):184-185

Pialoux, P et al, "Vaccinations and Deafness", Ann Otolaryng (Paris), Dec 1963, 80:1012-1013.

Angerstein, W, et al, "Solitary Hearing and Equilibrium Damage After Vaccinations", Gesundheitswesen, May 1995, 57(5): 264-268.

Brodsky, Stanievich, "Sensorineural Hearing Loss Following Live Measles Virus Vaccination", Int J Ped Oto, 1985 Nov; 10(2):159-163

Koga, et al, "Bilateral Acute Profound Deafness After MMR Vaccination- Report of a Case", Nippon Jibiin Gakkai Kai, 1991 Aug;94(8):1142-5

Seiferth, LB, "Deafness after Oral Poliomyelitis Vaccination – a Case Report and Review", HNO, 1977 Aug; 25(8): 297-300

Pantazopoulos, PE, "Perceptive Deafness Following Prophylactic use of Tetanus antitoxin", Laryngoscope, Dec 1965, 75:1832-1836.

Zimmerman, W, "Observation of a case of Acute Bilateral Hearing Impairment Following Preventive Poliomyelitis Vaccination (type 3)", Arch Ohr Nas Kehlkopfheilk, 1965, 185:723-725. Vaccinations and Kidney Disorders Citations:

Jacquot, C et al, "Renal Risk in Vaccination", Nouv Presse Med, Nov 6, 1982, 11(44):3237-3238.

Giudicelli, et al, "Renal Risk in Vaccination", Presse Med, Jun 11, 1982, 12(25):1587-1590.

Tan, SY, et al, "Vaccine Related Glomerulonephritis", BMJ, Jan 23, 1993, 306(6872):248.

Pillai, JJ, et al, "Renal Involvement in Association with Post-vaccination Varicella", Clin Infect Disorder, Dec 1993, 17(6): 1079-1080.

Eisinger, AJ et al, "Acute Renal Failure after TAB and Cholera Vaccination", B Med J, Feb 10, 1979, 1(6160):381-382.

Silina, ZM, et al, "Causes of Postvaccinal Complications in the Kidneys in Young Infants", Pediatria, Dec 1978, (12):59-61.

Na, "Albuminurias", Concours Med, Mar 1964, 85:5095-5098. [vaccination adverse reactions]

Oyrl, A, et al, "Can Vaccinations Harm the Kidney?", Clin Nephrol, 1975, 3(5):204-205.

Mel'man Nia, "[Renal lesions after use of vaccines and sera]." Vrach Delo 1978 Oct;(10):67-9, [Article in Russian]

Silina ZM, Galaktionova Tla, Shabunina NR, "[Causes of postvaccinal complications in the kidneys in young infants]." Pediatriia 1978 Dec;(12):59-61, [Article in Russian]

Silina EM, et al, "[Some diseases of the kidneys in children during the 1st year of life, following primary smallpox vaccination and administration of pertussis-diphtheria-tetanus vaccine]." Vopr Okhr Materin Det 1968 Mar; 13(3):79-80, [Article in Russian] Vaccines and Skin Disorders Citations:

Illingsworth R, "Skin rashes after triple vaccine," Arch Dis Child 1987 Sep; 62(9):979.

Lupton GP, "Discoid lupus erythematosus occurring in a smallpox vaccination scar," J Am Acad Dermatol, 1987 Oct; 17(4):688-690.

Kompier, A J, "Some Skin Diseases caused by Vaccinia Virus [Smallpox]," Ned Milt Geneesk T, 15:149-157, May 1962.

Weber, G et al, "Skin Lesions Following Vaccinations," Deutsch Med Wschr, 88:1878-1886, S7 Sept 1963.

Copeman, P W, "Skin Complications of Smallpox Vaccination," Practitioner, 197:793-800, Dec 1966.

Denning, DW, et al, "Skin Rashes After Triple Vaccine," Arch Disorder Child, May 1987, 62(5): 510-511.
Vaccinations and Abscesses:

Sterler, HC, et al, "Outbreaks of Group A Streptococcal Abscesses Following DTP Vaccination",
Pediatrics, Feb 1985, 75(2):299-303.

DiPiramo, D, et al, "Abscess Formation at the Site of Inoculation of Calmette-Guerin Bacillus (BCG)," Riv
Med Aeronaut Spaz, Jul-Dec 1981, 46(3-4):190-199. Vaccinations and Shock:

Caileba, A et al, "Shock associated with Disseminated Intravascular Coagulation Syndrome following
Injection of DT.TAB Vaccine, Prese Med, Sept 15, 1984, 13(3):1900. Vaccines: The Weird, The Wild and
The Hilarious Citations: Sometimes there are articles published about the strangest facts related to
vaccines that defies our imagination and ability to understand them. They were written seriously by
well-meaning scientific persons, but their titles can be seen differently. Some are funny, some are sad
and some are purely scientific folly. See if you can figure these out:

Pathel, JC, et al, "Tetanus Following Vaccination Against Small-pox", J Pediatr, Jul 1960; 27:251-263.
[Now you need a tetanus vaccination!]

Favez, G, "Tuberculous Superinfection Following a Smallpox Re-Vaccination", Praxis, July 21, 1960;
49:698-699. [Super means large/big/great!]

Bonifacio, A et al, "Traffic Accidents as an expression of "Iatrogenic damage", Minerva Med, Feb 24,
1971, 62:735-740. [But officer I was just vaccinated!]

Baker, J et al, "Accidental Vaccinia: Primary Inoculation of a Scrotum", Clin Pediatr (Phila), Apr 1972,
11:244-245. [Ooops, the needle slipped.]

Edwards, K, "Danger of Sunburn Following Vaccination", Papua New Guinea Med J, Dec 1977,
20(4):203. [Are vaccines phototoxic?]

Stroder, J, "Incorrect Therapy in Children", Folia Clin Int (Barc), Feb 1966, 16:82-90. [Agreed.]

Wehrle PF, "Injury associated with the use of vaccines," Clin Ther 1985;7(3):282-284. [Dah!]

Alberts ME, "When and where will it stop", Iowa Med 1986 Sep; 76(9):424. [When!]

Breiman RF, Zanca JA, "Of floors and ceilings — defining, assuring, and communicating vaccine
safety", Am J Public Health 1997 Dec;87(12):1919-1920. [What is in between floors and ceilings?]

Stewart, AM, et al, "Aetiology of Childhood Leukaemia", Lancet, 16 Oct, 1965, 2:789-790.

Nelson, ST, "John Hutchinson On Vaccination Syphilis (Hutchinson, J)", Arch Derm, (Chic), May 1969,
99:529-535. [Vaccinations and STDs!]

Mather, C, "Cotton Mather Anguishes Over the Consequences of His Son's Inoculation Against
Smallpox", Pediatrics, May 1974; 53:756. [Is it for or against?]

Thoman M, "The Toxic Shot Syndrome", *Vet Hum Toxicol*, Apr 1986, 28(2):163-166. [Animals are not exempt from vaccination damage either!]

Johnson, RH, et al, "Nosocomial Vaccinia Infection", *West J Med*, Oct 1976, 125(4):266-270. [Nosocomial means a disease acquired in a doctor's office or hospital.]

Heed, JR, "Human Immunization With Rabies Vaccine in Suckling Mice Brain," *Salud Publica*, May-Jun 1974, 16(3): 469-480. [Have you had your suckling mice brains today?]

Tesovic, G et al, "Aseptic Meningitis after Measles, Mumps and Rubella Vaccine", *Lancet*, Jun 12, 1993, 341(8859):1541. [AM has same symptoms as poliomyelitis!]

Buddle, BM et al, "Contagious Ecthyma Virus-Vaccination Failures", *Am J Vet Research*, Feb 1984, 45(2):263-266.

Freter, R et al, "Oral Immunization And Production of Coproantibody in Human Volunteers", *J Immunol*, Dec 1963, 91:724-729. [Guess what copro- means Feces.]

NA, "Vaccination, For and Against", 1964, *Belg T Geneesk*, 20:125-130. [Is it for or against?]

Sahadevan, MG et al, "Post-vaccinal Myelitis", *J Indian Med Ass*, Feb 16, 1966, 46:205-206. [Did I mention myelitis?]

Castan, P et al, "Coma Revealing an acute Leukosis in a child, 15 days after an Oral Anti-poliomyelitis Vaccination," *Acta Neurol Belg*, May 1965, 65:349-367. [Coma from vaccines!]

Stickl, H, et al, "Purulent [pus] meningitides Following Smallpox Vaccination. On the Problem of Post-Vaccinal Decrease of Resistance", *Deutsch Med Wschr*, Jul 22, 1966, 91:1307-1310. [Vaccines are the injection of viruses cultured from pus ...]

[Reference Source 183](#)

Syllabus

NOTE: Where it is feasible, a syllabus (headnote) will be released, as is being done in connection with this case, at the time the opinion is issued. The syllabus constitutes no part of the opinion of the Court but has been prepared by the Reporter of Decisions for the convenience of the reader. See *United States v. Detroit Timber & Lumber Co.*, 200 U. S. 321, 337.

SUPREME COURT OF THE UNITED STATES

Syllabus

BRUESEWITZ ET AL. *v.* WYETH LLC, FKA WYETH, INC.,
ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR
THE THIRD CIRCUIT

No. 09–152. Argued October 12, 2010—Decided February 22, 2011

The National Childhood Vaccine Injury Act of 1986 (NCVIA or Act) created a no-fault compensation program to stabilize a vaccine market adversely affected by an increase in vaccine-related tort litigation and to facilitate compensation to claimants who found pursuing legitimate vaccine-inflicted injuries too costly and difficult. The Act provides that a party alleging a vaccine-related injury may file a petition for compensation in the Court of Federal Claims, naming the Health and Human Services Secretary as the respondent; that the court must resolve the case by a specified deadline; and that the claimant can then decide whether to accept the court’s judgment or reject it and seek tort relief from the vaccine manufacturer. Awards are paid out of a fund created by an excise tax on each vaccine dose. As a *quid pro quo*, manufacturers enjoy significant tort-liability protections. Most importantly, the Act eliminates manufacturer liability for a vaccine’s unavoidable, adverse side effects.

Hannah Bruesewitz’s parents filed a vaccine-injury petition in the Court of Federal Claims, claiming that Hannah became disabled after receiving a diphtheria, tetanus, and pertussis (DTP) vaccine manufactured by Lederle Laboratories (now owned by respondent Wyeth). After that court denied their claim, they elected to reject the unfavorable judgment and filed suit in Pennsylvania state court, alleging, *inter alia*, that the defective design of Lederle’s DTP vaccine caused Hannah’s disabilities, and that Lederle was subject to strict liability and liability for negligent design under Pennsylvania common law. Wyeth removed the suit to the Federal District Court. It granted Wyeth summary judgment, holding that the relevant Pennsylvania law was preempted by 42 U. S. C. §300aa–22(b)(1), which

Syllabus

provides that “[n]o vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side-effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.” The Third Circuit affirmed.

Held: The NCVIA preempts all design-defect claims against vaccine manufacturers brought by plaintiffs seeking compensation for injury or death caused by a vaccine’s side effects. Pp. 7–19.

(a) Section 300aa–22(b)(1)’s text suggests that a vaccine’s design is not open to question in a tort action. If a manufacturer could be held liable for failure to use a different design, the “even though” clause would do no work. A vaccine side effect could always have been avoidable by use of a different vaccine not containing the harmful element. The language of the provision thus suggests the design is not subject to question in a tort action. What the statute establishes as a complete defense must be unavoidability (given safe manufacture and warning) with respect to the particular design. This conclusion is supported by the fact that, although products-liability law establishes three grounds for liability—defective manufacture, inadequate directions or warnings, and defective design—the Act mentions only manufacture and warnings. It thus seems that the Act’s failure to mention design-defect liability is “by deliberate choice, not inadvertence.” *Barnhart v. Peabody Coal Co.*, 537 U. S. 149, 168. Pp. 7–8.

(b) Contrary to petitioners’ argument, there is no reason to believe that §300aa–22(b)(1)’s term “unavoidable” is a term of art incorporating Restatement (Second) of Torts §402A, Comment *k*, which exempts from strict liability rules “unavoidably unsafe products.” “Unavoidable” is hardly a rarely used word, and cases interpreting comment *k* attach special significance only to the term “unavoidably unsafe products,” not the word “unavoidable” standing alone. Moreover, reading the phrase “side effects that were unavoidable” to exempt injuries caused by flawed design would require treating “even though” as a coordinating conjunction linking independent ideas when it is a concessive, subordinating conjunction conveying that one clause weakens or qualifies the other. The canon against superfluity does not undermine this Court’s interpretation because petitioners’ competing interpretation has superfluity problems of its own. Pp. 8–12.

(c) The structure of the NCVIA and of vaccine regulation in general reinforces what §300aa–22(b)(1)’s text suggests. Design defects do not merit a single mention in the Act or in Food and Drug Administration regulations that pervasively regulate the drug manufacturing process. This lack of guidance for design defects, combined with

Syllabus

the extensive guidance for the two liability grounds specifically mentioned in the Act, strongly suggests that design defects were not mentioned because they are not a basis for liability. The Act's mandates lead to the same conclusion. It provides for federal agency improvement of vaccine design and for federally prescribed compensation, which are other means for achieving the two beneficial effects of design-defect torts—prompting the development of improved designs, and providing compensation for inflicted injuries. The Act's structural *quid pro quo* also leads to the same conclusion. The vaccine manufacturers fund an informal, efficient compensation program for vaccine injuries in exchange for avoiding costly tort litigation and the occasional disproportionate jury verdict. Taxing their product to fund the compensation program, while leaving their liability for design defect virtually unaltered, would hardly coax them back into the market. Pp. 13–16.

561 F. 3d 233, affirmed.

SCALIA, J., delivered the opinion of the Court, in which ROBERTS, C. J., and KENNEDY, THOMAS, BREYER, and ALITO, JJ., joined. BREYER, J., filed a concurring opinion. SOTOMAYOR, J., filed a dissenting opinion, in which GINSBURG, J., joined. KAGAN, J., took no part in the consideration or decision of the case.

Opinion of the Court

NOTICE: This opinion is subject to formal revision before publication in the preliminary print of the United States Reports. Readers are requested to notify the Reporter of Decisions, Supreme Court of the United States, Washington, D. C. 20543, of any typographical or other formal errors, in order that corrections may be made before the preliminary print goes to press.

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.*
WYETH LLC, FKA WYETH, INC., FKA WYETH
LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF
APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE SCALIA delivered the opinion of the Court.

We consider whether a preemption provision enacted in the National Childhood Vaccine Injury Act of 1986 (NCVIA)¹ bars state-law design-defect claims against vaccine manufacturers.

I
A

For the last 66 years, vaccines have been subject to the same federal premarket approval process as prescription drugs, and compensation for vaccine-related injuries has been left largely to the States.² Under that regime, the elimination of communicable diseases through vaccination became “one of the greatest achievements” of public health in the 20th century.³ But in the 1970’s and 1980’s vac-

¹ 42 U. S. C. §300aa–22(b)(1).

² See P. Hutt, R. Merrill, & L. Grossman, *Food and Drug Law* 912–913, 1458 (3d ed. 2007).

³ Centers for Disease Control, *Achievements in Public Health, 1900–1999: Impact of Vaccines Universally Recommended for Children*, 48 *Morbidity and Mortality Weekly Report* 243, 247 (Apr. 2, 1999).

Opinion of the Court

cines became, one might say, victims of their own success. They had been so effective in preventing infectious diseases that the public became much less alarmed at the threat of those diseases,⁴ and much more concerned with the risk of injury from the vaccines themselves.⁵

Much of the concern centered around vaccines against diphtheria, tetanus, and pertussis (DTP), which were blamed for children's disabilities and developmental delays. This led to a massive increase in vaccine-related tort litigation. Whereas between 1978 and 1981 only nine product-liability suits were filed against DTP manufacturers, by the mid-1980's the suits numbered more than 200 each year.⁶ This destabilized the DTP vaccine market, causing two of the three domestic manufacturers to withdraw; and the remaining manufacturer, Lederle Laboratories, estimated that its potential tort liability exceeded its annual sales by a factor of 200.⁷ Vaccine shortages arose when Lederle had production problems in 1984.⁸

Despite the large number of suits, there were many complaints that obtaining compensation for legitimate vaccine-inflicted injuries was too costly and difficult.⁹ A

⁴See Mortimer, *Immunization Against Infectious Disease*, 200 *Science* 902, 906 (1978).

⁵See National Vaccine Advisory Committee, *A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities* 2–3 (Dec. 2008) (hereinafter NVAC), <http://www.hhs.gov/nvpo/nvac/documents/vaccine-safety-review.pdf> (as visited Feb. 18, 2011, and available in Clerk of Court's case file).

⁶See Sing & Willian, *Supplying Vaccines: An Overview of the Market and Regulatory Context*, in *Supplying Vaccines: An Economic Analysis of Critical Issues* 45, 51–52 (M. Pauly, C. Robinson, S. Sepe, M. Sing, & M. William eds. 1996).

⁷See *id.*, at 52.

⁸See Centers for Disease Control, *Diphtheria-Tetanus-Pertussis Vaccine Shortage*, 33 *Morbidity and Mortality Weekly Report* 695–696 (Dec. 14, 1984).

⁹See Apolinsky & Van Detta, *Rethinking Liability for Vaccine Injury*, 19 *Cornell J. L. & Pub. Pol'y* 537, 550–551 (2010); T. Burke, *Lawyers*,

Opinion of the Court

significant number of parents were already declining vaccination for their children,¹⁰ and concerns about compensation threatened to depress vaccination rates even further.¹¹ This was a source of concern to public health officials, since vaccines are effective in preventing outbreaks of disease only if a large percentage of the population is vaccinated.¹²

To stabilize the vaccine market and facilitate compensation, Congress enacted the NCVIA in 1986. The Act establishes a no-fault compensation program “designed to work faster and with greater ease than the civil tort system.” *Shalala v. Whitecotton*, 514 U. S. 268, 269 (1995). A person injured by a vaccine, or his legal guardian, may file a petition for compensation in the United States Court of Federal Claims, naming the Secretary of Health and Human Services as the respondent.¹³ A special master then makes an informal adjudication of the petition within (except for two limited exceptions) 240 days.¹⁴ The Court of Federal Claims must review objections to the special master’s decision and enter final judgment under a similarly tight statutory deadline.¹⁵ At that point, a claimant has two options: to accept the court’s judgment and forgo a traditional tort suit for damages, or to reject the judgment and seek tort relief from the vaccine manufacturer.¹⁶

Fast, informal adjudication is made possible by the Act’s Vaccine Injury Table, which lists the vaccines covered under the Act; describes each vaccine’s compensable,

Lawsuits, and Legal Rights: The Battle over Litigation in American Society 146 (2002).

¹⁰Mortimer, *supra*, at 906.

¹¹See Hagan, 45 Food Drug Cosm. L. J. 477, 479 (1990).

¹²See R. Merrill, Introduction to Epidemiology 65–68 (2010).

¹³See 42 U. S. C. §300aa–11(a)(1).

¹⁴See §300aa–12(d)(3).

¹⁵See §300aa–12(e), (g).

¹⁶See §300aa–21(a).

Opinion of the Court

adverse side effects; and indicates how soon after vaccination those side effects should first manifest themselves.¹⁷ Claimants who show that a listed injury first manifested itself at the appropriate time are prima facie entitled to compensation.¹⁸ No showing of causation is necessary; the Secretary bears the burden of disproving causation.¹⁹ A claimant may also recover for unlisted side effects, and for listed side effects that occur at times other than those specified in the Table, but for those the claimant must prove causation.²⁰ Unlike in tort suits, claimants under the Act are not required to show that the administered vaccine was defectively manufactured, labeled, or designed.

Successful claimants receive compensation for medical, rehabilitation, counseling, special education, and vocational training expenses; diminished earning capacity; pain and suffering; and \$250,000 for vaccine-related deaths.²¹ Attorney's fees are provided, not only for successful cases, but even for unsuccessful claims that are not frivolous.²² These awards are paid out of a fund created by an excise tax on each vaccine dose.²³

The *quid pro quo* for this, designed to stabilize the vaccine market, was the provision of significant tort-liability protections for vaccine manufacturers. The Act requires claimants to seek relief through the compensation program before filing suit for more than \$1,000.²⁴ Manufacturers are generally immunized from liability for fail-

¹⁷ See §300aa-14(a); 42 CFR §100.3 (2009) (current Vaccine Injury Table).

¹⁸ See 42 U. S. C. §§300aa-11(c)(1), 300aa-13(a)(1)(A).

¹⁹ See §300aa-13(a)(1)(B).

²⁰ See §300aa-11(c)(1)(C)(ii).

²¹ See §300aa-15(a).

²² See §300aa-15(e).

²³ See §300aa-15(i)(2); 26 U. S. C. §§4131, 9510.

²⁴ See 42 U. S. C. §300aa-11(a)(2).

Opinion of the Court

ure to warn if they have complied with all regulatory requirements (including but not limited to warning requirements) and have given the warning either to the claimant or the claimant’s physician.²⁵ They are immunized from liability for punitive damages absent failure to comply with regulatory requirements, “fraud,” “intentional and wrongful withholding of information,” or other “criminal or illegal activity.”²⁶ And most relevant to the present case, the Act expressly eliminates liability for a vaccine’s unavoidable, adverse side effects:

“No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.”²⁷

B

The vaccine at issue here is a DTP vaccine manufactured by Lederle Laboratories. It first received federal approval in 1948 and received supplemental approvals in 1953 and 1970. Respondent Wyeth purchased Lederle in 1994 and stopped manufacturing the vaccine in 1998.

Hannah Bruesewitz was born on October 20, 1991. Her pediatrician administered doses of the DTP vaccine according to the Center for Disease Control’s recommended childhood immunization schedule. Within 24 hours of her April 1992 vaccination, Hannah started to experience

²⁵ See §300aa–22(b)(2), (c). The immunity does not apply if the plaintiff establishes by clear and convincing evidence that the manufacturer was negligent, or was guilty of fraud, intentional and wrongful withholding of information, or other unlawful activity. See §§300aa–22(b)(2), 300aa–23(d)(2).

²⁶ §300aa–23(d)(2).

²⁷ §300aa–22(b)(1).

Opinion of the Court

seizures.²⁸ She suffered over 100 seizures during the next month, and her doctors eventually diagnosed her with “residual seizure disorder” and “developmental delay.”²⁹ Hannah, now a teenager, is still diagnosed with both conditions.

In April 1995, Hannah’s parents, Russell and Robalee Bruesewitz, filed a vaccine injury petition in the United States Court of Federal Claims, alleging that Hannah suffered from on-Table residual seizure disorder and encephalopathy injuries.³⁰ A Special Master denied their claims on various grounds, though they were awarded \$126,800 in attorney’s fees and costs. The Bruesewitzes elected to reject the unfavorable judgment, and in October 2005 filed this lawsuit in Pennsylvania state court. Their complaint alleged (as relevant here) that defective design of Lederle’s DTP vaccine caused Hannah’s disabilities, and that Lederle was subject to strict liability, and liability for negligent design, under Pennsylvania common law.³¹

Wyeth removed the suit to the United States District Court for the Eastern District of Pennsylvania, which granted Wyeth summary judgment on the strict-liability and negligence design-defect claims, holding that the Pennsylvania law providing those causes of action was preempted by 42 U. S. C. §300aa–22(b)(1).³² The United States Court of Appeals for the Third Circuit affirmed.³³ We granted certiorari. 559 U. S. ___ (2010).

²⁸ See *Bruesewitz v. Secretary of Health and Human Servs.*, No. 95–0266V, 2002 WL 31965744, *3 (Ct. Cl., Dec. 20, 2002).

²⁹ 561 F. 3d 233, 236 (CA3 2009).

³⁰ See *id.*, at *1.

³¹ See 561 F. 3d at 237. The complaint also made claims based upon failure to warn and defective manufacture. These are no longer at issue.

³² See *id.*, at 237–238.

³³ *Id.*, at 235.

Opinion of the Court

II

A

We set forth again the statutory text at issue:

“No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.”³⁴

The “even though” clause clarifies the word that precedes it. It delineates the preventative measures that a vaccine manufacturer *must* have taken for a side-effect to be considered “unavoidable” under the statute. Provided that there was proper manufacture and warning, any remaining side effects, including those resulting from design defects, are deemed to have been unavoidable. State-law design-defect claims are therefore preempted.

If a manufacturer could be held liable for failure to use a different design, the word “unavoidable” would do no work. A side effect of a vaccine could *always* have been avoidable by use of a differently designed vaccine not containing the harmful element. The language of the provision thus suggests that the *design* of the vaccine is a given, not subject to question in the tort action. What the statute establishes as a complete defense must be unavailability (given safe manufacture and warning) *with respect to the particular design*. Which plainly implies that the design itself is not open to question.³⁵

³⁴ 42 U. S. C. §300aa–22(b)(1).

³⁵ The dissent advocates for another possibility: “[A] side effect is ‘unavoidable’ . . . where there is no feasible alternative design that would eliminate the side effect of the vaccine without compromising its cost and utility.” *Post*, at 15 (opinion of SOTOMAYOR, J.). The dissent makes no effort to ground that position in the text of §300aa–22(b)(1).

Opinion of the Court

A further textual indication leads to the same conclusion. Products-liability law establishes a classic and well known triumvirate of grounds for liability: defective manufacture, inadequate directions or warnings, and defective design.³⁶ If all three were intended to be preserved, it would be strange to mention specifically only two, and leave the third to implication. It would have been much easier (and much more natural) to provide that manufacturers would be liable for “defective manufacture, defective directions or warning, and defective design.” It seems that the statute fails to mention design-defect liability “by deliberate choice, not inadvertence.” *Barnhart v. Peabody Coal Co.*, 537 U. S. 149, 168 (2003). *Expressio unius, exclusio alterius*.

B

The dissent’s principal textual argument is mistaken. We agree with its premise that “‘side effects that were unavoidable’ must refer to side effects caused by a vaccine’s *design*.”³⁷ We do not comprehend, however, the second step of its reasoning, which is that the use of the conditional term “if” in the introductory phrase “if the injury or death resulted from side effects that were unavoidable” “plainly implies that some side effects stemming from a vaccine’s design are ‘unavoidable,’ while

We doubt that Congress would introduce such an amorphous test by implication when it otherwise micromanages vaccine manufacturers. See *infra*, at 13–14. We have no idea how much more expensive an alternative design can be before it “compromis[es]” a vaccine’s cost or how much efficacy an alternative design can sacrifice to improve safety. Neither does the dissent. And neither will the judges who must rule on motions to dismiss, motions for summary judgment, and motions for judgment as a matter of law. Which means that the test would probably have no real-world effect.

³⁶W. Keeton, D. Dobbs, R. Keeton, & D. Owen, *Prosser and Keeton on Law of Torts* 695 (5th ed. 1984); *Restatement (Third) of Torts* §2 (1999).

³⁷*Post*, at 3.

Opinion of the Court

others are avoidable.”³⁸ That is not so. The “if” clause makes total sense whether the design to which “unavoidable” refers is (as the dissent believes) any feasible design (making the side effects of the design used for the vaccine at issue avoidable), or (as we believe) the particular design used for the vaccine at issue (making its side effects unavoidable). Under the latter view, the condition established by the “if” clause is that the vaccine have been properly labeled and manufactured; and under the former, that it have been properly *designed*, labeled, and manufactured. Neither view renders the “if” clause a nullity. Which of the two variants must be preferred is addressed by our textual analysis, and is in no way determined by the “if” clause.

Petitioners’ and the dissent’s textual argument also rests upon the proposition that the word “unavoidable” in §300aa–22(b)(1) is a term of art that incorporates comment *k* to Restatement (Second) of Torts §402A (1963–1964).³⁹ The Restatement generally holds a manufacturer strictly liable for harm to person or property caused by “any product in a defective condition unreasonably dangerous to the user.”⁴⁰ Comment *k* exempts from this strict-liability rule “unavoidably unsafe products.” An unavoidably unsafe product is defined by a hodge-podge of criteria and a few examples, such as the Pasteur rabies vaccine and experimental pharmaceuticals. Despite this lack of clarity, petitioners seize upon one phrase in the comment *k* analysis, and assert that by 1986 a majority of courts had made this a *sine qua non* requirement for an “unavoidably unsafe product”: a case-specific showing that the product was “quite incapable of being made safer for

³⁸ *Ibid.*

³⁹ See Brief for Petitioners 29.

⁴⁰ Restatement §402A, p. 347.

Opinion of the Court

[its] intended . . . use.”⁴¹

We have no need to consider the finer points of comment *k*. Whatever consistent judicial gloss that comment may have been given in 1986, there is no reason to believe that §300aa–22(b)(1) was invoking it. The comment creates a special category of “unavoidably unsafe products,” while the statute refers to “side effects that were unavoidable.” That the latter uses the adjective “unavoidable” and the former the adverb “unavoidably” does not establish that Congress had comment *k* in mind. “Unavoidable” is hardly a rarely used word. Even the cases petitioners cite as putting a definitive gloss on comment *k* use the precise phrase “unavoidably unsafe product”;⁴² none attaches special significance to the term “unavoidable” standing alone.

The textual problems with petitioners’ interpretation do

⁴¹*Id.*, Comment *k*, p. 353; Petitioners cite, *inter alia*, *Kearl v. Lederle Labs.*, 172 Cal. App. 3d 812, 828–830, 218 Cal. Rptr. 453, 463–464 (1985); *Belle Bonfils Memorial Blood Bank v. Hansen*, 665 P. 2d 118, 122 (Colo. 1983).

Though it is not pertinent to our analysis, we point out that a large number of courts disagreed with that reading of comment *k*, and took it to say that manufacturers did not face strict liability for side effects of properly manufactured prescription drugs that were accompanied by adequate warnings. See, e.g., *Brown v. Superior Court*, 227 Cal. Rptr. 768, 772–775 (Cal. App. 1986), (officially depublished), *aff’d* 44 Cal. 3d 1049, 751 P. 2d 470 (1988); *McKee v. Moore*, 648 P. 2d 21, 23 (Okla. 1982); *Stone v. Smith, Kline & French Labs.*, 447 So. 2d 1301, 1303–1304 (Ala. 1984); *Lindsay v. Ortho Pharm. Corp.*, 637 F. 2d 87, 90–91 (CA2 1980) (applying N. Y. law); *Wolfgruber v. Upjohn Co.*, 72 App. Div. 2d 59, 61, 423 N. Y. S. 2d 95, 96 (1979); *Chambers v. G. D. Searle & Co.*, 441 F. Supp. 377, 380–381 (D Md. 1975); *Basko v. Sterling Drug, Inc.*, 416 F. 2d 417, 425 (CA2 1969) (applying Conn. law).

⁴²See, e.g., *Johnson v. American Cyanamid Co.*, 239 Kan. 279, 285, 718 P. 2d 1318, 1323 (1986); *Feldman v. Lederle Labs.*, 97 N. J. 429, 440, 446–447, 479 A. 2d 374, 380, 383–384 (1984); *Belle Bonfils Memorial Blood Bank supra*, at 121–123; *Cassisi v. Maytag Co.*, 396 So. 2d 1140, 1144, n. 4, 1146 (Fla. App. 1981); *Racer v. Utterman*, 629 S. W. 2d 387, 393 (Mo. App. 1981).

Opinion of the Court

not end there. The phrase “even though” in the clause “even though the vaccine was properly prepared and [labeled]” is meant to signal the unexpected: unavoidable side effects persist *despite* best manufacturing and labeling practices.⁴³ But petitioners’ reading eliminates any opposition between the “even though” clause—called a concessive subordinate clause by grammarians—and the word “unavoidable.”⁴⁴ Their reading makes preemption turn equally on unavoidability, proper preparation, and proper labeling. Thus, the dissent twice refers to the requirements of proper preparation and proper labeling as “two additional prerequisites” for preemption independent of unavoidability.⁴⁵ The primary textual justification for the dissent’s position depends on that independence.⁴⁶ But linking independent ideas is the job of a coordinating junction like “and,” not a subordinating junction like “even though.”⁴⁷

⁴³The dissent’s assertion that we treat “even though” as a synonym for “because” misses the subtle distinction between “because” and “despite.” See *post*, at 17, n. 14. “Even though” is a close cousin of the latter. See Webster’s New International Dictionary 709, 2631 (2d ed. 1957). The statement “the car accident was unavoidable despite his quick reflexes” indicates that quick reflexes could not avoid the accident, and leaves open two unstated possibilities: (1) that other, unstated means of avoiding the accident besides quick reflexes existed, but came up short as well; or (2) that quick reflexes were the only possible way to avoid the accident. Our interpretation of §300aa–22(b)(1) explains why we think Congress meant the latter in this context. (Incidentally, the statement “the car accident was unavoidable because of his quick reflexes” makes no sense.)

⁴⁴See W. Follett, *Modern American Usage: A Guide* 61 (1966).

⁴⁵*Post*, at 9, 17.

⁴⁶*Post*, at 3–5.

⁴⁷The dissent responds that these “additional prerequisites” act “in a concessive, subordinating fashion,” *post*, at 17, n. 14 (internal quotation marks and brackets omitted). But that is no more true of the dissent’s conjunctive interpretation of the present text than it is of *all* provisions that set forth additional requirements—meaning that we could eliminate “even though” from our English lexicon, its function being entirely

Opinion of the Court

Petitioners and the dissent contend that the interpretation we propose would render part of §300aa–22(b)(1) superfluous: Congress could have more tersely and more clearly preempted design-defect claims by barring liability “if . . . the vaccine was properly prepared and was accompanied by proper directions and warnings.” The intervening passage (“the injury or death resulted from side effects that were unavoidable even though”) is unnecessary. True enough. But the rule against giving a portion of text an interpretation which renders it superfluous does not prescribe that a passage which could have been more terse does not mean what it says. The rule applies only if verbosity and prolixity can be eliminated by giving the offending passage, or the remainder of the text, a competing interpretation. That is not the case here.⁴⁸ To be sure, petitioners’ and the dissent’s interpretation gives independent meaning to the intervening passage (the supposed meaning of comment *k*); but it does so only at the expense of rendering the remainder of the provision superfluous. Since a vaccine is not “quite incapable of being made safer for [its] intended use” if manufacturing defects could have been eliminated or better warnings provided, the entire “even though” clause is a useless appendage.⁴⁹ It would suffice to say “if the injury or death resulted from side effects that were unavoidable”—full stop.

performed by “and.” No, we think “even though” has a distinctive concessive, subordinating role to play.

⁴⁸Because the dissent has a superfluity problem of its own, its reliance on *Bates v. Dow Agrosciences LLC*, 544 U. S. 431 (2005), is misplaced. See *id.*, at 449 (adopting an interpretation that was “the only one that makes sense of each phrase” in the relevant statute).

⁴⁹That is true regardless of whether §300aa–22(b)(1) incorporates comment *k*. See Restatement §402A, Comment *k*, pp. 353, 354 (noting that “unavoidably unsafe products” are exempt from strict liability “with the qualification that they are properly prepared and marketed, and proper warning is given”).

Opinion of the Court

III

The structure of the NCVIA and of vaccine regulation in general reinforces what the text of §300aa–22(b)(1) suggests. A vaccine’s license spells out the manufacturing method that must be followed and the directions and warnings that must accompany the product.⁵⁰ Manufacturers ordinarily must obtain the Food and Drug Administration’s (FDA) approval before modifying either.⁵¹ Deviations from the license thus provide objective evidence of manufacturing defects or inadequate warnings. Further objective evidence comes from the FDA’s regulations—more than 90 of them⁵²—that pervasively regulate the manufacturing process, down to the requirements for plumbing and ventilation systems at each manufacturing facility.⁵³ Material noncompliance with any one of them, or with any other FDA regulation, could cost the manufacturer its regulatory-compliance defense.⁵⁴

Design defects, in contrast, do not merit a single mention in the NCVIA or the FDA’s regulations. Indeed, the FDA has never even spelled out in regulations the criteria it uses to decide whether a vaccine is safe and effective for its intended use.⁵⁵ And the decision is surely not an easy one. Drug manufacturers often could trade a little less efficacy for a little more safety, but the safest design is not always the best one. Striking the right balance between safety and efficacy is especially difficult with respect to vaccines, which affect public as well as individual health. Yet the Act, which in every other respect micromanages manufacturers, is silent on how to evaluate competing designs. Are manufacturers liable only for failing to em-

⁵⁰ See 42 U. S. C. §262(a), (j); 21 CFR §§601.2(a), 314.105(b) (2010).

⁵¹ See §601.12.

⁵² See §§211.1 *et seq.*, 600.10–600.15, 600.21–600.22, 820.1 *et seq.*

⁵³ See §§211.46, 211.48.

⁵⁴ See 42 U. S. C. §300aa–22(b)(2).

⁵⁵ Hutt, Merrill, & Grossman, *Food and Drug Law*, at 685, 891.

Opinion of the Court

ploy an alternative design that the FDA has approved for distribution (an approval it takes years to obtain⁵⁶)? Or does it suffice that a vaccine design has been approved in other countries? Or could there be liability for failure to use a design that exists only in a lab? Neither the Act nor the FDA regulations provide an answer, leaving the universe of alternative designs to be limited only by an expert's imagination.

Jurors, of course, often decide similar questions with little guidance, and we do not suggest that the absence of guidance alone suggests preemption. But the lack of guidance for design defects combined with the extensive guidance for the two grounds of liability specifically mentioned in the Act strongly suggests that design defects were not mentioned because they are not a basis for liability.

The mandates contained in the Act lead to the same conclusion. Design-defect torts, broadly speaking, have two beneficial effects: (1) prompting the development of improved designs, and (2) providing compensation for inflicted injuries. The NCVIA provides other means for achieving both effects. We have already discussed the Act's generous compensation scheme. And the Act provides many means of improving vaccine design. It directs the Secretary of Health and Human Services to promote "the development of childhood vaccines that result in fewer and less serious adverse reactions."⁵⁷ It establishes a National Vaccine Program, whose Director is "to achieve optimal prevention of human infectious diseases . . . and to achieve optimal prevention against adverse reactions."⁵⁸ The Program is to set priorities for federal vaccine research, and to coordinate federal vaccine safety and effi-

⁵⁶ See Sing & William, *Supplying Vaccines*, at 66–67.

⁵⁷ 42 U. S. C. §300aa–27(a)(1).

⁵⁸ §300aa–1.

Opinion of the Court

cacy testing.⁵⁹ The Act requires vaccine manufacturers and health-care providers to report adverse side effects,⁶⁰ and provides for monitoring of vaccine safety through a collaboration with eight managed-care organizations.⁶¹ And of course whenever the FDA concludes that a vaccine is unsafe, it may revoke the license.⁶²

These provisions for federal agency improvement of vaccine design, and for federally prescribed compensation, once again suggest that §300aa–22(b)(1)’s silence regarding design-defect liability was not inadvertent. It instead reflects a sensible choice to leave complex epidemiological judgments about vaccine design to the FDA and the National Vaccine Program rather than juries.⁶³

And finally, the Act’s structural *quid pro quo* leads to the same conclusion: The vaccine manufacturers fund from their sales an informal, efficient compensation program for vaccine injuries;⁶⁴ in exchange they avoid costly tort litigation and the occasional disproportionate jury verdict.⁶⁵ But design-defect allegations are the most speculative and difficult type of products liability claim to

⁵⁹ See §§300aa–2(a)(1)–(3), 300aa–3.

⁶⁰ See §300aa–25(b).

⁶¹ See NVAC 18–19.

⁶² See 21 CFR §601.5(b)(1)(vi) (2010).

⁶³ The dissent quotes just part of this sentence, to make it appear that we believe complex epidemiological judgments ought to be assigned in that fashion. See *post*, at 26. We do not state our preference, but merely note that it is Congress’s expressed preference—and in order to preclude the argument that it is absurd to think Congress enacted such a thing, we assert that the choice is reasonable and express some of the reasons why. Leaving it to the jury may (or may not) be reasonable as well; we express no view.

⁶⁴ See 42 U. S. C. §300aa–15(i)(2); Pub. L. 99–660, §323(a), 100 Stat. 3784. The dissent’s unsupported speculation that demand in the vaccine market is inelastic, see *post*, at 24, n. 22, sheds no light on whether Congress regarded the tax as a *quid pro quo*, most Members of Congress being neither professional economists nor law-and-economics scholars.

⁶⁵ See 42 U. S. C. §§300aa–11(a)(2), 300aa–22.

Opinion of the Court

litigate. Taxing vaccine manufacturers' product to fund the compensation program, while leaving their liability for design defect virtually unaltered, would hardly coax manufacturers back into the market.

The dissent believes the Act's mandates are irrelevant because they do not spur innovation in precisely the same way as state-law tort systems.⁶⁶ That is a novel suggestion. Although we previously have expressed doubt that Congress would quietly preempt product-liability claims without providing a federal substitute, see *Medtronic, Inc. v. Lohr*, 518 U. S. 470, 486–488 (1996) (plurality opinion), we have never suggested we would be skeptical of preemption unless the congressional substitute operated like the tort system. We decline to adopt that stance today. The dissent's belief that the FDA and the National Vaccine Program cannot alone spur adequate vaccine innovation is probably questionable, but surely beside the point.

IV

Since our interpretation of §300aa–22(b)(1) is the only interpretation supported by the text and structure of the NCVIA, even those of us who believe legislative history is a legitimate tool of statutory interpretation have no need to resort to it. In any case, the dissent's contention that it would contradict our conclusion is mistaken.

The dissent's legislative history relies on the following syllogism: A 1986 House Committee Report states that §300aa–22(b)(1) “sets forth the principle contained in Comment k of Section 402A of the Restatement of Torts (Second);”⁶⁷ in 1986 comment *k* was “commonly understood” to require a case-specific showing that “no feasible alternative design” existed; Congress therefore must have intended §300aa–22(b)(1) to require that showing.⁶⁸ The

⁶⁶ See *post*, at 21–24.

⁶⁷ H. R. Rep. No. 99–908, pt. 1, p. 25 (1986) (hereinafter 1986 Report).

⁶⁸ *Post*, at 7–8.

Opinion of the Court

sylogism ignores unhelpful statements in the Report and relies upon a term of art that did not exist in 1986.

Immediately after the language quoted by the dissent, the 1986 Report notes the difficulty a jury would have in faithfully assessing whether a feasible alternative design exists when an innocent “young child, often badly injured or killed” is the plaintiff.⁶⁹ Eliminating that concern is why the Report’s authors “strongly believ[e] that Comment k is appropriate and necessary as the policy for civil actions seeking damages in tort.”⁷⁰ The dissent’s interpretation of §300aa–22(b)(1) and its version of “the principle in Comment K” adopted by the 1986 Report leave that concern unaddressed.

The dissent buries another unfavorable piece of legislative history. Because the Report believes that §300aa–22(b)(1) should incorporate “the principle in Comment K” and because the Act provides a generous no-fault compensation scheme, the Report counsels injured parties who cannot prove a manufacturing or labeling defect to “pursue recompense in the compensation system, not the tort system.”⁷¹ That counsel echoes our interpretation of §300aa–22(b)(1).

Not to worry, the dissent retorts, a Committee Report by a later Congress “authoritative[ly]” vindicates its interpretation.⁷² Post-enactment legislative history (a contradiction in terms) is not a legitimate tool of statutory interpretation. See *Jones v. United States*, 526 U. S. 227, 238

⁶⁹ 1986 Report, at 26; see *ibid.* (“[E]ven if the defendant manufacturer may have made as safe a vaccine as anyone reasonably could expect, a court or jury undoubtedly will find it difficult to rule in favor of the ‘innocent’ manufacturer if the equally ‘innocent’ child has to bear the risk of loss with no other possibility of recompense”).

⁷⁰ *Ibid.*

⁷¹ *Ibid.*

⁷² *Post*, at 12. This is a courageous adverb since we have previously held that the only authoritative source of statutory meaning is the text that has passed through the Article I process. See *Exxon Mobil Corp. v. Allapattah Services, Inc.*, 545 U. S. 546, 568 (2005).

Opinion of the Court

(1999); *United States v. Mine Workers*, 330 U. S. 258, 281–282 (1947). Real (pre-enactment) legislative history is persuasive to some because it is thought to shed light on what legislators understood an ambiguous statutory text to mean when they voted to enact it into law. See *Exxon Mobil Corp. v. Allapattah Services, Inc.*, 545 U. S. 546, 568 (2005). But post-enactment legislative history by definition “could have had no effect on the congressional vote,” *District of Columbia v. Heller*, 554 U. S. 570, 605 (2008).

It does not matter that §300aa–22(b)(1) did not take effect until the later Congress passed the excise tax that funds the compensation scheme,⁷³ and that the supposedly dispositive Committee Report is attached to that funding legislation.⁷⁴ Those who voted on the relevant statutory language were not necessarily the same persons who crafted the statements in the later Committee Report; or if they were did not necessarily have the same views at that earlier time; and no one voting at that earlier time could possibly have been informed by those later statements. Permitting the legislative history of subsequent funding legislation to alter the meaning of a statute would set a dangerous precedent. Many provisions of federal law depend on appropriations or include sunset provisions;⁷⁵ they cannot be made the device for unenacted statutory revision.

That brings us to the second flaw in the dissent’s syllogism: Comment *k* did not have a “commonly understood meaning”⁷⁶ in the mid-1980’s. Some courts thought it required a case-specific showing that a product was “unavoidably unsafe”; many others thought it categorically exempted certain types of products from strict liability.⁷⁷

⁷³Pub. L. 99–960, §323(a), 100 Stat. 3784.

⁷⁴H. R. Rep. No. 100–391, pt. 1, p. 701 (1987).

⁷⁵See, e.g., Pub. L. 104–208, §§401, 403(a), 110 Stat. 3009–655 to 3009–656, 3009–659 to 3009–662, as amended, note following 8 U. S. C. §1324a (2006 ed., Supp. III) (E-Verify program expires Sept. 30, 2012).

⁷⁶*Post*, at 8.

⁷⁷See n. 39, *supra*; *post*, at 7–8, n. 5.

Opinion of the Court

When “all (or nearly all) of the” relevant judicial decisions have given a term or concept a consistent judicial gloss, we presume Congress intended the term or concept to have that meaning when it incorporated it into a later-enacted statute. *Merck & Co. v. Reynolds*, 559 U. S. ____, ____ (2010) (SCALIA, J., concurring in part and concurring in judgment) (slip op., at 5). The consistent gloss represents the public understanding of the term. We cannot make the same assumption when widespread disagreement exists among the lower courts. We must make do with giving the term its most plausible meaning using the traditional tools of statutory interpretation. That is what we have done today.

* * *

For the foregoing reasons, we hold that the National Childhood Vaccine Injury Act preempts all design-defect claims against vaccine manufacturers brought by plaintiffs who seek compensation for injury or death caused by vaccine side effects. The judgment of the Court of Appeals is affirmed.

It is so ordered.

JUSTICE KAGAN took no part in the consideration or decision of this case.

BREYER, J., concurring

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.*
WYETH LLC, FKA WYETH, INC., FKA WYETH
LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF
APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE BREYER, concurring.

I join the Court’s judgment and opinion. In my view, the Court has the better of the purely textual argument. But the textual question considered alone is a close one. Hence, like the dissent, I would look to other sources, including legislative history, statutory purpose, and the views of the federal administrative agency, here supported by expert medical opinion. Unlike the dissent, however, I believe these other sources reinforce the Court’s conclusion.

I

House Committee Report 99–908 contains an “authoritative” account of Congress’ intent in drafting the pre-emption clause of the National Childhood Vaccine Injury Act of 1986 (NCVIA or Act). See *Garcia v. United States*, 469 U. S. 70, 76 (1984) (“[T]he authoritative source for finding the Legislature’s intent lies in the Committee Reports on the bill”). That Report says that, “if” vaccine-injured persons

“cannot demonstrate under applicable law either that a vaccine was improperly prepared or that it was accompanied by improper directions or inadequate warnings [they] should pursue recompense in the

BREYER, J., concurring

compensation system, not the tort system.” H. R. Rep. No. 99–908, pt. 1, p. 24 (1986) (hereinafter H. R. Rep.).

The Report lists two specific kinds of tort suits that the clause does not pre-empt (suits based on improper manufacturing and improper labeling), while going on to state that compensation for other tort claims, *e.g.*, design-defect claims, lies in “the [NCVIA’s no-fault] compensation system, not the tort system.” *Ibid.*

The strongest contrary argument rests upon the Report’s earlier description of the statute as “set[ting] forth the principle contained in Comment k” (of the Restatement Second of Torts’ *strict liability* section, 402A) that “a vaccine manufacturer should not be liable for injuries or deaths resulting from *unavoidable* side effects.” *Id.*, at 23 (emphasis added). But the appearance of the word “unavoidable” in this last-mentioned sentence cannot provide petitioners with much help. That is because nothing in the Report suggests that the statute means the word “unavoidable” to summon up an otherwise unmentioned third exception encompassing suits based on design defects. Nor can the Report’s reference to comment *k* fill the gap. The Report itself refers, not to comment *k*’s details, but only to its “*principle*,” namely, that vaccine manufacturers should *not* be held liable for unavoidable injuries. It says nothing at all about who—judge, jury, or federal safety agency—should decide whether a safer vaccine could have been designed. Indeed, at the time Congress wrote this Report, different state courts had come to very different conclusions about that matter. See Cupp, Rethinking Conscious Design Liability for Prescription Drugs: The *Restatement (Third)* Standard Versus a Negligence Approach, 63 *Geo. Wash. L. Rev.* 76, 79 (1994–1995) (“[C]ourts [had] adopted a broad range of conflicting interpretations” of comment *k*). Neither the word “unavoid-

BREYER, J., concurring

able” nor the phrase “the principle of Comment k” tells us which courts’ view Congress intended to adopt. Silence cannot tell us to follow those States where juries decided the design-defect question.

II

The legislative history describes the statute more generally as trying to protect the lives of children, in part by ending “the instability and unpredictability of the childhood vaccine market.” H. R. Rep., at 7; see *ante*, at 2–3. As the Committee Report makes clear, routine vaccination is “one of the most spectacularly effective public health initiatives this country has ever undertaken.” H. R. Rep., at 4. Before the development of routine whooping cough vaccination, for example, “nearly all children” in the United States caught the disease and more than 4,000 people died annually, most of them infants. U. S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, What Would Happen if We Stopped Vaccinations? <http://www.cdc.gov/vaccines/vac-gen/whatifstop.htm> (all Internet materials as visited Feb. 17, 2011, and available in Clerk of Court’s case file); Preventing Tetanus, Diphtheria, and Pertussis Among Adolescents: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccines, 55 Morbidity and Mortality Weekly Report, No. RR–3, p. 2 (Mar. 24, 2006) (hereinafter Preventing Tetanus) (statistics for 1934–1943), <http://www.cdc.gov/mmwr/PDF/rr/rr5503.pdf>; U. S. Dept. of Health and Human Services, Centers for Disease Control and Prevention, Epidemiology and Prevention of Vaccine-Preventable Diseases 200 (11th ed. rev. May 2009). After vaccination became common, the number of annual cases of whooping cough declined from over 200,000 to about 2,300, and the number of deaths from about 4,000 to about 12. Preventing Tetanus 2; Childhood Immunizations, House Committee on Energy and Com-

BREYER, J., concurring

merce, 99th Cong., 2d Sess., 10 (Comm. Print 1986) (hereinafter *Childhood Immunizations*).

But these gains are fragile; “[t]he causative agents for these preventable childhood illnesses are ever present in the environment, waiting for the opportunity to attack the unprotected individual.” Hearing on S. 827 before the Senate Committee on Labor and Human Resources, 99th Cong., 2d Sess., pt. 2, pp. 20–21 (1985) (hereinafter *Hearings*) (testimony of the American Academy of Pediatrics); see California Dept. of Public Health, *Pertussis Report* (Jan. 7, 2011), www.cdph.ca.gov/programs/immunize/Documents/PertussisReport2011-01-07.pdf (In 2010, 8,383 people in California caught whooping cough, and 10 infants died). Even a brief period when vaccination programs are disrupted can lead to children’s deaths. *Hearings* 20–21; see Gangarosa et al., *Impact of Anti-Vaccine Movements on Pertussis Control: The Untold Story*, 351 *Lancet* 356–361 (Jan. 31, 1998) (when vaccination programs are disrupted, the number of cases of whooping cough skyrockets, increasing by orders of magnitude).

In considering the NCVIA, Congress found that a sharp increase in tort suits brought against whooping cough and other vaccine manufacturers between 1980 and 1985 had “prompted manufacturers to question their continued participation in the vaccine market.” H. R. Rep., at 4; *Childhood Immunizations* 85–86. Indeed, two whooping cough vaccine manufacturers withdrew from the market, and other vaccine manufacturers, “fac[ing] great difficulty in obtaining [product liability] insurance,” told Congress that they were considering “a similar course of action.” H. R. Rep., at 4; *Childhood Immunizations* 68–70. The Committee Report explains that, since there were only one or two manufacturers of many childhood vaccines, “[t]he loss of any of the existing manufacturers of childhood vaccines . . . could create a genuine public health hazard”; it “would present the very real possibility of vaccine short-

BREYER, J., concurring

ages, and, in turn, increasing numbers of unimmunized children, and, perhaps, a resurgence of preventable diseases.” H. R. Rep., at 5. At the same time, Congress sought to provide generous compensation to those whom vaccines injured—as determined by an expert compensation program. *Id.*, at 5, 24.

Given these broad general purposes, to read the preemption clause as preserving design-defect suits seems anomalous. The Department of Health and Human Services (HHS) decides when a vaccine is safe enough to be licensed and which licensed vaccines, with which associated injuries, should be placed on the Vaccine Injury Table. 42 U. S. C. §300aa–14; *ante*, at 3–4; A Comprehensive Review of Federal Vaccine Safety Programs and Public Health Activities 13–15, 32–34 (Dec. 2008), <http://www.hhs.gov/nvpo/nvac/documents/vaccine-safety-review.pdf>. A special master in the Act’s compensation program determines whether someone has suffered an injury listed on the Injury Table and, if not, whether the vaccine nonetheless caused the injury. *Ante*, at 3–4; §300aa–13. To allow a jury in effect to second-guess those determinations is to substitute less expert for more expert judgment, thereby threatening manufacturers with liability (indeed, strict liability) in instances where any conflict between experts and nonexperts is likely to be particularly severe—instances where Congress intended the contrary. That is because potential tort plaintiffs are unlikely to bring suit unless the specialized compensation program has determined that they are not entitled to compensation (say, because it concludes that the vaccine did not cause the injury). Brief for United States as *Amicus Curiae* 28 (“99.8% of successful Compensation Program claimants have accepted their awards, foregoing any tort remedies against vaccine manufacturers”). It is difficult to reconcile these potential conflicts and the resulting tort liabilities with a statute that seeks to diminish

BREYER, J., concurring

manufacturers' product liability while simultaneously augmenting the role of experts in making compensation decisions.

III

The United States, reflecting the views of HHS, urges the Court to read the Act as I and the majority would do. It notes that the compensation program's listed vaccines have survived rigorous administrative safety review. It says that to read the Act as permitting design-defect lawsuits could lead to a recurrence of "exactly the crisis that precipitated the Act," namely withdrawals of vaccines or vaccine manufacturers from the market, "disserv[ing] the Act's central purposes," and hampering the ability of the agency's "expert regulators, in conjunction with the medical community, [to] control the availability and withdrawal of a given vaccine." Brief for United States as *Amicus Curiae* 30, 31.

The United States is supported in this claim by leading public health organizations, including the American Academy of Pediatrics, the American Academy of Family Physicians, the American College of Preventive Medicine, the American Public Health Association, the American Medical Association, the March of Dimes Foundation, the Pediatric Infectious Diseases Society, and 15 other similar organizations. Brief for American Academy of Pediatrics et al. as *Amici Curiae* (hereinafter AAP Brief). The American Academy of Pediatrics has also supported the retention of vaccine manufacturer tort liability (provided that federal law structured state-law liability conditions in ways that would take proper account of federal agency views about safety). Hearings 14–15. But it nonetheless tells us here, in respect to the specific question before us, that the petitioners' interpretation of the Act would undermine its basic purposes by threatening to "halt the future production and development of childhood vaccines

BREYER, J., concurring

in this country,” *i.e.*, by “threaten[ing] a resurgence of the very problems which . . . caused Congress to intervene” by enacting this statute. AAP Brief 24 (internal quotation marks omitted).

I would give significant weight to the views of HHS. The law charges HHS with responsibility for overseeing vaccine production and safety. It is “likely to have a thorough understanding” of the complicated and technical subject matter of immunization policy, and it is comparatively more “qualified to comprehend the likely impact of state requirements.” *Geier v. American Honda Motor Co., Inc.*, 529 U. S. 861, 883 (2000) (internal quotation marks omitted); see *Medtronic, Inc. v. Lohr*, 518 U. S. 470, 506 (1996) (BREYER, J., concurring in part and concurring in judgment) (the agency is in the best position to determine “whether (or the extent to which) state requirements may interfere with federal objectives”). HHS’s position is particularly persuasive here because expert public health organizations support its views and the matter concerns a medical and scientific question of great importance: how best to save the lives of children. See *Skidmore v. Swift & Co.*, 323 U. S. 134 (1944).

In sum, congressional reports and history, the statute’s basic purpose as revealed by that history, and the views of the expert agency along with those of relevant medical and scientific associations, all support the Court’s conclusions. I consequently agree with the Court.

SOTOMAYOR, J., dissenting

SUPREME COURT OF THE UNITED STATES

No. 09–152

RUSSELL BRUESEWITZ, ET AL., PETITIONERS *v.*
WYETH LLC, FKA WYETH, INC., FKA WYETH
LABORATORIES, ET AL.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF
APPEALS FOR THE THIRD CIRCUIT

[February 22, 2011]

JUSTICE SOTOMAYOR, with whom JUSTICE GINSBURG
joins, dissenting.

Vaccine manufacturers have long been subject to a legal duty, rooted in basic principles of products liability law, to improve the designs of their vaccines in light of advances in science and technology. Until today, that duty was enforceable through a traditional state-law tort action for defective design. In holding that §22(b)(1) of the National Childhood Vaccine Injury Act of 1986 (Vaccine Act or Act), 42 U. S. C. §300aa–22(b)(1), pre-empts all design defect claims for injuries stemming from vaccines covered under the Act, the Court imposes its own bare policy preference over the considered judgment of Congress. In doing so, the Court excises 13 words from the statutory text, misconstrues the Act’s legislative history, and disturbs the careful balance Congress struck between compensating vaccine-injured children and stabilizing the childhood vaccine market. Its decision leaves a regulatory vacuum in which no one ensures that vaccine manufacturers adequately take account of scientific and technological advancements when designing or distributing their products. Because nothing in the text, structure, or legislative history of the Vaccine Act remotely suggests that Congress intended such a result, I respectfully dissent.

SOTOMAYOR, J., dissenting

I
A

Section 22 of the Vaccine Act provides “[s]tandards of responsibility” to govern civil actions against vaccine manufacturers. 42 U. S. C. §300aa–22. Section 22(a) sets forth the “[g]eneral rule” that “State law shall apply to a civil action brought for damages for a vaccine-related injury or death.” §300aa–22(a). This baseline rule that state law applies is subject to three narrow exceptions, one of which, §22(b)(1), is at issue in this case. Section 22(b)(1) provides:

“No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.” §300aa–22(b)(1).

The provision contains two key clauses: “if the injury or death resulted from side effects that were unavoidable” (the “if” clause), and “even though the vaccine was properly prepared and was accompanied by proper directions and warnings” (the “even though” clause).

Blackletter products liability law generally recognizes three different types of product defects: design defects, manufacturing defects, and labeling defects (*e.g.*, failure to warn).¹ The reference in the “even though” clause to a “properly prepared” vaccine “accompanied by proper directions and warnings” is an obvious reference to two such defects—manufacturing and labeling defects. The plain terms of the “even though” clause thus indicate that

¹W. Keeton, D. Dobbs, R. Keeton, & D. Owen, *Prosser and Keeton on Law of Torts* 695 (5th ed. 1984).

SOTOMAYOR, J., dissenting

§22(b)(1) applies only where neither kind of defect is present. Because §22(b)(1) is invoked by vaccine manufacturers as a defense to tort liability, it follows that the “even though” clause requires a vaccine manufacturer in each civil action to demonstrate that its vaccine is free from manufacturing and labeling defects to fall within the liability exemption of §22(b)(1).²

Given that the “even though” clause requires the absence of manufacturing and labeling defects, the “if” clause’s reference to “side effects that were unavoidable” must refer to side effects caused by something other than manufacturing and labeling defects. The only remaining kind of product defect recognized under traditional products liability law is a design defect. Thus, “side effects that were unavoidable” must refer to side effects caused by a vaccine’s *design* that were “unavoidable.” Because §22(b)(1) uses the conditional term “if,” moreover, the text plainly implies that some side effects stemming from a vaccine’s design are “unavoidable,” while others are avoidable. See Webster’s Third New International Dictionary 1124 (2002) (“if” means “in the event that,” “so long as,” or “on condition that”). Accordingly, because the “if” clause (like the “even though” clause) sets forth a condition to invoke §22(b)(1)’s defense to tort liability, Congress must also have intended a vaccine manufacturer to demonstrate in each civil action that the particular side effects of a vaccine’s design were “unavoidable.”

Congress’ use of conditional “if” clauses in two other provisions of the Vaccine Act supports the conclusion that §22(b)(1) requires an inquiry in each case in which a manufacturer seeks to invoke the provision’s exception to

²See *Silkwood v. Kerr-McGee Corp.*, 464 U. S. 238, 255 (1984); *Brown v. Earthboard Sports USA, Inc.*, 481 F. 3d 901, 912 (CA6 2007) (“[F]ederal preemption is an affirmative defense upon which the defendants bear the burden of proof” (quoting *Fifth Third Bank v. CSX Corp.*, 415 F. 3d 741, 745 (CA7 2005))).

SOTOMAYOR, J., dissenting

state tort liability. In §22(b)(2), Congress created a presumption that, for purposes of §22(b)(1), “a vaccine shall be presumed to be accompanied by proper directions and warnings if the vaccine manufacturer shows that it complied in all material respects with” federal labeling requirements. 42 U. S. C. §300aa–22(b)(2). Similarly, in §23(d)(2), Congress created an exemption from punitive damages “[i]f . . . the manufacturer shows that it complied, in all material respects,” with applicable federal laws, unless it engages in “fraud,” “intentional and wrongful withholding of information” from federal regulators, or “other criminal or illegal activity.” §300aa–23(d)(2). It would be highly anomalous for Congress to use a conditional “if” clause in §§22(b)(2) and 23(d)(2) to require a specific inquiry in each case while using the same conditional “if” clause in §22(b)(1) to denote a categorical exemption from liability. Cf. *Erlenbaugh v. United States*, 409 U. S. 239, 243 (1972) (“[A] legislative body generally uses a particular word with a consistent meaning in a given context”).

Indeed, when Congress intends to pre-empt design defect claims categorically, it does so using categorical (*e.g.*, “all”) and/or declarative language (*e.g.*, “shall”), rather than a conditional term (“if”). For example, in a related context, Congress has authorized the Secretary of Health and Human Services to designate a vaccine designed to prevent a pandemic or epidemic as a “covered countermeasure.” 42 U. S. C. §§247d–6d(b), (i)(1), (i)(7)(A)(i). With respect to such “covered countermeasure[s],” Congress provided that subject to certain exceptions, “a covered person *shall* be immune from suit and liability under Federal and State law with respect to *all* claims for loss caused by, arising out of, relating to, or resulting from the administration to or the use by an individual of a covered countermeasure,” §247d–6d(a)(1) (emphasis added), including specifically claims relating to

SOTOMAYOR, J., dissenting

“the design” of the countermeasure, §247d–6d(a)(2)(B).

The plain text and structure of the Vaccine Act thus compel the conclusion that §22(b)(1) pre-empts some—but not all—design defect claims. Contrary to the majority’s and respondent’s categorical reading, petitioners correctly contend that, where a plaintiff has proved that she has suffered an injury resulting from a side effect caused by a vaccine’s design, a vaccine manufacturer may invoke §22(b)(1)’s liability exemption only if it demonstrates that the side effect stemming from the particular vaccine’s design is “unavoidable,” and that the vaccine is otherwise free from manufacturing and labeling defects.³

B

The legislative history confirms petitioners’ interpretation of §22(b)(1) and sheds further light on its pre-emptive scope. The House Energy and Commerce Committee Report accompanying the Vaccine Act, H. R. Rep. No. 99–908, pt. 1 (1986) (hereinafter 1986 Report), explains in relevant part:

*“Subsection (b)—Unavoidable Adverse Side Effects; Direct Warnings.—*This provision sets forth the principle contained in Comment K of Section 402A of the Restatement of Torts (Second) that a vaccine manufacturer should not be liable for injuries or deaths resulting from unavoidable side effects even though the vaccine was properly prepared and accompanied by proper directions and warnings.

“The Committee has set forth Comment K in this bill because it intends that the principle in Comment K regarding ‘unavoidably unsafe’ products, i.e., those products which in the present state of human skill and knowledge cannot be made safe, apply to the vac-

³This leaves the question of what precisely §22(b)(1) means by “unavoidable” side effects, which I address in the next section.

SOTOMAYOR, J., dissenting

cines covered in the bill and that such products not be the subject of liability in the tort system.” *Id.*, at 25–26.

The Report expressly adopts comment *k* of §402A of the Restatement of Torts (Second) (1963–1964) (hereinafter Restatement), which provides that “unavoidably unsafe” products—*i.e.*, those that “in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use”—are not defective.⁴ As “[a]n outstanding example” of an “[u]navoidably unsafe” product, comment *k* cites “the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected”;

⁴ Comment *k* provides as follows:

“*Unavoidably unsafe products.* There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper directions and warning, is not defective, nor is it *unreasonably* dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot legally be sold except to physicians, or under the prescription of a physician. It is also true in particular of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even of purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk. The seller of such products, again with the qualification that they are properly prepared and marketed, and proper warning is given, where the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.” Restatement 353–354.

SOTOMAYOR, J., dissenting

“[s]ince the disease itself invariably leads to a dreadful death, both the marketing and the use of the vaccine are fully justified, notwithstanding the unavoidable high degree of risk which they involve.” *Id.*, at 353. Comment *k* thus provides that “seller[s]” of “[u]navoidably unsafe” products are “not to be held to strict liability” provided that such products “are properly prepared and marketed, and proper warning is given.” *Ibid.*

As the 1986 Report explains, Congress intended that the “principle in Comment K regarding ‘unavoidably unsafe’ products” apply to the vaccines covered in the bill. 1986 Report 26. That intent, in turn, is manifested in the plain text of §22(b)(1)—in particular, Congress’ use of the word “unavoidable,” as well as the phrases “properly prepared” and “accompanied by proper directions and warnings,” which were taken nearly verbatim from comment *k*. 42 U. S. C. §300aa–22(b)(1); see Restatement 353–354 (“Such a[n unavoidably unsafe] product, properly prepared, and accompanied by proper directions and warning, is not defective”). By the time of the Vaccine Act’s enactment in 1986, numerous state and federal courts had interpreted comment *k* to mean that a product is “unavoidably unsafe” when, given proper manufacture and labeling, no feasible alternative design would reduce the safety risks without compromising the product’s cost and utility.⁵ Given Con-

⁵See, e.g., *Smith ex rel. Smith v. Wyeth Labs., Inc.*, No. Civ. A 84–2002, 1986 WL 720792, *5 (SD W. Va., Aug. 21, 1986) (“[A] prescription drug is not ‘unavoidably unsafe’ when its dangers can be eliminated through design changes that do not unduly affect its cost or utility”); *Kearl v. Lederle Labs.*, 172 Cal. App. 3d 812, 830, 218 Cal. Rptr. 453, 464 (1985) (“unavoidability” turns on “(i) whether the product was designed to minimize—to the extent scientifically knowable at the time it was distributed—the risk inherent in the product, and (ii) the availability . . . of any alternative product that would have *as effectively* accomplished the *full intended purpose* of the subject product”), disapproved in part by *Brown v. Superior Ct.*, 44 Cal. 3d 1049, 751 P. 2d 470 (1988); *Belle Bonfils Memorial Blood Bank v. Hansen*, 665 P. 2d 118,

SOTOMAYOR, J., dissenting

gress’ expressed intent to codify the “principle in Comment K,” 1986 Report 26, the term “unavoidable” in §22(b)(1) is best understood as a term of art, which incorporates the commonly understood meaning of “unavoidably unsafe” products under comment *k* at the time of the Act’s enactment in 1986. See *McDermott Int’l, Inc. v. Wilander*, 498 U. S. 337, 342 (1991) (“[W]e assume that when a statute uses . . . a term [of art], Congress intended it to have its established meaning”); *Morissette v. United States*, 342 U. S. 246, 263 (1952) (same).⁶ Similarly, courts applying

122 (Colo. 1983) (“[A]pplicability of comment *k* . . . depends upon the co-existence of several factors,” including that “the product’s benefits must not be achievable in another manner; and the risk must be unavoidable under the present state of knowledge”); see also 1 L. Frumer & M. Friedman, *Products Liability* §§8.07[1]–[2], pp. 8–277 to 8–278 (2010) (comment *k* applies “only to defects in design,” and there “must be no feasible alternative design which on balance accomplishes the subject product’s purpose with a lesser risk” (internal quotation marks omitted)). To be sure, a number of courts at the time of the Vaccine Act’s enactment had interpreted comment *k* to preclude design defect claims categorically for certain kinds of products, see *Hill v. Searle Labs.*, 884 F. 2d 1064, 1068 (CA8 1989) (collecting cases), but as indicated by the sources cited above, the courts that had construed comment *k* to apply on a case-specific basis generally agreed on the basic elements of what constituted an “unavoidably unsafe” product. See also n. 8, *infra*. The majority’s suggestion that “judges who must rule on motions to dismiss, motions for summary judgment, and motions for judgment as a matter of law” are incapable of adjudicating claims alleging “unavoidable” side effects, *ante*, at 7–8, n. 35, is thus belied by the experience of the many courts that had adjudicated such claims for years by the time of the Vaccine Act’s enactment.

⁶The majority refuses to recognize that “unavoidable” is a term of art derived from comment *k*, suggesting that “[u]navoidable’ is hardly a rarely used word.” *Ante*, at 10. In fact, however, “unavoidable” is an extremely rare word in the relevant context. It appears exactly *once* (*i.e.*, in §300aa–22(b)(1)) in the entirety of Title 42 of the U. S. Code (“Public Health and Welfare”), which governs, *inter alia*, Social Security, see 42 U. S. C. §301 *et seq.*, Medicare, see §1395 *et seq.*, and several other of the Federal Government’s largest entitlement programs. The singular rarity in which Congress used the term supports the conclu-

SOTOMAYOR, J., dissenting

comment *k* had long required manufacturers invoking the defense to demonstrate that their products were not only “unavoidably unsafe” but also properly manufactured and labeled.⁷ By requiring “prope[r] prepar[ation]” and “proper directions and warnings” in §22(b)(1), Congress plainly intended to incorporate these additional comment *k* requirements.

The 1986 Report thus confirms petitioners’ interpretation of §22(b)(1). The Report makes clear that “side effects that were unavoidable” in §22(b)(1) refers to side effects stemming from a vaccine’s design that were “unavoidable.” By explaining what Congress meant by the term “unavoidable,” moreover, the Report also confirms that whether a side effect is “unavoidable” for purposes of §22(b)(1) involves a specific inquiry in each case as to whether the vaccine “in the present state of human skill and knowledge cannot be made safe,” 1986 Report 26—*i.e.*, whether a feasible alternative design existed that would have eliminated the adverse side effects of the vaccine without compromising its cost and utility. See Brief for Kenneth W. Starr et al. as *Amici Curiae* 14–15 (“If a particular plaintiff could show that her injury at issue was avoidable . . . through the use of a feasible alternative design for a specific vaccine, then she would satisfy the plain language of the statute, because she would have demonstrated that the side effects were *not* unavoidable”). Finally, the Report confirms that the “even though” clause is properly read to establish two additional prerequisites—proper manufacturing and proper labeling—to qualify for

sion that “unavoidable” is a term of art.

⁷See, *e.g.*, *Brochu v. Ortho Pharmaceutical Corp.*, 642 F. 2d 652, 657 (CA1 1981); *Needham v. White Labs., Inc.*, 639 F. 2d 394, 402 (CA7 1981); *Reyes v. Wyeth Labs.*, 498 F. 2d 1264, 1274–1275 (CA5 1974); *Davis v. Wyeth Labs.*, 399 F. 2d 121, 127–129 (CA9 1968); *Feldman v. Lederle Labs.*, 97 N. J. 429, 448, 479 A. 2d 374, 384 (1984); see also *Toner v. Lederle Labs.*, 112 Idaho 328, 336, 732 P. 2d 297, 305 (1987).

SOTOMAYOR, J., dissenting

§22(b)(1)'s liability exemption.⁸

In addition to the 1986 Report, one other piece of the Act's legislative history provides further confirmation of the petitioners' textual reading of §22(b)(1). When Congress enacted the Vaccine Act in 1986, it did not initially include a source of payment for the no-fault compensation program the Act established. The Act thus "made the compensation program and accompanying tort reforms contingent on the enactment of a tax to provide funding

⁸Respondent suggests an alternative reading of the 1986 Report. According to respondent, "the principle in Comment K" is simply that of nonliability for "unavoidably unsafe" products, and thus Congress' stated intent in the 1986 Report to apply the "principle in Comment K" to "the vaccines covered in the bill" means that Congress viewed the covered vaccines as a class to be "unavoidably unsafe." 1986 Report 25–26; Brief for Respondent 42. The concurrence makes a similar argument. *Ante*, at 1–2 (opinion of BREYER, J.). This interpretation finds some support in the 1986 Report, which states that "if [injured individuals] cannot demonstrate under applicable law either that a vaccine was improperly prepared or that it was accompanied by improper directions or inadequate warnings [they] should pursue recompense in the compensation system, not the tort system." 1986 Report 26. It also finds some support in the pre-Vaccine Act case law, which reflected considerable disagreement in the courts over "whether comment k applies to pharmaceutical products across the board or only on a case-by-case basis." Ausness, *Unavoidably Unsafe Products and Strict Products Liability: What Liability Rule Should be Applied to the Sellers of Pharmaceutical Products?* 78 Ky. L. J. 705, 708, and n. 11 (1989–1990) (collecting cases). This interpretation, however, is undermined by the fact that Congress has never directed the Food and Drug Administration (FDA) or any other federal agency to review vaccines for optimal vaccine design, see *infra*, at 20–22, and n. 19, and thus it seems highly unlikely that Congress intended to eliminate the traditional mechanism for such review (*i.e.*, design defect liability), particularly given its express retention of state tort law in the Vaccine Act, see 42 U. S. C. §300aa–22(a). In any event, to the extent there is ambiguity as to how precisely Congress intended the "principle in Comment K" to apply to the covered vaccines, that ambiguity is explicitly resolved in petitioners' favor by the 1987 House Energy and Commerce Committee Report, H. R. Rep. No. 100–391, pt. 1, pp. 690–691 (hereinafter 1987 Report). See *infra* this page and 11–12.

SOTOMAYOR, J., dissenting

for the compensation.” 1987 Report 690. In 1987, Congress passed legislation to fund the compensation program. The House Energy and Commerce Committee Report⁹ accompanying that legislation specifically stated that “the codification of Comment (k) of The Restatement (Second) of Torts was not intended to decide as a matter of law the circumstances in which a vaccine should be deemed unavoidably unsafe.” *Id.*, at 691. The Committee noted that “[a]n amendment to establish . . . that a manufacturer’s failure to develop [a] safer vaccine was not grounds for liability was rejected by the Committee during its original consideration of the Act.” *Ibid.* In light of that rejection, the Committee emphasized that “there should be no misunderstanding that the Act undertook to decide as a matter of law whether vaccines were unavoidably unsafe or not,” and that “[t]his question is left to the courts to determine in accordance with applicable law.” *Ibid.*

To be sure, postenactment legislative history created by a subsequent Congress is ordinarily a hazardous basis from which to infer the intent of the enacting Congress. See *Sullivan v. Finkelstein*, 496 U. S. 617, 631–632 (1990) (SCALIA, J., concurring in part). But unlike ordinary postenactment legislative history, which is justifiably given little or no weight, the 1987 Report reflects the intent of the Congress that enacted the funding legislation necessary to give operative effect to the principal provisions of the Vaccine Act, including §22(b)(1).¹⁰ Congress in

⁹The Third Circuit’s opinion below expressed uncertainty as to whether the 1987 Report was authored by the House Budget Committee or the House Energy and Commerce Committee. See 561 F. 3d 233, 250 (2009). As petitioners explain, although the Budget Committee compiled and issued the Report, the Energy and Commerce Committee wrote and approved the relevant language. Title IV of the Report, entitled “Committee on Energy and Commerce,” comprises “two Committee Prints approved by the Committee on Energy and Commerce for inclusion in the forthcoming reconciliation bill.” 1987 Report 377, 380.

¹⁰The majority suggests that the 1987 legislation creating the fund-

SOTOMAYOR, J., dissenting

1987 had a number of options before it, including adopting an entirely different compensation scheme, as the Reagan administration was proposing;¹¹ establishing different limitations on tort liability, including eliminating design defect liability, as pharmaceutical industry leaders were advocating;¹² or not funding the compensation program at all, which would have effectively nullified the relevant portions of the Act. Because the tort reforms in the 1986 Act, including §22(b)(1), had no operative legal effect unless and until Congress provided funding for the compensation program, the views of the Congress that enacted that funding legislation are a proper and, indeed, authoritative guide to the meaning of §22(b)(1). Those views, as reflected in the 1987 Report, provide unequivocal confir-

ing mechanism is akin to appropriations legislation and that giving weight to the legislative history of such legislation “would set a dangerous precedent.” *Ante*, at 18. The difference, of course, is that appropriations legislation ordinarily funds congressional enactments that already have operative legal effect; in contrast, operation of the tort reforms in the 1986 Act, including §22(b)(1), was expressly conditioned on the enactment of a separate tax to fund the compensation program. See §323(a), 100 Stat. 3784. Accordingly, this Court’s general reluctance to view appropriations legislation as modifying substantive legislation, see, *e.g.*, *TVA v. Hill*, 437 U. S. 153, 190 (1978), has no bearing here.

¹¹See 1987 Report 700 (describing the administration’s alternative proposal).

¹²See, *e.g.*, Hearings on Funding of the Childhood Vaccine Program before the Subcommittee on Select Revenue Measures of the House Committee on Ways and Means, 100th Cong., 1st Sess., 85 (1987) (“[T]he liability provisions of the 1986 Act should be amended to assure that manufacturers will not be found liable in the tort system if they have fully complied with applicable government regulations. In particular, manufacturers should not face liability under a ‘design defect’ theory in cases where plaintiffs challenge the decisions of public health authorities and federal regulators that the licensed vaccines are the best available way to protect children from deadly diseases” (statement of Robert B. Johnson, President, Lederle Laboratories Division, American Cyanamid Co.)).

SOTOMAYOR, J., dissenting

mation of petitioners' reading of §22(b)(1).

In sum, the text, structure, and legislative history of the Vaccine Act are fully consistent with petitioners' reading of §22(b)(1). Accordingly, I believe §22(b)(1) exempts vaccine manufacturers from tort liability only upon a showing by the manufacturer in each case that the vaccine was properly manufactured and labeled, and that the side effects stemming from the vaccine's design could not have been prevented by a feasible alternative design that would have eliminated the adverse side effects without compromising the vaccine's cost and utility.

II

In contrast to the interpretation of §22(b)(1) set forth above, the majority's interpretation does considerable violence to the statutory text, misconstrues the legislative history, and draws the wrong conclusions from the structure of the Vaccine Act and the broader federal scheme regulating vaccines.

A

As a textual matter, the majority's interpretation of §22(b)(1) is fundamentally flawed in three central respects. First, the majority's categorical reading rests on a faulty and untenable premise. Second, its reading functionally excises 13 words from the statutory text, including the key term "unavoidable." And third, the majority entirely ignores the Vaccine Act's default rule preserving state tort law.

To begin, the majority states that "[a] side effect of a vaccine could *always* have been avoidable by use of a differently designed vaccine not containing the harmful element." *Ante*, at 7. From that premise, the majority concludes that the statute must mean that "the *design* of the vaccine is a given, not subject to question in the tort action," because construing the statute otherwise would

SOTOMAYOR, J., dissenting

render §22(b)(1) a nullity. *Ibid.* A tort claimant, according to the majority, will always be able to point to a differently designed vaccine not containing the “harmful element,” and if that were sufficient to show that a vaccine’s side effects were not “unavoidable,” the statute would preempt nothing.

The starting premise of the majority’s interpretation, however, is fatally flawed. Although in the most literal sense, as the majority notes, a side effect can always be avoided “by use of a differently designed vaccine not containing the harmful element,” *ibid.*, this interpretation of “unavoidable” would effectively read the term out of the statute, and Congress could not have intended that result. Indeed, §22(b)(1) specifically uses the conditional phrase “if the injury or death resulted from side effects that were unavoidable,” which plainly indicates that Congress contemplated that there would be some instances in which a vaccine’s side effects are “unavoidable” and other instances in which they are not. See *supra*, at 3. The majority’s premise that a vaccine’s side effects can always be “avoid[ed] by use of a differently designed vaccine not containing the harmful element,” *ante*, at 7, entirely ignores the fact that removing the “harmful element” will often result in a less effective (or entirely ineffective) vaccine. A vaccine, by its nature, ordinarily employs a killed or weakened form of a bacteria or virus to stimulate antibody production;¹³ removing that bacteria or virus might remove the “harmful element,” but it would also necessarily render the vaccine inert. As explained above, the legislative history of the Vaccine Act and the cases interpreting comment *k* make clear that a side effect is

¹³ See American Academy of Pediatrics, Questions and Answers about Vaccine Ingredients (Oct. 2008), <http://www.aap.org/immunization/families/faq/Vaccineingredients.pdf> (all Internet materials as visited Feb. 18, 2011, and available in Clerk of Court’s case file).

SOTOMAYOR, J., dissenting

“unavoidable” for purposes of §22(b)(1) only where there is no feasible alternative design that would eliminate the side effect of the vaccine without compromising its cost and utility. See *supra*, at 7. The majority’s premise—that side effects stemming from a vaccine’s design are always avoidable—is thus belied by the statutory text and legislative history of §22(b)(1). And because its starting premise is invalid, its conclusion—that the design of a vaccine is not subject to challenge in a tort action—is also necessarily invalid.

The majority’s reading suffers from an even more fundamental defect. If Congress intended to exempt vaccine manufacturers categorically from all design defect liability, it more logically would have provided: “No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the vaccine was properly prepared and was accompanied by proper directions and warnings.” There would have been no need for Congress to include the additional 13 words “the injury or death resulted from side effects that were unavoidable even though.” See *TRW Inc. v. Andrews*, 534 U. S. 19, 31 (2001) (noting “cardinal principle of statutory construction that a statute ought, upon the whole, to be so construed that, if it can be prevented, no clause, sentence, or word shall be superfluous, void, or insignificant” (internal quotation marks omitted)).

In *Bates v. Dow Agrosciences LLC*, 544 U. S. 431 (2005), this Court considered an analogous situation where an express pre-emption provision stated that certain States “shall not impose or continue in effect any requirements for labeling or packaging in addition to or different from those required under this subchapter.” *Id.*, at 436 (quoting 7 U. S. C. §136v(b) (2000 ed.)). The *Bates* Court stated:

SOTOMAYOR, J., dissenting

“Conspicuously absent from the submissions by [respondent] and the United States is any plausible alternative interpretation of ‘in addition to or different from’ that would give that phrase meaning. Instead, they appear to favor reading those words out of the statute, which would leave the following: ‘Such State shall not impose or continue in effect any requirements for labeling or packaging.’ This amputated version of [the statute] would no doubt have clearly and succinctly commanded the pre-emption of *all* state requirements concerning labeling. That Congress added the remainder of the provision is evidence of its intent to draw a distinction between state labeling requirements that are pre-empted and those that are not.” 544 U. S., at 448–449.

As with the statutory interpretation rejected by this Court in *Bates*, the majority’s interpretation of §22(b)(1) functionally excises 13 words out of the statute, including the key term “unavoidable.” See *Duncan v. Walker*, 533 U. S. 167, 174 (2001) (“We are especially unwilling” to treat a statutory term as surplusage “when the term occupies so pivotal a place in the statutory scheme”). Although the resulting “amputated version” of the statutory provision “would no doubt have clearly and succinctly commanded the pre-emption of *all* state” design defect claims, the fact “[t]hat Congress added the remainder of the provision” is strong evidence of its intent not to pre-empt design defect claims categorically. *Bates*, 544 U. S., at 449; see also *American Home Prods. Corp. v. Ferrari*, 284 Ga. 384, 393, 668 S. E. 2d 236, 242 (2008) (“If Congress had intended to deprive injured parties of a long available form of compensation, it surely would have expressed that intent more clearly” (quoting *Bates*, 544 U. S., at 449)), cert. pending, No. 08–1120.

Strikingly, the majority concedes that its interpretation

SOTOMAYOR, J., dissenting

renders 13 words of the statute entirely superfluous. See *ante*, at 12 (“The intervening passage (‘the injury or death resulted from side effects that were unavoidable even though’) is unnecessary. True enough”). Nevertheless, the majority contends that “the rule against giving a portion of text an interpretation which renders it superfluous . . . applies only if verbosity and prolixity can be eliminated by giving the offending passage, or the remainder of the text, a competing interpretation.” *Ibid.* According to the majority, petitioners’ reading of §22(b)(1) renders the “even though” clause superfluous because, to reach petitioners’ desired outcome, “[i]t would suffice to say ‘if the injury or death resulted from side effects that were unavoidable’—full stop.” *Ibid.* As explained above, however, the “even though” clause establishes two additional prerequisites—proper manufacturing and proper labeling—to qualify for §22(b)(1)’s exemption from liability. Contrary to the majority’s contention, then, the “even though” clause serves an important function by limiting the scope of the preemption afforded by the preceding “if” clause.¹⁴

The majority’s only other textual argument is based on

¹⁴In this manner, the “even though” clause functions in a “concessive subordinat[ing]” fashion, *ante*, at 11, in accord with normal grammatical usage. According to the majority, however, the “even though” clause “clarifies the word that precedes it” by “delineat[ing]” the conditions that make a side effect “unavoidable” under the statute. *Ante*, at 7. The majority’s interpretation hardly treats the clause as “concessive,” and indeed strains the meaning of “even though.” In the majority’s view, proper manufacturing and labeling are the sole prerequisites that render a vaccine’s side effects unavoidable. Thus, an injurious side effect is unavoidable *because* the vaccine was properly prepared and labeled, not “even though” it was. The two conjunctions are not equivalent: The sentence “I am happy *even though* it is raining” can hardly be read to mean that “I am happy *because* it is raining.” In any event, the more fundamental point is that petitioners’ interpretation actually gives meaning to the words “even though,” whereas the majority concedes that its interpretation effectively reads those words entirely out of the statute. See *supra* this page.

SOTOMAYOR, J., dissenting

the *expressio unius, exclusio alterius* canon. According to the majority, because blackletter products liability law generally recognizes three different types of product defects, “[i]f all three were intended to be preserved, it would be strange [for Congress] to mention specifically only two”—namely, manufacturing and labeling defects in the “even though” clause—“and leave the third to implication.” *Ante*, at 8. The majority’s argument, however, ignores that the default rule under the Vaccine Act is that state law is preserved. As explained above, §22(a) expressly provides that the “[g]eneral rule” is that “State law shall apply to a civil action brought for damages for a vaccine-related injury or death.” 42 U. S. C. §300aa–22(a). Because §22(a) already preserves state-law design defect claims (to the extent the exemption in §22(b)(1) does not apply), there was no need for Congress separately and expressly to preserve design defect claims in §22(b)(1). Indeed, Congress’ principal aim in enacting §22(b)(1) was not to preserve manufacturing and labeling claims (those, too, were already preserved by §22(a)), but rather, to federalize comment *k*-type protection for “unavoidably unsafe” vaccines. The “even though” clause simply functions to limit the applicability of that defense. The lack of express language in §22(b)(1) specifically preserving design defect claims thus cannot fairly be understood as impliedly (and categorically) pre-empting such traditional state tort claims, which had already been preserved by §22(a).¹⁵

¹⁵This Court, moreover, has long operated on “the assumption that the historic police powers of the States are not to be superseded by the Federal Act unless that was the clear and manifest purpose of Congress.” *Altria Group, Inc. v. Good*, 555 U. S. ___, ___ (2008) (slip op., at 5) (internal quotation marks and alteration omitted). Given the long history of state regulation of vaccines, see Brief for Petitioners 3–6, the presumption provides an additional reason not to read §22(b)(1) as pre-empting all design defect claims, especially given Congress’ inclusion of

SOTOMAYOR, J., dissenting

The majority also suggests that if Congress wished to preserve design defect claims, it could have simply provided that manufacturers would be liable for “defective manufacture, defective directions or warning, and defective design.” *Ante*, at 8 (internal quotation marks omitted). Putting aside the fact that §22(a) already preserves design defect claims (to the extent §22(b)(1) does not apply), the majority’s proposed solution would not have fully effectuated Congress’ intent. As the legislative history makes clear, Congress used the term “unavoidable” to effectuate its intent that the “principle in Comment K regarding ‘unavoidably unsafe’ products . . . apply to the vaccines covered in the bill.” 1986 Report 26; see also 1987 Report 691. At the time of the Vaccine Act’s enactment in 1986, at least one State had expressly rejected comment *k*,¹⁶ while many others had not addressed the applicability of comment *k* specifically to vaccines or applied comment *k* to civil actions proceeding on a theory other than strict liability (*e.g.*, negligence¹⁷). A statute

an express saving clause in the same statutory section, see 42 U. S. C. §300aa–22(a), and its use of the conditional “if” clause in defining the pre-emptive scope of the provision. See *Bates v. Dow Agrosciences LLC*, 544 U. S. 431, 449 (2005) (“In areas of traditional state regulation, we assume that a federal statute has not supplanted state law unless Congress has made such an intention clear and manifest” (internal quotation marks omitted)).

¹⁶See *Collins v. Eli Lilly Co.*, 116 Wis. 2d 166, 197, 342 N. W. 2d 37, 52 (1984) (“We conclude that the rule embodied in comment k is too restrictive and, therefore, not commensurate with strict products liability law in Wisconsin”). *Collins* did, however, “recognize that in some exigent circumstances it may be necessary to place a drug on the market before adequate testing can be done.” *Ibid.* It thus adopted a narrower defense (based on “exigent circumstances”) than that recognized in other jurisdictions that had expressly adopted comment *k*.

¹⁷See, *e.g.*, *Kearl*, 172 Cal. App. 3d, at 831, n. 15, 218 Cal. Rptr., at 465, n. 15 (“[T]he unavoidably dangerous product doctrine merely exempts the product from a strict liability design defect analysis; a plaintiff remains free to pursue his design defect theory on the basis of

SOTOMAYOR, J., dissenting

that simply stated that vaccine manufacturers would be liable for “defective design” would be silent as to the availability of a comment *k*-type defense for “unavoidably unsafe” vaccines, and thus would not have fully achieved Congress’ aim of extending greater liability protection to vaccine manufacturers by providing comment *k*-type protection in all civil actions as a matter of federal law.

B

The majority’s structural arguments fare no better than its textual ones. The principal thrust of the majority’s position is that, since nothing in the Vaccine Act or the FDA’s regulations governing vaccines expressly mentions design defects, Congress must have intended to remove issues concerning the design of FDA-licensed vaccines from the tort system. *Ante*, at 13. The flaw in that reasoning, of course, is that the FDA’s silence on design defects existed long before the Vaccine Act was enacted. Indeed, the majority itself concedes that the “FDA has never even spelled out in regulations the criteria it uses to decide whether a vaccine is safe and effective for its intended use.”¹⁸ *Ibid.* And yet it is undisputed that prior to the Act, vaccine manufacturers had long been subject to liability under state tort law for defective vaccine design. That the Vaccine Act did not itself set forth a comprehensive regulatory scheme with respect to design defects is thus best understood to mean not that Congress suddenly decided to change course *sub silentio* and pre-empt a

negligence”); *Toner*, 112 Idaho, at 340, 732 P. 2d, at 309–310 (“The authorities universally agree that where a product is deemed unavoidably unsafe, the plaintiff is deprived of the advantage of a strict liability cause of action, but may proceed under a negligence cause of action”).

¹⁸See 42 U. S. C. §262(a)(2)(C)(i)(I) (“The Secretary shall approve a biologics license application . . . on the basis of a demonstration that . . . the biological product that is the subject of the application is safe, pure, and potent”).

SOTOMAYOR, J., dissenting

longstanding, traditional category of state tort law, but rather, that Congress intended to leave the status quo alone (except, of course, with respect to those aspects of state tort law that the Act expressly altered). See 1987 Report 691 (“It is not the Committee’s intention to preclude court actions under applicable law. The Committee’s intent at the time of considering the Act . . . was . . . to leave otherwise applicable law unaffected, except as expressly altered by the Act”).

The majority also suggests that Congress necessarily intended to pre-empt design defect claims since the aim of such tort suits is to promote the development of improved designs and provide compensation for injured individuals, and the Vaccine Act “provides other means for achieving both effects”—most notably through the no-fault compensation program and the National Vaccine Program. *Ante*, at 14, and nn. 57–60 (citing 42 U. S. C. §§300aa–1, 300aa–2(a)(1)–(3), 300aa–3, 300aa–25(b), 300aa–27(a)(1)). But the majority’s position elides a significant difference between state tort law and the federal regulatory scheme. Although the Vaccine Act charges the Secretary of Health and Human Services with the obligation to “promote the development of childhood vaccines” and “make or assure improvements in . . . vaccines, and research on vaccines,” §300aa–27(a), neither the Act nor any other provision of federal law places a legal *duty* on vaccine manufacturers to improve the design of their vaccines to account for scientific and technological advances. Indeed, the FDA does not condition approval of a vaccine on it being the most optimally designed among reasonably available alternatives, nor does it (or any other federal entity) ensure that licensed vaccines keep pace with technological and scientific advances.¹⁹ Rather, the function of ensuring

¹⁹See, e.g., *Hurley v. Lederle Labs.*, 863 F. 2d 1173, 1177 (CA5 1988) (“[T]he FDA is a passive agency: it considers whether to approve

SOTOMAYOR, J., dissenting

that vaccines are optimally designed in light of existing science and technology has traditionally been left to the States through the imposition of damages for design defects. Cf. *Bates*, 544 U. S., at 451 (“[T]he specter of damage actions may provide manufacturers with added dynamic incentives to continue to keep abreast of all possible injuries stemming from use of their product[s] so as to forestall such actions through product improvement”); *Wyeth v. Levine*, 555 U. S. ___, ___ (2009) (slip op., at 22–

vaccine designs only if and when manufacturers come forward with a proposal”); *Jones v. Lederle Labs.*, 695 F. Supp. 700, 711 (EDNY 1988) (“[T]he agency takes the drugs and manufacturers as it finds them. While its goal is to oversee inoculation with the best possible vaccine, it is limited to reviewing only those drugs submitted by various manufacturers, regardless of their flaws”). Although the FDA has authority under existing regulations to revoke a manufacturer’s biologics licenses, that authority can be exercised only where (as relevant here) “[t]he licensed product is not safe and effective for all of its intended uses.” 21 CFR §601.5(b)(1)(vi) (2010); see §600.3(p) (defining “safety” as “relative freedom from harmful effect to persons affected, directly or indirectly, by a product when prudently administered, taking into consideration the character of the product in relation to the condition of the recipient at the time”). The regulation does not authorize the FDA to revoke a biologics license for a manufacturer’s failure to adopt an optimal vaccine design in light of existing science and technology. See Conk, *Is There a Design Defect in the Restatement (Third) of Torts: Products Liability?* 109 *Yale L. J.* 1087, 1128–1129 (1999–2000) (“The FDA does not claim to review products for optimal design FDA review thus asks less of drug . . . manufacturers than the common law of products liability asks of other kinds of manufacturers”). At oral argument, counsel for *amicus* United States stated that the Centers for Disease Control and Prevention (CDC) routinely performs comparative analyses of vaccines that are already on the market. See Tr. of Oral Arg. 44–45; *id.*, at 52–53 (describing CDC’s comparison of Sabin and Salk polio vaccines). Neither the United States nor any of the parties, however, has represented that CDC examines whether a safer alternative vaccine *could have been designed* given practical and scientific limits, the central inquiry in a state tort law action for design defect. CDC does not issue biologics licenses, moreover, and thus has no authority to require a manufacturer to adopt a different vaccine design.

SOTOMAYOR, J., dissenting

23) (noting that the FDA has “traditionally regarded state law as a complementary form of drug regulation” as “[s]tate tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly”).²⁰ The importance of the States’ traditional regulatory role is only underscored by the unique features of the vaccine market, in which there are “only one or two manufacturers for a majority of the vaccines listed on the routine childhood immunization schedule.” Brief for Respondent 55. The normal competitive forces that spur innovation and improvements to existing product lines in other markets thus operate with less force in the vaccine market, particularly for vaccines that have already been released and marketed to the public. Absent a clear statutory mandate to the contrary, there is no reason to think that Congress intended in the vaccine context to eliminate the traditional incentive and deterrence functions served by state tort liability in favor of a federal regulatory scheme providing only carrots and no sticks.²¹ See *Levine*, 555 U. S., at ____ (slip op., at 18) (“The

²⁰Indeed, we observed in *Levine* that the FDA is perpetually understaffed and underfunded, see 555 U. S., at ___, n. 11 (slip op., at 22, n. 11), and the agency has been criticized in the past for its slow response in failing to withdraw or warn about potentially dangerous products, see, e.g., L. Leveton, H. Sox, & M. Soto, *Institute of Medicine, HIV and the Blood Supply: An Analysis of Crisis Decisionmaking* (1995) (criticizing FDA response to transmission of AIDS through blood supply). These practical shortcomings reinforce the conclusion that “state law offers an additional, and important, layer of consumer protection that complements FDA regulation.” *Levine*, 555 U. S., at ____ (slip op., at 23).

²¹The majority mischaracterizes my position as expressing a general “skepticalism” of preemption unless the congressional substitute operate[s] like the tort system.” *Ante*, at 16. Congress could, of course, adopt a regulatory regime that operates differently from state tort systems, and such a difference is not necessarily a reason to question Congress’ pre-emptive intent. In the specific context of the Vaccine Act, however, the relevant point is that this Court should not lightly assume

SOTOMAYOR, J., dissenting

case for federal pre-emption is particularly weak where Congress has indicated its awareness of the operation of state law in a field of federal interest, and has nonetheless decided to stand by both concepts and to tolerate whatever tension there is between them.” (internal quotation marks and alteration omitted)).

III

In enacting the Vaccine Act, Congress established a carefully wrought federal scheme that balances the competing interests of vaccine-injured persons and vaccine manufacturers. As the legislative history indicates, the Act addressed “two overriding concerns”: “(a) the inadequacy—from both the perspective of vaccine-injured persons as well as vaccine manufacturers—of the current approach to compensating those who have been damaged by a vaccine; and (b) the instability and unpredictability of the childhood vaccine market.” 1986 Report 7. When viewed in the context of the Vaccine Act as a whole, §22(b)(1) is just one part of a broader statutory scheme that balances the need for compensating vaccine-injured children with added liability protections for vaccine manufacturers to ensure a stable childhood vaccine market.

The principal innovation of the Act was the creation of the no-fault compensation program—a scheme funded entirely through an excise tax on vaccines.²² Through that

that Congress intended *sub silentio* to displace a longstanding species of state tort liability where, as here, Congress specifically included an express saving clause preserving state law, there is a long history of state-law regulation of vaccine design, and pre-emption of state law would leave an important regulatory function—*i.e.*, ensuring optimal vaccine design—entirely unaddressed by the congressional substitute.

²²The majority’s suggestion that “vaccine manufacturers fund from their sales” the compensation program is misleading. *Ante*, at 15. Although the manufacturers nominally pay the tax, the amount of the tax is specifically included in the vaccine price charged to purchasers. See CDC Vaccine Price List (Feb. 15, 2011), <http://www.cdc.gov/>

SOTOMAYOR, J., dissenting

program, Congress relieved vaccine manufacturers of the burden of compensating victims of vaccine-related injuries in the vast majority of cases²³—an extremely significant economic benefit that “functionally creat[es] a valuable insurance policy for vaccine-related injuries.” Reply Brief for Petitioners 10. The structure and legislative history, moreover, point clearly to Congress’ intention to divert would-be tort claimants into the compensation program, rather than eliminate a longstanding category of traditional tort claims. See 1986 Report 13 (“The Committee anticipates that the speed of the compensation program, the low transaction costs of the system, the no-fault nature of the required findings, and the relative certainty and generosity of the system’s awards will divert a significant number of potential plaintiffs from litigation”). Indeed, although complete pre-emption of tort claims would have eliminated the principal source of the “unpredictability” in the vaccine market, Congress specifically chose *not* to pre-empt state tort claims categorically. See 42 U. S. C. §300aa–22(a) (providing as a “[g]eneral rule” that “State law shall apply to a civil action brought for damages for a vaccine-related injury or death”). That decision reflects Congress’ recognition that court actions are essential

vaccines/programs/vfc/cdc-vac-price-list.htm. Accordingly, the only way the vaccine manufacturers can be said to actually “fund” the compensation program is if the cost of the excise tax has an impact on the number of vaccines sold by the vaccine manufacturer. The majority points to no evidence that the excise tax—which ordinarily amounts to 75 cents per dose, 26 U. S. C. §4131(b)—has any impact whatsoever on the demand for vaccines.

²³See Brief for United States as *Amicus Curiae* 28 (“Department of Justice records indicate that 99.8% of successful Compensation Program claimants have accepted their awards, foregoing any tort remedies against vaccine manufacturers”); S. Plotkin, W. Orenstein, & P. Offit, *Vaccines* 1673 (5th ed. 2008) (noting that “[v]irtually all . . . petitioners, even those who were not awarded compensation” under the compensation program, choose to accept the program’s determination).

SOTOMAYOR, J., dissenting

because they provide injured persons with significant procedural tools—including, most importantly, civil discovery—that are not available in administrative proceedings under the compensation program. See §§300aa–12(d)(2)(E), (d)(3). Congress thus clearly believed there was still an important function to be played by state tort law.

Instead of eliminating design defect liability entirely, Congress enacted numerous measures to reduce manufacturers’ liability exposure, including a limited regulatory compliance presumption of adequate warnings, see §300aa–22(b)(2), elimination of claims based on failure to provide direct warnings to patients, §300aa–22(c), a heightened standard for punitive damages, §300aa–23(d)(2), and, of course, immunity from damages for “unavoidable” side effects, §300aa–22(b)(1). Considered in light of the Vaccine Act as a whole, §22(b)(1)’s exemption from liability for unavoidably unsafe vaccines is just one part of a broader statutory scheme that reflects Congress’ careful balance between providing adequate compensation for vaccine-injured children and conferring substantial benefits on vaccine manufacturers to ensure a stable and predictable childhood vaccine supply.

The majority’s decision today disturbs that careful balance based on a bare policy preference that it is better “to leave complex epidemiological judgments about vaccine design to the FDA and the National Vaccine Program rather than juries.” *Ante*, at 15.²⁴ To be sure, reasonable minds can disagree about the wisdom of having juries weigh the relative costs and benefits of a particular vaccine design. But whatever the merits of the majority’s

²⁴ JUSTICE BREYER’s separate concurrence is even more explicitly policy driven, reflecting his own preference for the “more expert judgment” of federal agencies over the “less expert” judgment of juries. *Ante*, at 5.

SOTOMAYOR, J., dissenting

policy preference, the decision to bar all design defect claims against vaccine manufacturers is one that Congress must make, not this Court.²⁵ By construing §22(b)(1) to

²⁵Respondent notes that there are some 5,000 petitions alleging a causal link between certain vaccines and autism spectrum disorders that are currently pending in an omnibus proceeding in the Court of Federal Claims (Vaccine Court). Brief for Respondent 56–57. According to respondent, a ruling that §22(b)(1) does not pre-empt design defect claims could unleash a “crushing wave” of tort litigation that would bankrupt vaccine manufacturers and deplete vaccine supply. *Id.*, at 28. This concern underlies many of the policy arguments in respondent’s brief and appears to underlie the majority and concurring opinions in this case. In the absence of any empirical data, however, the prospect of an onslaught of autism-related tort litigation by claimants denied relief by the Vaccine Court seems wholly speculative. As an initial matter, the special masters in the autism cases have thus far uniformly rejected the alleged causal link between vaccines and autism. See Brief for American Academy of Pediatrics et al. as *Amici Curiae* 20–21, n. 4 (collecting cases). To be sure, those rulings do not necessarily mean that no such causal link exists, cf. Brief for United States as *Amicus Curiae* 29 (noting that injuries have been added to the Vaccine Injury Table for existing vaccines), or that claimants will not ultimately be able to prove such a link in a state tort action, particularly with the added tool of civil discovery. But these rulings do highlight the substantial hurdles to recovery a claimant faces. See *Schafer v. American Cyanamid Co.*, 20 F. 3d 1, 5 (CA1 1994) (“[A] petitioner to whom the Vaccine Court gives nothing may see no point in trying to overcome tort law’s yet more serious obstacles to recovery”). Trial courts, moreover, have considerable experience in efficiently handling and disposing of meritless products liability claims, and decades of tort litigation (including for design defect) in the prescription-drug context have not led to shortages in prescription drugs. Despite the doomsday predictions of respondent and the various *amici* cited by the concurrence, *ante*, at 6–7, the possibility of a torrent of meritless lawsuits bankrupting manufacturers and causing vaccine shortages seems remote at best. More fundamentally, whatever the merits of these policy arguments, the issue in this case is what Congress has decided, and as to that question, the text, structure, and legislative history compel the conclusion that Congress intended to leave the courthouse doors open for children who have suffered severe injuries from defectively designed vaccines. The majority’s policy-driven decision to the contrary usurps Congress’ role and deprives such vaccine-injured children of a key remedy that Congress intended them to have.

SOTOMAYOR, J., dissenting

pre-empt all design defect claims against vaccine manufacturers for covered vaccines, the majority's decision leaves a regulatory vacuum in which no one—neither the FDA nor any other federal agency, nor state and federal juries—ensures that vaccine manufacturers adequately take account of scientific and technological advancements. This concern is especially acute with respect to vaccines that have already been released and marketed to the public. Manufacturers, given the lack of robust competition in the vaccine market, will often have little or no incentive to improve the designs of vaccines that are already generating significant profit margins. Nothing in the text, structure, or legislative history remotely suggests that Congress intended that result.

I respectfully dissent.

Pilot comparative study on the health of vaccinated and unvaccinated 6- to 12-year-old U.S. children

Anthony R Mawson^{1*}, Brian D Ray², Azad R Bhuiyan³ and Binu Jacob⁴

¹Professor, Department of Epidemiology and Biostatistics, School of Public Health, Jackson State University, Jackson, MS 39213, USA

²President, National Home Education Research Institute, PO Box 13939, Salem, OR 97309, USA

³Associate Professor, Department of Epidemiology and Biostatistics, School of Public Health, Jackson State University, Jackson, MS 39213, USA

⁴Former graduate student, Department of Epidemiology and Biostatistics School of Public Health, Jackson State University, Jackson, MS 39213, USA

Abstract

Vaccinations have prevented millions of infectious illnesses, hospitalizations and deaths among U.S. children, yet the long-term health outcomes of the vaccination schedule remain uncertain. Studies have been recommended by the U.S. Institute of Medicine to address this question. This study aimed 1) to compare vaccinated and unvaccinated children on a broad range of health outcomes, and 2) to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors. A cross-sectional study of mothers of children educated at home was carried out in collaboration with homeschool organizations in four U.S. states: Florida, Louisiana, Mississippi and Oregon. Mothers were asked to complete an anonymous online questionnaire on their 6- to 12-year-old biological children with respect to pregnancy-related factors, birth history, vaccinations, physician-diagnosed illnesses, medications used, and health services. NDD, a derived diagnostic measure, was defined as having one or more of the following three closely-related diagnoses: a learning disability, Attention Deficient Hyperactivity Disorder, and Autism Spectrum Disorder. A convenience sample of 666 children was obtained, of which 261 (39%) were unvaccinated. The vaccinated were less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but more likely to have been diagnosed with pneumonia, otitis media, allergies and NDD. After adjustment, vaccination, male gender, and preterm birth remained significantly associated with NDD. However, in a final adjusted model with interaction, vaccination but not preterm birth remained associated with NDD, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% CI: 2.8, 15.5). In conclusion, vaccinated homeschool children were found to have a higher rate of allergies and NDD than unvaccinated homeschool children. While vaccination remained significantly associated with NDD after controlling for other factors, preterm birth coupled with vaccination was associated with an apparent synergistic increase in the odds of NDD. Further research involving larger, independent samples and stronger research designs is needed to verify and understand these unexpected findings in order to optimize the impact of vaccines on children's health.

Abbreviations: ADHD: Attention Deficit Hyperactivity Disorder; ASD: Autism Spectrum Disorder; AOM: Acute Otitis Media; CDC: Centers for Disease Control and Prevention; CI: Confidence Interval; NDD: Neurodevelopmental Disorders; NHERI: National Home Education Research Institute; OR: Odds Ratio; PCV-7: Pneumococcal Conjugate Vaccine-7; VAERS: Vaccine Adverse Events Reporting System.

Introduction

Vaccines are among the greatest achievements of biomedical science and one of the most effective public health interventions of the 20th century [1]. Among U.S. children born between 1995 and 2013, vaccination is estimated to have prevented 322 million illnesses, 21 million hospitalizations and 732,000 premature deaths, with overall cost savings of \$1.38 trillion [2]. About 95% of U.S. children of kindergarten age receive all of the recommended vaccines as a requirement for school and daycare attendance [3,4], aimed at preventing the occurrence and spread of targeted infectious diseases [5]. Advances in biotechnology are contributing to the development of new vaccines for widespread use [6].

Under the currently recommended pediatric vaccination schedule [7], U.S. children receive up to 48 doses of vaccines for 14 diseases from birth to age six years, a figure that has steadily increased since the 1950s, most notably since the Vaccines for Children program was created in 1994. The Vaccines for Children program began with vaccines targeting nine diseases: diphtheria, tetanus, pertussis, polio,

Haemophilus influenzae type b disease, hepatitis B, measles, mumps, and rubella. Between 1995 and 2013, new vaccines against five other diseases were added for children age 6 and under: varicella, hepatitis A, pneumococcal disease, influenza, and rotavirus vaccine.

Although short-term immunologic and safety testing is performed on vaccines prior to their approval by the U.S. Food and Drug Administration, the long-term effects of individual vaccines and of the vaccination program itself remain unknown [8]. Vaccines are acknowledged to carry risks of severe acute and chronic adverse effects, such as neurological complications and even death [9], but such risks are considered so rare that the vaccination program is believed to be safe and effective for virtually all children [10].

There are very few randomized trials on any existing vaccine recommended for children in terms of morbidity and mortality, in

***Correspondence to:** Anthony R Mawson, Professor, Department of Epidemiology and Biostatistics, School of Public Health, Jackson State University, Jackson, MS 39213, USA, E-mail: Anthony.r.mawson@jsums.edu

Key words: acute diseases, chronic diseases, epidemiology, evaluation, health policy, immunization, neurodevelopmental disorders, vaccination

Received: March 22, 2017; **Accepted:** April 21, 2017; **Published:** April 24, 2017

part because of ethical concerns involving withholding vaccines from children assigned to a control group. One exception, the high-titer measles vaccine, was withdrawn after several randomized trials in west Africa showed that it interacted with the diphtheria-tetanus-pertussis vaccine, resulting in a significant 33% increase in child mortality [11]. Evidence of safety from observational studies includes a limited number of vaccines, e.g., the measles, mumps and rubella vaccine, and hepatitis B vaccine, but none on the childhood vaccination program itself. Knowledge is limited even for vaccines with a long record of safety and protection against contagious diseases [12]. The safe levels and long-term effects of vaccine ingredients such as adjuvants and preservatives are also unknown [13]. Other concerns include the safety and cost-effectiveness of newer vaccines against diseases that are potentially lethal for individuals but have a lesser impact on population health, such as the group B meningococcus vaccine [14].

Knowledge of adverse events following vaccinations is largely based on voluntary reports to the Vaccine Adverse Events Reporting System (VAERS) by physicians and parents. However, the rate of reporting of serious vaccine injuries is estimated to be <1% [15]. These considerations led the former Institute of Medicine (now the National Academy of Medicine) in 2005 to recommend the development of a five-year plan for vaccine safety research by the Centers for Disease Control and Prevention (CDC) [16,17]. In its 2011 and 2013 reviews of the adverse effects of vaccines, the Institute of Medicine concluded that few health problems are caused by or associated with vaccines, and found no evidence that the vaccination schedule was unsafe [18,19]. Another systematic review, commissioned by the US Agency for Healthcare Research and Quality to identify gaps in evidence on the safety of the childhood vaccination program, concluded that severe adverse events following vaccinations are extremely rare [20]. The Institute of Medicine, however, noted that studies were needed: to compare the health outcomes of vaccinated and unvaccinated children; to examine the long-term cumulative effects of vaccines; the timing of vaccination in relation to the age and condition of the child; the total load or number of vaccines given at one time; the effect of other vaccine ingredients in relation to health outcomes; and the mechanisms of vaccine-associated injury [19].

A complicating factor in evaluating the vaccination program is that vaccines against infectious diseases have complex nonspecific effects on morbidity and mortality that extend beyond prevention of the targeted disease. The existence of such effects poses a challenge to the assumption that individual vaccines affect the immune system independently of each other and have no physiological effect other than protection against the targeted pathogen [21]. The nonspecific effects of some vaccines appear to be beneficial, while in others they appear to increase morbidity and mortality [22,23]. For instance, both the measles and Bacillus Calmette–Guérin vaccine reportedly reduce overall morbidity and mortality [24], whereas the diphtheria-tetanus-pertussis [25] and hepatitis B vaccines [26] have the opposite effect. The mechanisms responsible for these nonspecific effects are unknown but may involve *inter alia*: interactions between vaccines and their ingredients, e.g., whether the vaccines are live or inactivated; the most recently administered vaccine; micronutrient supplements such as vitamin A; the sequence in which vaccines are given; and their possible combined and cumulative effects [21].

A major current controversy is the question of whether vaccination plays a role in neurodevelopmental disorders (NDDs), which broadly include learning disabilities, Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). The controversy has

been fueled by the fact that the U.S. is experiencing what has been described as a “silent pandemic” of mostly subclinical developmental neurotoxicity, in which about 15% of children suffer from a learning disability, sensory deficits, and developmental delays [27,28]. In 1996 the estimated prevalence of ASD was 0.42%. By 2010 it had risen to 1.47% (1 in 68), with 1 in 42 boys and 1 in 189 girls affected [29]. More recently, based on a CDC survey of parents in 2011–2014, 2.24% of children (1 in 45) were estimated to have ASD. Rates of other developmental disabilities, however, such as intellectual disability, cerebral palsy, hearing loss, and vision impairments, have declined or remained unchanged [30]. Prevalence rates of Attention Deficit Hyperactivity Disorder (ADHD) have also risen markedly in recent decades [31]. Earlier increases in the prevalence of learning disability have been followed by declining rates in most states, possibly due to changes in diagnostic criteria [32].

It is believed that much of the increase in NDD diagnoses in recent decades has been due to growing awareness of autism and more sensitive screening tools, and hence to greater numbers of children with milder symptoms of autism. But these factors do not account for all of the increase [33]. The geographically widespread increase in ASD and ADHD suggests a role for an environmental factor to which virtually all children are exposed. Agricultural chemicals are a current focus of research [34-37].

A possible contributory role for vaccines in the rise in NDD diagnoses remains unknown because data on the health outcomes of vaccinated and unvaccinated children are lacking. The need for such studies is suggested by the fact that the Vaccine Injury Compensation Program has paid \$3.2 billion in compensation for vaccine injury since its creation in 1986 [38]. A study of claims compensated by the Vaccine Injury Compensation Program for vaccine-induced encephalopathy and seizure disorder found 83 claims that were acknowledged as being due to brain damage. In all cases it was noted by the Court of Federal Claims, or indicated in settlement agreements, that the children had autism or ASD [39]. On the other hand, numerous epidemiological studies have found no association between receipt of selected vaccines (in particular the combined measles, mumps, and rubella vaccine) and autism [10,40-45], and there is no accepted mechanism by which vaccines could induce autism [46].

A major challenge in comparing vaccinated and unvaccinated children has been to identify an accessible pool of unvaccinated children, since the vast majority of children in the U.S. are vaccinated. Children educated at home (“homeschool children”) are suitable for such studies as a higher proportion are unvaccinated compared to public school children [47]. Homeschool families have an approximately equal median income to that of married-couple families nationwide, somewhat more years of formal education, and a higher average family size (just over three children) compared to the national average of just over two children [48-50]. Homeschooling families are slightly overrepresented in the south, about 23% are nonwhite, and the age distribution of homeschool children in grades K-12 is similar to that of children nationwide [51]. About 3% of the school-age population was homeschooled in the 2011-2012 school year [52].

The aims of this study were 1) to compare vaccinated and unvaccinated children on a broad range of health outcomes, including acute and chronic conditions, medication and health service utilization, and 2) to determine whether an association found between vaccination and NDDs, if any, remained significant after adjustment for other measured factors.

Methods

Study planning

To implement the study, a partnership was formed with the National Home Education Research Institute (NHERI), an organization that has been involved in educational research on homeschooling for many years and has strong and extensive contacts with the homeschool community throughout the country (www.nheri.org). The study protocol was approved by the Institutional Review Board of Jackson State University.

Study design

The study was designed as a cross-sectional survey of homeschooling mothers on their vaccinated and unvaccinated biological children ages 6 to 12. As contact information on homeschool families was unavailable, there was no defined population or sampling frame from which a randomized study could be carried out, and from which response rates could be determined. However, the object of our pilot study was not to obtain a representative sample of homeschool children but a convenience sample of unvaccinated children of sufficient size to test for significant differences in outcomes between the groups.

We proceeded by selecting 4 states (Florida, Louisiana, Mississippi, and Oregon) for the survey (Stage 1). NHERI compiled a list of statewide and local homeschool organizations, totaling 84 in Florida, 18 in Louisiana, 12 in Mississippi and 17 in Oregon. Initial contacts were made in June 2012. NHERI contacted the leaders of each statewide organization by email to request their support. A second email was then sent, explaining the study purpose and background, which the leaders were asked to forward to their members (Stage 2). A link was provided to an online questionnaire in which no personally identifying information was requested. With funding limited to 12 months, we sought to obtain as many responses as possible, contacting families only indirectly through homeschool organizations. Biological mothers of children ages 6-12 years were asked to serve as respondents in order to standardize data collection and to include data on pregnancy-related factors and birth history that might relate to the children's current health. The age-range of 6 to 12 years was selected because most recommended vaccinations would have been received by then.

Recruitment and informed consent

Homeschool leaders were asked to sign Memoranda of Agreement on behalf of their organizations and to provide the number of member families. Non-responders were sent a second notice but few provided the requested information. However, follow-up calls to the leaders suggested that all had contacted their members about the study. Both the letter to families and the survey questions were stated in a neutral way with respect to vaccines. Our letter to parents began:

“Dear Parent, This study concerns a major current health question: namely, whether vaccination is linked in any way to children's long-term health. Vaccination is one of the greatest discoveries in medicine, yet little is known about its long-term impact. The objective of this study is to evaluate the effects of vaccination by comparing vaccinated and unvaccinated children in terms of a number of major health outcomes...”

Respondents were asked to indicate their consent to participate, to provide their home state and zip code of residence, and to confirm that they had biological children 6 to 12 years of age. The communications company Qualtrics (<http://qualtrics.com>) hosted the survey website. The questionnaire included only closed-ended questions requiring yes or no responses, with the aim of improving both response and completion rates.

A number of homeschool mothers volunteered to assist NHERI promote the study to their wide circles of homeschool contacts. A number of nationwide organizations also agreed to promote the study in the designated states. The online survey remained open for three months in the summer of 2012. Financial incentives to complete the survey were neither available nor offered.

Definitions and measures

Vaccination status was classified as unvaccinated (i.e., no previous vaccinations), partially vaccinated (received some but not all recommended vaccinations) and fully vaccinated (received all recommended age-appropriate vaccines), as reported by mothers. These categories were developed on the premise that any long-term effects of vaccines would be more evident in fully-vaccinated than in partially-vaccinated children, and rare or absent in the unvaccinated. Mothers were asked to use their child's vaccination records to indicate the recommended vaccines and doses their child had received. Dates of vaccinations were not requested in order not to overburden respondents and to reduce the likelihood of inaccurate reporting; nor was information requested on adverse events related to vaccines, as this was not our purpose. We also did not ask about dates of diagnoses because chronic illnesses are often gradual in onset and made long after the appearance of symptoms. Since most vaccinations are given before age 6, vaccination would be expected to precede the recognition and diagnosis of most chronic conditions.

Mothers were asked to indicate on a list of more than 40 acute and chronic illnesses all those for which her child or children had received a diagnosis by a physician. Other questions included the use of health services and procedures, dental check-ups, “sick visits” to physicians, medications used, insertion of ventilation ear tubes, number of days in the hospital, the extent of physical activity (number of hours the child engaged in “vigorous” activities on a typical weekday), number of siblings, family structure (mother and father living in the home, divorced or separated), family income and/or highest level of education of mother or father, and social interaction with children outside the home (i.e., amount of time spent in play or other contact with children outside the household). Questions specifically for the mother included pregnancy-related conditions and birth history, use of medications during pregnancy, and exposure to an adverse environment (defined as living within 1-2 miles of a furniture manufacturing factory, hazardous waste site, or lumber processing factory). NDD, a derived diagnostic category, was defined as having one or more of the following three closely related and overlapping diagnoses: a learning disability, Attention Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) [53].

Statistical methods

Unadjusted bivariate analyses using chi-square tests were performed initially to test the null hypothesis of no association between vaccination status and health outcomes, i.e., physician-diagnosed acute and chronic illnesses, medications, and the use of health services. In most analyses, partially and fully vaccinated children were grouped together as the “vaccinated” group, with unvaccinated children as the control group. The second aim of the study was to determine whether any association found between vaccination and neurodevelopmental disorders remained significant after controlling for other measured factors. Descriptive statistics on all variables were computed to determine frequencies and percentages for categorical variables and means (\pm SD) for continuous variables. The strength of associations

between vaccination status and health outcomes were tested using odds ratios (OR) and 95% Confidence Intervals (CI). Odds ratios describe the strength of the association between two categorical variables measured simultaneously and are appropriate measures of that relationship in a cross-sectional study [54]. Unadjusted and adjusted logistic regression analyses were carried out using SAS (Version 9.3) to determine the factors associated with NDDs.

Results

Socio-Demographic characteristics of respondents

The information contained in 415 questionnaires provided data on 666 homeschool children. Table 1 shows the characteristics of the survey respondents. Mothers averaged about 40 years of age, were typically white, college graduates, with household incomes between \$50,000 to \$100,000, Christian, and married. The reasons for homeschooling for the majority of respondents (80-86%) were for a moral environment, better family relationships, or for more contact with their child or children.

The children as a group were similarly mostly white (88%), with a slight preponderance of females (52%), and averaged 9 years of age. With regard to vaccination status, 261 (39%) were unvaccinated, 208 (31%) were partially vaccinated, and 197 (30%) had received all of the recommended vaccinations. All statistical analyses are based on these numbers.

Acute illness

Vaccinated children (N=405), combining the partially and fully vaccinated, were significantly less likely than the unvaccinated to have had chickenpox (7.9% vs. 25.3%, $p < 0.001$; Odds Ratio = 0.26, 95% Confidence Interval: 0.2, 0.4) and whooping cough (pertussis) (2.5% vs. 8.4%, $p < 0.001$; OR 0.3, 95% CI: 0.1, 0.6), and less likely, but not significantly so, to have had rubella (0.3% vs. 1.9%, $p = 0.04$; OR 0.1, 95% CI: 0.01, 1.1). However, the vaccinated were significantly more likely than the unvaccinated to have been diagnosed with otitis media (19.8% vs. 5.8%, $p < 0.001$; OR 3.8, 95% CI: 2.1, 6.6) and pneumonia (6.4% vs. 1.2%, $p = 0.001$; OR 5.9, 95% CI: 1.8, 19.7). No significant differences were seen with regard to hepatitis A or B, high fever in the past 6 months, measles, mumps, meningitis (viral or bacterial), influenza, or rotavirus (Table 2).

Chronic illness

Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following: allergic rhinitis (10.4% vs. 0.4%, $p < 0.001$; OR 30.1, 95% CI: 4.1, 219.3), other allergies (22.2% vs. 6.9%, $p < 0.001$; OR 3.9, 95% CI: 2.3, 6.6), eczema/atopic dermatitis (9.5% vs. 3.6%, $p = 0.035$; OR 2.9, 95% CI: 1.4, 6.1), a learning disability (5.7% vs. 1.2%, $p = 0.003$; OR 5.2, 95% CI: 1.6, 17.4), ADHD (4.7% vs. 1.0%, $p = 0.013$; OR 4.2, 95% CI: 1.2, 14.5), ASD (4.7% vs. 1.0%, $p = 0.013$; OR 4.2, 95% CI: 1.2, 14.5), any neurodevelopmental disorder (i.e., learning disability, ADHD or ASD) (10.5% vs. 3.1%, $p < 0.001$; OR 3.7, 95% CI: 1.7, 7.9) and any chronic illness (44.0% vs. 25.0%, $p < 0.001$; OR 2.4, 95% CI: 1.7, 3.3). No significant differences were observed with regard to cancer, chronic fatigue, conduct disorder, Crohn's disease, depression, Types 1 or 2 diabetes, encephalopathy, epilepsy, hearing loss, high blood pressure, inflammatory bowel disease, juvenile rheumatoid arthritis, obesity, seizures, Tourette's syndrome, or services received under the Individuals with Disabilities Education Act (Table 3).

Partial versus full vaccination

Partially vaccinated children had an intermediate position between the fully vaccinated and unvaccinated in regard to several but not all health outcomes. For instance, as shown in Table 4, the partially vaccinated had an intermediate (apparently detrimental) position in terms of allergic rhinitis, ADHD, eczema, and learning disability.

Gender differences in chronic illness

Among the vaccinated (combining partially and fully vaccinated children), boys were more likely than girls to be diagnosed with a chronic condition – significantly so in the case of allergic rhinitis (13.9% vs. 7.2%, $p = 0.03$; OR 2.1, 95% CI: 1.1, 4.1), ASD (7.7% vs. 1.9%, $p = 0.006$; OR 4.3, 95% CI: 1.4, 13.2), and any neurodevelopmental disorder (14.4% vs. 6.7%, $p = 0.01$; OR 2.3, 95% CI: 1.2, 4.6) (Table 5).

Use of medications and health services

The vaccinated (combining the partially and fully vaccinated) were significantly more likely than the unvaccinated to use medication for allergies (20.0% vs. 1.2%, $p < 0.001$; OR 21.5, 95% CI: 6.7, 68.9), to have used antibiotics in the past 12 months (30.8% vs. 15.4%, $p < 0.001$; OR 2.4, 95% CI: 1.6, 3.6), and to have used fever medications at least once (90.7% vs. 67.8%, $p < 0.001$; OR 4.6, 95% CI: 3.0, 7.1). The vaccinated were also more likely to have seen a doctor for a routine checkup in the past 12 months (57.6% vs. 37.2%, $p < 0.001$; OR 2.3, 95% CI: 1.7, 3.2), visited a dentist during the past year (89.4% vs. 80.5%, $p < 0.001$; OR 2.0, 95% CI: 1.3, 3.2), visited a doctor or clinic due to illness in the past year (36.0% vs. 16.0%, $p < 0.001$; OR 3.0, 95% CI: 2.0, 4.4), been fitted with ventilation ear tubes (3.0% vs. 0.4%, $p = 0.018$; OR 8.0, 95% CI: 1.0, 66.1), and spent one or more nights in a hospital (19.8% vs. 12.3%, $p = 0.012$; OR 1.8, 95% CI: 1.1, 2.7) (Table 6).

Table 1. Characteristics of the respondents*

	Mean (SD) ^a
Age (n=407)	40.59 (6.7)
	Number (%)^a
Race	
White	382 (92.5%)
Non-White	21 (7.6%)
Total	413
Education	
High School Graduate or Less	35 (8.5%)
Some College	114 (27.5%)
College Graduate	187 (45.2%)
Post-Graduates	78 (18.5%)
Total	414
Total Gross Household Income	
< \$49,999	123 (30.8%)
\$50,000-100,000	182 (45.5%)
> \$100,000	95 (23.8%)
Total	400
Religious Affiliation	
Christianity	375 (91.2%)
Non-Christianity	36 (8.8%)
Total	411
Marital Status	
Married	386 (93.7%)
Not Married	26 (6.3%)
Total	412

*Missing observations are excluded.

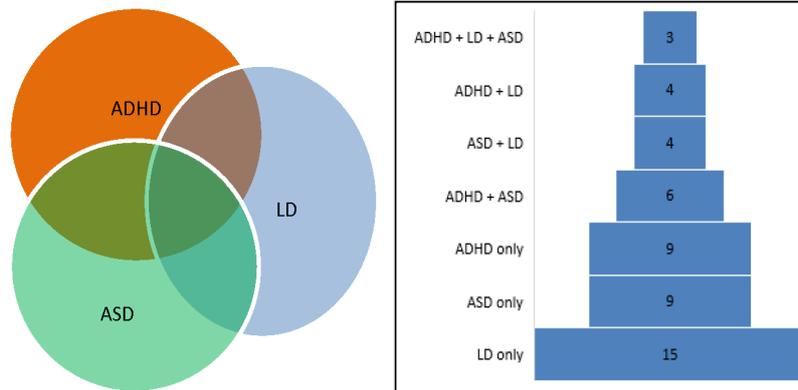


Figure 1. The overlap and distribution of physician-diagnosed neurodevelopmental disorders, based on mothers' reports

Table 2. Vaccination status and health outcomes – Acute Conditions

	Vaccinated (n=405)	Unvaccinated (n=261)	Total (n=666)	Chi-square	P-value	Odds Ratio (95% CI)
Chickenpox						
Yes	32 (7.9%)	66 (25.3%)	98 (14.7%)	38.229	< 0.001	0.26 (0.2 - 0.4)
No	373 (92.1%)	195 (74.7%)	568 (85.3%)			
Otitis media						
Yes	80 (19.8%)	16(5.8%)	96 (14.4%)	26.643	< 0.001	3.8 (2.1 - 6.6)
No	325 (80.2%)	245 (94.2%)	507 (85.6%)			
Pneumonia						
Yes	26 (6.4%)	3 (1.2%)	29 (4.4%)	10.585	< 0.001	5.9 (1.8 - 19.7)
No	379 (93.6%)	258 (98.8%)	637 (95.6%)			
Whooping cough						
Yes	10 (2.5%)	22 (8.4%)	32 (4.8%)	12.326	< 0.001	0.3 (0.1 - 0.6)
No	395 (97.5%)	239 (91.6%)	634 (95.2%)			
Rubella						
Yes	1 (0.3%)	5 (1.9%)	6 (0.9%)	4.951	0.037	0.1 (0.01 - 1.1)
No	404 (99.6%)	256 (98.1%)	660 (99.1%)			

Table 3. Vaccination status and health outcomes – Chronic Conditions

Chronic Disease	Vaccinated (n=405)	Unvaccinated (n=261)	Chi-square	P-value	Odds Ratio (95% CI)
Allergic rhinitis					
Yes	42 (10.4%)	1 (0.4%)	26.21	< 0.001	30.1 (4.1 - 219.3)
No	363 (89.6%)	260 (99.6%)			
Allergies					
Yes	90 (22.2%)	18 (6.9%)	29.44	< 0.001	3.9 (2.3 - 6.6)
No	315 (77.9%)	243 (93.1%)			
ADHD					
Yes	19 (4.7%)	3 (1.0%)	6.23	0.013	4.2 (1.2 - 14.5)
No	386 (95.3%)	258 (99.0%)			
ASD					
Yes	19 (4.7%)	3 (1.0%)	6.23	0.013	4.2 (1.2 - 14.5)
No	386 (95.3%)	258 (99.0%)			
Eczema (atopic dermatitis)					
Yes	38 (9.5%)	9 (3.6%)	8.522	0.035	2.9 (1.4 - 6.1)
No	367 (90.5%)	252 (96.4%)			
Learning Disability					
Yes	23 (5.7%)	3 (1.2%)	8.6803	0.003	5.2 (1.6 - 17.4)
No	382 (94.3%)	258 (98.9%)			
Neurodevelopment Disorder					
Yes	42 (10.5%)	8 (3.1%)	12.198	< 0.001	3.7 (1.7 - 7.9)
No	313 (89.5%)	253 (96.9%)			
Any Chronic Condition					
Yes	178 (44.0%)	65 (24.9%)	24.8456	< 0.001	2.4 (1.7 - 3.3)
No	227 (56.0%)	196 (75.1%)			

Table 4. Partial versus full vaccination and chronic health conditions

	Unvaccinated (n=261)	Partially Vaccinated (n=208)	Fully Vaccinated (n=197)	Total (n=666)	Chi-Square	P-value
Chronic Conditions						
Allergic rhinitis						
Yes	1 (0.4%)	17 (8.2%)	25 (12.7%)	43 (6.5%)	29.6306	< 0.001
No	260 (99.6%)	191 (91.8%)	172 (87.3%)	623 (93.5%)		
Allergies						
Yes	18 (6.9%)	47 (22.6%)	43 (21.8%)	108 (16.2%)	27.4819	< 0.001
No	243 (93.1%)	161 (77.4%)	154 (78.2%)	558 (83.8%)		
ADHD						
Yes	3 (1.2%)	8 (3.9%)	11 (5.6%)	22 (3.3%)	7.1900	0.075
No	258 (98.8%)	200 (96.1%)	186 (94.4%)	644 (96.7%)		
ASD						
Yes	3 (1.2%)	11 (5.3%)	8 (4.6%)	22 (3.3%)	6.7109	0.034
No	258 (98.8%)	197 (94.7%)	189 (95.4%)	644 (96.7%)		
Eczema (atopic dermatitis)						
Yes	9 (3.5%)	18 (8.7%)	20 (10.2%)	47 (7.1%)	8.8683	0.012
No	252 (96.5%)	190 (91.3%)	177 (89.8%)	619 (92.9%)		
Learning Disability						
Yes	3 (1.2%)	11 (5.3%)	12 (6.1%)	26 (3.9%)	8.8541	0.012
No	258 (98.8%)	197 (94.7%)	185 (93.9%)	640 (96.1%)		
NDD						
Yes	8 (3.1%)	21 (10.1%)	21 (10.7%)	50 (7.5%)	12.2443	0.002
No	253 (96.9%)	187 (89.9%)	176 (89.3%)	616 (92.5%)		
Any Chronic Condition						
Yes	65 (24.9%)	94 (45.2%)	84 (42.6%)	243 (36.5%)	25.1301	< 0.001
No	196 (75.1%)	114 (54.8%)	113 (57.4%)	423 (63.5%)		

Table 5. Chronic conditions and gender among vaccinated children

	Male (n=194)	Female (n=209)	Total (n=403)	Chi-square	P-value	Odds Ratio (95% CI)
Allergic rhinitis						
Yes	27 (13.9%)	15 (7.2%)	42 (10.4%)	4.8964	0.0269	2.1 (1.1 - 4.1)
No	167 (86.1%)	194 (92.8%)	361 (90.0%)			
Allergies						
Yes	50 (25.8%)	40 (19.1%)	90 (22.3%)	2.5531	0.1101	1.5 (0.91 - 2.4)
No	144 (74.2%)	168 (80.9%)	313 (77.7%)			
ADHD						
Yes	13 (6.7%)	6 (2.9%)	19 (4.7%)	3.2856	0.0699	2.4 (0.90 - 6.5)
No	181 (93.3%)	203 (97.1%)	384 (95.3%)			
ASD						
Yes	15 (7.7%)	4 (1.9%)	19 (4.7%)	7.5810	0.0059	4.3 (1.4 - 13.2)
No	178 (92.3%)	205 (98.1%)	384 (95.3%)			
Eczema						
Yes	19 (9.89%)	19 (9.1%)	38 (9.4%)	0.0582	0.8094	1.1 (0.6 - 2.1)
No	175 (90.2%)	190 (90.9%)	365 (90.6%)			
Learning Disability						
Yes	14 (7.2%)	9 (4.3%)	23 (5.7%)	1.5835	0.2083	1.7 (0.7 - 4.1)
No	180 (92.8%)	200 (95.7%)	380 (94.3%)			
NDD						
Yes	28 (14.4%)	14 (6.7%)	42 (10.4%)	6.4469	0.0111	2.3 (1.2 - 4.6)
No	166 (85.6%)	195 (93.3%)	361 (89.6%)			
Any Chronic Condition						
Yes	94 (48.5%)	83 (39.7%)	177 (43.9%)	3.1208	0.0773	1.4 (1.0 - 2.1)
No	100 (51.5%)	126 (60.3%)	226 (56.1%)			

Factors associated with neurodevelopmental disorders

The second aim of the study focused on a specific health outcome and was designed to determine whether vaccination was associated with neurodevelopmental disorders (NDD) and, if so, whether the

association remained significant after adjustment for other measured factors. As noted, because of the relatively small numbers of children with specific diagnoses, NDD was a derived variable combining children with a diagnosis of one or more of ASD, ADHD and a learning disability. The close association and overlap of these diagnoses in the

Table 6. Vaccination status, medication use and health services utilization

	Vaccinated (n=405)	Unvaccinated (n=261)	Total (n=666)	Chi-square	P-value	Odds Ratio (95% CI)
Medication Use						
Medication for Allergy						
Yes	81 (20.0%)	3 (1.2%)	84 (12.6%)	51.170	< 0.001	21.5 (6.7 - 68.9)
No	324 (80.0%)	258 (98.8%)	582 (87.4%)			
Used antibiotics in the past 12 months						
Yes	124 (30.8%)	40 (15.4%)	164 (24.7%)	20.092	< 0.001	2.4 (1.6 - 3.6)
No	279 (69.2%)	220 (84.6%)	499 (75.3%)			
Used fever medication 1+ times						
Yes	350 (90.7%)	173 (67.8%)	523 (81.6%)	53.288	< 0.001	4.6 (3.0 - 7.1)
No	36 (9.3%)	82 (32.2%)	118 (18.4%)			
Using fitted ear drainage tubes						
Yes	12 (3.0%)	1 (0.4%)	13 (2.0%)	5.592	0.018	8.0 (1.0 - 66.1)
No	389 (97.0%)	260 (99.6%)	649 (98.0%)			
Used medication for ADHD						
Yes	7 (1.7%)	3 (1.2%)	10 (1.5%)	0.346	0.556	-
No	398 (98.3%)	256 (98.8%)	654 (98.5%)			
Used medication for Seizures						
Yes	4 (1.0%)	1 (0.4%)	5 (0.8%)	0.769	0.653	-
No	400 (99.0%)	258 (99.6%)	658 (99.2%)			
Health Services Utilization						
Emergency Department visit in the past 12 months						
Yes	38 (9.5%)	23 (9.0%)	61 (9.3%)	0.047	0.828	-
No	364 (90.5%)	234 (91.0%)	598 (90.7%)			
Sick visit to doctor in the past year						
Yes	145 (36.0%)	41 (16.0%)	186 (28.2%)	31.096	< 0.001	3.0 (2.0 - 4.4)
No	258 (64.0%)	216 (84.0%)	474 (71.8%)			
Ever spent one or more nights in the hospital						
Yes	80 (19.8%)	32 (12.3%)	112 (16.8%)	6.267	0.012	1.8 (1.1 - 2.7)
No	325 (80.2%)	228 (87.7%)	553 (83.2%)			
Seen doctor for checkup in past 12 months						
Yes	233 (57.6%)	97 (37.2%)	330 (49.6%)	26.336	< 0.001	2.3 (1.7 - 3.2)
No	172 (42.4%)	164 (62.8%)	336 (50.4%)			
Seen dentist in the past 12 months						
Yes	362 (89.4%)	210 (80.5%)	572 (85.9%)	10.424	< 0.001	2.0 (1.3 - 3.2)
No	43 (10.6%)	51 (19.5%)	94 (14.1%)			

study is shown in the figure above (Figure 1). The figure shows that the single largest group of diagnoses was learning disability (n=15) followed by ASD (n=9), and ADHD (n=9), with smaller numbers comprising combinations of the three diagnoses.

Unadjusted analysis

Table 7 shows that the factors associated with NDD in unadjusted logistic regression analyses were: vaccination (OR 3.7, 95% CI: 1.7, 7.9); male gender (OR 2.1, 95% CI: 1.1, 3.8); adverse environment, defined as living within 1-2 miles of a furniture manufacturing factory, hazardous waste site, or lumber processing factory (OR 2.9, 95% CI: 1.1, 7.4); maternal use of antibiotics during pregnancy (OR 2.3, 95% CI: 1.1, 4.8); and preterm birth (OR 4.9, 95% CI: 2.4, 10.3). Two factors that almost reached statistical significance were vaccination during pregnancy (OR 2.5, 95% CI: 1.0, 6.3) and three or more fetal ultrasounds (OR 3.2, 95% CI: 0.92, 11.5). Factors that were not associated with NDD in this study included mother's education, household income, and religious affiliation; use of acetaminophen, alcohol, and antacids during pregnancy; gestational diabetes; preeclampsia; Rhogham shot during pregnancy; and breastfeeding (data not shown).

Adjusted analysis

After adjustment for all other significant factors, those that remained significantly associated with NDD were: vaccination (OR 3.1, 95% CI: 1.4, 6.8); male gender (OR 2.3, 95% CI: 1.2, 4.3); and preterm birth (OR 5.0, 95% CI: 2.3, 11.1). The apparently strong association between both vaccination and preterm birth and NDD suggested the possibility of an interaction between these factors.

In a final adjusted model designed to test for this possibility, controlling for the interaction of preterm birth and vaccination, the following factors remained significantly associated with NDD: vaccination (OR 2.5, 95% CI: 1.1, 5.6), nonwhite race (OR 2.4, 95% CI: 1.1, 5.4), and male gender (OR 2.3, 95% CI: 1.2, 4.4). Preterm birth itself, however, was not significantly associated with NDD, whereas the combination (interaction) of preterm birth and vaccination was associated with 6.6-fold increased odds of NDD (95% CI: 2.8, 15.5) (Table 8).

Discussion

Following a recommendation of the Institute of Medicine [19] for studies comparing the health outcomes of vaccinated and unvaccinated

Table 7. Unadjusted analysis of potential risk factors for neurodevelopmental disorders

Vaccination Status	NDD			Chi-Square	P-value	OR (95% CI)**
	Yes (N=50)	No (N=616)	Total* (N=666)			
Vaccinated	42	363	405	12.198	<0.001	3.7 (1.7 - 7.9)
Not Vaccinated	8	253	261			Ref
Race						
Non-White	9	71	80	1.8208	0.177	1.7 (0.7 - 3.6)
White	41	544	585			Ref
Child's Gender						
Male	32	283	315	5.9471	0.015	2.1 (1.1 - 3.8)
Female	18	331	349			Ref
Adverse Environment						
Yes	6	27	33	5.8706	0.053	2.9 (1.1 - 7.4)
No	40	523	563			Ref
Do not know	4	66	70			0.8 (0.3 - 2.3)
Medication during Pregnancy - Antibiotics						
Yes	10	61	71	4.950	0.026	2.3 (1.1 - 4.8)
No	40	555	595			Ref
Medication during Pregnancy –Vaccinated						
Yes	6	32	38	3.965	0.057	2.5 (1.0 - 6.3)
No	44	583	627			Ref
Preterm birth						
Yes	12	37	49	22.910	< 0.001	4.9 (2.4 - 10.3)
No	38	578	616			Ref
Ultrasound						
None	3	71	74	5.898	0.052	Ref
1-3 times	30	419	449			1.7 (0.5 - 5.7)
> 3 times	17	124	141			3.2 (0.92 - 11.5)

*Numbers may not add to column totals due to missing or incomplete data.

**Note that Odds Ratios are the cross-product ratios of the entries in the 2-by-2 tables, and are an estimate of the relative incidence (or risk) of the outcome associated with the exposure factor.

Table 8. Adjusted logistic regression analyses of risk factors and NDD*

	Adjusted Model (Model 1)	Adjusted Model with Interaction (Model 2)
Vaccination Status		
Vaccinated	3.1 (1.4 - 6.8)	2.5 (1.1 - 5.6)
Not Vaccinated	Ref	Ref
Race		
Non-White	2.3 (1.0 - 5.2)	2.4 (1.1 - 5.4)
White	Ref	Ref
Child's Gender		
Male	2.3 (1.2 - 4.3)	2.3 (1.2 - 4.4)
Female	Ref	Ref
Preterm birth		
Yes	5.0 (2.3 - 11.1)	NS
No	Ref	
Preterm birth and Vaccination interaction		
No interaction	Not in the model	Ref
Preterm and Vaccinated		6.6 (2.8 - 15.5)

*Number of observation read 666, number of observations used 629. NDD=47, Not NDD = 582

children, this study focused on homeschool children ages 6 to 12 years based on mothers' anonymous reports of pregnancy-related conditions, birth histories, physician-diagnosed illnesses, medications and healthcare use. Respondents were mostly white, married, and college-educated, upper income women who had been contacted and

invited to participate in the study by the leaders of their homeschool organizations. Data from the survey were also used to determine whether vaccination was associated specifically with NDDs, a derived diagnostic category combining children with the diagnoses of learning disability, ASD and/or ADHD.

With regard to acute and chronic conditions, vaccinated children were significantly less likely than the unvaccinated to have had chickenpox and pertussis but, contrary to expectation, were significantly more likely to have been diagnosed with otitis media, pneumonia, allergic rhinitis, eczema, and NDD. The vaccinated were also more likely to have used antibiotics, allergy and fever medications; to have been fitted with ventilation ear tubes; visited a doctor for a health issue in the previous year, and been hospitalized. The reason for hospitalization and the age of the child at the time were not determined, but the latter finding appears consistent with a study of 38,801 reports to the VAERS of infants who were hospitalized or had died after receiving vaccinations. The study reported a linear relationship between the number of vaccine doses administered at one time and the rate of hospitalization and death; moreover, the younger the infant at the time of vaccination, the higher was the rate of hospitalization and death [55]. The hospitalization rate increased from 11% for 2 vaccine doses to 23.5% for 8 doses ($r^2 = 0.91$), while the case fatality rate increased significantly from 3.6% for those receiving from 1-4 doses to 5.4 % for those receiving from 5-8 doses.

In support of the possibility that the number of vaccinations received could be implicated in risks of associated chronic illness, a

comparison of unvaccinated, partially and fully vaccinated children in the present study showed that the partially vaccinated had increased but intermediate odds of chronic disease, between those of unvaccinated and fully vaccinated children, specifically for allergic rhinitis, ADHD, eczema, a learning disability, and NDD as a whole.

The national rates of ADHD and LD are comparable to those of the study. The U.S. rate of ADHD for ages 4-17 (twice the age range of children than the present study), is 11% [31]. The study rate of ADHD for ages 6 to 12 is 3.3%, and 4.7% when only vaccinated children are included. The national LD rate is 5% [32], and the study data show a rate of LD of 3.9% for all groups, and 5.6% when only vaccinated children are included. However, the ASD prevalence of 2.24% from a CDC parent survey is lower than the study rate of 3.3%. Vaccinated males were significantly more likely than vaccinated females to have been diagnosed with allergic rhinitis, and NDD. The percentage of vaccinated males with an NDD in this study (14.4%) is consistent with national findings based on parental responses to survey questions, indicating that 15% of U.S. children ages 3 to 17 years in the years 2006-2008 had an NDD [28]. Boys are also more likely than girls to be diagnosed with an NDD, and ASD in particular [29].

Vaccination was strongly associated with both otitis media and pneumonia, which are among the most common complications of measles infection [56,57]. The odds of otitis media were almost four-fold higher among the vaccinated (OR 3.8, 95% CI: 2.1, 6.6) and the odds of myringotomy with tube placement were eight-fold higher than those of unvaccinated children (OR 8.0, 95% CI: 1.0, 66.1). Acute otitis media (AOM) is a very frequent childhood infection, accounting for up to 30 million physician visits each year in the U.S., and the most common reason for prescribing antibiotics for children [58,59]. The incidence of AOM peaks at ages 3 to 18 months and 80% of children have experienced at least one episode by 3 years of age. Rates of AOM have increased in recent decades [60]. Worldwide, the incidence of AOM is 10.9%, with 709 million cases each year, 51% occurring in children under 5 years of age [61]. Pediatric AOM is a significant concern in terms of healthcare utilization in the U.S., accounting for \$2.88 billion in annual health care costs [62].

Numerous reports of AOM have been filed with VAERS. A search of VAERS for "Cases where age is under 1 and onset interval is 0 or 1 or 2 or 3 or 4 or 5 or 6 or 7 days and Symptom is otitis media" [63] revealed that 438,573 cases were reported between 1990 and 2011, often with fever and other signs and symptoms of inflammation and central nervous system involvement. One study [64] assessed the nasopharyngeal carriage of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* during AOM in fully immunized, partly immunized children with 0 or 1 dose of Pneumococcal Conjugate Vaccine-7 (PCV7), and "historical control" children from the pre-PCV-7 era, and found an increased frequency of *M. catarrhalis* colonization in the vaccinated group compared to the partly immunized and control groups (76% vs. 62% and 56%, respectively). A high rate of *Moraxella catarrhalis* colonization is associated with an increased risk of AOM [65].

Successful vaccination against pneumococcal infections can lead to replacement of the latter in the nasopharyngeal niche by nonvaccine pneumococcal serotypes and disease [66]. Vaccination with PCV-7 has a marked effect on the complete microbiota composition of the upper respiratory tract in children, going beyond shifts in the distribution of pneumococcal serotypes and known potential pathogens and resulting in increased anaerobes, gram-positive bacteria and gram-negative bacterial species. PCV-7 administration also correlates highly with the emergence and expansion of oropharyngeal types of species.

These observations have suggested that eradication of vaccine serotype pneumococci can be followed by colonization of other bacterial species in the vacant nasopharyngeal niche, leading to disequilibria of bacterial composition (dysbiosis) and increased risks of otitis media. Long-term monitoring has been recommended as essential for understanding the full implications of vaccination-induced changes in microbiota structure [67].

The second aim of the paper focused on a specific health outcome and sought to determine whether vaccination remained associated with neurodevelopmental disorders (NDD) after controlling for other measured factors. After adjustment, the factors that remained significantly associated with NDD were vaccination, nonwhite race, male gender, and preterm birth. The apparently strong association between both vaccination and preterm birth and NDD suggested the possibility of an interaction between these factors. This was shown in a final adjusted model with interaction (controlling for the interaction of preterm birth with vaccination). In this model, vaccination, nonwhite race and male gender remained associated with NDD, whereas preterm birth itself was no longer associated with NDD. However, preterm birth combined with vaccination was associated with a 6.6-fold increased odds of NDD.

In summary, vaccination, nonwhite race, and male gender were significantly associated with NDD after controlling for other factors. Preterm birth, although significantly associated with NDD in unadjusted and adjusted analyses, was no longer associated with NDD in the final model with interaction. However, preterm birth and vaccination combined was strongly associated with NDD in the final adjusted model with interaction, more than doubling the odds of NDD compared to vaccination alone. Preterm birth has long been known as a major factor for NDD [68,69], but since preterm infants are routinely vaccinated, the separate effects of preterm birth and vaccination have not been examined. The present study suggests that vaccination could be a contributing factor in the pathogenesis of NDD but also that preterm birth by itself may have a lesser or much reduced role in NDD (defined here as ASD, ADHD and/or a learning disability) than currently believed. The findings also suggest that vaccination coupled with preterm birth could increase the odds of NDD beyond that of vaccination alone.

Potential limitations

We did not set out to test a specific hypothesis about the association between vaccination and health. The aim of the study was to determine whether the health outcomes of vaccinated children differed from those of unvaccinated homeschool children, given that vaccines have nonspecific effects on morbidity and mortality in addition to protecting against targeted pathogens [11]. Comparisons were based on mothers' reports of pregnancy-related factors, birth histories, vaccinations, physician-diagnosed illnesses, medications, and the use of health services. We tested the null hypothesis of no difference in outcomes using chi-square tests, and then used Odds Ratios and 96% Confidence Intervals to determine the strength and significance of the association.

If the effects of vaccination on health were limited to protection against the targeted pathogens, as is assumed to be the case [21], no difference in outcomes would be expected between the vaccinated and unvaccinated groups except for reduced rates of the targeted infectious diseases. However, in this homogeneous sample of 666 children there were striking differences in diverse health outcomes between the groups. The vaccinated were less likely to have had chickenpox or whooping cough, as expected, but more likely to have been diagnosed with pneumonia and ear infections as well as allergies and NDDs.

What credence can be given to the findings? This study was not intended to be based on a representative sample of homeschool children but on a convenience sample of sufficient size to test for significant differences in outcomes. Homeschoolers were targeted for the study because their vaccination completion rates are lower than those of children in the general population. In this respect our pilot survey was successful, since data were available on 261 unvaccinated children.

To eliminate opportunities for subjectivity or opinion in the data, only factual information was requested and the questions involved memorable events such as physician-diagnosed diseases in a child. With regard to minimizing potential bias in the information provided by mothers, all communications with the latter emphasized neutrality regarding vaccination and vaccine safety. To minimize recall bias, respondents were asked to use their child's vaccination records. To enhance reliability, closed-ended questions were used and each set of questions had to be completed before proceeding to the next. To enhance validity, parents were asked to report only physician-diagnosed illnesses.

Mothers' reports could not be validated by clinical records because the survey was designed to be anonymous. However, self-reports about significant events provide a valid proxy for official records when medical records and administrative data are unavailable [70]. Had mothers been asked to provide copies of their children's medical records it would no longer have been an anonymous study and would have resulted in few completed questionnaires. We were advised by homeschool leaders that recruitment efforts would have been unsuccessful had we insisted on obtaining the children's medical records as a requirement for participating in the study.

A further potential limitation is under-ascertainment of disease in unvaccinated children. Could the unvaccinated have artificially reduced rates of illness because they are seen less often by physicians and would therefore have been less likely to be diagnosed with a disease? The vaccinated were indeed more likely to have seen a doctor for a routine checkup in the past 12 months (57.5% vs. 37.1%, $p < 0.001$; OR 2.3, 95% CI: 1.7, 3.1). Such visits usually involve vaccinations, which non-vaccinating families would be expected to refuse. However, fewer visits to physicians would not necessarily mean that unvaccinated children are less likely to be seen by a physician if their condition warranted it. In fact, since unvaccinated children were more likely to be diagnosed with chickenpox and whooping cough, which would have involved a visit to the pediatrician, differences in health outcomes are unlikely to be due to under-ascertainment.

Strengths of the study include the unique design of the study, involving homeschool mothers as respondents, and the relatively large sample of unvaccinated children, which made it possible to compare health outcomes across the spectrum of vaccination coverage. Recruitment of biological mothers as respondents also allowed us to test hypotheses about the role of pregnancy-related factors and birth history as well as vaccination in NDD and other specific conditions. In addition, this was a within-group study of a demographically homogeneous population of mainly white, higher-income and college-educated homeschooling families in which the children were all 6-12 years of age. Information was provided anonymously by biological mothers, obviously well-informed about their own children's vaccination status and health, which likely increased the validity of the reports.

Conclusions

Assessment of the long-term effects of the vaccination schedule on morbidity and mortality has been limited [71]. In this pilot study of

vaccinated and unvaccinated homeschool children, reduced odds of chickenpox and whooping cough were found among the vaccinated, as expected, but unexpectedly increased odds were found for many other physician-diagnosed conditions. Although the cross-sectional design of the study limits causal interpretation, the strength and consistency of the findings, the apparent "dose-response" relationship between vaccination status and several forms of chronic illness, and the significant association between vaccination and NDDs all support the possibility that some aspect of the current vaccination program could be contributing to risks of childhood morbidity. Vaccination also remained significantly associated with NDD after controlling for other factors, whereas preterm birth, long considered a major risk factor for NDD, was not associated with NDD after controlling for the interaction between preterm birth and vaccination. In addition, preterm birth coupled with vaccination was associated with an apparent synergistic increase in the odds of NDD above that of vaccination alone. Nevertheless, the study findings should be interpreted with caution. First, additional research is needed to replicate the findings in studies with larger samples and stronger research designs. Second, subject to replication, potentially detrimental factors associated with the vaccination schedule should be identified and addressed and underlying mechanisms better understood. Such studies are essential in order to optimize the impact of vaccination of children's health.

Competing Interests

The authors declare that they have no financial interests that had any bearing on any aspect of the conduct or conclusions of the study and the submitted manuscript.

Author contributions

AM designed the study, contributed to data analysis and interpretation, and drafted the paper. BR designed the study, contributed to data collection, and edited the paper. AB contributed to data analyses and edited the paper. BJ contributed to data analyses and editing. All authors read and approved the final version of the paper.

Funding sources

This study was supported by grants from Generation Rescue, Inc., and the Children's Medical Safety Research Institute, charitable organizations that support research on children's health and safety. The funders had no role or influence on the design and conduct of the research or the preparation of reports.

Acknowledgments

The authors thank all those who contributed critical comments, suggestions and financial support for the project. We also thank the collaborating homeschool organizations and especially the mothers who participated in the survey.

Disclaimer

This study was approved by the Institutional Review Board of Jackson State University and completed prior to Dr. Mawson's tenure-track appointment at Jackson State University.

References

- Centers for Disease Control and Prevention (CDC) (1999) Ten great public health achievements--United States, 1900-1999. *MMWR Morb Mortal Wkly Rep* 48: 241-243. [[Crossref](#)]

2. Whitney CG, Zhou F, Singleton J, Schuchat A; Centers for Disease Control and Prevention (CDC) (2014) Benefits from immunization during the vaccines for children program era - United States, 1994-2013. *MMWR Morb Mortal Wkly Rep* 63: 352-355. [Crossref]
3. Centers for Disease Control and Prevention (CDC) (2007) Vaccination coverage among children in kindergarten--United States, 2006-07 school year. *MMWR Morb Mortal Wkly Rep* 56: 819-821. [Crossref]
4. Centers for Disease Control and Prevention (CDC) (2013) Vaccination coverage among children in kindergarten - United States, 2012-13 school year. *MMWR Morb Mortal Wkly Rep* 62: 607-612. [Crossref]
5. <http://www.cdc.gov/vaccines/vacgen/whatifstop.htm> (Accessed 19 June 2016)
6. http://www.hhs.gov/nvpo/vacc_plan/index.html (Accessed 19 June 2015).
7. <http://www.cdc.gov/vaccines/schedules/index.html> (Accessed 19 June 2016).
8. Ward BJ (2000) Vaccine adverse events in the new millennium: is there reason for concern? *Bull World Health Organ* 78: 205-215. [Crossref]
9. Sienkiewicz D, Kulak W, Okurowska-Zawada B, Paszko-Pateg G (2012) Neurologic adverse events following vaccination. *Prog Health Sci* 2:129-141.
10. Pollard AJ (2007) Childhood immunisation: what is the future? *Arch Dis Child* 92: 426-433. [Crossref]
11. Aaby P, Whittle H, Benn CS (2012) Vaccine programmes must consider their effect on general resistance. *BMJ* 344: e3769. [Crossref]
12. Cunningham AS (2015) Vaccine mandates in the US are doing more harm than good. *BMJ* 351: h4576. [Crossref]
13. Dórea JG. Exposure to mercury and aluminum in early life: developmental vulnerability as a modifying factor in neurologic and immunologic effects. *Int J Environ Res Public Health*(2015) 12(2):1295-313.
14. Crowcroft NS1, Deeks SL2, Upshur RE2 (2015) Do we need a new approach to making vaccine recommendations? *BMJ* 350: h308. [Crossref]
15. Kessler DA1 (1993) Introducing MEDWatch. A new approach to reporting medication and device adverse effects and product problems. *JAMA* 269: 2765-2768. [Crossref]
16. http://www.nap.edu/catalog.php?record_id=11234 (Accessed 19 June 2016).
17. http://www.cdc.gov/vaccinesafety/pdf/iso-finalscientific_agenda-nov-10.pdf (Accessed 19 June 2016).
18. Institute of Medicine (2012) Adverse Effects of Vaccines: Evidence and Causality. The National Academies Press, Washington, DC.
19. Institute of Medicine (2013) The childhood immunization schedule and safety: Stakeholder concerns, scientific evidence, and future studies. The National Academies Press, Washington, DC.
20. Maglione MA, Das L, Raaen L, Smith A, Chari R, et al. (2014) Safety of vaccines used for routine immunization of US children: a systematic review. *Pediatrics* 134:325-337. [Crossref]
21. Siegrist CA (2008) Vaccine Immunology. Vaccines. (5thEdtn). Saunders Elsevier.
22. Benn CS, Netea MG, Selin LK, Aaby P (2013) A small jab - a big effect: nonspecific immunomodulation by vaccines. *Trends Immunol* 34: 431-439. [Crossref]
23. Jensen KJ, Benn CS, van Crevel R (2016) Unravelling the nature of non-specific effects of vaccines - A challenge for innate immunologists. *Semin Immunol* 28:377-383. [Crossref]
24. Sorup S, Benn CS, Poulsen A, Krause TG, Aaby P, et al. (2014) Live vaccine against measles, mumps, and rubella and the risk of hospital admissions for nontargeted infections. *JAMA* 311: 826-835. [Crossref]
25. Aaby P, Benn C, Nielsen J, Lisse IM, Rodrigues A, et al. (2012) Testing the hypothesis that diphtheria-tetanus-pertussis vaccine has negative non-specific and sex-differential effects on child survival in high-mortality countries. *BMJ Open* 2:e000707. [Crossref]
26. Garly ML1, Jensen H, Martins CL, Balé C, Baldé MA, et al. (2004) Hepatitis B vaccination associated with higher female than male mortality in Guinea-Bissau: an observational study. *Pediatr Infect Dis J* 23:10861092. [Crossref]
27. Grandjean P, Landrigan PJ (2006) Developmental neurotoxicity of industrial chemicals. *Lancet* 368: 2167-2178. [Crossref]
28. Boyle CA, Boulet S, Schieve LA, Cohen RA, Blumberg SJ, et al. (2011) Trends in the prevalence of developmental disabilities in US Children, 1997-2008. *Pediatrics* 127:10341042. [Crossref]
29. Baio J (2014) Prevalence of Autism Spectrum Disorder among children aged 8 years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2010 Surveillance Summaries. *MMWR* 63:1-21.
30. Zablotsky B, Black LI, Maenner MJ, Schieve LA, Blumberg SJ (2015) Estimated prevalence of autism and other developmental disabilities following questionnaire changes in the 2014 National Health Interview Survey. *Natl Health Stat Report* 13:1-20.
31. Visser SN, Danielson ML, Bitsko RH, Holbrook JR, Kogan MD, et al. (2014) Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003-2011. *J Am Acad Child Adolesc Psychiatry* 53:34-46.e2. [Crossref]
32. Cortiella C, Horowitz SH (2014) The State of Learning Disabilities: Facts, Trends and Emerging Issues. National Center for Learning Disabilities, New York:.
33. Cornwall W (2015) Autism rates are up, but is it really on the rise? *Science Magazine*.
34. Landrigan PJ (2010) What causes autism? Exploring the environmental contribution. *Curr Opin Pediatr* 22: 219-225. [Crossref]
35. Nevison CD (2014) A comparison of temporal trends in United States autism prevalence to trends in suspected environmental factors. *Environ Health* 13: 73. [Crossref]
36. Shaw CA, Seneff S, Kette SD, Tomljenovic L, Oller JW Jr, et al. (2014) Aluminum-induced entropy in biological systems: implications for neurological disease. *J Toxicol* 2014: 491316. [Crossref]
37. Sealey LA, Hughes BW, Sriskanda AN1, Guest JR1, Gibson AD1, et al. (2016) Environmental factors in the development of autism spectrum disorders. *Environ Int* 88: 288-298. [Crossref]
38. <http://www.hrsa.gov/vaccinecompensation/data.html> (Accessed 20 June 2016).
39. Holland M, Conte L, Krakow R, Colin L (2011) Unanswered questions from the Vaccine Injury Compensation Program: A review of compensated cases of vaccine-induced brain injury. *Pace Envtl L Rev* 28:480.
40. Doja A, Roberts W (2006) Immunizations and autism: a review of the literature. *Can J Neurol Sci* 33: 341-346. [Crossref]
41. Price CS, Thompson WW, Goodson B, Weintraub ES, Croen LA, et al. (2010) Prenatal and infant exposure to thimerosal from vaccines and immunoglobulins and risk of autism. *Pediatrics* 126: 656-664. [Crossref]
42. DeStefano F, Price CS, Weintraub ES (2013) Increasing exposure to antibody-stimulating proteins and polysaccharides in vaccines is not associated with risk of autism. *J Pediatr* 163:561-567. [Crossref]
43. McNeil MM, Gee J, Weintraub ES, Belongia EA, Lee GM, et al. (2014) The Vaccine Safety Datalink: successes and challenges monitoring vaccine safety. *Vaccine* 32: 5390-5398. [Crossref]
44. Taylor LE, Swerdfeger AL, Eslick GD (2014) Vaccines are not associated with autism: an evidence-based meta-analysis of case-control and cohort studies. *Vaccine* 32: 3623-3629. [Crossref]
45. Jain A, Marshall J, Buikema A, Bancroft T, Kelly JP, et al. (2015) Autism occurrence by MMR vaccine status among US children with older siblings with and without autism. *JAMA* 313: 1534-1540. [Crossref]
46. Gerber JS, Offit PA (2009) Vaccines and autism: a tale of shifting hypotheses. *Clin Infect Dis* 48: 456-461. [Crossref]
47. Choi BK, Manning ML (2010) The immunization status of home-schooled children in America. *J Pediatr Health Care* 24: 42-47. [Crossref]
48. Ray BD (2010) Academic achievement and demographic traits of homeschool students: a nationwide study. *J Acad Leadership* 8: 1.
49. https://www.census.gov/library/publications/time-series/statistical_abstracts.html (Accessed 19 August 2016).
50. <http://files.eric.ed.gov/fulltext/ED505409.pdf> (Accessed 22 August 2016).
51. <http://nces.ed.gov/pubs2006/2006042.pdf> (Accessed 22 August 2016).
52. <http://eric.ed.gov/?id=ED544174> (Accessed 22 August 2016).

53. Surén P, Bakken IJ, Aase H, Chin R, Gunnes N, et al. (2012) Autism spectrum disorder, ADHD, epilepsy, and cerebral palsy in Norwegian children. *Pediatrics* 130: e152-158. [Crossref]
54. Zocchetti C, Consonni D, Bertazzi PA (1997) Relationship between prevalence rate ratios and odds ratios in cross-sectional studies. *Int J Epidemiol* 26: 220-223. [Crossref]
55. Goldman GS, Miller NZ (2012) Relative trends in hospitalizations and mortality among infants by the number of vaccine doses and age, based on the Vaccine Adverse Event Reporting System (VAERS), 1990-2010. *Hum Exp Toxicol* 31:1012-1021. [Crossref]
56. Orenstein WA, Perry RT, Halsey NA (2004) The clinical significance of measles: a review. *J Infect Dis* 189:S4-S16. [Crossref]
57. CDC (2013) Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP). Recommendations and Reports. *MMWR* 62:1-34.
58. Dhooge IJ (2003) Risk factors for the development of otitis media. *Curr Allergy Asthma Rep* 3: 321-325. [Crossref]
59. Siegel RM (2010) Acute otitis media guidelines, antibiotic use, and shared medical decision-making. *Pediatrics* 125:384-386. [Crossref]
60. Casselbrant ML, Mandel EM (2003) Epidemiology. Evidence-based otitis media. BC Decker, Hamilton, ON, Canada. Pp. 147-162.
61. Monasta L1, Ronfani L, Marchetti F, Montico M, VecchiBrumatti L, et al. (2012) Burden of disease caused by otitis media: systematic review and global estimates. *PLoS One* 7: e36226. [Crossref]
62. Ahmed S1, Shapiro NL, Bhattacharyya N (2014) Incremental health care utilization and costs for acute otitis media in children. *Laryngoscope* 124: 301-305. [Crossref]
63. [http://www.medicare.gov/vaersdb/findfield.php?TABLE=ON&GROUP1=AGE&EVENTS=ON&SYMPTOMS\[\]=Otitis+media+%2810033078%29&NUMDAYS\[\]=0&NUMDAYS\[\]=1&NUMDAYS\[\]=2&NUMDAYS\[\]=3&NUMDAYS\[\]=4&NUMDAYS\[\]=5&NUMDAYS\[\]=6&NUMDAYS\[\]=7&WhicAge=range&LOWAGE=0.0&HIGHAGE=1.0](http://www.medicare.gov/vaersdb/findfield.php?TABLE=ON&GROUP1=AGE&EVENTS=ON&SYMPTOMS[]=Otitis+media+%2810033078%29&NUMDAYS[]=0&NUMDAYS[]=1&NUMDAYS[]=2&NUMDAYS[]=3&NUMDAYS[]=4&NUMDAYS[]=5&NUMDAYS[]=6&NUMDAYS[]=7&WhicAge=range&LOWAGE=0.0&HIGHAGE=1.0) (Accessed 25 August, 2016).
64. Revai K, McCormick DP, Patel J, Grady JJ, Saeed K, et al. (2006) Effect of pneumococcal conjugate vaccine on nasopharyngeal bacterial colonization during acute otitis media. *Pediatrics* 117:1823-1829. [Crossref]
65. Faden H, Harabuchi Y, Hong JJ (1994) Epidemiology of *Moraxella catarrhalis* in children during the first 2 years of life: relationship to otitis media. *J Infect Dis* 169: 1312-1317. [Crossref]
66. Weinberger DM, Malley R, Lipsitch M (2011) Serotype replacement in disease after pneumococcal vaccination. *Lancet* 378:1962-1973. [Crossref]
67. Biesbroek G, Wang X, Keijsers BJ, Eijkemans RM, Trzcinski K, et al. (2014) Seven-valent pneumococcal conjugate vaccine and nasopharyngeal microbiota in healthy children. *Emerg Infect Dis* 20: 201-210.
68. Goldin RL, Matson JL (2016) Premature birth as a risk factor for autism spectrum disorder. *Dev Neurorehabil* 19: 203-206. [Crossref]
69. Padilla N, Eklöf E, Mårtensson GE, Bölte S, Lagercrantz H, et al. (2015) Poor brain growth in extremely preterm neonates long before the onset of autism spectrum disorder symptoms. *Cereb Cortex* 27: 1245-1252. [Crossref]
70. Short ME, Goetzl RZ, Pei X, Tabrizi MJ, Ozminkowski RJ, et al. (2009) How accurate are self-reports? Analysis of self-reported health care utilization and absence when compared with administrative data. *J Occup Environ Med* 51:786-796. [Crossref]
71. Fisker AB, Hornshøj L, Rodrigues A, Balde I, Fernandes M, et al. (2014) Effects of the introduction of new vaccines in Guinea-Bissau on vaccine coverage, vaccine timeliness, and child survival: an observational study. *Lancet Glob Health* 2:e478-e487.



Health Resources & Services Administration



Advanced Search

[Grants](#) [Loans & Scholarships](#) [Data Warehouse](#) [About HRSA](#)
[share](#) | [print](#) [email](#) [facebook](#) [twitter](#)
[Home](#) > [National Vaccine Injury Compensation Program](#) > Vaccine Injury Compensation Data

Vaccine Injury Compensation Data



Most Recent Data Report

[National Vaccine Injury Compensation Program Data Report](#) (PDF - 318 KB) - updated December 1, 2018.

Updated monthly, and includes the number of:

- petitions filed,
- adjudications compensated and dismissed,
- awards paid by type and amount,
- claims by vaccine, and
- adjudication categories by vaccine.

The United States has the safest, most effective vaccine supply in history. In the majority of cases, vaccines cause no side effects, however they can occur, as with any medication—but most are mild. Very rarely, people experience more serious side effects, like allergic reactions.

In those instances, the National Vaccine Injury Compensation Program (VICP) allows individuals to file a petition for compensation.

What does it mean to be awarded compensation?

Being awarded compensation for a petition does not necessarily mean that the vaccine caused the alleged injury. In fact:

- Almost 80% of all compensation awarded by the VICP comes as result of a negotiated settlement between the parties in which HHS has not concluded, based upon review of the evidence, that the alleged vaccine(s) caused the alleged injury.
- Attorneys are eligible for reasonable attorneys' fees, whether or not the petitioner is awarded compensation by the Court, if certain minimal requirements are met. In those circumstances, attorneys are paid by the VICP directly. By statute, attorneys may not charge any other fee, including a contingency fee, for his or her services in representing a petitioner in the VICP.

What reasons might a petition result in a negotiated settlement?

- Consideration of prior U.S. Court of Federal Claims decisions, both parties decide to minimize risk of loss through settlement
- A desire to minimize the time and expense of litigating a case
- The desire to resolve a petition quickly

How many petitions have been awarded compensation?

According to the CDC, from 2006 to 2016 over 3.1 billion doses of covered vaccines were distributed in the U.S. For petitions filed in this time period, 5,576 petitions were adjudicated by

National Vaccine Injury Compensation Program

[Home](#)
[About the Program](#)
[Infographic](#) (PDF - 1.1 MB)

[Covered Vaccines](#)
[Vaccine Injury Table \(Revised and Effective March 21, 2017\)](#) (PDF - 119 KB)

[Vaccine Injury Table \(Effective between July 23, 2015 and March 20, 2017\)](#) (PDF - 139 KB)

[Who Can File a Petition](#)
[How to File a Petition](#)
[Vaccine Injury Compensation Data](#)
[Frequently Asked Questions](#)
[Resources](#)
[Job and Advisory Committee Opportunities](#)

National Vaccine Injury Compensation Program (VICP) Fact Sheet (PDF - 200 KB)

the Court, and of those 3,785 were compensated. This means for every 1 million doses of vaccine that were distributed, 1 individual was compensated.

Since 1988, over 20,123 petitions have been filed with the VICP. Over that 30-year time period, 17,576 petitions have been adjudicated, with 6,313 of those determined to be compensable, while 11,263 were dismissed. Total compensation paid over the life of the program is approximately \$4.0 billion.

Disclaimer

The content of this website reflects the current thinking of the United States Department of Health and Human Services on the topics addressed and does not create or confer any rights for or on any person and does not operate to bind the Department or the public. The ultimate decision about the scope of the statutes authorizing the VICP is within the authority of the United States Court of Federal Claims, which is responsible for resolving petitions for compensation under the VICP.

If you have additional questions, call: 1-800-338-2382.

Date Last Reviewed: December 2018

 About HRSA

 Connect with HRSA

 Find Health Services

- [Bureaus & Offices](#)
- [Budget](#)
- [Strategic Plan](#)
- [Working at HRSA](#)
- [About HRSA](#)



Sign up for email updates

Health Center
HIV Medical Care and Treatment

[Locate other health services](#) 

[Contact Us](#) | [Viewers & Players](#) | [Privacy Policy](#) | [Disclaimers](#) | [Accessibility](#) | [Freedom of Information Act](#) | [No Fear Act](#)
U.S. Department of Health and Human Services | [USA.gov](#) | [Whitehouse.gov](#)

Language Assistance Available

- | | | | |
|--------------------------|-------------------------|----------------------------|--------------------------------|
| Español | 繁體中文 | Tiếng Việt | 한국어 |
| Tagalog | Русский | العربية | Kreyòl Ayisyen |
| Français | Polski | Português | Italiano |
| Deutsch | 日本語 | فارسی | English |

USA & CANADA - ABORTED FETAL CELL LINE PRODUCTS AND ETHICAL ALTERNATIVES (Aug 2016) [References](#)

Disease	Product Name	Manufacturer	Fetal Cell Line	Ethical Version	Manufacturer	Cell Line
Acute Respiratory	Adenovirus 4,7 Oral	Barr Labs	WI-38	None	N/A	N/A
Chickenpox	All Varivax, Varilrix	Merck, GSK	WI-38, MRC-5	None	N/A	N/A
Cystic Fibrosis	Pulmozyme	Genentech	HEK-293	N-acetylcysteine, Hyper-sal	Various	N/A
Anemia (Cancer patients, severe kidney disease)	Procrit, Epoetin alfa Epogen, Aranesp, Darbepoetin alfa	Amgen	Human erythropoietin gene from fetal liver lambda.hE1/	None	N/A	N/A
Ebola - In Development	NIAID/GSK ChAd3 AdVacEbola VSV-EBOV	GSK J&J/Crucell, NewLink /BioProtSv	Procell92/HEK-293 PER C6, HEK-293	rVSV-ZEBOV-GP GOVOX-E301, E-302 ZMapp Therapeutic	Merck/New Link GeoVax LeafBio	Vero Chick eggs Tobacco
Heart problems	Abciximab (Repro)	Eli Lilly	HEK-293	Integrilin, Angiomax	Merck, Medicine Co.	N/A
Hemophilia	rhFVI, VIII, Elocbate	Octapharma, BioGen	HEK-293	Advate, Kogenate	Baxter	Hamster
Hepatitis A	Vaqta, Havrix Avaxim, Epaxal	Merck, GSK Sanofi, Berna	MRC-5 MRC-5	Aimmugen None in US or Canada	Kaketsuken (Japan, Asia & Europe)	Vero (monkey)
Hepatitis A & B Hepatitis A & Typhoid	Twinrix Vivaxim	GSK Sanofi	MRC-5 MRC-5	Engerix Hep-B Only Recombivax Hep-B Only	GSK Merck	Yeast Yeast
Infection prevention	G-CSF	Octapharma	HEK-293	Neupogen, Zarxio	Amgen, Sandoz	E-coli
Measles/Mumps/Rubella	MMR, Priorix	Merck, GSK	RA273, WI-38, MRC-5	MR+M (Japan only)	Kitasato Daiichi Sankyo	Hen, rabbit
Measles-Rubella	MR Vax, Eolarix	Merck, GSK.	RA273, WI-38, MRC-5	Attenuvax (Measles Only)* MR (Japan only)	Merck Kitasato Daiichi Sankyo	Hen eggs Hen, rabbit
Mumps-Rubella	Biavax II	Merck	RA273, WI-38	Mumpsvax (Mumps Only)*	Merck	Hen eggs
Rubella	Meruvax II	Merck	RA273, WI-38	Takahashi (Japan only)	Kitasato Daiichi Sankyo	Rabbit
MMR + Chickenpox	ProQuad/MMR-V Priorix Tetra	Merck GSK	RA273, WI-38, MRC-5	None	N/A	N/A
Polio	Poliovax, DT PolAds Polio Sabin (oral)	Sanofi Pasteur GSK	MRC-5 MRC-5	IPOL, IMOVAX® Polio**	Sanofi Pasteur	Vero
Polio Combination (DTaP + polio+ HiB)	Pentacel, Quadracel	Sanofi Pasteur	MRC-5	Pediacel, Pediarix, Any HiB DTap, IPOL, InfanrixHexa,	Sanofi, GSK	Vero
Rabies	Imovax**	Sanofi Pasteur	MRC-5	RabAvert	Novartis	Hen eggs
Rheumatoid Arthritis	Enbrel	Amgen	WI-26 VA4 - RDNA	Humira, Cimzia, Orencia	Abbott, UCB, BMS	Hamster
Shingles	Zostavax	Merck.	WI-38, MRC-5	In Development: Shingrix	GSK	Yeast
Smallpox	Acambis 1000	Acambis	MRC-5	ACAM2000, MVA3000	Acambis/Baxter	Vero

Note: Immune-Globulin shots will provide temporary immunity (4-6 months) for Hepatitis-A and Rubella (3-4 months)

***Moral versions of Measles and Mumps are currently UNAVAILABLE as of January 2010 – TELL MERCK TO PROVIDE THEM!**

****NOTE: IMOVAX®Polio is a moral version for polio vaccine in Canada and is not the same as IMOVAX for rabies.**

ANY VACCINE NOT LISTED ABOVE DOES NOT USE ABORTED FETAL CELL LINES Copy Permissible with Credit Children of God for Life ©

VACCINE SAFETY

Introduction to Vaccine Safety Science & Policy in the United States



Published: October 2, 2017 (Version 1.0)

Address for correspondence: whitepaper@icandecide.org

This white paper provides an introduction to vaccine safety science and policy in the United States.

Section “I” discusses how Congress granted pharmaceutical companies immunity from liability for vaccine injuries and transferred all responsibility for vaccine safety to the United States Department of Health & Human Services (HHS) and its agencies, including the Food & Drug Administration (FDA), the Centers for Disease Control (CDC) and the National Institutes of Health (NIH).

Section “II” discusses how most pediatric vaccines were licensed based on inadequate clinical trials, including follow-up periods too brief to capture adverse outcomes, and illegitimate placebos (e.g., other vaccines).

Section “III” discusses the CDC’s deficient post-licensure vaccine safety surveillance.

Section “IV” discusses the conflicts of interest at HHS regarding vaccine safety, including the issues resulting from placing HHS in charge of vaccine safety and the conflicting duty of promoting and defending vaccines against any claim of injury.

Until a frank conversation is possible regarding vaccine safety, children susceptible to vaccine injury will not be protected from such injury. Nor will children injured by vaccines be able to access the services they need. We can do better in protecting and serving children who are susceptible or succumb to serious injuries from vaccination.

The first step in avoiding vaccine injuries and helping those already harmed is understanding the state of vaccine safety science and policy in America. This paper provides this understanding and highlights areas in need of improvement.

I. Who is responsible for vaccine safety?

Unlike nearly every other company in America, pharmaceutical companies have almost no liability for injuries caused by their vaccine products. How did this happen? As

explained by the Institute of Medicine (IOM)¹, by 1986, the “litigation costs associated with claims of damage from vaccines had forced several companies to end their vaccine

¹ In 2016, the IOM formally changed its name to the National Academies of Sciences, Engineering, and Medicine.

research and development programs as well as to stop producing already licensed vaccines.”² Instead of letting market forces compel vaccine makers to create safer vaccines, Congress granted pharmaceutical companies financial immunity from injuries caused by vaccines recommended by the CDC.³ Congress did so by passing the National Childhood Vaccine Injury Act (the **1986 Act**).⁴

By granting immunity from actual or potential liability from injuries caused by vaccines, Congress eliminated the market forces that are generally relied upon to assure the safety of all other products. As the 1986 Act expressly provides: “No person may bring a civil action ... against a vaccine administrator or manufacturer in a State or Federal court for damages arising from a vaccine-related injury or death.”⁵

The 1986 Act even shields vaccine makers from liability where it is clear and unmistakable that the vaccine in question could have been designed safer.⁶ As recently explained in a U.S. Supreme Court opinion:

[N]o one—neither the FDA nor any other federal agency, nor state and federal juries—ensures that vaccine manufacturers adequately take account of scientific and technological advancements. This concern is especially acute with respect to vaccines that have already been

*released and marketed to the public. Manufacturers ... will often have little or no incentive to improve the designs of vaccines that are already generating significant profit margins.*⁷

Recognizing that the 1986 Act eliminated the incentive for vaccine makers to assure the safety of their vaccine products, the 1986 Act explicitly places this responsibility in the hands of the United States Department of Health & Human Services (**HHS**).⁸

As provided in the 1986 Act, HHS is responsible for “research ... to prevent adverse reactions to vaccines,” “develop[ing] the techniques needed to produce safe ... vaccines,” “safety ... testing of vaccines,” “monitoring ... adverse effects of vaccines,” and “shall make or assure improvements in ... the licensing, manufacturing, processing, testing, labeling, warning, use instructions, distribution, storage, administration, field surveillance, adverse reaction reporting, ... and research on vaccines in order to reduce the risks of adverse reactions to vaccines.”⁹

Since passage of the 1986 Act, the number of required pediatric vaccines has grown rapidly. In 1983, the CDC’s childhood vaccine schedule included 11 injections of 4 vaccines.¹⁰ As of 2017, the CDC’s childhood vaccine schedule includes 56 injections of 30 different vaccines.¹¹

² <https://www.nap.edu/read/2138/chapter/2#2>

³ 42 U.S.C. § 300aa-1 et seq.

⁴ Ibid.

⁵ 42 U.S.C. § 300aa-11

⁶ *Bruesewitz v. Wyeth LLC*, 562 U.S. 223 (2011)

⁷ Ibid.

⁸ 42 U.S.C. § 300aa-2; 42 U.S.C. § 300aa-27

⁹ Ibid.

¹⁰ https://www.cdc.gov/vaccines/schedules/images/schedule_1983s.jpg

¹¹ https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adol_escent.html (note that the influenza vaccine is different every year)

CDC Childhood Immunization Schedule ¹²		
1986	2017	
DTP (2 months)	Influenza (pregnancy)	Influenza (18 months)
Polio (2 months)	TDaP (pregnancy)	Influenza (2 years)
DTP (4 months)	Hepatitis B (one day)	Influenza (3 years)
Polio (4 months)	Hepatitis B (one month)	Influenza (4 years)
DTP (6 months)	DTaP (2 months)	DTaP (4 years)
MMR (15 months)	Polio (2 months)	Polio (4 years)
DTP (18 months)	Hib (2 months)	MMR (4 years)
Polio (18 months)	PCV (2 months)	Varicella (4 years)
DTP (4 years)	Rotavirus (2 months)	Influenza (5 years)
Polio (4 years)	DTaP (4 months)	Influenza (6 years)
Tetanus (14 years)	Polio (4 months)	Influenza (7 years)
	Hib (4 months)	Influenza (8 years)
	PCV (4 months)	Influenza (9 years)
	Rotavirus (4 months)	Influenza (10 years)
	DTaP (6 months)	HPV (11 years)
	Polio (6 months)	Men (11 years)
	Hepatitis B (6 months)	TDaP (11 years)
	Hib (6 months)	Influenza (11 years)
	PCV (6 months)	HPV (11 ½ years)
	Rotavirus (6 months)	Influenza (12 years)
	Influenza (6 months)	HPV (12 years)
	MMR (12 months)	Influenza (13 years)
	Varicella (12 months)	Influenza (14 years)
	Hib (12 months)	Influenza (15 years)
	Hepatitis A (12 months)	Men (16 years)
	PCV (12 months)	Influenza (16 years)
	DTaP (15 months)	Influenza (17 years)
	Hepatitis A (18 months)	Influenza (18 years)

It is only when the CDC adds a vaccine to its recommended vaccine schedule that the manufacturer is granted immunity from

liability for vaccine injuries. And due to a federal funding scheme, CDC recommended vaccines are then made compulsory to American children under state laws and subsidized by the Federal government for children unable to afford the vaccine.¹³

The end result is that under the 1986 Act, every pediatric vaccine recommended by the CDC creates for its manufacturer a liability-free captive market of 78 million children with guaranteed payment. This incentive structure is unequal in the marketplace and eliminates the normal market forces driving product safety. Hence the 1986 Act transferred essentially all responsibility for vaccine safety from the pharmaceutical companies to HHS.

II. Pre-Licensure Vaccine Safety Review

HHS, through the FDA, licenses all vaccines used by the American public.

All non-vaccine drugs licensed by the FDA undergo long-term multi-year double-blind safety studies during which the rate of adverse reactions in the group receiving the drug under review is compared to the rate of adverse reactions in a group receiving an inert placebo, such as a sugar pill or saline injection.

For example: Enbrel’s pre-licensure trials followed subjects up to 80 months and

controls received a saline injection.¹⁴ Lipitor’s pre-licensure trials lasted a median of 4.8 years and controls received a sugar pill.¹⁵ Botox’s pre-licensure trials lasted a median of 51 weeks and controls received a saline injection.¹⁶ And even with these long-term studies, drugs are still often recalled.

While most drugs, like the ones above, are given to sick adults, pediatric vaccines are typically given universally to babies and toddlers. And while pharmaceutical companies remain liable for injuries caused by their

¹² The rapid growth of CDC’s vaccine schedule is expected to accelerate since there were 271 new vaccines under development in 2013 and far more currently under development. <http://www.phrma.org/press-release/medicines-in-development-vaccines> (listing 2,300 trials in search for “vaccines” between 2013 and 2017)

¹³ See Section IV below.

¹⁴ https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103795s5503lbl.pdf

¹⁵ https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020702s0561lbl.pdf

¹⁶ https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/103000s5302lbl.pdf

non-vaccine drugs, as discussed above, they have no liability for injuries caused by their vaccines. One would therefore expect that pre-licensure safety testing for vaccines would be more rigorous than that conducted for drugs.

Unfortunately, unlike all non-vaccine drugs licensed by the FDA, vaccines are *not* required to undergo long-term double-blind inert-placebo controlled trials to assess safety. In fact, not a single one of the clinical trials for vaccines given to babies and toddlers had a control group receiving an inert placebo. Further, most pediatric vaccines currently on the market have been approved based on studies with inadequate follow-up periods of only a few days or weeks.

For example, there are two Hepatitis B vaccines licensed for one day old babies in the United States – one manufactured by Merck and the other by GlaxoSmithKline. Merck’s Hepatitis B vaccine was licensed by the FDA after trials which solicited adverse reactions for *only five days* after vaccination.¹⁷ Similarly, GlaxoSmithKline’s Hepatitis B vaccine was licensed by the FDA after trials which solicited adverse reactions for *only four days* after vaccination.¹⁸

Follow-up periods of 4 or 5 days are not nearly long enough to detect possible adverse effects such as autoimmune or neurological disorders, seizures, or death. Worse is that since neither of these clinical trials used a control group, it was impossible to scientifically determine if any adverse

reaction in the limited four or five day safety review period was even caused by the Hepatitis B vaccine being evaluated.

Similarly, the HiB vaccines manufactured by Merck and GlaxoSmithKline were licensed by the FDA based on trials in which adverse reactions were monitored for only three days and four days, respectively, after vaccination.¹⁹ The only stand-alone polio vaccine in the United States was licensed after a mere 48-hour follow-up period.²⁰

Even more amazing is that unlike every drug licensed by the FDA, the control groups in these vaccine trials did not receive an inert placebo.²¹ Rather, the control group was given one or more previously licensed vaccines as the “placebo.”²² This means each new vaccine need only be roughly as safe as one (or in some cases numerous) previously licensed vaccines. Such flawed and unscientific study designs cannot establish the actual safety profile of any vaccine. The real adverse event rate for a vaccine can only be determined by comparing subjects receiving the vaccine with those receiving an inert placebo. Yet, this study design, required for every drug, is never required before or after licensing a vaccine.

It is unacceptable that the FDA licensing process for vaccines fails to assess the safety profile of each vaccine. It is also unacceptable that the FDA does not require the use of inert placebo controls to assure the integrity of even the minimal safety review conducted. As HHS’s own paid experts, the

¹⁷ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM110114.pdf>

¹⁸ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM224503.pdf>

¹⁹ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM253652.pdf>

<https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM179530.pdf>

²⁰ <https://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM133479.pdf>

²¹ Ibid. (prior two footnotes)

²² Ibid.

IOM, explains: “Because [vaccine] trials are primarily ... for determination of efficacy,

conclusions about vaccine safety derived from these trials are limited.”²³

III. Post-Licensure Surveillance of Vaccine Safety & the Known and Unknown Risks of Vaccination

HHS also fails to conduct proper post-licensure monitoring and studies of vaccine safety.

1. CDC Blocks Automation of Vaccine Adverse Events Reporting

The paucity of pre-licensure safety reviews for vaccines (see discussion above) leaves the assessment of adverse reactions to the post-licensing period when they are being administered to children in the “real world.”

In order to capture adverse events that may arise from vaccination in the “real world,” the 1986 Act established the Vaccine Adverse Events Reporting System (VAERS) operated by HHS and co-sponsored by the CDC and FDA.²⁴ VAERS is a passive, not mandatory, reporting system.²⁵ Anyone, including health care providers, on a voluntary basis, may report adverse vaccine reactions to VAERS.²⁶ HHS compiles these adverse reaction reports in VAERS and the CDC uses VAERS as a “safety signal detection and hypothesis generating system” to identify potential injuries caused by vaccines.²⁷

In 2016, VAERS received 59,117 reports of adverse reactions following vaccination including 432 deaths, 1,091 permanent disabilities, 4,132 hospitalizations, and 10,284 emergency room visits.²⁸

A problem with VAERS is that it is a passive reporting system, relying on voluntary, rather than mandatory, reporting.²⁹ As such, numerous reviews of VAERS have found that only a tiny fraction of vaccine adverse events are reported. For example, an HHS-funded review of vaccine adverse events over a three-year period by Harvard Medical School involving 715,000 patients found that “fewer than 1% of vaccine adverse events are reported.”³⁰ A U.S. House Report similarly stated: “Former FDA Commissioner David A. Kessler has estimated that VAERS reports currently represent only a fraction of the serious adverse events.”³¹

Assuming VAERS captures 1 percent of adverse events (which is more than is estimated), then the number of adverse events reported to VAERS in 2016 would reflect for that year 5,911,700 adverse events, 43,200 deaths, 109,100 permanent disabilities, 413,200 hospitalizations, and 1,028,400 emergency

²³ <https://www.nap.edu/read/13563/chapter/4>

²⁴ <https://wonder.cdc.gov/vaers.html>

²⁵ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

²⁶ Ibid.

²⁷ Ibid.

²⁸ <https://wonder.cdc.gov/vaers.html>

²⁹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

³⁰ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

³¹ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

room visits. If accurate, these figures are very troubling.

Of course, these figures are merely estimates. It would be far better if adverse events reports were automatically created and submitted to VAERS to avoid the issue of underreporting. Automated reporting would provide invaluable information that could clarify which vaccines might cause which harms and to whom, potentially allowing us to avoid these injuries and deaths.

The idea of automating adverse event reporting to VAERS is not new or even difficult to achieve.³² The Agency for Healthcare Research and Quality, an agency within HHS, sought to do exactly that in 2007 when it provided an approximately \$1 million grant to automate VAERS reporting at Harvard Pilgrim Health Care.³³ The result was the successful automation of adverse event reports at Harvard Pilgrim:

*Preliminary data were collected from June 2006 through October 2009 on 715,000 patients, and 1.4 million doses (of 45 different vaccines) were given to 376,452 individuals. Of these doses, 35,570 possible reactions ... were identified.*³⁴

These results should have been startling to HHS since they show that over only a three-year period, there were 35,570 reportable reactions in just 376,452 vaccine recipients. Given HHS's statutory mandate to assure safer vaccines, it should have rushed forward with automating VAERS reporting. However, this is not what happened.

³² <https://healthit.ahrq.gov/ahrq-funded-projects/electronic-support-public-health-vaccine-adverse-event-reporting-system>

³³ <https://healthit.ahrq.gov/sites/default/files/docs/publication/r18hs017045-lazarus-final-report-2011.pdf>

³⁴ Ibid.

After automating adverse event reports at Harvard Pilgrim, the developers of this system asked the CDC to take the final step of linking VAERS with the Harvard Pilgrim system so that these reports could be automatically transmitted into VAERS. Instead, the CDC refused to cooperate. As the Harvard grant recipients explained:

*Unfortunately, there was never an opportunity to perform system performance assessments because the necessary CDC contacts were no longer available and the CDC consultants responsible for receiving data were no longer responsive to our multiple requests to proceed with testing and evaluation.*³⁵

After three years and spending \$1 million of taxpayers' money, the CDC refused to even communicate with the HHS' Harvard Medical School grant recipients.

While HHS generally strongly supports automating public health surveillance systems, when it comes to vaccine safety, the CDC has only supported projects that would limit VAERS to passive surveillance.³⁶ Automation would improve safety and address many of the long-standing issues and limitations raised by CDC regarding VAERS.³⁷

Capturing "fewer than 1% of vaccine adverse events" thirty years after the passage of the 1986 Act is unacceptable – and potentially deadly.

³⁵ Ibid.

³⁶ [http://www.ajpmonline.org/article/S0749-3797\(12\)00249-8/pdf](http://www.ajpmonline.org/article/S0749-3797(12)00249-8/pdf); <https://www.ncbi.nlm.nih.gov/pubmed/26209838>; <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632204/>

³⁷ Ibid.

2. CDC Ignores IOM's Calls to Identify Injuries Caused by Vaccines

The IOM was formed in 1863 by congressional charter, to “provide expert advice on some of the most pressing challenges facing the nation and the world.”³⁸ The IOM further claims its “members are among the world's most distinguished scientists, engineers, physicians, and researchers; more than 300 members are Nobel laureates.”³⁹

Under the 1986 Act, the IOM was charged with issuing reports on injuries from vaccination. In 1991, the IOM examined 22 commonly reported serious injuries following the DTP vaccine.⁴⁰ The IOM concluded the scientific literature supported a causal relationship between the DTP vaccine and 6 of these injuries: acute encephalopathy, chronic arthritis, acute arthritis, shock and unusual shock-like state, anaphylaxis, and protracted inconsolable crying.⁴¹

While this picture was troubling enough, equally concerning was that the IOM found that the scientific literature was insufficient to conclude whether or not the DTP vaccine can cause 12 other serious injuries commonly reported from this vaccine:

Aseptic meningitis (serious inflammation of the brain); Chronic neurologic damage; Learning disabilities and attention-deficit disorder; Hemolytic anemia; Juvenile diabetes; Guillain-Barre syndrome;

*Erythema multiforme; Autism; Peripheral mononeuropathy (nerve damage); Radiculoneuritis and other neuropathies; Thrombocytopenia; Thrombocytopenic purpura*⁴²

These commonly reported serious injuries *could* be caused by this vaccine – the IOM just couldn't determine one way or another due to a lack of science.

The IOM lamented that it “encountered many gaps and limitations in knowledge bearing directly and indirectly on the safety of vaccines.”⁴³ The IOM also remarked on the poor design of the few vaccine studies that had been conducted, stating these “studies are too small or have inadequate length of follow-up to have a reasonable chance of detecting true adverse reactions.”⁴⁴ Moreover, the IOM reported that “existing surveillance systems of vaccine injury have limited capacity to provide persuasive evidence of causation.”⁴⁵

The IOM thus cautioned in its 1991 report that: “If research capacity and accomplishment in this field are not improved, future reviews of vaccine safety will be similarly handicapped.”⁴⁶

As charged under the 1986 Act, the IOM issued another report in 1994 entitled *Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causation*.⁴⁷ This second IOM Report examined the scientific literature for evidence that could either prove or disprove a causal link between 54

³⁸ <http://www.national-academies.org/about/whoweare/index.html>

³⁹ Ibid.

⁴⁰ <https://www.nap.edu/read/1815/chapter/2#7>

⁴¹ Ibid.

⁴² Ibid.

⁴³ <https://www.nap.edu/read/1815/chapter/2#8>

⁴⁴ <https://www.nap.edu/read/1815/chapter/9>

⁴⁵ Ibid.

⁴⁶ Ibid.

⁴⁷ <https://www.nap.edu/read/2138/chapter/1>

commonly reported serious injuries and vaccination for diphtheria, tetanus, measles, mumps, polio, hepatitis B, and Hib.⁴⁸

For this Report, the IOM located sufficient science to support a causal connection between these vaccines and 12 injuries, including death, anaphylaxis, thrombocytopenia, and Guillain-Barre syndrome.⁴⁹

Again, as with the IOM Report from 1991, for “the majority of vaccine-adverse event pairs the evidence was considered inadequate to accept or reject causality.”⁵⁰ The problem that basic scientific studies had not been done continued to persist. The IOM could not determine whether there was a causal connection between vaccination and 38 of the most common serious injuries parents reported their children experienced following these vaccines, including:

*Demyelinating diseases of the central nervous system, Sterility, Arthritis, Neuropathy, Residual seizure disorder, Transverse myelitis, Sensorineural deafness, Optic neuritis, Aseptic meningitis, Insulin-dependent diabetes mellitus, SIDS*⁵¹

This means that of the 54 vaccine-injury pairs studied, there was sufficient science to find a causal relationship of harm for 12, and to reject a relationship for 4.⁵² But for the remaining 38, there was insufficient science to reach any conclusion.⁵³

As in 1991, this IOM Report from 1994 again stated: “The lack of adequate data regarding many of the adverse events under study was of major concern to the committee. Presentations at public meeting indicated that many parents and physicians share this concern.”⁵⁴

Another acute concern raised by the IOM in 1994 was the potential risks posed by combining vaccines. The IOM noted that this subject simply had not been studied: “The committee was able to identify little information pertaining to the risk of serious adverse events following administration of multiple vaccines simultaneously. This is an issue of increasing concern as more vaccines and vaccine combinations are developed for routine use.”⁵⁵

In 2011, HHS paid the IOM to conduct another assessment regarding vaccine safety.⁵⁶ This Report, entitled *Adverse Effects of Vaccines: Evidence and Causality*, was the culmination of the largest review by the IOM regarding vaccine safety since the IOM’s reports from 1991 and 1994.⁵⁷

This third IOM Report reviewed the 158 most common vaccine injuries claimed to have occurred from vaccination for varicella, hepatitis B, tetanus, measles, mumps, and/or rubella.⁵⁸ The IOM located science which “convincingly supports a causal relationship” for 14 of these serious injuries, including pneumonia, meningitis, hepatitis, MIBE (deadly brain inflammation a year after vaccination), febrile seizures, and

⁴⁸ <https://www.nap.edu/read/2138/chapter/2#12>

⁴⁹ <https://www.nap.edu/read/2138/chapter/2#12>

⁵⁰ <https://www.nap.edu/read/2138/chapter/1#vi>

⁵¹ <https://www.nap.edu/read/2138/chapter/2#12>

⁵² Ibid.

⁵³ Ibid.

⁵⁴ <https://www.nap.edu/read/2138/chapter/12>

⁵⁵ <https://www.nap.edu/read/2138/chapter/12#307>

⁵⁶ <https://www.nap.edu/read/13164/chapter/2#2>

⁵⁷ Ibid.

⁵⁸ Ibid.

anaphylaxis.⁵⁹ The review found sufficient evidence to support “acceptance of a causal relationship” for 4 additional serious injuries.⁶⁰

The IOM, however, found the scientific literature was insufficient to conclude whether or not those vaccines caused 135 other serious injuries commonly reported after their administration, including:

Encephalitis (brain inflammation), Encephalopathy (gradual degeneration of brain function, including memory, cognitive ability, concentration, lethargy, and eventually consciousness), Infantile Spasms, Afebrile Seizures, Seizures, Cerebellar Ataxia (inflammation of and/or damage to the cerebellum), Ataxia (the loss of full control of bodily movements), Acute Disseminated Encephalomyelitis (brief but widespread attack of inflammation in the brain and spinal cord that damages myelin – the protective covering of nerve fibers), Transverse Myelitis (neurological disorder caused by inflammation across both sides of one level, or segment, of the spinal cord that typically results in permanent impairments), Optic Neuritis (inflammation of the optic nerve and symptoms are usually unilateral, with eye pain and partial or complete vision loss), Neuromyelitis Optica (body’s immune system over time repeatedly mistakenly attacks healthy cells and proteins in the body, most often those in the spinal cord and eyes resulting in permanent disability), Multiple Sclerosis, Guillain-Barre Syndrome (body’s immune system attacks part of the peripheral nervous system), Chronic Inflammatory

Demyelinating Polyneuropathy (auto-immune inflammatory disorder of the peripheral nervous system resulting in loss of nerve axons), Brachial Neuritis (auto-immune reaction against nerve fibers of the brachial plexus), Amyotrophic Lateral Sclerosis (rapidly progressive, invariably fatal neurological disease that attacks the nerve cells responsible for controlling voluntary muscles), Small Fiber Neuropathy (damage to the small unmyelinated peripheral nerve fibers), Chronic Urticaria (chronic hives), Erythema Nodosum (skin inflammation in the fatty layer of skin), Systemic Lupus Erythematosus (autoimmune disease in which the body’s immune system mistakenly attacks healthy tissue), Polyarteritis Nodosa (inflammation resulting in injury to organ systems), Psoriatic Arthritis, Reactive Arthritis, Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, Arthralgia (joint pain), Autoimmune Hepatitis, Stroke, Chronic Headache, Fibromyalgia, Sudden Infant Death Syndrome, Hearing Loss, Thrombocytopenia, Immune Thrombocytopenic Purpura⁶¹

Thus, out of the 158 most common serious injuries reported to have been caused by the vaccines under review, the evidence “convincingly supports a causal relationship” for 14, “favors acceptance of a causal relationship” for 4, and “favors rejection of a causal relationship” for only 5 of them.⁶² For the remaining 135 vaccine-injury pairs, over 86 percent of those reviewed, the IOM found

⁵⁹ <https://www.nap.edu/read/13164/chapter/2#3>

⁶⁰ Ibid.

⁶¹ Ibid.

⁶² Ibid.

that the science simply had not been performed.⁶³

3. CDC Ignores IOM's Calls to Identify Children Susceptible to Vaccine Injury

Compounding the lack of adequate science to simply ascertain whether the most commonly reported serious adverse reactions following vaccination are caused by vaccines, the IOM Reports discussed above have consistently acknowledged there is individual susceptibility to serious vaccine injuries.

The IOM has also acknowledged that research on such susceptibility must be done on an individual basis, considering a child's personal genome, behaviors, microbiome, intercurrent illness, and present and past environmental exposure.⁶⁴ Unfortunately, HHS has not conducted this research.

In 1994, the IOM, building on concerns raised in its 1991 Report, stated: "The committee was able to identify little information pertaining to why some individuals react adversely to vaccines when most do not."⁶⁵ The IOM urged that "research should be encouraged to elucidate the factors that put certain people at risk."⁶⁶

Yet, seventeen years later, in 2011, the IOM acknowledged this research had still not been done:

Both epidemiologic and mechanistic research suggest that most individuals who experience an adverse reaction to vaccines

have a preexisting susceptibility. These predispositions can exist for a number of reasons—genetic variants (in human or microbiome DNA), environmental exposures, behaviors, intervening illness, or developmental stage, to name just a few—all of which can interact as suggested graphically in Figure 3-1.

Some of these adverse reactions are specific to the particular vaccine, while others may not be. Some of these predispositions may be detectable prior to the administration of vaccine. ... [M]uch work remains to be done to elucidate and to develop strategies to document the immunologic mechanisms that lead to adverse effects in individual patients.

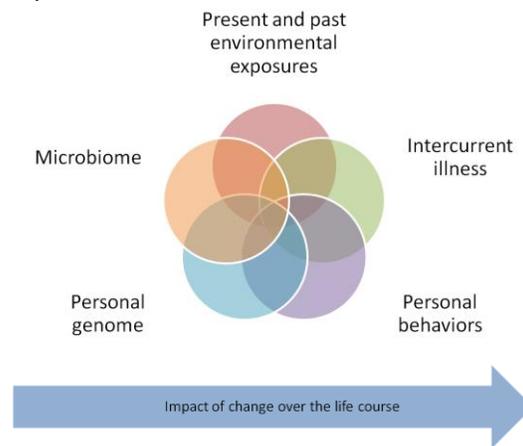


FIGURE 3-1 Present and past environmental exposures.⁶⁷

In 2013, HHS commissioned the IOM to review the safety of the entire vaccine schedule.⁶⁸ The IOM again explained that while "most children who experience an adverse reaction to immunization have preexisting susceptibility," the IOM:

⁶³ Ibid.

⁶⁴ <https://www.nap.edu/read/13164/chapter/5#82>

⁶⁵ <https://www.nap.edu/read/2138/chapter/12#307>. See also <https://www.nap.edu/read/1815/chapter/9>

⁶⁶ Ibid.

⁶⁷ <https://www.nap.edu/read/13164/chapter/5#82>

⁶⁸ <https://www.nap.edu/read/13563/chapter/1>

*found that evidence assessing outcomes in sub populations of children who may be potentially susceptible to adverse reactions to vaccines (such as children with a family history of autoimmune disease or allergies or children born prematurely) was limited and is characterized by uncertainty about the definition of populations of interest and definitions of exposures and outcomes.*⁶⁹

HHS had failed to even define the terminology for the study of susceptible subpopulations; hence IOM admonished HHS to “develop a framework that clarifies and standardizes definitions of ... populations that are potentially susceptible to adverse events.”⁷⁰ While every vaccine brand is the same, it is plain that every child is different.

The IOM correctly points out in 2011 that given the “widespread use of vaccines” and “state mandates requiring vaccination of children ... it is essential that safety concerns receive assiduous attention.”⁷¹ This is the same call for diligent attention that the IOM made in 1991 and 1994. Unfortunately, all of these calls for action have gone unheeded. The critical scientific inquiry to identify individuals susceptible to serious vaccine injury has simply never commenced.

Since the IOM’s first call for this science in 1991, HHS has spent tens of billions promoting and purchasing vaccines, and

vaccine makers have accumulated hundreds of billions in vaccine revenue.⁷² Yet, during this time, no material funds have been allocated to identify susceptible subpopulations, let alone what injuries are caused by vaccines.⁷³

4. CDC Views Vaccine Safety as a Public Relations Issue

The CDC, unfortunately, has treated vaccine safety as a public relations issue rather than a public health imperative. For example, the CDC claims on its website that “Vaccines Do Not Cause Autism” even though this broad claim is plainly not supported by the scientific literature.⁷⁴

Indeed, as part of the IOM’s 2011 review of vaccine safety, it was asked by HHS whether there is a causal relationship between autism and the DTaP vaccine administered to children at two, four, six, and fifteen months of age.⁷⁵ The IOM could not locate a single study supporting that DTaP does not cause autism.⁷⁶ The IOM therefore concluded: “The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid–, tetanus toxoid–, or acellular pertussis–containing vaccine and autism.”⁷⁷ The IOM’s full explanation for this finding is as follows:

⁶⁹ <https://www.nap.edu/read/13563/chapter/9#130>

⁷⁰ Ibid.

⁷¹ <https://www.nap.edu/read/13164/chapter/3#28>

⁷² <https://www.hhs.gov/about/budget/index.html#previous>; <https://www.statista.com/statistics/265102/revenues-in-the-global-vaccine-market/>; <https://www.ft.com/content/93374f4a-e538-11e5-a09b-1f8b0d268c39>

⁷³ For example, while in 2016 vaccine makers reported over \$33 billion from vaccine sales and the CDC reported spending over

\$5 billion promoting and purchasing vaccines (Ibid.), the CDC Immunization Safety Office’s budget is apparently only around \$20 million. [http://www.ajpmonline.org/article/S0749-3797\(15\)00314-1/pdf](http://www.ajpmonline.org/article/S0749-3797(15)00314-1/pdf)

⁷⁴ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁷⁵ <https://www.nap.edu/read/13164/chapter/2#2>

⁷⁶ <https://www.nap.edu/read/13164/chapter/12#545>

⁷⁷ Ibid.

AUTISM

Epidemiologic Evidence

The committee reviewed one study to evaluate the risk of autism after the administration of DTaP vaccine. This one study (Geier and Geier, 2004) was not considered in the weight of epidemiologic evidence because it provided data from a passive surveillance system and lacked an unvaccinated comparison population.

Weight of Epidemiologic Evidence

The epidemiologic evidence is insufficient or absent to assess an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.

Mechanistic Evidence

The committee did not identify literature reporting clinical, diagnostic, or experimental evidence of autism after the administration of vaccines containing diphtheria toxoid, tetanus toxoid, and acellular pertussis antigens alone or in combination.

Weight of Mechanistic Evidence

The committee assesses the mechanistic evidence regarding an association between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism as lacking.

Causality Conclusion

Conclusion 10.6: The evidence is inadequate to accept or reject a causal relationship between diphtheria toxoid-, tetanus toxoid-, or acellular pertussis-containing vaccine and autism.⁷⁸

It is troubling that the only study the IOM could locate regarding whether DTaP causes autism, (Geier and Geier, 2004), concluded there *was* an association between DTaP and autism.⁷⁹ No research has been published since 2011 that could change the IOM's conclusion. Based on the foregoing, the CDC cannot validly make the blanket assertion that "Vaccines Do Not Cause Autism."

As with DTaP, there are also no published studies showing that autism is not caused by Hepatitis B, Rotavirus, Hib, Pneumococcal, Inactivated Poliovirus, Influenza, Varicella, or Hepatitis A vaccines – all of which HHS recommends babies receive by one year of age.⁸⁰

Instead, HHS's claim that "Vaccines Do Not Cause Autism" relies almost entirely upon studies exclusively studying only one vaccine, MMR (which is administered no earlier than one year of age), or only one vaccine ingredient, thimerosal, with regard to autism.⁸¹ Putting aside the controversy surrounding these studies, studies which focus on only one vaccine and one ingredient while ignoring the entire balance of the CDC's pediatric vaccine schedule cannot support the

⁷⁸ Ibid.

⁷⁹ Ibid. Ironically, this study was disregarded "because it provided data from a passive surveillance system [VAERS] and lacked an unvaccinated comparison population," which would be true of any study using VAERS data.

⁸⁰ <https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html>

⁸¹ <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

CDC's overarching declaration that "Vaccines Do Not Cause Autism."

As for the MMR vaccine, the CDC's senior scientist for its seminal MMR-autism study has recently revealed that the CDC concealed an association between MMR and autism. Dr. William Thompson has been a scientist at CDC for nearly two decades and is the CDC's Senior Scientist on dozens of the CDC's peer-reviewed publications, including the core group of the CDC's vaccine-autism safety studies.⁸²

Dr. Thompson recently provided a statement through his attorney that the CDC "omitted statistically significant information" showing an association between the MMR vaccine and autism in the first and only MMR-autism study ever conducted by the CDC with American children.⁸³

Dr. Thompson, in a recorded phone call in 2014, described how the CDC concealed a finding indicating that healthy children who received the MMR vaccine may be eight times more likely to develop autism than those without the vaccine.⁸⁴ He stated: "Oh my God, I can't believe we did what we did. But we did. It's all there. It's all there. I have handwritten notes."⁸⁵ Dr. Thompson stated that "If I were forced to testify or something like that, I'm not gonna lie ... I basically have stopped lying."⁸⁶ Expressing contrition for concealing the MMR-autism association, Dr. Thompson stated:

I have great shame now when I meet families with kids with autism because I

*have been part of the problem ... the CDC is so paralyzed right now by anything related to autism. They're not doing what they should be doing because they're afraid to look for things that might be associated. So anyway there's still a lot of shame with that. ... I am completely ashamed of what I did.*⁸⁷

Dr. Thompson also provided the following statement explaining the CDC's concealment of the autism-MMR association with regard to African-American males:

My primary job duties while working in the immunization safety branch from 2000 to 2006, were to later co-lead three major vaccine safety studies. ... We hypothesized that if we found statistically significant effects at either 18 or 36 month thresholds, we would conclude that vaccinating children early with MMR vaccine could lead to autism-like characteristics or features. We all met and finalized the study protocol and analysis plan ... [and after implementing this plan we found] the adjusted race effect statistical significance was huge.

All the authors and I [therefore] met and decided ... to exclude reporting any race effects. The co-authors scheduled a meeting to destroy documents related to the study. The remaining four co-authors all met and brought a big garbage can into the meeting room, and reviewed and went through all the hardcopy documents that we had thought we should discard, and put them into a huge garbage can. However,

⁸² <https://www.ncbi.nlm.nih.gov/pubmed/?term=Thompson+WW%5BAuthor%5D>

⁸³ <http://www.rescuepost.com/files/william-thompson-statement-27-august-2014-3.pdf>

⁸⁴ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

⁸⁵ Ibid.

⁸⁶ Ibid.

⁸⁷ Ibid.

*because I assumed it was illegal and would violate both FOIA and DOJ requests, I kept hardcopies of all documents in my office, and I retain all associated computer files. I believe we intentionally withheld controversial findings from the final draft of the Pediatrics paper.*⁸⁸

Hence, for the only vaccine (MMR) actually studied by the CDC with regard to autism, it appears the CDC concealed an association between that vaccine and autism.

When the former Director of the National Institutes of Health, Dr. Bernadine Healy, was asked about whether public health authorities are correct to claim that vaccines do not cause autism, she answered: “You can’t say that.”⁸⁹ When asked again, Dr. Healy explained: “The more you delve into it – if you look at the basic science – if you look at the research that’s been done, in animals – if you also look at some of these individual cases – and, if you look at the evidence that there is no link - what I come away with is: *The question has not been answered.*”⁹⁰

Former NIH Director Dr. Healy goes on to explain:

This is the time when we do have the opportunity to understand whether or not there are susceptible children, perhaps genetically, perhaps they have a metabolic issue, mitochondrial disorder, immunological issue, that makes them more susceptible to vaccines plural, or to one particular vaccine, or to a component of vaccine. ... A susceptible group does not

mean that vaccines are not good. What a susceptible group will tell us is that maybe there is a group of individuals, or a group of children, that shouldn’t have a particular vaccine or shouldn’t have vaccine on the same schedule. ...

I think the government, or certain health officials in the government, are - have been too quick to dismiss the concerns of these families without studying the population that got sick. I haven’t seen major studies that focus on - three hundred kids, who got autistic symptoms within a period of a few weeks of a vaccine.

I think that the public health officials have been too quick to dismiss the hypothesis as irrational, without sufficient studies of causation. I think that they often have been too quick to dismiss studies in the animal laboratory, either in mice, in primates, that do show some concerns with regard to certain vaccines. ...

*The reason why they didn’t want to look for those susceptibility groups was because they’re afraid if they found them – however big or small they were – that that would scare the public away. First of all, I think the public’s smarter than that; the public values vaccines. But, more importantly, I don’t think you should ever turn your back on any scientific hypothesis because you’re afraid of what it might show!*⁹¹

The CDC’s claim that “Vaccines Do Not Cause Autism” also fails to address the

⁸⁸ <https://www.c-span.org/video/?c4546453/senator-posey-calls-investigation-cdc-fraud>

⁸⁹ <http://www.cbsnews.com/news/the-open-question-on-vaccines-and-autism/>

⁹⁰ Ibid.

⁹¹ Ibid.

science supporting a link between vaccines and autism.⁹² For example, the CDC has not addressed a study which found a 300% increased rate of autism among newborns receiving the hepatitis B vaccine at birth compared to those that did not.⁹³ Nor a recent and first ever vaccinated vs. unvaccinated pilot study which found vaccinated children had a 420% increased rate of autism and that vaccinated preterm babies had an even higher rate of autism.⁹⁴ There is also a persuasive body of science supporting a connection between aluminum adjuvants in vaccines and autism which the CDC has, despite request, failed to directly or persuasively address.⁹⁵

The CDC also failed to address the fact that a review of vaccine injuries compensated by HHS, through the vaccine injury compensation program established by the 1986 Act, “found eighty-three cases of autism among those compensated for vaccine-induced brain damage.”⁹⁶

The CDC ignores all the foregoing and continues to rely on its prior MMR-autism studies which, even putting aside Dr. Thompson’s claims of concealment, are not applicable to any of the 25 doses of seven vaccines the CDC advised doctors to inject into babies during the first year of life.⁹⁷

The critical need for the CDC to properly engage in vaccine safety science regarding autism is made even more vital by the fact that vaccine makers are immune from liability for vaccine injury and vaccines are not

safety-tested prior to licensure to assess whether they cause autism. Without proper *long-term* safety studies comparing those receiving the vaccine to a true placebo group, it is impossible to know prior to licensure whether these products cause autism. There are also no follow-up studies which compare vaccinated to unvaccinated individuals and hence no supportable basis to claim that vaccines do not cause any cases of autism. For the CDC to make this claim, it must demonstrate that a child receiving the entire vaccine schedule is at no greater risk of becoming autistic than a child that is unvaccinated. No such study has ever been done.

The IOM Report referenced above has confirmed that the CDC cannot make this claim even for children receiving only the DTaP, let alone the entire vaccine schedule. It is thus plain that the CDC cannot validly claim that “Vaccines Do Not Cause Autism.” The truth is, the CDC, at best, does not know.

5. CDC & IOM Ignore Massive Body of Science Supporting Vaccine Injuries

While the 2011 IOM Report has 75 pages of citations to peer-reviewed sources, there are far more peer-reviewed articles documenting vaccine injuries apparently not even considered by the 2011 IOM Report. Resources for references to these citations can be provided upon request.

⁹² <https://www.cdc.gov/vaccinesafety/concerns/autism.html>

⁹³ http://hisunim.org.il/images/documents/scientific_literature/Gallagher_Goodman_HepB_2010.pdf

⁹⁴ http://www.cmsri.org/wp-content/uploads/2017/05/Mawson_StudyHealthOutcomes5.8.2017.pdf

⁹⁵ http://vaccine-safety.s3.amazonaws.com/WhitePaper-Alum_AdjuvantAutism.pdf

⁹⁶ <http://digitalcommons.pace.edu/cgi/viewcontent.cgi?article=1681&context=pehr>

⁹⁷ Further, studies of MMR and autism are simply erroneous because of healthy user bias, which has been emphasized as a serious source of error in epidemiological vaccine safety studies by the CDC’s own scientists. <https://www.ncbi.nlm.nih.gov/pubmed/1415136>

A major theme among these peer-reviewed vaccine papers is the connection between vaccination and chronic disease, mainly autoimmunity and immune mediated neurological disorders and injuries. As detailed above, in the last 30 years, the CDC's childhood vaccine schedule has rapidly increased from 11 injections of 4 vaccines in 1986 to 56 injections of 30 vaccines in 2017. This upsurge has occurred in lock step with the precipitous increase in childhood chronic illness and developmental disabilities which have, during this same period, risen among American children from 12.8% to 54%.⁹⁸

Many of the same disorders that have sharply risen during this period, including neurological and autoimmune disorders, are associated with vaccination as reflected in VAERS⁹⁹, manufacturer inserts for vaccines¹⁰⁰, and claims in the Vaccine Injury Compensation Program¹⁰¹.

The causal mechanisms of these disorders are increasingly understood, and increasingly implicate vaccine exposure during early development.¹⁰² For example, it is now known that early life immune activation can cause autism, mental illnesses, and immune disorders.¹⁰³ Vaccines and vaccine adjuvants (particularly in cases of adverse reactions) can cause the types of immune activation known to cause these disorders later in life.¹⁰⁴ Accordingly, there is an urgent and long-overdue need for higher quality vaccine safety research looking at long term neurological and immune outcomes.

Nonetheless, the 2011 IOM Report makes it clear that little has been ruled out with regard to what injures are caused by vaccines. In 2013, the IOM was again engaged by HHS to review the safety of the entire vaccine schedule on a population level.¹⁰⁵ The "committee's literature searches and review were intended to identify health outcomes associated with some aspect of the childhood immunization schedule."¹⁰⁶ "Allergy and asthma, autoimmunity, autism, other neurodevelopmental disorders (e.g., learning disabilities, tics, behavioral disorders, and intellectual disability), seizures, and epilepsy were included as search terms."¹⁰⁷

Instead of answers, the IOM found that no studies had been conducted to validly assess the safety of the entire vaccine schedule or even portions of the vaccine schedule:

[F]ew studies have comprehensively assessed the association between the entire immunization schedule or variations in the overall schedule and categories of health outcomes, and no study ... compared the differences in health outcomes ... between entirely unimmunized populations of children and fully immunized children. Experts who addressed the committee pointed not to a body of evidence that had been overlooked but rather to the fact that existing research has not been designed to test the entire immunization schedule. ...

⁹⁸ <https://www.ncbi.nlm.nih.gov/pubmed/20159870>

⁹⁹ <https://wonder.cdc.gov/vaers.html>

¹⁰⁰ <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm>; See also Section III(7) below.

¹⁰¹ <http://www.usfc.uscourts.gov/aggregator/sources/7>; See also Section IV(4) below.

¹⁰² <https://www.ncbi.nlm.nih.gov/pubmed/27540164>

¹⁰³ <https://www.ncbi.nlm.nih.gov/pubmed/25311587>

¹⁰⁴ <https://www.ncbi.nlm.nih.gov/pubmed/26531688>;

<https://www.ncbi.nlm.nih.gov/pubmed/27908630>

¹⁰⁵ <https://www.nap.edu/read/13563/chapter/1>

¹⁰⁶ <https://www.nap.edu/read/13563/chapter/2#5>

¹⁰⁷ Ibid.

*[Also,] studies designed to examine the long-term effects of the cumulative number of vaccines or other aspects of the immunization schedule have not been conducted.*¹⁰⁸

While most of the 78 million children in America follow the CDC's childhood vaccine schedule, currently at 56 injections, no science has been done to confirm the safety of this schedule.¹⁰⁹ Even more alarming is that the IOM acknowledges that science does not yet even know "if there is a relationship between short-term adverse events following vaccination and long-term health issues."¹¹⁰

Due to the lack of science regarding the safety of the CDC vaccine schedule, the best the IOM could do was conclude: "There is no evidence that the schedule is not safe."¹¹¹ Left unsaid, but equally true: There is no evidence that the schedule is safe.

6. CDC Refuses to Conduct Vaccinated vs. Unvaccinated Study

The best and most efficient way to answer a large portion of the questions raised regarding vaccine safety would be a long-term, properly powered (*i.e.*, sized) study comparing the overall health outcomes of vaccinated and completely unvaccinated children. Parents and safety advocacy groups

have been demanding for decades that HHS perform such a study. Even the CDC's internal vaccine committee recognizes that assessing "adverse events require more detailed epidemiologic studies to compare the incidence of the event among vaccinees to the incidence among unvaccinated persons."¹¹²

HHS has nonetheless consistently refused to study health outcomes of the completely unvaccinated. There have been, however, small-scale studies performed outside of HHS comparing vaccinated with completely unvaccinated children. And these smaller studies have consistently reported that the unvaccinated have much better health outcomes.

Dr. Peter Aaby is renowned for studying and promoting vaccines in Africa with over 300 published studies.¹¹³ In 2017, he published a study finding children vaccinated with DTP were 10 times more likely to die in the first 6 months of life than the unvaccinated.¹¹⁴ Dr. Aaby's study therefore concluded that: "All currently available evidence suggests that DTP vaccine may kill more children from other causes than it saves from diphtheria, tetanus or pertussis."¹¹⁵ More disturbing is that children vaccinated with DTP were dying from causes never associated with this vaccine, such as respiratory infections, diarrhea, and malaria.¹¹⁶ This indicated that while DTP

increasingly recognized problem in vaccine safety studies is that subjects are typically not well-matched. People with pre-existing health problems are reluctant to receive a vaccine, and are therefore unwittingly used as controls. When this happens, the control group is sicker than the vaccine-exposed group at the outset of the study. Studies with this problem give wrong results, and make the vaccine look much safer than it really is. Dr. Aaby's study was one of the few specifically designed to avoid this error.

¹⁰⁸ Ibid.

¹⁰⁹ Ibid.

¹¹⁰ <https://www.nap.edu/read/13563/chapter/5#45>

¹¹¹ <https://www.nap.edu/read/13563/chapter/2#12>

¹¹² <https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6002a1.htm>

¹¹³ <https://www.ncbi.nlm.nih.gov/pubmed/?term=PETER+AABY%5BAuthor+-+Full%5D>

¹¹⁴ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360569/>

Dr. Aaby's study was more reliable than other vaccine safety studies because the subjects were accurately matched. An

¹¹⁵ Ibid.

¹¹⁶ Ibid.

reduced the incidence of diphtheria, tetanus, and pertussis, it increased susceptibility to other infections.¹¹⁷

It is equally troubling that Dr. Aaby's study was based on data that had been collecting dust for over 30 years.¹¹⁸ This begs the question: what other serious vaccine injuries are we missing because of neglect to conduct proper vaccine safety science?

A pilot study comparing 650 vaccinated and unvaccinated homeschooled children in the United States provides a glimpse of the potential scope of vaccine harm.¹¹⁹ The study found that, compared to completely-unvaccinated children, fully-vaccinated children had an increased risk of 390% for allergies, 420% for ADHD, 420% for autism, 290% for eczema, 520% for learning disabilities, and 370% for any neuro-developmental delay.¹²⁰ Fully-vaccinated pre-term infants had an increased risk of 1,450% for a neurodevelopmental disorder, which includes a learning disability, ADHD or autism, compared to completely unvaccinated preterm infants.¹²¹

Another recent study compared children receiving the flu shot with those receiving a saline injection in a prospective randomized double-blind study.¹²² Both groups had the same rate of influenza but the group receiving the flu shot had a 440% increased rate of non-influenza infection.¹²³

Like the DTP study, the flu vaccine increased susceptibility to other infections.

As a final example, the CDC in 2001 unwittingly conducted a narrow vaccinated versus unvaccinated study comparing children receiving the Hepatitis B vaccine during the first month of life versus those who did not.¹²⁴ The results of this study were never released by the CDC, and an abstract of the study was only recently obtained under a FOIA request.¹²⁵ Children vaccinated with Hepatitis B vaccine in the first month of life, compared to children receiving no vaccines in the first month of life, had an increased risk of 829% for ADHD, 762% for autism, 638% for ADD, 565% for tics, 498% for sleep disorders, and 206% for speech delays.¹²⁶

The foregoing limited studies should have raised alarm bells at the CDC regarding the urgency of a proper vaccinated versus unvaccinated study that stakeholders have been demanding the CDC perform for over 20 years. The IOM has even confirmed such a study can be conducted using the CDC's VSD, a database of health records for almost ten million individuals maintained by the CDC.¹²⁷ As explained by the IOM: "It is possible to make this comparison [between vaccinated and unvaccinated children] through analyses of patient information contained in large databases such as VSD."¹²⁸ Such a retrospective epidemiological study would be quick, cheap and efficient; CDC could literally

¹¹⁷ Ibid.

¹¹⁸ Ibid.

¹¹⁹ <http://www.oatext.com/pdf/JTS-3-186.pdf>

¹²⁰ Ibid.

¹²¹ <http://www.oatext.com/pdf/JTS-3-187.pdf>

¹²² <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3404712/>

¹²³ Ibid.

¹²⁴ http://vaccine-safety.s3.amazonaws.com/CDC_FOIA_Response_UnpublishedStudy.pdf The CDC's study abstract discusses comparing thimerosal exposure by one month of age.

Since the only vaccine recommended by one month of age was Hepatitis B, and since only thimerosal containing Hepatitis B vaccine was available at the time of this study, this study primarily compared children receiving Hepatitis B with children that did not receive this vaccine.

¹²⁵ Ibid.

¹²⁶ Ibid.

¹²⁷ <https://www.nap.edu/read/13563/chapter/2#13>

¹²⁸ Ibid.

conduct this study using the VSD in a matter of minutes. Yet it has never, as far as the public knows, been done.¹²⁹

Every year tens of millions of American children are compelled to receive pediatric vaccines. Yet a large-scale study with completely-unvaccinated controls has never been performed to assess the long-term safety of the CDC's recommended vaccine schedule.¹³⁰ When vaccine makers are generating over \$33 billion in vaccine revenue annually and the CDC is spending over \$5 billion annually to promote and purchase vaccines, there is no justification for not performing this study.¹³¹

7. CDC Ignores Vaccine Manufacturer Disclosures of Potential Adverse Reactions

Vaccine makers are required by law to report to the FDA complaints they receive from consumers of serious adverse reactions from their vaccines.¹³² A partial list of these serious adverse reactions is detailed below. While studies have been conducted for a few of these to confirm whether they are in fact caused by vaccines, the CDC has failed to conduct such studies for most of them.

¹²⁹ The CDC's inaction does not appear to be mere neglect since CDC Senior Scientist, Dr. Thompson, recently stated that a proper large scale vaccine safety study "needs to be done" but that the CDC is "not doing what they should be doing because they're afraid to look for things that might be associated." <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio> Dr. Thompson even explained that they have the data to conduct such a study and that "we're insane to be sitting on this data and not have an independent group" conduct this study but that it will not happen because "they don't really want people to know that this data exists." Ibid.

Meningitis (*acute inflammation of protective membranes covering the brain and spinal cord*); Thrombocytopenia (*low blood platelet count which can result from autoimmune action*); Stevens-Johnson's Syndrome (*severe autoimmune reaction in which the top layer of skin is burned off and dies*); Alopecia Areata (*autoimmune skin disease resulting in the loss of hair on the scalp and elsewhere on the body*); Arthritis (*painful and disabling autoimmune disease that includes joint pain, swelling and progressive stiffness in the fingers, arms, legs and wrists*); Rhinitis (*irritation and inflammation of nasal mucous membranes impacting ability to breathe properly*); Insomnia; Lupus Erythematosus (*autoimmune disease in which immune system attacks healthy tissue, including skin, joint, kidney, brain, and other organs*); Hypotension (*abnormally low blood pressure*); Guillian-Barre Syndrome (*autoimmune disease that attacks the nerves in the legs, upper body, arms and/or face*); Polyarteritis Nodosa (*systemic vasculitis that affect medium-sized and small muscular arteries resulting in ruptures and other damage*); Encephalitis (*inflammation of the brain, which can result in permanent injury*); Bell's Palsy (*disfiguring paralysis or weakness on one side of the face*); Radiculopathy (*compressed or pinched nerve*); Myelitis (*inflammation of spinal cord that can involve nerve pain, paralysis and incontinence*); Multiple Sclerosis (*immune system attacks nerve fibers, causing them to deteriorate*); Optic Neuritis (*inflammation*

¹³⁰ In fact, due to the CDC's refusal to act, bills have been proposed in Congress to require such a study, but, the political clout for passage could not be mustered. See, e.g., H.R. 1757 (2013) and H.R. 1636 (2015) ("to conduct or support a comprehensive study comparing total health outcomes ... in vaccinated populations in the United States with such outcomes in unvaccinated populations in the United States").

¹³¹ <https://www.hhs.gov/sites/default/files/fy2017-budget-in-brief.pdf>; <https://www.bccresearch.com/market-research/pharmaceuticals/vaccine-technologies-markets-report-phm014f.html>

¹³² [21 C.F.R. § 600.80\(c\)](#)

causing eye pain and partial or complete vision loss); Aplastic anemia (damage to the bone marrow which slows or shuts down the production of new blood cells); Aseptic Meningitis (acute inflammation of the brain and spinal cord which can lead to death); Henoch-Schonlein purpura (abnormal immune response resulting in inflammation of microscopic blood vessels which can result in multiple organ damage); Myalgia (muscle pain that can become chronic); Radial nerve and recurrent nerve paralysis (nerve injury to the radial nerve that can cause weakness or difficulty moving the wrist, hand or fingers); Encephalopathy with EEG disturbances (damage or malfunction of the brain with severity ranging from altered mental status to dementia, seizures and coma); Grand Mal Convulsion (loss of consciousness and violent muscle contractions); Sudden Infant Death Syndrome (sudden death of infant in good health); Diabetes mellitus (chronic, lifelong condition effecting ability to use

energy found in food); Pancreatitis (pancreas attacks its own digestive enzymes); Encephalomyelitis (inflammation of the brain and spinal cord); Transverse myelitis (autoimmunity causing inflamed spinal cord which may result in paralysis); Pneumonitis (inflammation of lung tissue); Ocular Palsies (damage to the nerve of the eye that controls eye movement); Ataxia (brain damage resulting loss of full control of bodily movement, impaired speech, eye movement, and swallowing); Retrobulbar Neuritis (inflammation and damage to the optic nerve between the back of the eye and the brain); Epididymitis (inflammation testicle tube which can lead to abscess formation, testicular pain, painful urination, tissue death, and decreased functionality of gonads); Orchitis (inflammation of one or more testicles that can cause infertility, testicular atrophy, pain, and severe pain); Nerve Deafness (hearing loss from damage to the nerve that runs from the ear to the brain).¹³³

IV. CONFLICTS OF INTEREST IN VACCINE SAFETY

The 1986 Act created a system in which vaccines are licensed, recommended, encouraged, subsidized, and defended by HHS (the **Vaccine Program**).

The lack of evidence supporting vaccine safety is partially the result of the 1986 Act's unfortunate scheme which places the same agency, HHS, in charge of two conflicting duties. On the one hand, HHS is responsible for vaccine safety. On the other hand, HHS is simultaneously required to promote vaccine uptake and defend against any claim that vaccines cause any harm.

Regrettably, it appears that HHS has chosen to focus almost entirely on its vaccine promotion and defense responsibilities to such a degree that it has essentially abandoned its vaccine safety responsibility.

The Vaccine Program has transformed what should be a government watchdog over the pharmaceutical industry with regard to vaccines into an industry partner, with the same interests of promoting and literally defending, with the Department of Justice (**DOJ**) as its defense firm, against any claim of

¹³³ See vaccine products inserts at <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm093833.htm>

vaccine injury. The result – as reflected in scathing reports by Congress and the HHS Inspector General – is that the Vaccine Program is fraught with pervasive conflicts of interests both structurally and literally with pharmaceutical company insiders.

Usually, when a government watchdog becomes ineffective or conflicted, consumers turn to the last line of recourse against harm caused by a product: class action and product liability attorneys. But in the case of vaccines, even they have been neutered because of the immunity from financial liability given to pharmaceutical companies for harms caused by their vaccines.

The Vaccine Program created by the 1986 Act has unfortunately resulted in a complete lack of accountability for vaccine safety.

1. HHS Licenses Vaccines

The introduction of a new vaccine begins with its licensure by the FDA. A committee at the FDA, the Vaccines and Related Biological Products Advisory Committee (VRBPAC), “advises the FDA on whether or not to license new vaccines for commercial use.”¹³⁴ In reality this committee effectively decides whether a new vaccine gets licensed since its recommendations for licensure are almost always accepted by the FDA. Unfortunately, the members of this board are often pharmaceutical insiders and, as discussed in Section II above, they license vaccines with virtually no safety data.

By the year 2000, most pediatric vaccines on the CDC’s vaccine schedule were already licensed by the FDA. That same year, the U.S. House of Representatives’ Committee on Government Reform (the **Committee**) issued a report revealing serious conflicts of interest in the VRBPAC.¹³⁵ The Committee “determined that conflict of interest rules employed by the FDA and the CDC have been weak, enforcement has been lax, and committee members with substantial ties to pharmaceutical companies have been given waivers to participate in committee proceedings.”¹³⁶ The Committee further explained that:

*Perhaps one of the major problems contributing to the overall influence of the pharmaceutical industry over the vaccine approval and recommendation process may be the loose standards that are used by the agency in determining whether a conflict actually exists. In many cases, significant conflicts of interest are not deemed to be conflicts at all.*¹³⁷

For instance, the Committee found that “3 out of 5 FDA advisory committee [VRBPAC] members who voted to approve the rotavirus vaccine in December 1997 [then the most recently approved vaccine by the VRBPAC] had financial ties to pharmaceutical companies that were developing different versions of the vaccine.”¹³⁸

Among these five VRBPAC members present and voting to license the rotavirus vaccine: one member’s employer had a \$9,586,000 contract for a rotavirus vaccine;

¹³⁴ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹³⁵ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹³⁶ Ibid.

¹³⁷ Ibid.

¹³⁸ Ibid.

another member was the principal investigator for a grant from Merck for the development of a rotavirus vaccine; two other members received almost \$1,000,000 from vaccine manufacturers toward vaccine development; and even the “consumer advocate” member (an ardent vaccine supporter) had received honoraria, in addition to travel expenses, from Merck.¹³⁹

These members voted to approve this pediatric vaccine even though a temporary voting member raised the following concern: “I would ask the FDA to work with the sponsor to further quantitate what these serious side effects are – specifically the adverse effects, driven in particular by febrile illness – is inducing hospitalizations and what is that level of access. I still don’t feel like I have a good grasp of that at this point.”¹⁴⁰

Regarding the VRBPAC, the Committee concluded: “The overwhelming majority of members, both voting members and consultants, have substantial ties to the pharmaceutical industry.”¹⁴¹ Hence, even putting aside the astonishing lack of safety review prior to licensure, extensive conflicts were found to pervade the HHS committee that largely determined whether to license the pediatric vaccines currently on the market.

2. HHS Recommends Vaccines

After a pediatric vaccine is licensed with virtually no safety data by an HHS

committee rife with conflicts of interest, another HHS committee, the CDC’s Advisory Committee on Immunization Practices (ACIP), decides whether to recommend the vaccine for all children in America.

ACIP is the only federal entity to make vaccination recommendations and these recommendations are consistently approved by the CDC.¹⁴² A recommendation by ACIP “for routine use of a vaccine is tantamount to a Federal mandate for vaccine use.”¹⁴³ This is because “HHS regulations require that all grants for childhood immunizations are subject to the States’ implementation of procedures to ensure routine vaccination ... [and] vigorous enforcement of school immunization laws.”¹⁴⁴

ACIP-recommended vaccines are also subsidized by the federal government.¹⁴⁵ In fact, 41% of the entire childhood vaccine market is purchased through ACIP resolutions.¹⁴⁶ This currently amounts to over \$4 billion paid to vaccine makers by the CDC, accounting for a third of the CDC’s current budget.¹⁴⁷

Putting all this together: as a result of the 1986 Act, **when the ACIP votes to recommend a pediatric vaccine for general use, the pharmaceutical industry is handed a liability-free, captive market of 78 million children with guaranteed payment.** It is not surprising that with this economic incentive,

without needing additional Congressional appropriations. As pointed out by the CDC: “It is unusual that a federal advisory committee has the power and authority to add benefits to an entitlement program.” It is also noteworthy that another 11% of the pediatric vaccine market is purchased through other Congressional appropriations and another 5% from state and local government funding.)

¹⁴⁷ <https://www.hhs.gov/sites/default/files/fy2017-budget-in-brief.pdf>

¹³⁹ Ibid.

¹⁴⁰ Ibid.

¹⁴¹ Ibid.

¹⁴² Ibid.

¹⁴³ Ibid.

¹⁴⁴ Ibid.

¹⁴⁵ <https://doi.org/10.1086/420748>

¹⁴⁶ Ibid. (Once ACIP votes to add a vaccine to the Vaccine for Children program, payment is provided to vaccine makers

the vaccine market has catapulted from \$170 million in 1982 to over \$33 billion in 2016.¹⁴⁸

Given these economic incentives, it is obvious that the ACIP should be scrupulously shielded from even an apparent – let alone actual – conflict of interest with vaccine makers. Unfortunately, government reports have found the exact opposite.

The ACIP is comprised of 15 voting members that are *not* federal government employees. Fourteen of these voting members must be medical professionals in the area of immunization.¹⁴⁹ There are also eight non-voting members who represent federal agencies with responsibility for immunization programs and an additional 26 non-voting members of liaison organizations, many of which receive financial support from vaccine makers.¹⁵⁰ As the U.S. House Committee on Government Reform concluded:

*The absence of any consumer advocates on the ACIP has resulted in an advisory committee that is inherently not 'fairly balanced.'*¹⁵¹

Far worse than the structural conflicts in ACIP's composition are the actual conflicts of interests of its members. These conflicts have been highlighted by multiple government reports but due to gridlock and disparate influence on Congress by pharmaceutical companies, Congress has never moved to fix the issues and conflicts it has identified.

One investigation by the U.S. House Committee on Government Reform resulted in a June 15, 2000 report entitled *Conflicts of Interest in Vaccine Policy Making*.¹⁵² The Committee found that ACIP members routinely fail to disclose conflicts with vaccine manufacturers.¹⁵³ Moreover, as a matter of routine, “[t]he CDC grants blanket waivers to the ACIP members each year that allow them to deliberate on any subject, regardless of their conflicts, for the entire year.”¹⁵⁴ In the congressional inquiry, legal counsel for the ACIP *conceded* that even when serious conflicts are identified, “we generally give them [waivers] to everyone ... we give them out freely.”¹⁵⁵ The Committee on Government Reform was troubled:

*The CDC's policy of issuing annual waivers creates an environment where people do not take the conflict of interest issue as seriously as they should. This policy, in concert with sloppy monitoring of the completeness of members' financial disclosure statements, allows for a clubby environment where ethical concerns are downplayed.*¹⁵⁶

As an example of this “clubby environment,” the Committee found: “Members of the ACIP are allowed to vote on a recommendation for one company's vaccine even if they have

¹⁴⁸ <https://www.bccresearch.com/market-research/pharmaceuticals/vaccine-technologies-markets-report-phm014f.html>;

<https://www.ncbi.nlm.nih.gov/books/NBK216815/>

¹⁴⁹ <https://www.cdc.gov/vaccines/acip/committee/downloads/nominations.pdf>

¹⁵⁰ <https://www.cdc.gov/vaccines/acip/committee/acip-charter-2016.pdf>

¹⁵¹ <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf>

¹⁵² Ibid.

¹⁵³ Ibid.

¹⁵⁴ Ibid.

¹⁵⁵ Ibid.

¹⁵⁶ Ibid.

financial ties to a competing firm developing a similar vaccine.”¹⁵⁷

Highlighting these conflict issues, the Committee drew focus on the vaccine most recently approved by the ACIP, a rotavirus vaccine, and whatever conflicts they could identify for the eight members of the ACIP that voted to approve that vaccine for routine pediatric use.¹⁵⁸ The Committee’s findings were damning: (1) The chairman served on Merck’s Immunization Advisory Board; (2) another member, who shared the patent on a rotavirus vaccine, had a \$350,000 grant from Merck to develop the vaccine, and was a consultant for Merck; (3) another member was under contract with the Merck Vaccine Division and received funds from various vaccine makers including Pasteur, and was a principal investigator for SmithKline; (4) another member received a salary and other payments from Merck; (5) another member participated in vaccine studies with Merck, Wyeth, and SmithKline; and (6) another member received grants from Merck and SmithKline.¹⁵⁹

The Committee was deeply troubled that these members were nonetheless allowed to vote to recommend a pediatric vaccine for universal use.¹⁶⁰

The Committee was further concerned by its finding that “ACIP liaison representatives have numerous ties to vaccine manufacturers.”¹⁶¹ The Committee found that these liaison members, through whom third-party organizations are permitted to provide

opinions regarding a vaccine under review, “provide more than just the opinions.”¹⁶² The Committee found them “more like” a voting member of ACIP “than an advisory representative.”¹⁶³ The advice of these liaison representatives “is solicited frequently by CDC personnel on issues where their organization has a financial interest.”¹⁶⁴

The ACIP also routinely forms subcommittees (called “working groups”) which convene behind closed doors and whose recommendations are typically rubber stamped by the ACIP.¹⁶⁵ The Committee was troubled by extensive and routine use of working groups since the participants in these working groups often had conflicts which would have prohibited them from voting during an actual ACIP meeting.¹⁶⁶ The Committee explained: “The ACIP’s prolific use of working groups to draft vaccine policy recommendations outside the specter of public scrutiny opens the door to undue special interest access.”¹⁶⁷ Regarding the ACIP’s most recent working group recommending approval of a vaccine, the Committee found:

The working group has ten members, seven of whom have identifiable conflicts of interest with vaccine manufacturers or vaccine interest groups. The group’s meetings were held in private with no minutes or records of the proceedings taken. It appears that members who were not allowed to vote because of conflicts of interest ... were allowed to work

¹⁵⁷ Ibid.

¹⁵⁸ Ibid.

¹⁵⁹ Ibid.

¹⁶⁰ Ibid.

¹⁶¹ Ibid.

¹⁶² Ibid.

¹⁶³ Ibid.

¹⁶⁴ Ibid.

¹⁶⁵ Ibid.

¹⁶⁶ Ibid.

¹⁶⁷ Ibid.

*extensively on the recommendation for a long period of time in the working group.*¹⁶⁸

The Committee's damning overall conclusion was that ACIP's process for recommending a vaccine reflected "a system where government officials make crucial decisions affecting American children without the advice and consent of the governed."¹⁶⁹

After the Committee's scathing report in 2000, one would expect nothing less than drastic reform of ACIP – something that would differentiate it from a biased and self-interested pharmaceutical company board so that the interests of American children are placed ahead of the companies with the resources to influence government. This expectation unfortunately has not been fulfilled.

Indeed, in December 2009, the HHS Office of Inspector General issued another report after an extensive review of the conflicts of CDC's advisory committee members, known as Special Government Employee (SGEs), with the first among these committees being the ACIP.¹⁷⁰ The Inspector General found that the "CDC had a systemic lack of oversight of the ethics program for SGEs."¹⁷¹ For example, the Inspector General found that: "Most of the experts who served on advisory panels in 2007 to evaluate vaccines for flu and cervical cancer had potential conflicts that were never resolved."¹⁷²

The Inspector General reached this conclusion after reviewing the conflict forms, Form 450's, filed by SGEs at the CDC. CDC "must obtain from SGEs" a completed Form 450, which includes "assets, sources of income, and non-income-earning activities."¹⁷³ Then, "[b]efore permitting SGEs to participate in committee meetings, CDC must review these forms and certify them to indicate that they are complete and that it has identified and resolved all conflicts of interest."¹⁷⁴ Reviewing CDC's compliance with these requirements, the Inspector General found that nothing had changed in the years since the scathing Congressional Committee on Government Reform report in 2000.¹⁷⁵

Indeed, the Inspector General found that "CDC certified OGE Forms 450 with at least one omission in 2007 for 97 percent ... of SGEs."¹⁷⁶ Almost all of these "had more than one type of omission."¹⁷⁷ Compounding this problem, the Inspector General found that "58 percent ... of SGEs had at least one potential conflict of interest that CDC did not identify."¹⁷⁸ Splicing down this 58% of unidentified conflicts, 40% involved employment or grants, 13% involved equity ownership, and 5% involved consulting.¹⁷⁹

These conflicts are serious, and the CDC "did not inform the SGEs that they would violate the criminal conflict-of-interest statute if they participated in committee work regarding particular matters affecting their specific employers' financial interests."¹⁸⁰

¹⁶⁸ Ibid.

¹⁶⁹ Ibid.

¹⁷⁰ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf>

¹⁷¹ Ibid.

¹⁷² <http://www.nytimes.com/2009/12/18/health/policy/18cdc.html?mcubz=0>

¹⁷³ <https://oig.hhs.gov/oei/reports/oei-04-07-00260.pdf>

¹⁷⁴ Ibid.

¹⁷⁵ Ibid.

¹⁷⁶ Ibid.

¹⁷⁷ Ibid.

¹⁷⁸ Ibid.

¹⁷⁹ Ibid.

¹⁸⁰ Ibid.

The Inspector General further concluded that even when the CDC actually identified a conflict, the CDC improperly granted broad waivers despite already being castigated for this improper practice in 2000.¹⁸¹ Even worse, “32 percent ... of SGEs with certified forms had at least one potential conflict of interest that CDC identified but did not resolve.”¹⁸² Amazingly, 13 percent of SGEs were allowed to participate in committee meetings without even having a Form 450 on file.¹⁸³

In sum, even after the blistering 2000 Committee on Government Reform report, and numerous damning Congressional hearings before that committee regarding CDC’s conflicts with vaccine makers, little changed.¹⁸⁴ Instead of resolving and avoiding these conflicts, the “incestuous relationship” between the CDC and vaccine makers has apparently become even more hardened and enmeshed.¹⁸⁵

Since an ACIP vote to recommend a vaccine hands a vaccine maker a liability-free market of 78 million American children with guaranteed payment, an ACIP vote must be completely insulated from any influence by pharmaceutical companies. Instead, the ACIP and its working groups, are inundated with conflicts of interest and ties to these companies.

3. HHS Promotes Vaccines

Not only is the process for licensing and recommending vaccines riddled with conflicts, so is HHS’s process for promoting vaccines.

While the CDC states on its website – not less than 130 times – that “CDC does not accept commercial support,” this is simply not true.¹⁸⁶ For example, in reviewing this very issue, the British Medical Journal, which it asserts is “one of the world’s most influential and widely read medical journals,” reported in 2015:

*The CDC’s image as an independent watchdog over the public health has given it enormous prestige, and its recommendations are occasionally enforced by law. Despite the agency’s disclaimer, the CDC does receive millions of dollars in industry gifts and funding, both directly and indirectly, and several recent CDC actions and recommendations have raised questions about the science it cites, the clinical guidelines it promotes, and the money it is taking.*¹⁸⁷

Explaining the concern with CDC receiving industry funding, the Journal described this as “classic stealth marketing, in which industry puts their message in the mouths of a trusted third party [here the CDC].”¹⁸⁸ The Journal quoted a methodologist and emeritus professor of medicine at UCLA stating, “Most of us were shocked to learn the CDC takes

¹⁸¹ Ibid.

¹⁸² Ibid.

¹⁸³ Ibid.

¹⁸⁴ Compare <http://vaccinesafetycommission.org/pdfs/Conflicts-Govt-Reform.pdf> with Ibid.

¹⁸⁵ https://cdn.voiceamerica.com/health/010278/arranga_040814.mp3

¹⁸⁶ <https://search.cdc.gov/search?query=%22cdc+does+not+accept+commercial+support%22&utf8=%E2%9C%93&affiliate=cdc-main>

¹⁸⁷ <http://vapors.org.uk/wp-content/uploads/2015/05/CDC-Industry-Funding.pdf>

¹⁸⁸ Ibid.

funding from industry,” adding that, “it is outrageous that industry apparently is allowed to punish the CDC if the agency conducts research that has the potential to cut into profits.”¹⁸⁹

As another example, Congress expressly created a private foundation, the “CDC Foundation,” through which private entities, such as pharmaceutical companies, can support programs at the CDC, endow positions at the CDC, and even place individuals to work at the CDC, paid through “private funding.”¹⁹⁰

Since 1995 the CDC Foundation has raised \$620 million to pay for 824 programs at the CDC.¹⁹¹ In 2015 alone, the CDC Foundation raised \$157 million for privately funded programs at the CDC, which then obtain the stamp of legitimacy of the CDC.¹⁹² Merck, for example, funded an \$832,916 program through the CDC Foundation to “expand CDC’s ... viral hepatitis prevention and vaccination activities.”¹⁹³ As a result, the CDC is reliant on the CDC Foundation for the continued funding of these projects, and even for the services of the staff placed at the CDC by the CDC Foundation, since the CDC is only permitted to use these funds as expressly directed by the CDC Foundation.¹⁹⁴ This foundation even funds and thus directs CDC “management training courses.”¹⁹⁵

Worse, the promotion track for CDC management extends into vaccine makers.

The most prominent example is former CDC Director Dr. Julie Gerberding who headed the CDC from 2002 to 2009. Dr. Gerberding oversaw several controversial studies regarding vaccines produced by Merck, including notably the MMR vaccine, which sought to silence those calling for an increase in the safety profile of those vaccines. When she left the CDC she was rewarded with the position of President of Merck Vaccines in 2010 with a reported estimated \$2.5 million annual salary and lucrative stock options.¹⁹⁶

In contrast, the few CDC officials who have attempted to blow the whistle on how vaccine safety research is conducted and treated at the CDC have become targets of character assassination. For example, following revelations of Dr. Thompson’s statements regarding the CDC’s improper conduct¹⁹⁷ (some of which was discussed above), he soon found himself marginalized and publicly maligned, despite the CDC’s prior reliance on him for over a decade to produce most of its core vaccine safety science.¹⁹⁸

As Congressman Bill Posey explained in 2014 after investigating the CDC’s approach to vaccine safety: the CDC and vaccine industry’s “media network [will] twist the truth to disparage, to malign, to vilify, to denigrate anybody who wants any kind of accountability” and added that his review of CDC emails discussing vaccine safety “will make you absolutely sick to your stomach.”¹⁹⁹

¹⁸⁹ Ibid.

¹⁹⁰ [42 U.S.C.A. §§ 280e-11\(h\)\(1\), \(2\)](#)

¹⁹¹ <http://www.cdcfoundation.org/FY2015>

¹⁹² Ibid.

¹⁹³ Ibid.

¹⁹⁴ [42 U.S.C.A. § 280e-11\(h\)\(2\)\(a\), \(7\)\(b\)](#)

¹⁹⁵ <https://www.cdcfoundation.org/sites/default/files/upload/pdf/CDCF-Form990-2014.pdf>

¹⁹⁶ <https://www.sec.gov/cgi-bin/own-disp?action=getowner&CIK=0001628884>

¹⁹⁷ <https://soundcloud.com/fomotion/cdc-whistle-blower-full-audio>

¹⁹⁸ <https://www.ncbi.nlm.nih.gov/pubmed/?term=Thompson+WW%5BAuthor%5D>

¹⁹⁹ <https://cdn.voiceamerica.com/health/010278/arranga040814.mp3>

4. HHS Defends Vaccines

After HHS licenses, effectively mandates, and promotes a vaccine to 78 million American children with virtually no safety data, *this very same government agency is mandated to defend against any claim that the vaccine caused harm.* There is no other product where the very agency responsible to regulate a product and assure its safety is statutorily required to defend against any claim it causes harm.

The Vaccine Injury Compensation Program (**VICP** or **Vaccine Court**) is effectively the only legal recourse in America to obtain compensation for a pediatric vaccine injury.²⁰⁰ The injured must file a claim in the VICP and litigate against HHS and the DOJ in a quasi-judicial process filed under seal where the injured child effectively cannot obtain documents from or depose vaccine makers to prove how the vaccine caused injury.²⁰¹ There is no jury, nor even a judge; special masters play the role of trial judges, with the final say.²⁰² DOJ and HHS have the government's vast resources while the injured must secure a private attorney.²⁰³ Moreover, an injured child's damages are limited to \$250,000 for death and pain and suffering.²⁰⁴

Worst of all, despite these limitations, the injured child must *still* almost always prove "causation" – the biological mechanism by which the vaccine caused the claimed injury. Requiring an injured child to prove causation adds insult to injury because, sadly, had HHS conducted the vaccine safety science it demands as proof in the VICP before

licensing a vaccine, the child's injury may have been avoided altogether.

There is a disconnect in requiring a child receiving a compulsory pharmaceutical product to medically prove how the vaccine caused his or her injury, where the science to understand vaccine injuries is not being done by the government agency tasked with this job.²⁰⁵ As confirmed by the IOM, HHS has not conducted the basic science needed to even determine whether commonly claimed vaccine injuries are caused by vaccines.²⁰⁶ It has failed to conduct even one properly sized study comparing vaccinated to unvaccinated children, despite all the resources at its disposal.²⁰⁷ It therefore may not be surprising that the Federal Circuit Court of Appeals found, medical science is "a field bereft of complete and direct proof of how vaccines affect the human body."²⁰⁸

The Committee on Government Reform explained the devastating consequences suffered by families when children are injured by a vaccine:

Every year, a number of children are seriously injured by adverse reactions to vaccines. When such a tragedy befalls a family, they are faced with devastating emotional and financial consequences. As the devastation of adverse reactions can lead to paralysis, permanent disability and death, families without adequate insurance can face enormous expenses, including

²⁰⁰ [42 U.S.C. § 300aa-10 et seq.](#)

²⁰¹ [42 U.S.C. § 300aa-12](#)

²⁰² *Ibid.*

²⁰³ [42 U.S.C. § 300aa-15](#)

²⁰⁴ *Ibid.*

²⁰⁵ See Sections II and III above.

²⁰⁶ See Section III(2) above.

²⁰⁷ See Section III(6) above.

²⁰⁸ [Althen v. Secretary of Health and Human Services, 418 F.3d 1274 \(Fed. Cir. 2005\)](#)

*residential care, therapy, medical equipment, and drugs.*²⁰⁹

Yet it is left to the injured child to prove the physiological mechanics by which the vaccine caused injury.²¹⁰

Moreover, Congress left HHS with the authority to set the rules for the VICP and so HHS has used this authority to shortcut its defense of claims for vaccine injuries by changing the rules in its favor. Indeed, the 1986 Act created a Vaccine Injury Table (the **Table**) which quickly compensated certain common injuries associated with each vaccine.²¹¹ If the petitioner suffered an injury on the Table, the burden would shift to HHS to prove the vaccine did not cause the injury.²¹² After passage of the 1986 Act, almost 90 percent of claims were Table claims and were quickly settled.²¹³ Soon after, in 1995 and 1997, HHS amended the Table such that 98% of new claims are off-Table.²¹⁴ This change greatly increased the difficulty of obtaining compensation for vaccine injuries.

While HHS changes the VICP rules in its favor, the Committee on Government Reform found “DOJ attorneys make full use of the apparently limitless resources available to them,” “pursued aggressive defenses in

compensation cases,” and “establish[ed] a cadre of attorneys specializing in vaccine injury” and “an expert witness program to challenge claims.”²¹⁵ The Committee even noted a VICP decision which stated:

*In the special master’s view, [HHS’s] counsel’s abrasive, tenacious, obstreperous litigation tactics were inappropriate in a program that is intended to be less adversarial; and hindered greatly a fair, expeditious resolution of the case. In addition, counsel lacks simply tact and compassion. Quite frankly; the special master is embarrassed that [HHS’s] counsel and ... life care planner represented the United States Government in this case.*²¹⁶

The length of time it has taken to adjudicate claims has also multiplied such that over half of claims now take over five years.²¹⁷

Even with all the foregoing barriers to obtaining compensation for a vaccine injury – notably requiring injured children to prove causation and capping damages for pain and suffering and death at \$250,000 – the VICP has paid over \$2.1 billion dollars for vaccine injury claims since 2007 and over \$3.7 billion since 1986.²¹⁸ Just a few of the serious vaccine injuries for which the VICP has paid include:

²⁰⁹ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

²¹⁰ Further compounding the above issues, babies are unable to describe their symptoms which may explain why most VICP claims are filed by adults. Most adults bring claims for injury after a single flu shot. (https://www.hrsa.gov/vaccinecompensation/data/vicpmonthlyreporttemplate8_1_17.pdf) In contrast, babies receive between five and seven injections of numerous vaccine doses at two months, four months, six months, etc. (See Section I above.) If babies could talk, they may be able to explain why they are crying inconsolably, have decreased activity/lethargy, drowsiness, irritability, fussiness, and loss of appetite – reactions that are considered “normal” side effects of vaccination. (See vaccine product inserts at <https://www.fda.gov/biologicsbloodvaccines/vaccines/approvedproducts/ucm>

<093833.htm>) But since babies can’t talk, the symptoms which would explain a neurological injury, for example, are not knowable until later in life when it is too late to assert a claim.

²¹¹ <https://www.hrsa.gov/vaccinecompensation/vaccineinjurytable.pdf>

²¹² 42 U.S.C. § 300aa-13

²¹³ *Stevens v. Secretary of the Department of Health & Human Services*, No. 99-594V (Office of Special Masters 2001)

²¹⁴ <http://www.gao.gov/assets/670/667136.pdf>

²¹⁵ <https://www.congress.gov/106/crpt/hrpt977/CRPT-106hrpt977.pdf>

²¹⁶ *Ibid.*

²¹⁷ <http://www.gao.gov/assets/670/667136.pdf>

²¹⁸ https://www.hrsa.gov/vaccinecompensation/data/vicpmonthlyreporttemplate8_1_17.pdf; 42 U.S.C.A. § 300aa-15(a)(2), (4)

*Guillain-Barre Syndrome, Transverse Myelitis, Encephalopathy (disease altering brain function), Seizure Disorder, Death, Brachial Neuritis, CIDP (inflammation damaging the brain and spinal cord), Acute Disseminated Encephalomyelitis, Premature Ovarian Failure, Bell's Palsy, Idiopathic Thrombocytopenic Purpura (ITP) (autoimmune disease of the blood), Juvenile Diabetes, Rheumatoid Arthritis, Multiple Sclerosis, Fibromyalgia, Infantile Spasms, Anaphylaxis, Ocular Myasthenia Gravis (autoimmune condition causing visual impairments), Hypoxic Seizure*²¹⁹

Recognizing the depths of the foregoing issues and conflicts, in 2006 a bipartisan group of seven congressmen proposed a bill to create an entirely new government agency solely devoted to vaccine safety.²²⁰ The primary sponsor of this bill explained the need for this bill as follows:

Federal agencies charged with overseeing vaccine safety research have failed. They have failed to provide sufficient resources for vaccine safety research. They have failed to fund extramural research. And, they have failed to free themselves from conflicts of interest that serve to undermine public confidence in the safety of vaccines.

The American public deserves better and increasingly parents and the public at large are demanding better.

I'm a physician. ... When I first began working on this issue about seven years ago, I was shocked at the dearth of resources dedicated to vaccine safety research. ...

When I first tasked my staff with investigating this issue we got a lot of confused responses from federal agencies. The FDA told us to check in with the CDC, saying CDC did most of the vaccine safety research. The CDC referred us over to the NIH. Then, the NIH referred us back to the CDC. ...

Several issues relating to vaccine safety have persisted for years. The response from public health agencies has been largely defensive from the outset and the studies plagued by conflicts of interest. ...

Presently, vaccine safety research is an in-house function conducted predominantly by the CDC – the very agency that makes vaccine

²¹⁹ See, e.g., *Kuperus v. Sec'y of the HHS*, No. 01-0060V, 2003 U.S. Claims LEXIS 397 (Fed. Cl. Oct. 23, 2003) (Acute Disseminated Encephalitis from DTaP); *Lerwick v. Sec'y of HHS*, No. 06-847V, 2010 U.S. Claims LEXIS 398 (Fed. Cl. May 26, 2010) (Acute Disseminated Encephalitis from DTaP); *Price v. Sec'y of HHS*, No. 11-442V, 2015 U.S. Claims LEXIS 1554 (Fed. Cl. Oct. 29, 2015) (Anaphylaxis from DTaP); *Rodriguez v. Sec'y of the HHS*, No. 06-559V, 2007 U.S. Claims LEXIS 685 (Fed. Cl. Sep. 14, 2007) (Death from DTaP); *Harry Tembenis & Gina Tembenis v. Sec'y of HHS*, No. 03-2820V, 2010 U.S. Claims LEXIS 950 (Fed. Cl. Nov. 29, 2010) (Death from DTaP); *Agresti v. Sec'y of HHS*, No. 05-0752V, 2009 U.S. Claims LEXIS 517 (Fed. Cl. Mar. 17, 2009) (Encephalopathy from DTaP); *Corzine v. Sec'y of the HHS*, No.

[01-230V](#), 2004 U.S. Claims LEXIS 116 (Fed. Cl. Apr. 23, 2004) (Hypoxic seizure leading to Death from DTaP); *Loving v. Sec'y of HHS*, No. 02-469V, 2013 U.S. Claims LEXIS 1570 (Fed. Cl. Sep. 20, 2013) (Infantile Spasms and Seizure Disorder from DTaP); *Herrell v. Sec'y of the HHS*, No. 08-123V, 2009 U.S. Claims LEXIS 577 (Fed. Cl. Jan. 6, 2009) (Idopathic Thrombocytopenic Purpura from MMR); *Zatuchni v. Sec'y of HHS (In re Snyder)*, No. 94-58V, 2006 U.S. Claims LEXIS 127 (Fed. Cl. May 10, 2006) (Fibromyalgia leading to death from MMR); *Francis v. Sec'y of the HHS*, No. 99-520V, 2007 U.S. Claims LEXIS 172 (Fed. Cl. May 23, 2007) (Ocular Myasthenia Gravis from Varicella).

²²⁰ <https://www.congress.gov/bill/109th-congress/house-bill/5887>

*recommendations and promotes their uptake. This should not be.*²²¹

This bill did not get out of committee, a fact which likely reflects the ratio of over 1,000 pharma lobbyists in Washington D.C. to virtually no vaccine safety lobbyists.

Many parents, doctors and scientists, as well as politicians, are legitimately concerned about the process whereby vaccines are licensed, recommended, promoted and defended by the same department. This is not because of any conspiracy, or belief in an insidious intent. Rather, the problem is with the structural conflicts and incentive scheme this system creates. There is no incentive for research to

uncover which long-term chronic conditions, including which immune and neurological disorders – which *can* clearly result from the current vaccination schedule – are caused by vaccines. Even worse is the disincentive to uncover susceptible populations to vaccine injury. The burden of judging whether a vaccine will seriously injure a child therefore falls on the child’s parents. But unless parents can identify with scientific accuracy how a vaccine will injure their child, parents cannot obtain a medical exemption from vaccinating their child. Worse, when a child is injured, the burden again falls on the parent to prove how the vaccine injured their child. This system is inherently unfair and unjust.

CONCLUSION

We can do better. With hundreds of vaccines in the pipeline we must do better. Children susceptible to vaccine injury are as deserving of protection as any other child. Avoiding injury to these children is not only a moral and ethical duty, but will, in fact, strengthen the Vaccine Program. Every parent that does not witness their child suffer a serious reaction after vaccination, such as a seizure or paralysis, is another parent that will not add their voice to the growing chorus of parents opposed to the Vaccine Program due to safety concerns.

These parents and their kindred doctors, scientists and politicians, are also in fact correct that the system for vaccine safety is broken. While we know that vaccines can

cause serious adverse reactions, the studies to quantify the rate at which it causes these harms have never been done. While we know that certain children are predisposed to serious injury from vaccines, the studies to identify which children are so disposed have never been done. While we know that valid pre-licensure safety trials take years and must use an inert placebo control, such pre-licensure safety trials are never done for any vaccine. While we know that post-licensure surveillance of vaccines captures less than one percent of adverse reactions, the CDC refused to cooperate to automate VAERS reporting.

In the zeal to protect the Vaccine Program the primary objective of protecting every child to the greatest extent possible from

²²¹ http://vaccine-safety.s3.amazonaws.com/Weldon_Statement_Vaccine_Safety_final.pdf

harm has been lost. Every child susceptible to a vaccine injury or injured by a vaccine deserves better.

The good news is that fixing this system is not complicated and would require a tiny fraction of the resources already devoted to the Vaccine Program. The quickest solution would be to repeal the 1986 Act and let normal market forces drive vaccine safety. Alternatively, the following actions would immediately correct many of the issues identified in this white-paper:

Reduce Conflicts

1. Prohibit any conflict waivers for members of HHS's vaccine committees.²²²
2. Prohibit HHS vaccine committee members or employees from accepting any compensation from a vaccine maker for twenty years.
3. Require that vaccine safety advocates comprise at least half of HHS's vaccine committees.

Increase Safety Profile

4. Conduct prospective double-blind saline-placebo controlled studies of each vaccine recommended by the CDC as well as the entire CDC vaccine schedule.
5. Conduct properly sized and controlled retrospective and prospective safety studies

comparing total health outcomes between vaccinated children and completely unvaccinated children.

6. Create a vaccine safety agency independent of HHS with a budget equal to 50% of HHS's budget for promoting and purchasing vaccines.
7. Automate creation and transmission of adverse reactions reports at hospital/clinic to VAERS.

²²² HHS's vaccine committees include the Advisory Committee on Immunization Practices (ACIP), the Vaccine and Related

Biological Products Advisory Committee (VRBPAC), the National Vaccine Advisory Committee (NVAC), and the Advisory Commission on Childhood Vaccines (ACCV).

APPENDIX: Vaccine Ingredients

Most pediatric vaccines do not contain live viruses.²²³ For example, (i) polio vaccine (IPV) only contains a killed virus, (ii) hepatitis b vaccine contains a portion of a killed virus, and (iii) diphtheria vaccine contains only a modified toxin released by the diphtheria bacteria.²²⁴ These pieces of killed bacteria or virus or modified toxins are commonly referred to as “antigens.” An injection of antigen alone, with nothing more, produces a weak immune response insufficient for creating long-term immunity.²²⁵

Therefore, many vaccines also contain an “adjuvant,” an immune-stimulating substance that increase the immune response to the antigen, so that immunity is created. Aluminum compounds are by far the most commonly used adjuvants in vaccines. They are made of particles of aluminum hydroxide, aluminum phosphate or aluminum sulfate, or mixtures thereof.²²⁶

It is universally accepted that aluminum is a potent neurotoxin, and toxic to all life.²²⁷ Accordingly, the FDA has established strict limits for aluminum in intravenous feeding solutions (.000005 grams per kg body weight per day). Exposure in infants exceeding this limit causes long term cognitive impairment.²²⁸

A significant safety problem with aluminum adjuvants is that, because they are made of microscopic particles, they can travel into the brain.²²⁹ Once in the brain, aluminum adjuvants cause long term chronic inflammation.²³⁰

Inflammation in the brain is a cause of neurodevelopmental disorders (e.g. autism) and mental illnesses (e.g. schizophrenia).²³¹ The resulting mental illness can occur years or decades after the inflammation starts.²³²

Exposure to aluminum adjuvants has increased dramatically in the last 50 years, in parallel with the increasing incidence of neurodevelopmental disorders in children.²³³

Some vaccines also contain other biological matter, both intended and unintended.²³⁴ These include cell lines from aborted human fetuses and biological material from animal tissue.²³⁵ Before being killed in the vaccine manufacturing process, the virus, disease, or toxin (against which the vaccine is supposed to protect) is grown on these human and biological mediums.²³⁶

Human cell portions in vaccines disclosed by the CDC include “human albumin, human diploid cell cultures (WI-38), human embryonic lung cultures, WI-38 human diploid lung fibroblasts, MRC-5 (human diploid) cells, MRC-5 cells, residual components of MRC-5 cells including DNA and protein, [and] recombinant human albumin.”²³⁷ These human cell portions also include billions of strands of human DNA from these aborted fetal cells lines that are of a length capable of inserting themselves into DNA to which they are exposed.²³⁸

²²³ <https://www.vaccines.gov/basics/types/index.html>

²²⁴ Ibid.

²²⁵ <https://www.cdc.gov/vaccinesafety/concerns/adjuvants.html>

²²⁶ Ibid.

²²⁷ <https://www.ncbi.nlm.nih.gov/pubmed/2940082>;
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819810/>;
<https://www.ncbi.nlm.nih.gov/pubmed/23932735>

²²⁸ <https://www.ncbi.nlm.nih.gov/pubmed/9164811>

²²⁹ <https://www.ncbi.nlm.nih.gov/pubmed/23557144>

²³⁰ <https://www.ncbi.nlm.nih.gov/pubmed/27908630>;

<https://www.ncbi.nlm.nih.gov/pubmed/19740540>

²³¹ <https://www.ncbi.nlm.nih.gov/pubmed/27540164>;

<https://www.ncbi.nlm.nih.gov/pubmed/25311587>

²³² Ibid.

²³³ <https://www.cdc.gov/vaccines/schedules/past.html>;

<https://www.ncbi.nlm.nih.gov/pubmed/20159870>

²³⁴ <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

²³⁵ Ibid.

²³⁶ Ibid.

²³⁷ Ibid.

²³⁸ <http://soundchoice.org/research/dna-fragments-research/>;

<http://soundchoice.org/wp-content/uploads/2012/08/DNA>

The CDC's list of ingredients for the vaccines also includes the following animal parts:

*monkey kidney cells, vero (monkey kidney) cells, embryonic guinea pig cell cultures, lactose, chick embryo cell culture, bovine calf serum, bovine serum albumin, calf serum protein, fetal bovine serum*²³⁹

These fragments of cultured human tissue and animal tissue, which have also been found to include various monkey, retro and other unintended viruses, are injected into the muscle tissue of babies and children, along with the adjuvant intended to generate a sustained immune response to the biological matter in the vaccine.²⁴⁰

[Contaminants in Vaccines Can Integrate Into Childrens Genes.pdf](#)

²³⁹ <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/b/excipient-table-2.pdf>

²⁴⁰ <https://www.fda.gov/biologicsbloodvaccines/scienceresearch/biologicsresearchareas/ucm127327.htm>; <https://www.ncbi.nlm.nih.gov/pubmed/20375174>. Vaccines also contain, among other ingredients, the following: *2-phenoxethanol, complex*

fermentation medium, detergent, 5rdimethyl 1-beta-cyclodextrin, Eagle MEM modified medium, enzymes, formaldehyde, gelatin, glutaraldehyde, hemin chloride, hydrolyzed galtin, lactalbumin hydrolysate, Medium 199, Minimum Essential Medium, modified Mueller's growth medium, modified Stainer-Scholte liquid medium, neomycin, neomycin sulfate, phenol polymyxin B, polymyxin B sulfate, polysorbate 80, soy peptone, Stainer-Scholte medium, streptomycin, yeast, yeast protein

VAERS Database Results for 11.14.2018

	Adverse Events	Died	Disabled	No Recovery	Hospitalized	Life Threatening
HPV	60,444	443	2813	9599	6015	958
Hepatitis A	34,981	109	582	3360	2325	526
Influenza	160,967	1520	3202	27,997	12,931	3230
Pneumococcal	114,355	2210	1837	16,807	16,956	2565
Rotavirus	28,132	712	328	3220	7947	1262
Meningococcal	21,410	69	204	2073	1199	266

Current belief is that less than 10% of all adverse events are reported to the VAERS system even though Federal Law requires health care workers to report vaccine related events. Imagine if the real VAERS results in the above chart were multiplied by 10X?

"No batch of vaccine can be proved safe before it is given to children"
 -Dr. Leonard Scheele, M.D., former Surgeon General of the U.S.

Henry Kissinger speech to world health organization Council on Eugenics 2009

Once the herd accepts mandatory forcible vaccination, it's game over! They will accept anything - forcible blood donation, or organ donation - for the "greater good". We can genetically modify children and sterilize them, for the "greater good". Control sheep minds and you control the herd. Vaccine makers stand to make billions, and many of you in this room today are investors. It's a big win-win! We thin out the herd, and the herd pays us for providing extermination services.

Now, what's for lunch, huh?



Is Aluminum in Vaccines Safe?

If a premature baby receives more than 10 mcg of aluminum in an IV, it can accumulate in the bones and brain, and can be toxic. The FDA maximum limit for aluminum received in an IV is 25 mcg per day. The suggested aluminum per kg of weight to give to a person is up to 5 mcg (a 5 pound baby should get no more than 11 mcg of aluminum). Anything that has more than 25 mcg of aluminum is "supposed" to have a Warning label "This product contains aluminum that may be toxic..."

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

• 8 pound healthy baby	18.2 mcg
• 15 pound healthy baby	34.1 mcg
• 30 pound healthy toddler	68.1 mcg
• 50 pound healthy child	113.0 mcg
• 150 pound adult	340.5 mcg
• 300 pound adult	794.5 mcg

So how much aluminum is in the vaccines that are routinely given to children?

• Hib (PedVaxHib brand only)	225 mcg
• Hepatitis B	250 mcg
• DTaP (varies with manufacturer)	170 – 625 mcg
• Pneumococcus	125 mcg
• Hepatitis A	250 mcg
• HPV	225 mcg
• Pentacel (DTaP, Hib & Polio combo vaccine)	330 mcg
• Pediarix (DTaP, Hep B & Polio combo vaccine)	850 mcg

Hepatitis B vaccine is recommended for all infants at birth and contains 250 mcg aluminum. This one vaccine alone is **±14 TIMES THE AMOUNT OF ALUMINUM THAT IS FDA-APPROVED.**

CDC recommends up to 8 vaccinations at 2, 4 & 6 months for a total of >1,000 mcg of aluminum. This amount is above the minimum for a 350 pound adult.

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=201.323>

<http://vaxtruth.org/2011/08/vaccine-ingredients/>

Immune Activation & Autism

In early life, the brain and immune system develop together. "Cytokines" are chemicals used by the immune system for communication, but they also guide brain development. Immune activation from an infection or vaccine [14] can cause elevated cytokines in the brain, thereby disrupting brain development. Specifically, immune activation can cause life-long brain injury and mental illnesses including autism, seizures/epilepsy, and schizophrenia. Developmental brain injury by cytokines has been studied extensively in humans, mice, and monkeys. [1-5]

Immune activation is recognized as a valid model for human autism, schizophrenia and other disorders. [1] Research has identified interleukin-6 (IL-6) and interleukin 17a (IL-17) as specific cytokines responsible for autism. IL-6 at low levels is necessary for healthy brain development, but elevated brain IL-6 during development causes autism. [6-12]

Immune activation in infants can cause brain injury [13-16]. This is because the brain develops for years after birth. For example, synapse formation, which is disrupted by IL-6, is most intense at ages 0-2, when vaccines are given. [17-19]

Early life immune activation causes many abnormalities associated with autism: mitochondrial dysfunction, Purkinje cell loss, microbiome dysbiosis, chronic brain inflammation, and autoimmunity. [20-25] It is established beyond reasonable doubt that autism is caused by immune/microglial activation and IL-6/IL-17 specifically.

Vaccines are designed to cause immune activation. But can vaccines cause immune activation in the brain? Can vaccines induce IL-6 in the brain? The answer to these questions is YES.

The aluminum (Al) adjuvant in vaccines can travel to the brain and stay there, causing long-term brain inflammation.

Aluminum Adjuvant & Immune Activation

Aluminum (Al) adjuvant is necessary in many vaccines for stimulating immunity. The Al adjuvant dosages infants receive in the CDC schedule cause neurological injury, brain inflammation, learning and memory impairment, and behavioral abnormalities in animal experiments (@ 100, 200, 300 and 550 mcg/kg). [27-30]

It is now clear that vaccines contain brain-damaging amounts of Al adjuvant.

Aluminum from CDC Schedule		
Birth	74 mcg/kg	(1 vaccine with 250 mcg, 3.4 kg infant)
2 months	245 mcg/kg	(6 vaccines with 1225 mcg, 5 kg infant)
4 months	150 mcg/kg	(5 vaccines with 975 mcg, 6.5 kg infant)
6 months	153 mcg/kg	(7 vaccines with 1225 mcg, 8 kg infant)
TOTAL	3675 mcg aluminum	

Aluminum dosage varies by vaccine manufacturer and infant weight. Chart shows maximum possible dosages for average-weight infants.

Al adjuvant is made of microscopic particles. The particles cause immune activation wherever they go, and they travel into the brain. Al adjuvant particles persist in the brain for months or years, [30-31] causing chronic immune activation. Aluminum elevates IL-6 in the brain. [32] Hepatitis B vaccine (contains Al adjuvant) elevates IL-6 in the brain. [41] Aluminum also causes methylation impairment, which is always present in autism. [42]

Al adjuvant particles are transported around the body by immune system cells (macrophages), in response to a signal called "MCP-1". [31] Elevated MCP-1 causes Al adjuvant transport into the brain. Infants that become autistic have high MCP-1 at birth. [33, 34] Vaccines (e.g. MMR) can trigger MCP-1, and thereby accelerate transport of Al particles into the brain. Brain accumulation of Al adjuvant can take months or years. Hence, brain injury can develop months or years after vaccination.

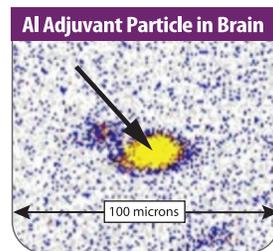
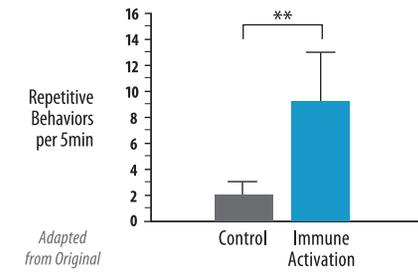


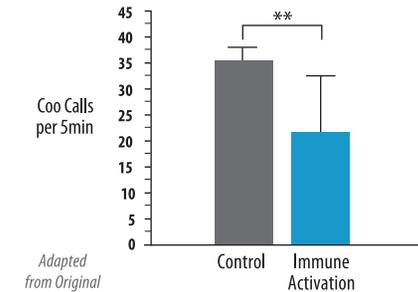
Image of Al adjuvant particle in brain of mouse injected with Al adjuvant into the leg 1 year earlier. [31] Yellow = Aluminum

Repetitive Behavior (in Monkeys)



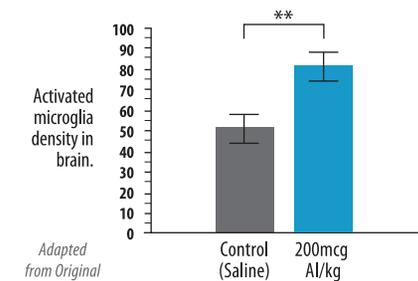
Immune activation increased repetitive behavior in monkeys. Repetitive behavior is a defining symptom of autism. $P < 0.01$ [26] **QUOTE:** "...alterations in behavior overlap with core diagnostic domains of autism." PMID: 24011823

Speech Impairment (in Monkeys)



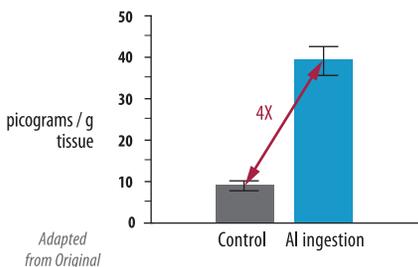
Immune activation reduced social speech in monkeys. This is a defining symptom of autism. $P < 0.01$ [26] **QUOTE:** "...alterations in behavior overlap with core diagnostic domains of autism." PMID: 24011823

Brain Inflammation



200mcg/kg Al adjuvant caused chronic inflammation (microglial activation) in the brains of mice, 6 months after Al adjuvant injection $P < 0.05$. This dosage increased brain aluminum content 50-fold. [30] Activated microglia play a causal role in autism. [35] PMID: 27908630

Al increases IL-6 in Brain



Ingestion of 3.4mg/Kg/d Al caused 4X increase in brain IL-6 level in rats. This is a vaccine-relevant dosage. Assurance of Al adjuvant safety is based on a single study showing no adverse effects from 26mg/Kg/day (ingested). Harm from 3.4 mg/kg/day disproves the safety assurances from CDC. $P < 0.05$. PMID: 26897372

How Aluminum Adjuvant Causes Autism



There is now strong scientific evidence that vaccines cause autism by an immune activation mechanism. Aluminum adjuvant is implicated because it travels into the brain where it causes microglial activation and elevated IL-6 production.

Today about 1 in 6 American children suffer from a neurodevelopmental disorder, a large increase compared to decades ago. Vaccines are a primary cause of this new crisis.

Vaccine advocates are silent about the science of Al adjuvant toxicity and immune activation.

“These MIA (maternal immune activation) animal models meet all of the criteria required for validity for a disease model: They mimic a known disease-related risk factor (construct validity), they exhibit a wide range of disease-related symptoms (face validity), and they can be used to predict the efficacy of treatments (predictive validity).”^[1]

— Dr. Kimberley McAllister, et al. (UC Davis MIND Institute), 2016

“...any factors that alter the number or activation state of microglia either in utero or during the early postnatal period can profoundly affect neural development, thus resulting in neurodevelopmental disorders, including autism.”^[35]

— Tomoyuki Takano (Shiga University of Medical Science, Japan), 2015

“...the existing evidence on the toxicology and pharmacokinetics of Al adjuvants... strongly implicate these compounds as contributors to the rising prevalence of neurobehavioral disorders in children.”^[3]

— Dr. C.A Shaw, et al. (University of British Columbia), 2013

“And what does a vaccination do? It activates the immune system. That’s the point of vaccination... I think that universal vaccination of pregnant women could get us into a whole new set of problems.”^[43]

— Dr. Paul Patterson, et al. (California Institute of Technology), 2006

OBJECTIONS ANSWERED

What about the studies showing vaccines do not cause autism?

They look only at MMR or thimerosal. MMR does not contain Al. Also, MMR-autism studies ignore healthy user bias, created when parents do not give MMR to children with neurological injury caused by prior Al-containing vaccines. Healthy user bias conceals evidence of harm in vaccine safety studies.^[40]

But aluminum has been used in vaccines for over 80 years.

TRUE. But it has not been studied for neurotoxicity or long-term safety until recently. Al dosage from vaccines increased dramatically in the last 25 years, in parallel with childhood neurodevelopmental disorders.

Aluminum is everywhere and ingested constantly. It cannot be harmful.

99.7% of ingested aluminum is not absorbed. The absorbed 0.3% comprises dissolved ions, which are rapidly eliminated in urine. Al adjuvant is made of **particles**, which remain in the body for years. Babies receive about 175X more Al from vaccines than mother’s milk in the first 6 months.

But immune activation studies are based on prenatal immune activation, not postnatal.

Studies of postnatal immune activation also show brain injury. The brain can be injured by immune activation prenatally or postnatally. The CDC recklessly promotes multiple vaccines for pregnant women. Influenza vaccination during pregnancy increases autism risk (4 additional autism cases per 1000 vaccinations).^[41]

But autism is an inherited, genetic disorder.

Autism is a gene-environment interaction between vaccines and genes that create a vulnerability to vaccines. Heritability estimates are from twin studies, which misclassify gene-environment interaction as purely genetic. Vaccines cause autism in people with the genes; the genes per se do not cause autism.^[44-45]

Are there ways to prevent damage from aluminum and immune activation?

YES. The nutrients silica, taurine and curcumin reduce Al neurotoxicity. Vitamin D reduces IL-17, and can prevent and reverse autism.^[37, 38, 39]

“Maternal immune activation yields male offspring with deficient social and communicative behavior, as well as high levels of repetitive behaviors, all of which are hallmarks of autism.”^[36]

— Dr. Paul Patterson, et al. (California Institute of Technology), 2012

“Interleukin-6 is necessary and sufficient for producing autism in the offspring...”^[12]

— Dr Eduardo Pineda, et al. (David Geffen School of Medicine, UCLA), 2013

REFERENCES

Citations available at: vaccinepapers.org/autism-brochure

Vaccines and Autism

New scientific evidence shows that vaccines cause autism and other brain injuries.

Vaccination ▶ Immune Activation ▶ Autism

New scientific discoveries show that autism is caused by early-life immune activation and brain inflammation. This brochure explains the science connecting vaccines, immune activation, aluminum adjuvant and autism.

VaccinePapers.org

"The CDC is a very troubled agency and it's not just me saying that. There has been four separate intensive federal investigations, by the United States Congress, a three year investigation: 2001, 2002, 2003, by the United States Senate Tom Coburn's committee, by the Inspector General of HHS in 2008, by The Office of Research Integrity in 2014.

...and all of them have painted the CDC as a cesspool of corruption. Of an agency that has become an absolute subsidiary of the pharmaceutical industry, and that has become a sock-puppet, a spokesperson, a shill for the industry.

The CDC is not an independent agency.

It is a vaccine company.

The CDC owns over 20 vaccine patents. It sells about 4.6 billion dollars of vaccines every year. Its primary metric for success in all of the departments in the agency are vaccine sales."

~ Robert F. Kennedy Jr.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GARDASIL 9 safely and effectively. See full prescribing information for GARDASIL 9.

GARDASIL[®]9

(Human Papillomavirus 9-valent Vaccine, Recombinant)

Suspension for intramuscular injection

Initial U.S. Approval: 2014

RECENT MAJOR CHANGES

Indications and Usage (1.1, 1.2, 1.3) 10/2018

Dosage and Administration, Dosage (2.1) 10/2018

INDICATIONS AND USAGE

GARDASIL 9 is a vaccine indicated in girls and women 9 through 45 years of age for the prevention of the following diseases:

- Cervical, vulvar, vaginal, and anal cancer caused by Human Papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58. (1.1)
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11. (1.1)

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma *in situ* (AIS). (1.1)
- Cervical intraepithelial neoplasia (CIN) grade 1. (1.1)
- Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3. (1.1)
- Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3. (1.1)
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3. (1.1)

GARDASIL 9 is indicated in boys and men 9 through 45 years of age for the prevention of the following diseases:

- Anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58. (1.2)
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11. (1.2)

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3. (1.2)

Limitations of Use and Effectiveness:

- GARDASIL 9 does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. (1.3, 17)
- Recipients of GARDASIL 9 should not discontinue anal cancer screening if it has been recommended by a health care provider. (1.3, 17)

GARDASIL 9 has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity. (1.3)

GARDASIL 9 has not been demonstrated to protect against diseases due to HPV types other than 6, 11, 16, 18, 31, 33, 45, 52, and 58. (1.3)

GARDASIL 9 is not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN; or AIN. (1.3)

Not all vulvar, vaginal, and anal cancers are caused by HPV, and GARDASIL 9 protects only against those vulvar, vaginal, and anal cancers caused by HPV 16, 18, 31, 33, 45, 52, and 58. (1.3)

GARDASIL 9 does not protect against genital diseases not caused by HPV. (1.3)

Vaccination with GARDASIL 9 may not result in protection in all vaccine recipients. (1.3)

DOSAGE AND ADMINISTRATION

For intramuscular administration only. (2)

Each dose of GARDASIL 9 is 0.5-mL

Administer GARDASIL 9 as follows: (2.1)

Age	Regimen	Schedule
9 through 14 years	2-dose	0, 6 to 12 months*
	3-dose	0, 2, 6 months
15 through 45 years	3-dose	0, 2, 6 months

*If the second dose is administered earlier than 5 months after the first dose, administer a third dose at least 4 months after the second dose. (14.2 and 14.5)

DOSAGE FORMS AND STRENGTHS

0.5-mL suspension for injection as a single-dose vial and prefilled syringe. (3, 11)

CONTRAINDICATIONS

Hypersensitivity, including severe allergic reactions to yeast (a vaccine component), or after a previous dose of GARDASIL 9 or GARDASIL[®]. (4, 11)

WARNINGS AND PRECAUTIONS

Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following HPV vaccination. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position. (5.1)

ADVERSE REACTIONS

The most common ($\geq 10\%$) local and systemic adverse reactions reported:

- In girls and women 16 through 26 years of age: injection-site pain (89.9%), injection-site swelling (40.0%), injection-site erythema (34.0%) and headache (14.6%). (6.1)
- In girls 9 through 15 years of age: injection-site pain (89.3%), injection-site swelling (47.8%), injection-site erythema (34.1%) and headache (11.4%). (6.1)
- In boys and men 16 through 26 years of age: injection-site pain (63.4%), injection-site swelling (20.2%) and injection-site erythema (20.7%). (6.1)
- In boys 9 through 15 years of age: injection-site pain (71.5%), injection-site swelling (26.9%), and injection-site erythema (24.9%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-877-888-4231 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

USE IN SPECIFIC POPULATIONS

Pregnancy registry: available at 1-800-986-8999. (8.1)

Safety and effectiveness of GARDASIL 9 have not been established in the following populations:

- Children below the age of 9 years. (8.4)
- Immunocompromised individuals. Response to GARDASIL 9 may be diminished. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

1.1 Girls and Women

1.2 Boys and Men

1.3 Limitations of Use and Effectiveness

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

2.2 Method of Administration

2.3 Administration of GARDASIL 9 in Individuals Who Have Been Previously Vaccinated with GARDASIL[®]

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Syncope

5.2 Managing Allergic Reactions

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

6.2 Post-Marketing Experience
7 DRUG INTERACTIONS
 7.1 Use with Systemic Immunosuppressive Medications
8 USE IN SPECIFIC POPULATIONS
 8.1 Pregnancy
 8.2 Lactation
 8.4 Pediatric Use
 8.5 Geriatric Use
 8.6 Immunocompromised Individuals
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
 12.1 Mechanism of Action
13 NONCLINICAL TOXICOLOGY
 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES

14.1 Efficacy and Effectiveness Data for GARDASIL
 14.2 Clinical Trials for GARDASIL 9
 14.3 Efficacy – HPV Types 31, 33, 45, 52 and 58 in Girls and Women 16 through 26 Years of Age
 14.4 Immunogenicity of a 3-Dose Regimen
 14.5 Immune Responses to GARDASIL 9 Using a 2-Dose Regimen in Individuals 9 through 14 Years of Age
 14.6 Studies with Menactra and Adacel
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Girls and Women

GARDASIL[®]9 is a vaccine indicated in girls and women 9 through 45 years of age for the prevention of the following diseases:

- Cervical, vulvar, vaginal, and anal cancer caused by Human Papillomavirus (HPV) types 16, 18, 31, 33, 45, 52, and 58-
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Cervical intraepithelial neoplasia (CIN) grade 2/3 and cervical adenocarcinoma *in situ* (AIS)
- Cervical intraepithelial neoplasia (CIN) grade 1
- Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3
- Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

1.2 Boys and Men

GARDASIL 9 is indicated in boys and men 9 through 45 years of age for the prevention of the following diseases:

- ~~Anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58-~~
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11

And the following precancerous or dysplastic lesions caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58:

- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3

1.3 Limitations of Use and Effectiveness

The health care provider should inform the patient, parent, or guardian that vaccination does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Women who receive GARDASIL 9 should continue to undergo cervical cancer screening per standard of care. [See Patient Counseling Information (17).]

Recipients of GARDASIL 9 should not discontinue anal cancer screening if it has been recommended by a health care provider [see Patient Counseling Information (17)].

GARDASIL 9 has not been demonstrated to provide protection against disease from vaccine HPV types to which a person has previously been exposed through sexual activity.

GARDASIL 9 has not been demonstrated to protect against diseases due to HPV types other than 6, 11, 16, 18, 31, 33, 45, 52, and 58.

GARDASIL 9 is not a treatment for external genital lesions; cervical, vulvar, vaginal, and anal cancers; CIN; VIN; VaIN; or AIN.

Not all vulvar, vaginal, and anal cancers are caused by HPV, and GARDASIL 9 protects only against those vulvar, vaginal, and anal cancers caused by HPV 16, 18, 31, 33, 45, 52, and 58.

GARDASIL 9 does not protect against genital diseases not caused by HPV.

Vaccination with GARDASIL 9 may not result in protection in all vaccine recipients.

How many
 re risks/year
 ORTH REWARDS?
 IN WE
 STOP IN
 OTHER WHY?
 VITAMIN C

Just the
 rest
 of this
 sentence
 or this
 whole
 insert?

2 DOSAGE AND ADMINISTRATION

2.1 Dosage

Each dose of GARDASIL 9 is 0.5-mL.
Administer GARDASIL 9 as follows:

Age	Regimen	Schedule
9 through 14 years	2-dose	0, 6 to 12 months*
	3-dose	0, 2, 6 months
15 through 45 years	3-dose	0, 2, 6 months

*If the second dose is administered earlier than 5 months after the first dose, administer a third dose at least 4 months after the second dose. [See Clinical Studies (14.2 and 14.5).]

2.2 Method of Administration

For intramuscular use only.

Shake well before use. Thorough agitation immediately before administration is necessary to maintain suspension of the vaccine. GARDASIL 9 should not be diluted or mixed with other vaccines. After thorough agitation, GARDASIL 9 is a white, cloudy liquid. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use the product if particulates are present or if it appears discolored.

Administer GARDASIL 9 intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.

Observe patients for 15 minutes after administration [see Warnings and Precautions (5)].

Single-Dose Vial Use

Withdraw the 0.5-mL dose of vaccine from the single-dose vial using a sterile needle and syringe and use promptly.

Prefilled Syringe Use

This package does not contain a needle. Shake well before use. Attach a needle by twisting in a clockwise direction until the needle fits securely on the syringe. Administer the entire dose as per standard protocol.

2.3 Administration of GARDASIL 9 in Individuals Who Have Been Previously Vaccinated with GARDASIL®

Safety and immunogenicity were assessed in individuals who completed a three-dose vaccination series with GARDASIL 9 and had previously completed a three-dose vaccination series with GARDASIL [see Adverse Reactions (6.1) and Clinical Studies (14.4)]. Studies using a mixed regimen of HPV vaccines to assess interchangeability were not performed for GARDASIL 9.

3 DOSAGE FORMS AND STRENGTHS

GARDASIL 9 is a suspension for intramuscular administration available in 0.5-mL single-dose vials and prefilled syringes. See Description (11) for the complete listing of ingredients.

4 CONTRAINDICATIONS

* Hypersensitivity, including severe allergic reactions to yeast (a vaccine component), or after a previous dose of GARDASIL 9 or GARDASIL [see Description (11)].

5 WARNINGS AND PRECAUTIONS

5.1 Syncope

Because vaccinees may develop syncope, sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended. Syncope, sometimes associated with tonic-clonic movements and other seizure-like activity, has been reported following HPV vaccination. When syncope is associated with tonic-clonic movements, the activity is usually transient and typically responds to restoring cerebral perfusion by maintaining a supine or Trendelenburg position.

if this is for people to read can you put it in simple terms for me?

particulates →
on you guarantee
all injections
have same
amounts of same
or listed ingredients
scope is there a

SAFETY STUDIES NOT
ADEQUATE (I'll learn
to spell)

→ please describe the details of severe allergic reactions.

5.2 Managing Allergic Reactions

* Will Schools have this?

Appropriate medical treatment and supervision must be readily available in case of anaphylactic reactions following the administration of GARDASIL 9.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine and may not reflect the rates observed in practice.

157703
PPI -
that's it?
There's
your
more,
Retr PPT!

The safety of GARDASIL 9 was evaluated in seven clinical studies that included 15,703 individuals who received at least one dose of GARDASIL 9 and had safety follow-up. Study 1 and Study 3 also included 7,378 individuals who received at least one dose of GARDASIL as a control and had safety follow-up. The vaccines were administered on the day of enrollment and the subsequent doses administered approximately two and six months thereafter. Safety was evaluated using vaccination report card (VRC)-aided surveillance for 14 days after each injection of GARDASIL 9 or GARDASIL.

Gardasil
control?

The individuals who were monitored using VRC-aided surveillance included 9,097 girls and women 16 through 26 years of age, 1,394 boys and men 16 through 26 years of age, and 5,212 girls and boys 9 through 15 years of age (3,436 girls and 1,776 boys) at enrollment who received GARDASIL 9; and 7,078 girls and women 16 through 26 years of age and 300 girls 9 through 15 years of age at enrollment who received GARDASIL. The race distribution of the integrated safety population for GARDASIL 9 was similar between girls and women 16 through 26 years of age (56.8% White; 25.2% Other Races or Multiracial; 14.1% Asian; 3.9% Black), girls and boys 9 through 15 years of age (62.0% White; 19.2% Other Races or Multiracial; 13.5% Asian; 5.4% Black), and boys and men 16 through 26 years of age (62.1% White; 22.6% Other Races or Multiracial; 9.8% Asian; 5.5% Black). The safety of GARDASIL 9 was compared directly to the safety of GARDASIL in two studies (Study 1 and Study 3) for which the overall race distribution of the GARDASIL cohorts (57.0% White; 26.3% Other Races or Multiracial; 13.6% Asian; 3.2% Black) was similar to that of the GARDASIL 9 cohorts.

Pacific
Island?
50 of
16,000
PPI only
25.2%

Safety of GARDASIL 9 in individuals 27 through 45 years of age is inferred from the safety data of GARDASIL in individuals 9 through 45 years of age and GARDASIL 9 in individuals 9 through 26 years of age.

were
"Other"
Races-

Injection-Site and Systemic Adverse Reactions

Injection-site reactions (pain, swelling, and erythema) and oral temperature were solicited using VRC-aided surveillance for five days after each injection of GARDASIL 9 during the clinical studies. The rates and severity of these solicited adverse reactions that occurred within five days following each dose of GARDASIL 9 compared with GARDASIL in Study 1 (girls and women 16 through 26 years of age) and Study 3 (girls 9 through 15 years of age) are presented in Table 1. Among subjects who received GARDASIL 9, the rates of injection-site pain were approximately equal across the three reporting time periods. Rates of injection-site swelling and injection-site erythema increased following each successive dose of GARDASIL 9. Recipients of GARDASIL 9 had numerically higher rates of injection-site reactions compared with recipients of GARDASIL.

break
down.
over
50%
white ->

25.
that's
study
#2?

Recommended: Monitor for 15 mins
Study - monitor 15 days/
5 days... etc. - so why
only 15 min?

NOT
TESTED
ON ALL
GENOME/
DNA TYPES
INNADEQUATE!

Table 1: Rates (%) and Severity of Solicited Injection-Site and Systemic Adverse Reactions Occurring within Five Days of Each Vaccination with GARDASIL 9 Compared with GARDASIL (Studies 1 and 3)

	GARDASIL 9				GARDASIL			
	Post-dose 1	Post-dose 2	Post-dose 3	Post any dose	Post-dose 1	Post-dose 2	Post-dose 3	Post any dose
Girls and Women 16 through 26 Years of Age								
Injection-Site Adverse Reactions	N=7069	N=6997	N=6909	N=7071	N=7076	N=6992	N=6909	N=7078
Pain, Any	70.7	73.5	71.6	89.9	58.2	62.2	62.6	83.5
Pain, Severe	0.7	1.7	2.6	4.3	0.4	1.0	1.7	2.6
Swelling, Any	12.5	23.3	28.3	40.0	9.3	14.6	18.7	28.8
Swelling, Severe	0.6	1.5	2.5	3.8	0.3	0.5	1.0	1.5
Erythema, Any	10.6	18.0	22.6	34.0	8.1	12.9	15.6	25.6
Erythema, Severe	0.2	0.5	1.1	1.6	0.2	0.2	0.4	0.8
Systemic Adverse Reactions	n=6995	n=6913	n=6743	n=7022	n=7003	n=6914	n=6725	n=7024
Temperature ≥100°F	1.7	2.6	2.7	6.0	1.7	2.4	2.5	5.9
Temperature ≥102°F	0.3	0.3	0.4	1.0	0.2	0.3	0.3	0.8
Girls 9 through 15 Years of Age								
Injection-Site Adverse Reactions	N=300	N=297	N=296	N=299	N=299	N=299	N=294	N=300
Pain, Any	71.7	71.0	74.3	89.3	66.2	66.2	69.4	88.3
Pain, Severe	0.7	2.0	3.0	5.7	0.7	1.3	1.7	3.3
Swelling, Any	14.0	23.9	36.1	47.8	10.4	17.7	25.2	36.0
Swelling, Severe	0.3	2.4	3.7	6.0	0.7	2.7	4.1	6.3
Erythema, Any	7.0	15.5	21.3	34.1	9.7	14.4	18.4	29.3
Erythema, Severe	0	0.3	1.4	1.7	0	0.3	1.7	2.0
Systemic Adverse Reactions	n=300	n=294	n=295	n=299	n=299	n=297	n=291	n=300
Temperature ≥100°F	2.3	1.7	3.0	6.7	1.7	1.7	0	3.3
Temperature ≥102°F	0	0.3	1.0	1.3	0.3	0.3	0	0.7

The data for girls and women 16 through 26 years of age are from Study 1 (NCT00543543), and the data for girls 9 through 15 years of age are from Study 3 (NCT01304498).

N=number of subjects vaccinated with safety follow-up

n=number of subjects with temperature data

Pain, Any=mild, moderate, severe or unknown intensity

Pain, Severe=incapacitating with inability to work or do usual activity

Swelling, Any=any size or size unknown

Swelling, Severe=maximum size greater than 2 inches

Erythema, Any=any size or size unknown

Erythema, Severe=maximum size greater than 2 inches

Unsolicited injection-site and systemic adverse reactions (assessed as vaccine-related by the investigator) observed among recipients of either GARDASIL 9 or GARDASIL in Studies 1 and 3 at a frequency of at least 1% are shown in Table 2. Few individuals discontinued study participation due to adverse experiences after receiving either vaccine (GARDASIL 9 = 0.1% vs. GARDASIL <0.1%).

Table 2: Rates (%) of Unsolicited Injection-Site and Systemic Adverse Reactions Occurring among $\geq 1.0\%$ of Individuals after Any Vaccination with GARDASIL 9 Compared with GARDASIL (Studies 1 and 3)

	Girls and Women 16 through 26 Years of Age		Girls 9 through 15 Years of Age	
	GARDASIL 9 N=7071	GARDASIL N=7078	GARDASIL 9 N=299	GARDASIL N=300
Injection-Site Adverse Reactions (1 to 5 Days Post-Vaccination, Any Dose)				
Pruritus	5.5	4.0	4.0	2.7
Bruising	1.9	1.9	0	0
Hematoma	0.9	0.6	3.7	4.7
Mass	1.3	0.6	0	0
Hemorrhage	1.0	0.7	1.0	2.0
Induration	0.8	0.2	2.0	1.0
Warmth	0.8	0.5	0.7	1.7
Reaction	0.6	0.6	0.3	1.0
Systemic Adverse Reactions (1 to 15 Days Post-Vaccination, Any Dose)				
Headache	14.6	13.7	11.4	11.3
Pyrexia	5.0	4.3	5.0	2.7
Nausea	4.4	3.7	3.0	3.7
Dizziness	3.0	2.8	0.7	0.7
Fatigue	2.3	2.1	0	2.7
Diarrhea	1.2	1.0	0.3	0
Oropharyngeal pain	1.0	0.6	2.7	0.7
Myalgia	1.0	0.7	0.7	0.7
Abdominal pain, upper	0.7	0.8	1.7	1.3
Upper respiratory tract infection	0.1	0.1	0.3	1.0

The data for girls and women 16 through 26 years of age are from Study 1 (NCT00543543), and the data for girls 9 through 15 years of age are from Study 3 (NCT01304498).

N=number of subjects vaccinated with safety follow-up

In an uncontrolled clinical trial with 639 boys and 1,878 girls 9 through 15 years of age (Study 2), the rates and severity of solicited adverse reactions following each dose of GARDASIL 9 were similar between boys and girls. Rates of solicited and unsolicited injection-site and systemic adverse reactions in boys 9 through 15 years of age were similar to those among girls 9 through 15 years of age. Solicited and unsolicited adverse reactions reported by boys in this study are shown in Table 3.

In another uncontrolled clinical trial with 1,394 boys and men and 1,075 girls and women 16 through 26 years of age (Study 7), the rates of solicited and unsolicited adverse reactions following each dose of GARDASIL 9 among girls and women 16 through 26 years of age were similar to those reported in Study 1. Rates of solicited and unsolicited adverse reactions reported by boys and men 16 through 26 years of age in this study are shown in Table 3.

where
is study
2?
why not
here?

16- to 26-year-old women (0, 2, 6) [†]	314	261	491.1	1
---	-----	-----	-------	---

*The PPI population consisted of individuals who received all assigned vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the last vaccination dose and blood collection for immunogenicity assessment, and were seronegative to the relevant HPV type(s) (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) prior to dose 1.

[†]2-dose regimen (0, 6): vaccination at Day 1 and Month 6; 2-dose regimen (0, 12): vaccination at Day 1 and Month 12; 3-dose regimen (0, 2, 6): vaccination at Day 1, Month 2, and Month 6. The data are from Study 8 (NCT01984697).

[‡]mMU=milli-Merck Units

[§]Demonstration of non-inferiority required that the lower bound of the 95% CI of the GMT ratio be greater than 0.67

[¶]Exploratory analysis; criterion for non-inferiority was not pre-specified

N = Number of individuals randomized to the respective vaccination group who received at least 1 injection

n = Number of individuals contributing to the analysis

CI=Confidence Interval

cLIA=competitive Luminex Immunoassay

GMT=Geometric Mean Titer

14.6 Studies with Menactra and Adacel

In Study 5, the safety and immunogenicity of co-administration of GARDASIL 9 with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] (same visit, injections at separate sites) were evaluated in 1,237 boys and girls 11 through 15 years of age at enrollment.

One group received GARDASIL 9 in one limb and both Menactra and Adacel, as separate injections, in the opposite limb concomitantly on Day 1 (n = 619). The second group received the first dose of GARDASIL 9 on Day 1 in one limb then Menactra and Adacel, as separate injections, at Month 1 in the opposite limb (n = 618). Subjects in both vaccination groups received the second dose of GARDASIL 9 at Month 2 and the third dose at Month 6. Immunogenicity was assessed for all vaccines one month post vaccination (one dose for Menactra and Adacel and three doses for GARDASIL 9).

Assessments of post-vaccination immune responses included type-specific antibody GMTs for each of the vaccine HPV types at four weeks following the last dose of GARDASIL 9; GMTs for anti-filamentous hemagglutinin, anti-pertactin, and anti-fimbrial antibodies at four weeks following Adacel; percentage of subjects with anti-tetanus toxin and anti-diphtheria toxin antibody concentrations ≥ 0.1 IU/mL at four weeks following Adacel; and percentage of subjects with ≥ 4 -fold rise from pre-vaccination baseline in antibody titers against *N. meningitidis* serogroups A, C, Y, and W-135 at four weeks following Menactra. Based on these measures, concomitant administration of GARDASIL 9 with Menactra and Adacel did not interfere with the antibody responses to any of the vaccines when compared with non-concomitant administration of GARDASIL 9 with Menactra and Adacel.

15 REFERENCES

1. Study 1 NCT00543543
2. Study 2 NCT00943722
3. Study 3 NCT01304498
4. Study 4 NCT01047345
5. Study 5 NCT00988884
6. Study 6 NCT01073293
7. Study 7 NCT01651949
8. Study 8 NCT01984697
9. Study A NCT01432574
10. Study B NCT00090285

↓ But what effect on the immune system overall?

How many... you guys sure?

Deaths in the Entire Study Population

Across the clinical studies, ten deaths occurred (five each in the GARDASIL 9 and GARDASIL groups); none were assessed as vaccine-related. Causes of death in the GARDASIL 9 group included one automobile accident, one suicide, one case of acute lymphocytic leukemia, one case of hypovolemic septic shock, and one unexplained sudden death 678 days following the last dose of GARDASIL 9. Causes of death in the GARDASIL control group included one automobile accident, one airplane crash, one cerebral hemorrhage, one gunshot wound, and one stomach adenocarcinoma.

Systemic Autoimmune Disorders

In all of the clinical trials with GARDASIL 9 subjects were evaluated for new medical conditions potentially indicative of a systemic autoimmune disorder. In total, 2.2% (351/15,703) of GARDASIL 9 recipients and 3.3% (240/7,378) of GARDASIL recipients reported new medical conditions potentially indicative of systemic autoimmune disorders, which were similar to rates reported following GARDASIL, AAHS control, or saline placebo in historical clinical trials.

Clinical Trials Experience for GARDASIL 9 in Individuals Who Have Been Previously Vaccinated with GARDASIL

A clinical study (Study 4) evaluated the safety of GARDASIL 9 in 12- through 26-year-old girls and women who had previously been vaccinated with three doses of GARDASIL. The time interval between the last injection of GARDASIL and the first injection of GARDASIL 9 ranged from approximately 12 to 36 months. Individuals were administered GARDASIL 9 or saline placebo and safety was evaluated using VRC-aided surveillance for 14 days after each injection of GARDASIL 9 or saline placebo in these individuals. The individuals who were monitored included 608 individuals who received GARDASIL 9 and 305 individuals who received saline placebo. Few (0.5%) individuals who received GARDASIL 9 discontinued due to adverse reactions. The vaccine-related adverse experiences that were observed among recipients of GARDASIL 9 at a frequency of at least 1.0% and also at a greater frequency than that observed among saline placebo recipients are shown in Table 4. Overall the safety profile was similar between individuals vaccinated with GARDASIL 9 who were previously vaccinated with GARDASIL and those who were naive to HPV vaccination with the exception of numerically higher rates of injection-site swelling and erythema among individuals who were previously vaccinated with GARDASIL (Tables 1 and 4).

saline placebo include AAHS control

1/600 = Adverse reactions → = ^{HPV cases} JUST NOT AGAIN

— / population of HI = vs. cervical cancer rates in HI

AAHS CONTROL →

AAHS is not a control.

Minimum injections ARE NOT CONTROLS!

Table 4: Rates (%) of Solicited and Unsolicited* Injection-Site and Systemic Adverse Reactions among Individuals Previously Vaccinated with GARDASIL Who Received GARDASIL 9 or Saline Placebo (Girls and Women 12 through 26 Years of Age) (Study 4)

	GARDASIL 9 N=608	Saline Placebo N=305
Solicited Adverse Reactions (1-5 Days Post-Vaccination, Any Dose)		
Injection-Site Pain	90.3	38.0
Injection-Site Erythema	42.3	8.5
Injection-Site Swelling	49.0	5.9
Oral Temperature $\geq 100.0^{\circ}\text{F}^{\dagger}$	6.5	3.0
Unsolicited Injection-Site Adverse Reactions (1-5 Days Post-Vaccination, Any Dose)		
Injection-Site Pruritus	7.7	1.3
Injection-Site Hematoma	4.8	2.3
Injection-Site Reaction	1.3	0.3
Injection-Site Mass	1.2	0.7
Unsolicited Systemic Adverse Reactions (1-15 Days Post-Vaccination, Any Dose)		
Headache	19.6	18.0
Pyrexia	5.1	1.6
Nausea	3.9	2.0
Dizziness	3.0	1.6
Abdominal pain, upper	1.5	0.7
Influenza	1.2	1.0

The data for GARDASIL 9 and saline placebo are from Study 4 (NCT01047345).

*Unsolicited adverse reactions reported by $\geq 1\%$ of individuals

N=number of subjects vaccinated with safety follow-up

[†]For oral temperature: number of subjects with temperature data GARDASIL 9 N=604; Saline Placebo N=304

Safety in Concomitant Use with Menactra and Adacel

In Study 5, the safety of GARDASIL 9 when administered concomitantly with Menactra [Meningococcal (Groups A, C, Y and W-135) Polysaccharide Diphtheria Toxoid Conjugate Vaccine] and Adacel [Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine Adsorbed (Tdap)] was evaluated in a randomized study of 1,241 boys (n = 620) and girls (n = 621) with a mean age of 12.2 years [see *Clinical Studies (14.6)*].

Of the 1,237 boys and girls vaccinated, 1,220 had safety follow-up for injection-site adverse reactions. The rates of injection-site adverse reactions were similar between the concomitant group and non-concomitant group (vaccination with GARDASIL 9 separated from vaccination with Menactra and Adacel by 1 month) with the exception of an increased rate of swelling reported at the injection site for GARDASIL 9 in the concomitant group (14.4%) compared to the non-concomitant group (9.4%). The majority of injection-site swelling adverse reactions were reported as being mild to moderate in intensity.

6.2 Post-Marketing Experience

There is limited post-marketing experience following administration of GARDASIL 9. However, the post-marketing safety experience with GARDASIL is relevant to GARDASIL 9 since the vaccines are manufactured similarly and contain the same antigens from HPV types 6, 11, 16, and 18. Because these events were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relationship to vaccine exposure. The following adverse experiences have been spontaneously reported during post-approval-use-of-GARDASIL and may also be seen in post-marketing experience with GARDASIL 9:

- Blood and lymphatic system disorders: Autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, lymphadenopathy.
- Respiratory, thoracic and mediastinal disorders: Pulmonary embolus.
- Gastrointestinal disorders: Nausea, pancreatitis, vomiting.
- General disorders and administration site conditions: Asthenia, chills, death, fatigue, malaise.
- Immune system disorders: Autoimmune diseases, hypersensitivity reactions including anaphylactic/anaphylactoid reactions, bronchospasm, and urticaria.
- Musculoskeletal and connective tissue disorders: Arthralgia, myalgia.
- Nervous system disorders: Acute disseminated encephalomyelitis, dizziness, Guillain-Barré syndrome, headache, motor neuron disease, paralysis, seizures, syncope (including syncope associated with tonic-

WATS.
DETIVE
P.S.

NEED
CONSENT

RISKS =
N/CENT

using
receipts
of one
not same
as next.
P.S.
changes
in
ingredients

NOT OKAY TO ATTEND SCHOOL WHEN
HPV & CERVICAL CANCER ARENT EPIDEMIC.

clonic movements and other seizure-like activity) sometimes resulting in falling with injury, transverse myelitis.

Infections and infestations: Cellulitis.

Vascular disorders: Deep venous thrombosis.

7 DRUG INTERACTIONS

7.1 Use with Systemic Immunosuppressive Medications

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune responses to vaccines [see Use in Specific Populations (8.6)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry to monitor pregnancy outcomes in women exposed to GARDASIL 9 during pregnancy. To enroll in or obtain information about the registry, call Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., at 1-800-986-8999.

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. There are no adequate and well-controlled studies of GARDASIL 9 in pregnant women. Available human data do not demonstrate vaccine-associated increase in risk of major birth defects and miscarriages when GARDASIL 9 is administered during pregnancy.

In one developmental toxicity study, 0.5 mL of a vaccine formulation containing between 1 and 1.5 – fold of each of the 9 HPV antigen types was administered to female rats prior to mating and during gestation. In another study, animals were administered a single human dose (0.5 mL) of GARDASIL 9 prior to mating, during gestation and during lactation. These animal studies revealed no evidence of harm to the fetus due to GARDASIL 9 [see Data].

Data

Human Data

In pre-licensure clinical studies of GARDASIL 9, women underwent pregnancy testing immediately prior to administration of each dose of GARDASIL 9 or control vaccine (GARDASIL). (Data from GARDASIL are relevant to GARDASIL 9 because both vaccines are manufactured using the same process and have overlapping compositions.) Subjects who were determined to be pregnant were instructed to defer vaccination until the end of their pregnancy. Despite this pregnancy screening regimen, some subjects were vaccinated very early in pregnancy before human chorionic gonadotropin (HCG) was detectable. An analysis was conducted to evaluate pregnancy outcomes for pregnancies with onset within 30 days before or after vaccination with GARDASIL 9 or GARDASIL. Among such pregnancies, there were 62 and 55 with known outcomes (excluding ectopic pregnancies and elective terminations) for GARDASIL 9 and GARDASIL, respectively, including 44 and 48 live births, respectively. The rates of pregnancies that resulted in a miscarriage were 27.4% (17/62) and 12.7% (7/55) in subjects who received GARDASIL 9 or GARDASIL, respectively. The rates of live births with major birth defects were 0% (0/44) and 2.1% (1/48) in subjects who received GARDASIL 9 or GARDASIL, respectively.

A five-year pregnancy registry enrolled 2,942 women who were inadvertently exposed to GARDASIL within one month prior to the last menstrual period (LMP) or at any time during pregnancy, 2,566 of whom were prospectively followed. After excluding elective terminations (n=107), ectopic pregnancies (n=5) and those lost to follow-up (n=814), there were 1,640 pregnancies with known outcomes. Rates of miscarriage and major birth defects were 6.8% of pregnancies (111/1,640) and 2.4% of live born infants (37/1,527), respectively. These rates of assessed outcomes in the prospective population were consistent with estimated background rates.

In two post-marketing studies of GARDASIL (one conducted in the U.S., and the other in Nordic countries), pregnancy outcomes among subjects who received GARDASIL during pregnancy were evaluated retrospectively. Among the 1,740 pregnancies included in the U.S. study database, outcomes

ADD STUDIES FOR PREDS

Overlapping (omparition) same data - same composition

→ I believe this type of testing is not ethical against my religion

same process: manufacturer doesn't mean same ingredients

were available to assess the rates of major birth defects and miscarriage. Among the 499 pregnancies included in the Nordic study database, outcomes were available to assess the rates of major birth defects. In both studies, rates of assessed outcomes did not suggest an increased risk with the administration of GARDASIL during pregnancy.

Animal Data

Developmental toxicity studies were conducted in female rats. In one study, animals were administered 0.5 mL of a vaccine formulation containing between 1 and 1.5 -fold of each of the 9 HPV antigen types 5 and 2 weeks prior to mating, and on gestation day 6. In a second study, animals were administered a single human dose (0.5 mL of GARDASIL 9) 5 and 2 weeks prior to mating, on gestation day 6, and on lactation day 7. No adverse effects on pre- and post-weaning development were observed. There were no vaccine-related fetal malformations or variations.

8.2 Lactation

Risk Summary

Available data are not sufficient to assess the effects of GARDASIL 9 on the breastfed infant or on milk production/excretion. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for GARDASIL 9 and any potential adverse effects on the breastfed child from GARDASIL 9 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

8.4 Pediatric Use

Safety and effectiveness have not been established in pediatric patients below 9 years of age.

8.5 Geriatric Use

The safety and effectiveness of GARDASIL 9 have not been evaluated in a geriatric population, defined as individuals aged 65 years and over.

8.6 Immunocompromised Individuals

The immunologic response to GARDASIL 9 may be diminished in immunocompromised individuals [see Drug Interactions (7.1)].

11 DESCRIPTION

GARDASIL 9, Human Papillomavirus 9-valent Vaccine, Recombinant, is a non-infectious recombinant 9-valent vaccine prepared from the purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58. The L1 proteins are produced by separate fermentations using recombinant *Saccharomyces cerevisiae* and self-assembled into VLPs. The fermentation process involves growth of *S. cerevisiae* on chemically-defined fermentation media which include vitamins, amino acids, mineral salts, and carbohydrates. The VLPs are released from the yeast cells by cell disruption and purified by a series of chemical and physical methods. The purified VLPs are adsorbed on preformed aluminum-containing adjuvant (Amorphous Aluminum Hydroxyphosphate Sulfate or AAHS). The 9-valent HPV VLP vaccine is a sterile liquid suspension that is prepared by combining the adsorbed VLPs of each HPV type and additional amounts of the aluminum-containing adjuvant and the final purification buffer.

GARDASIL 9 is a sterile suspension for intramuscular administration. Each 0.5-mL dose contains approximately 30 mcg of HPV Type 6 L1 protein, 40 mcg of HPV Type 11 L1 protein, 60 mcg of HPV Type 16 L1 protein, 40 mcg of HPV Type 18 L1 protein, 20 mcg of HPV Type 31 L1 protein, 20 mcg of HPV Type 33 L1 protein, 20 mcg of HPV Type 45 L1 protein, 20 mcg of HPV Type 52 L1 protein, and 20 mcg of HPV Type 58 L1 protein.

~~Each 0.5-mL dose of the vaccine also contains approximately 500 mcg of aluminum (provided as AAHS), 9.56 mg of sodium chloride, 0.78 mg of L-histidine, 50 mcg of polysorbate 80, 35 mcg of sodium borate, <7 mcg yeast protein, and water for injection. The product does not contain a preservative or antibiotics.~~

After thorough agitation, GARDASIL 9 is a white, cloudy liquid.

NOT
W/O
INJECT
SENT
HOME

AAHS
ALUMINUM →
effects?
NOT CONTROL

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

HPV only infects human beings. Animal studies with analogous animal papillomaviruses suggest that the efficacy of L1 VLP vaccines may involve the development of humoral immune responses. Efficacy of GARDASIL 9 against anogenital diseases related to the vaccine HPV types in human beings is thought to be mediated by humoral immune responses induced by the vaccine, although the exact mechanism of protection is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

GARDASIL 9 has not been evaluated for the potential to cause carcinogenicity, genotoxicity or impairment of male fertility. GARDASIL 9 administered to female rats had no effects on fertility [see Pregnancy (8.1)].

NOT STUDIED = NEEDS CONSENT? NOT MANIPATED

14 CLINICAL STUDIES

In these studies, seropositive is defined as anti-HPV titer greater than or equal to the pre-specified serostatus cutoff for a given HPV type. Seronegative is defined as anti-HPV titer less than the pre-specified serostatus cutoff for a given HPV type. The serostatus cutoff is the antibody titer level above the assay's lower limit of quantification that reliably distinguishes sera samples classified by clinical likelihood of HPV infection and positive or negative status by previous versions of competitive Luminex Immunoassay (cLIA). The lower limits of quantification and serostatus cutoffs for each of the 9 vaccine HPV types are shown in Table 5 below. PCR positive is defined as DNA detected for a given HPV type. PCR negative is defined as DNA not detected for a given HPV type. The lower limit of detection for the multiplexed HPV PCR assays ranged from 5 to 34 copies per test across the 9 vaccine HPV types.

Table 5: Competitive Luminex Immunoassay (cLIA) Limits of Quantification and Serostatus Cutoffs for GARDASIL 9 HPV Types

HPV Type	cLIA Lower Limit of Quantification (mMU*/mL)	cLIA Serostatus Cutoff (mMU*/mL)
HPV 6	16	30
HPV 11	6	16
HPV 16	12	20
HPV 18	8	24
HPV 31	4	10
HPV 33	4	8
HPV 45	3	8
HPV 52	3	8
HPV 58	4	8

*mMU=milli-Merck Units

14.1 Efficacy and Effectiveness Data for GARDASIL

Efficacy and effectiveness of GARDASIL are relevant to GARDASIL 9 since the vaccines are manufactured similarly and contain four of the same HPV L1 VLPs.

Individuals 16 through 26 Years of Age

Efficacy of GARDASIL was assessed in five AAHS-controlled, double-blind, randomized clinical trials evaluating 24,596 individuals 16 through 26 years of age (20,541 girls and women and 4,055 boys and men). The results of these trials are shown in Table 6 below.

Table 6: Analysis of Efficacy of GARDASIL in the PPE* Population for Vaccine HPV Types

Disease Endpoints	GARDASIL		AAHS Control		% Efficacy (95% CI)
	N	Number of cases	N	Number of cases	
16- through 26-Year-Old Girls and Women†					
HPV 16- or 18-related CIN 2/3 or AIS	8493	2	8464	112	98.2 (93.5, 99.8)
HPV 16- or 18-related VIN 2/3	7772	0	7744	10	100.0 (55.5, 100.0)
HPV 16- or 18-related VaIN 2/3	7772	0	7744	9	100.0 (49.5, 100.0)
HPV 6-, 11-, 16-, or 18-related CIN (CIN 1, CIN 2/3) or AIS	7864	9	7865	225	96.0 (92.3, 98.2)
HPV 6-, 11-, 16-, or 18-related Genital Warts	7900	2	7902	193	99.0 (96.2, 99.9)
HPV 6- and 11-related Genital Warts	6932	2	6856	189	99.0 (96.2, 99.9)
16- through 26-Year-Old Boys and Men					
External Genital Lesions HPV 6-, 11-, 16-, or 18-related					
External Genital Lesions	1394	3	1404	32	90.6 (70.1, 98.2)
Condyloma	1394	3	1404	28	89.3 (65.3, 97.9)
PIN 1/2/3	1394	0	1404	4	100.0 (-52.1, 100.0)
HPV 6-, 11-, 16-, or 18-related Endpoint					
AIN 1/2/3	194	5	208	24	77.5 (39.6, 93.3)
AIN 2/3	194	3	208	13	74.9 (8.8, 95.4)
AIN 1	194	4	208	16	73.0 (16.3, 93.4)
Condyloma Acuminatum	194	0	208	6	100.0 (8.2, 100.0)
Non-acuminate	194	4	208	11	60.4 (-33.5, 90.8)

*The PPE population consisted of individuals who received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 6, 11, 16, and 18) prior to dose 1 and who remained PCR negative to the relevant HPV type(s) through one month post-dose 3 (Month 7).

†Analyses of the combined trials were prospectively planned and included the use of similar study entry criteria.

N=Number of individuals with at least one follow-up visit after Month 7

CI=Confidence Interval

Note 1: Point estimates and confidence intervals are adjusted for person-time of follow-up.

Note 2: Table 6 does not include cases due to HPV types not covered by the vaccine.

AAHS = Amorphous Aluminum Hydroxyphosphate Sulfate, CIN = Cervical Intraepithelial Neoplasia, VIN = Vulvar Intraepithelial Neoplasia, VaIN=Vaginal Intraepithelial Neoplasia, PIN=Penile Intraepithelial Neoplasia, AIN=Anal Intraepithelial Neoplasia, AIS=Adenocarcinoma *In Situ*

In an extension study in females 16 through 26 years of age at enrollment, prophylactic efficacy of GARDASIL through Month 60 against overall cervical and genital disease related to HPV 6, 11, 16, and 18 was 100% (95% CI: 12.3%, 100%) compared to AAHS control.

An extension study in girls and women 16 through 23 years of age used national healthcare registries in Denmark, Iceland, Norway, and Sweden to monitor endpoint cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, cervical cancer, vulvar cancer, or vaginal cancer among 2,650 girls and women 16 through 23 years of age at enrollment who were randomized to vaccination with GARDASIL. An interim analysis of the per-protocol effectiveness population included 1,902 subjects who completed the GARDASIL vaccination series within one year, were naïve to the relevant HPV type through 1 month post-dose 3, had no protocol violations, and had follow-up data available. The median follow-up from the first dose of vaccine was 6.7 years with a range of 2.8 to 8.4 years. At the time of interim analysis, no cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, cervical cancer, vulvar cancer, or vaginal cancer were observed over a total of 5,765 person-years at risk.

Girls and Boys 9 through 15 Years of Age

An extension study of 614 girls and 565 boys 9 through 15 years of age at enrollment who were randomized to vaccination with GARDASIL actively followed subjects for endpoint cases of HPV 6-, 11-, 16-, or 18-related persistent infection, CIN (any grade), AIS, VIN, VaIN, cervical cancer, vulvar cancer, vaginal cancer, and external genital lesions from the initiation of sexual activity or age 16 onwards. An interim analysis of the per-protocol effectiveness population included 246 girls and 168 boys who completed the GARDASIL vaccination series within one year, were seronegative to the relevant HPV type at initiation of the vaccination series, and had not initiated sexual activity prior to receiving the third dose of GARDASIL. The median follow-up from the first dose of vaccine was 7.2 years with a range of

0.5 to 8.5 years. At the time of interim analysis, no cases of persistent infection of at least 12 months' duration and no cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade), AIS, VIN, VaIN, cervical cancer, vulvar cancer, vaginal cancer, or external genital lesions were observed over a total 1,105 person-years at risk. There were 4 cases of HPV 6-, 11-, 16-, or 18-related persistent infection of at least 6 months' duration, including 3 cases related to HPV 16 and 1 case related to HPV 6, none of which persisted to 12 months' duration.

Known to clear naturally during this time

doesn't protect

AAHS: NOT CONTROL

Individuals 27 through 45 Years of Age

A clinical trial evaluated efficacy of GARDASIL in 3,253 women 27 through 45 years of age, based on a combined endpoint of HPV 6-, 11-, 16- or 18-related persistent infection, genital warts, vulvar and vaginal dysplastic lesions of any grade, CIN of any grade, AIS, and cervical cancer. These women were randomized 1:1 to receive either GARDASIL or AAHS control. The clinical trial was conducted in two phases: a base study and a long-term study extension. The per-protocol efficacy (PPE) population received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 6, 11, 16 and 18) prior to dose 1 and remained PCR negative to the relevant HPV type(s) through one month post-dose 3 (Month 7).

In the base study (median duration of follow-up of 3.5 years post-dose 3), the efficacy of GARDASIL against the combined incidence of HPV 6-, 11-, 16-, and 18-related persistent infection, genital warts, VIN, VaIN, vulvar cancer, vaginal cancer, cervical dysplasia (any grade CIN), AIS and cervical cancer in the PPE population was 87.7% (95% CI: 75.4%, 94.6%). The efficacy estimate for the combined endpoint was driven primarily by prevention of persistent infection. The efficacy of GARDASIL against the combined incidence of HPV 6-, 11-, 16-, and 18-related genital warts or cervical dysplasia was 95.0% (95% CI: 68.7%, 99.9%) in the PPE population. While no statistically significant efficacy was demonstrated for GARDASIL in the base study for prevention of cervical intraepithelial neoplasia grades 2 and 3 (CIN 2/3), adenocarcinoma *in situ* (AIS) or cervical cancer related to HPV types 16 and 18, there was 1 case of CIN 2/3 observed in the GARDASIL group and 5 cases in the placebo group. The CIN 2 case in the GARDASIL group tested positive by PCR for HPV 16 and HPV 51.

In the long-term extension of this study, subjects from Colombia (n=600) randomized to the GARDASIL group in the base study were monitored for HPV 6-, 11-, 16-, and 18-related genital warts or cervical dysplasia. The median follow-up post-dose 3 was 8.9 years with a range of 0.1 to 10.1 years over a total of 3,518 person-years. During the long-term extension phase, no cases of HPV 6-, 11-, 16-, or 18-related CIN (any grade) or genital warts were observed in the PPE population.

Effectiveness of GARDASIL in men 27 through 45 years of age is inferred from efficacy data in women 27 through 45 years of age as described above and supported by immunogenicity data from a clinical trial in which 150 men, 27 through 45 years of age, received a 3-dose regimen of GARDASIL (0, 2, 6 months). A cross-study analysis of per-protocol immunogenicity populations compared Month 7 anti-HPV 6, 11, 16, and 18 GMTs of these 27- through 45-year-old men (Study A) to those of 16- through 26-year old boys and men (Study B) in whom efficacy of GARDASIL had been established (see Table 6). GMT ratios (Study A/Study B) for HPV 6, 11, 16, and 18 were 0.82 (95%CI: 0.65, 1.03), 0.79 (95%CI: 0.66, 0.93), 0.91 (95%CI: 0.72, 1.13), and 0.74 (95%CI: 0.59, 0.92), respectively.

14.2 Clinical Trials for GARDASIL 9

Efficacy and/or immunogenicity of the 3-dose regimen of GARDASIL 9 were assessed in six clinical trials. Study 1 evaluated the efficacy of GARDASIL 9 to prevent HPV-related cervical, vulvar, and vaginal disease using GARDASIL as a comparator.

The analysis of efficacy for GARDASIL 9 was evaluated in the per-protocol efficacy (PPE) population of 16- through 26-year-old girls and women, who received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, and were naïve to the relevant HPV type(s) by serology and PCR of cervicovaginal specimens prior to dose one and who remained PCR negative for the relevant HPV type(s) through one month post-dose 3 (Month 7). Overall, approximately 52% of subjects were negative to all vaccine HPV types by both PCR and serology at Day 1.

The primary analysis of efficacy against HPV Types 31, 33, 45, 52, and 58 is based on a combined endpoint of Cervical Intraepithelial Neoplasia (CIN) 2, CIN 3, Adenocarcinoma *in situ* (AIS), invasive cervical carcinoma, Vulvar Intraepithelial Neoplasia (VIN) 2/3, Vaginal Intraepithelial Neoplasia (VaIN)

2/3, vulvar cancer, or vaginal cancer. Other endpoints evaluated include cervical, vulvar and vaginal disease of any grade, persistent infection, cytological abnormalities and invasive procedures. For all endpoints, the efficacy against the HPV Types 31, 33, 45, 52 and 58 in GARDASIL 9 was evaluated compared with GARDASIL. Efficacy of GARDASIL 9 against anal lesions caused by HPV Types 31, 33, 45, 52, and 58 was not assessed due to low incidence. Effectiveness of GARDASIL 9 against anal lesions was inferred from the efficacy of GARDASIL against anal lesions caused by HPV types 6, 11, 16 and 18 in men and antibody responses elicited by GARDASIL 9 against the HPV types covered by the vaccine.

Effectiveness against disease caused by HPV Types 6, 11, 16, and 18 was assessed by comparison of geometric mean titers (GMTs) of type-specific antibodies following vaccination with GARDASIL 9 with those following vaccination with GARDASIL (Study 1 and Study 3). The effectiveness of GARDASIL 9 in girls and boys 9 through 15 years old and in boys and men 16 through 26 years old was inferred based on a comparison of type-specific antibody GMTs to those of 16 through 26-year-old girls and women following vaccination with GARDASIL 9. Immunogenicity analyses were performed in the per-protocol immunogenicity (PPI) population consisting of individuals who received all three vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met pre-defined day range for serum collection for assessment of antibody response and were naïve [PCR negative (in girls and women 16 through 26 years of age; Studies 1 and 2) and seronegative (Studies 1, 2, 3, 5, 7 and 8)] to the relevant HPV type(s) prior to dose 1 and among 16- through 26-year-old girls and women (Studies 1 and 2) remained PCR negative to the relevant HPV type(s) through Month 7. Pre-defined day ranges for vaccinations were relative to Day 1 (dose 1). For the 3-dose schedule, dose 2 was at 2 months (\pm 3 weeks) and dose 3 was at 6 months (\pm 4 weeks). For the 2-dose schedule, dose 2 was at 6 or 12 months (\pm 4 weeks). Pre-defined day range for serum collection for assessment of antibody response was 21 to 49 days after the last dose.

Study 1 evaluated immunogenicity of GARDASIL 9 and efficacy to prevent infection and disease caused by HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in 16- through 26-year-old girls and women. ~~Study 2 evaluated immunogenicity of GARDASIL 9 in girls and boys 9 through 15 years of age and women 16 through 26 years of age. Study 3 evaluated immunogenicity of GARDASIL 9 compared with GARDASIL in girls 9 through 15 years of age. Study 4 evaluated administration of GARDASIL 9 to girls and women 12 through 26 years of age previously vaccinated with GARDASIL. Study 5 evaluated GARDASIL 9 concomitantly administered with Menactra and Adacel in girls and boys 11 through 15 years of age. Together, these five clinical trials evaluated 12,233 individuals who received GARDASIL 9 (8,048 girls and women 16 through 26 years of age at enrollment with a mean age of 21.8 years; 2,927 girls 9 through 15 years of age at enrollment with a mean age of 11.9 years; and 1,258 boys 9 through 15 years of age at enrollment with a mean age of 11.9 years. Study 7 evaluated immunogenicity of GARDASIL 9 in boys and men, including 1,106 self-identified as heterosexual men (HM) and 313 self-identified as men having sex with men (MSM), 16 through 26 years of age at enrollment (mean ages 20.8 years and 22.2 years, respectively) and 1,101 girls and women 16 through 26 years of age at enrollment (mean age 21.3 years).~~

The race distribution of the 16- through 26-year-old girls and women in the clinical trials was as follows: 56.8% White; 25.2% Other; 14.1% Asian; and 3.9% Black. The race distribution of the 9- through 15-year-old girls in the clinical trials was as follows: 60.3% White; 19.3% Other; 13.5% Asian; and 7.0% Black. The race distribution of the 9- through 15-year-old boys in the clinical trials was as follows: 46.6% White; 34.3% Other; 13.3% Asian; and 5.9% Black. The race distribution of the 16- through 26-year-old boys and men in the clinical trials was as follows: 62.1% White; 22.6% Other; 9.8% Asian; and 5.5% Black.

One clinical trial (Study 8) assessed the 2-dose regimen of GARDASIL 9. Study 8 evaluated the immunogenicity of 2 doses of GARDASIL 9 in girls and boys 9 through 14 years of age and 3 doses of GARDASIL 9 in girls 9 through 14 years of age and women 16 through 26 years of age; (N=1,518; 753 girls; 451 boys and 314 women). The mean age for the girls and boys 9 through 14 years of age was 11.5 years; the mean age for girls and women 16 through 26 years of age was 21.0 years. In Study 8, the race distribution was as follows: 61.1% White; 16.3% Asian; 13.3% Other; and 8.9% Black.

14.3 Efficacy – HPV Types 31, 33, 45, 52 and 58 in Girls and Women 16 through 26 Years of Age

Studies Supporting the Efficacy of GARDASIL 9 against HPV Types 31, 33, 45, 52, and 58

The efficacy of GARDASIL 9 in 16- through 26-year-old girls and women was assessed in an active comparator-controlled, double-blind, randomized clinical trial (Study 1) that included a total of 14,204 women (GARDASIL 9 = 7,099; GARDASIL = 7,105) who were enrolled and vaccinated without pre-screening for the presence of HPV infection. Subjects were followed up with a median duration of 40 months (range 0 to 64 months) after the last vaccination.

The primary efficacy evaluation was conducted in the PPE population based on a composite clinical endpoint of HPV 31-, 33-, 45-, 52-, and 58-related cervical cancer, vulvar cancer, vaginal cancer, CIN 2/3 or AIS, VIN 2/3, and VaIN 2/3. Efficacy was further evaluated with the clinical endpoints of HPV 31-, 33-, 45-, 52-, and 58-related CIN 1, vulvar and vaginal disease of any grade, and persistent infection. In addition, the study also evaluated the impact of GARDASIL 9 on the rates of HPV 31-, 33-, 45-, 52-, and 58-related abnormal Papanicolaou (Pap) tests, cervical and external genital biopsy, and definitive therapy [including loop electrosurgical excision procedure (LEEP) and conization]. Efficacy for all endpoints was measured starting after the Month 7 visit.

GARDASIL 9 prevented HPV 31-, 33-, 45-, 52-, and 58-related persistent infection and disease and also reduced the incidence of HPV 31-, 33-, 45-, 52-, and 58-related Pap test abnormalities, cervical and external genital biopsy, and definitive therapy (Table 7).

Table 7: Analysis of Efficacy of GARDASIL 9 against HPV Types 31, 33, 45, 52, and 58 in the PPE* Population of 16- through 26-Year-old Girls and Women (Study 1)

Disease Endpoint	GARDASIL 9 N [†] =7099		GARDASIL N [†] =7105		GARDASIL 9 Efficacy % (95% CI)
	n [‡]	Number of cases	n [‡]	Number of cases	
HPV 31-, 33-, 45-, 52-, 58-related CIN 2/3, AIS, Cervical Cancer, VIN 2/3, VaIN 2/3, Vulvar Cancer, and Vaginal Cancer	6016	1	6017	30	96.7 (80.9, 99.8)
HPV 31-, 33-, 45-, 52-, 58-related CIN 1	5948	1	5943	69	98.6 (92.4, 99.9)
HPV 31-, 33-, 45-, 52-, 58-related CIN 2/3 or AIS	5948	1	5943	27	96.3 (79.5, 99.8)
HPV 31-, 33-, 45-, 52-, 58-related Vulvar or Vaginal Disease	6009	1	6012	16	93.8 (61.5, 99.7)
HPV 31-, 33-, 45-, 52-, 58-related Persistent Infection ≥6 Months [§]	5939	26	5953	642	96.2 (94.4, 97.5)
HPV 31-, 33-, 45-, 52-, 58-related Persistent Infection ≥12 Months [¶]	5939	15	5953	375	96.1 (93.7, 97.9)
HPV 31-, 33-, 45-, 52-, 58-related ASC-US HR-HPV Positive or Worse Pap [#] Abnormality	5881	35	5882	462	92.6 (89.7, 94.8)
HPV 31-, 33-, 45-, 52-, 58-related Biopsy	6016	7	6017	222	96.9 (93.6, 98.6)
HPV 31-, 33-, 45-, 52-, 58-related Definitive Therapy [‡]	6012	4	6014	32	87.5 (65.7, 96.0)

*The PPE population consisted of individuals who received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, were naïve (PCR negative and seronegative) to the relevant HPV type(s) (Types 31, 33, 45, 52, and 58) prior to dose 1, and who remained PCR negative to the relevant HPV type(s) through one month post-dose 3 (Month 7); data from Study 1 (NCT00543543).

[†]N=Number of individuals randomized to the respective vaccination group who received at least one injection

[‡]n=Number of individuals contributing to the analysis

[§]Persistent infection detected in samples from two or more consecutive visits at least six months apart

[¶]Persistent infection detected in samples from two or more consecutive visits over 12 months or longer

[#]Papanicolaou test

[‡]Including loop electrosurgical excision procedure (LEEP) and conization

CI=Confidence Interval

CIN=Cervical Intraepithelial Neoplasia, VIN=Vulvar Intraepithelial Neoplasia, VaIN=Vaginal Intraepithelial Neoplasia,

AIS=Adenocarcinoma *In Situ*, ASC-US=Atypical squamous cells of undetermined significance

HR=High Risk

14.4 Immunogenicity of a 3-Dose Regimen

The minimum anti-HPV titer that confers protective efficacy has not been determined.

LAB
PARTS
NO POST MARKET
- (MARKETING) -

Type-specific immunoassays (i.e., cLIA) with type-specific standards were used to assess immunogenicity to each vaccine HPV type. These assays measured antibodies against neutralizing epitopes for each HPV type. The scales for these assays are unique to each HPV type; thus, comparisons across types and to other assays are not appropriate. Immunogenicity was measured by (1) the percentage of individuals who were seropositive for antibodies against the relevant vaccine HPV type, and (2) the Geometric Mean Titer (GMT).

Studies Supporting the Effectiveness of GARDASIL 9 against HPV Types 6, 11, 16, and 18

Effectiveness of GARDASIL 9 against persistent infection and disease related to HPV Types 6, 11, 16, or 18 was inferred from non-inferiority comparisons in Study 1 (16- through 26-year-old girls and women) and Study 3 (9- through 15-year-old girls) of GMTs following vaccination with GARDASIL 9 with those following vaccination with GARDASIL. A low number of efficacy endpoint cases related to HPV types 6, 11, 16 and 18 in both vaccination groups precluded a meaningful assessment of efficacy using disease endpoints associated with these HPV types. The primary analyses were conducted in the per-protocol population, which included subjects who received all three vaccinations within one year of enrollment, did not have major deviations from the study protocol, and were HPV-naïve. HPV-naïve individuals were defined as seronegative to the relevant HPV type(s) prior to dose 1 and among female subjects 16 through 26 years of age in Study 1 PCR negative to the relevant HPV type(s) in cervicovaginal specimens prior to dose 1 through Month 7.

Anti-HPV 6, 11, 16 and 18 GMTs at Month 7 for GARDASIL 9 among girls 9 through 15 years of age and young women 16 through 26 years of age were non-inferior to those among the corresponding populations for GARDASIL (Table 8). At least 99.7% of individuals included in the analyses for each HPV type became seropositive by Month 7.

Table 8: Comparison of Immune Responses (Based on cLIA) Between GARDASIL 9 and GARDASIL for HPV Types 6, 11, 16, and 18 in the PPI* Population of 9- through 26-Year-Old Girls and Women (Studies 1 and 3)

Population	GARDASIL 9		GARDASIL		GARDASIL 9/ GARDASIL	
	N [†] (n [‡])	GMT mMU [§] /mL	N [†] (n [‡])	GMT mMU [§] /mL	GMT Ratio	(95% CI) [†]
Anti-HPV 6						
9- through 15-year-old girls	300 (273)	1679.4	300 (261)	1565.9	1.07	(0.93, 1.23)
16- through 26-year-old girls and women	6792 (3993)	893.1	6795 (3975)	875.2	1.02	(0.99, 1.06)
Anti-HPV 11						
9- through 15-year-old girls	300 (273)	1315.6	300 (261)	1417.3	0.93	(0.80, 1.08)
16- through 26-year-old girls and women	6792 (3995)	666.3	6795 (3982)	830.0	0.80	(0.77, 0.83)
Anti-HPV 16						
9- through 15-year-old girls	300 (276)	6739.5	300 (270)	6887.4	0.97	(0.85, 1.11)
16- through 26-year-old girls and women	6792 (4032)	3131.1	6795 (4062)	3156.6	0.99	(0.96, 1.03)
Anti-HPV 18						

Population	GARDASIL 9		GARDASIL		GARDASIL 9/ GARDASIL	
	N [†] (n [‡])	GMT mMU [§] /mL	N [†] (n [‡])	GMT mMU [§] /mL	GMT Ratio	(95% CI) [¶]
9- through 15-year-old girls	300 (276)	1956.6	300 (269)	1795.6	1.08	(0.91, 1.29)
16- through 26-year-old girls and women	6792 (4539)	804.6	6795 (4541)	678.7	1.19	(1.14, 1.23)

*The PPI population consisted of individuals who received all three vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the Month 6 and Month 7 visit, were naïve (PCR negative [among 16- through 26-year old girls and women] and seronegative) to the relevant HPV type(s) (types 6, 11, 16, and 18) prior to dose 1, and among 16- through 26-year-old girls and women remained PCR negative to the relevant HPV type(s) through one month post-dose 3 (Month 7). The data for 16- through 26-year-old girls and women are from Study 1 (NCT00543543), and the data for 9- through 15-year-old girls are from Study 3 (NCT01304498).

[†]N=Number of individuals randomized to the respective vaccination group who received at least one injection

[‡]n=Number of individuals contributing to the analysis

[§]mMU=milli-Merck Units

[¶]Demonstration of non-inferiority required that the lower bound of the 95% CI of the GMT ratio be greater than 0.67

CI=Confidence Interval

GMT=Geometric Mean Titer

cLIA=competitive Luminex Immunoassay

Study Supporting the Effectiveness of GARDASIL 9 against Vaccine HPV Types in 9- through 15-Year-Old Girls and Boys

Effectiveness of GARDASIL 9 against persistent infection and disease related to vaccine HPV types in 9- through 15-year-old girls and boys was inferred from non-inferiority comparison conducted in the PPI population in Study 2 of GMTs following vaccination with GARDASIL 9 among 9- through 15-year-old girls and boys with those among 16- through 26-year-old girls and women. Anti-HPV GMTs at Month 7 among 9- through 15-year-old girls and boys were non-inferior to anti-HPV GMTs among 16- through 26-year-old girls and women (Table 9).

Table 9: Comparison of Immune Responses (Based on cLIA) between the PPI* Populations of 16- through 26-Year-Old Girls and Women, 9- through 15-Year-Old Girls, and 9- through 15-Year-Old Boys for All GARDASIL 9 Vaccine HPV Types (Study 2)

Population	N [†]	n [‡]	GMT mMU [§] /mL	GMT Ratio relative to 16- through 26-year-old girls and women (95% CI) [¶]
Anti-HPV 6				
9- through 15-year-old girls	630	503	1703.1	1.89 (1.68, 2.12)
9- through 15-year-old boys	641	537	2083.4	2.31 (2.06, 2.60)
16- through 26-year-old girls and women	463	328	900.8	1
Anti-HPV 11				
9- through 15-year-old girls	630	503	1291.5	1.83 (1.63, 2.05)
9- through 15-year-old boys	641	537	1486.3	2.10 (1.88, 2.36)
16- through 26-year-old girls and women	463	332	706.6	1
Anti-HPV 16				
9- through 15-year-old girls	630	513	6933.9	1.97 (1.75, 2.21)
9- through 15-year-old boys	641	546	8683.0	2.46 (2.20, 2.76)
16- through 26-year-old girls and women	463	329	3522.6	1
Anti-HPV 18				
9- through 15-year-old girls	630	516	2148.3	2.43 (2.12, 2.79)
9- through 15-year-old boys	641	544	2855.4	3.23 (2.83, 3.70)
16- through 26-year-old girls and women	463	345	882.7	1
Anti-HPV 31				
9- through 15-year-old girls	630	506	1894.7	2.51 (2.21, 2.86)
9- through 15-year-old boys	641	543	2255.3	2.99 (2.63, 3.40)
16- through 26-year-old girls and women	463	340	753.9	1
Anti-HPV 33				

9- through 15-year-old girls	630	518	985.8	2.11 (1.88, 2.37)
9- through 15-year-old boys	641	544	1207.4	2.59 (2.31, 2.90)
16- through 26-year-old girls and women	463	354	466.8	1
Anti-HPV 45				
9- through 15-year-old girls	630	518	707.7	2.60 (2.25, 3.00)
9- through 15-year-old boys	641	547	912.1	3.35 (2.90, 3.87)
16- through 26-year-old girls and women	463	368	272.2	1
Anti-HPV 52				
9- through 15-year-old girls	630	517	962.2	2.21 (1.96, 2.49)
9- through 15-year-old boys	641	545	1055.5	2.52 (2.22, 2.84)
16- through 26-year-old girls and women	463	337	419.6	1
Anti-HPV 58				
9- through 15-year-old girls	630	516	1288.0	2.18 (1.94, 2.46)
9- through 15-year-old boys	641	544	1593.3	2.70 (2.40, 3.03)
16- through 26-year-old girls and women	463	332	590.5	1

*The PPI population consisted of individuals who received all three vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the Month 6 and Month 7 visit, were naïve (PCR negative [among 16- through 26-year old girls and women] and seronegative) to the relevant HPV type(s) prior to dose 1 and among 16- through 26-year-old girls and women remained PCR negative to the relevant HPV types through one month post-dose 3 (Month 7). The data are from Study 2 (NCT00943722).

[†]N=Number of individuals randomized to the respective vaccination group who received at least one injection

[‡]n=Number of individuals contributing to the analysis

[§]mMU=milli-Merck Units

[¶]Demonstration of non-inferiority required that the lower bound of the 95% CI of the GMT ratio be greater than 0.67

cLIA=competitive Luminex Immunoassay

CI=Confidence Interval

GMT=Geometric Mean Titer

Study Supporting the Effectiveness of GARDASIL 9 against Vaccine HPV Types in 16- through 26-Year-Old Boys and Men

Effectiveness of GARDASIL 9 against persistent infection and disease related to vaccine HPV types in 16- through 26-year-old boys and men was inferred from non-inferiority comparison conducted in the PPI population in Study 7 of GMTs following vaccination with GARDASIL 9 among 16- through 26-year-old HM with those among 16- through 26-year-old girls and women. Anti-HPV GMTs at Month 7 among 16- through 26-year-old HM were non-inferior to anti-HPV GMTs among 16- through 26-year-old girls and women (Table 10). Study 7 also enrolled 313 16- through 26-year-old HIV-negative MSM. At Month 7, anti-HPV GMT ratios for MSM relative to HM ranged from 0.6 to 0.8, depending on HPV type. The GMT ratios for MSM relative to HM were generally similar to those previously observed in clinical trials with GARDASIL.

Table 10: Comparison of Immune Responses (Based on cLIA) between the PPI* Populations of 16- through 26-Year-Old Girls and Women and 16- through 26-Year-Old Boys and Men Self-Identified as Heterosexual (HM) for All GARDASIL 9 Vaccine HPV Types (Study 7)

Population	N [†]	n [‡]	GMT mMU [§] /mL	GMT Ratio relative to 16- through 26-year-old girls and women (95% CI) [†]
Anti-HPV 6				
16- through 26-year-old HM	1103	847	782.0	1.11 (1.02, 1.21)
16- through 26-year-old girls and women	1099	708	703.9	1
Anti-HPV 11				
16- through 26-year-old HM	1103	851	616.7	1.09 (1.00, 1.19)
16- through 26-year-old girls and women	1099	712	564.9	1
Anti-HPV 16				
16- through 26-year-old HM	1103	899	3346.0	1.20 (1.10, 1.30)
16- through 26-year-old girls and women	1099	781	2788.3	1
Anti-HPV 18				
16- through 26-year-old HM	1103	906	808.2	1.19 (1.08, 1.31)
16- through 26-year-old girls and women	1099	831	679.8	1
Anti-HPV 31				
16- through 26-year-old HM	1103	908	708.5	1.24 (1.13, 1.37)
16- through 26-year-old girls and women	1099	826	570.1	1
Anti-HPV 33				
16- through 26-year-old HM	1103	901	384.8	1.19 (1.10, 1.30)
16- through 26-year-old girls and women	1099	853	322.0	1
Anti-HPV 45				
16- through 26-year-old HM	1103	909	235.6	1.27 (1.14, 1.41)
16- through 26-year-old girls and women	1099	871	185.7	1
Anti-HPV 52				
16- through 26-year-old HM	1103	907	386.8	1.15 (1.05, 1.26)
16- through 26-year-old girls and women	1099	849	335.2	1
Anti-HPV 58				
16- through 26-year-old HM	1103	897	509.8	1.25 (1.14, 1.36)
16- through 26-year-old girls and women	1099	839	409.3	1

*The PPI population consisted of individuals who received all three vaccinations within pre-defined day ranges, did not have major deviations from the study protocol, met predefined criteria for the interval between the Month 6 and Month 7 visit, and were seronegative to the relevant HPV type(s) (types 6, 11, 16, 18, 31, 33, 45, 52, and 58) prior to dose 1. The data are from Study 7 (NCT01651949).

[†]Number of individuals randomized to the respective vaccination group who received at least one injection

[‡]Number of individuals contributing to the analysis

[§]mMU=milli-Merck Units

[†]Demonstration of non-inferiority required that the lower bound of the 95% CI of the GMT ratio be greater than 0.67

cLIA=competitive Luminex Immunoassay

CI=Confidence Interval

GMT=Geometric Mean Titer

Immune Response to GARDASIL 9 across All Clinical Trials

Across all clinical trials, at least 99.5% of individuals included in the analyses for each of the nine vaccine HPV types became seropositive by Month 7. Anti-HPV GMTs at Month 7 among 9- through 15-year-old girls and boys and 16- through 26-year-old boys and men were comparable to anti-HPV responses among 16- through 26-year-old girls and women in the combined database of immunogenicity studies for GARDASIL 9.

how about AAHS

Persistence of Immune Response to GARDASIL 9

The duration of immunity following a 3-dose schedule of vaccination with GARDASIL 9 has not been established. The peak anti-HPV GMTs for each vaccine HPV type occurred at Month 7. Proportions of individuals who remained seropositive to each vaccine HPV type at Month 24 were similar to the corresponding seropositive proportions at Month 7.

Administration of GARDASIL 9 to Individuals Previously Vaccinated with GARDASIL

Study 4 evaluated the immunogenicity of 3 doses of GARDASIL 9 in 921 girls and women (12 through 26 years of age) who had previously been vaccinated with 3 doses of GARDASIL. Prior to enrollment in

the study, over 99% of subjects had received three injections of GARDASIL within a one year period. The time interval between the last injection of GARDASIL and the first injection of GARDASIL 9 ranged from approximately 12 to 36 months.

Seropositivity to HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 in the per protocol population ranged from 98.3 to 100% by Month 7 in individuals who received GARDASIL 9. The anti-HPV 31, 33, 45, 52 and 58 GMTs for the population previously vaccinated with GARDASIL were 25-63% of the GMTs in the combined populations from Studies 1, 2, 3, and 5, who had not previously received GARDASIL, although the clinical relevance of these differences is unknown. Efficacy of GARDASIL 9 in preventing infection and disease related to HPV Types 31, 33, 45, 52, and 58 in individuals previously vaccinated with GARDASIL has not been assessed.

Concomitant Use of Hormonal Contraceptives

Among 7,269 female recipients of GARDASIL 9 (16 through 26 years of age), 60.2% used hormonal contraceptives during the vaccination period of clinical studies 1 and 2. Use of hormonal contraceptives did not appear to affect the type specific immune responses to GARDASIL 9.

14.5 Immune Responses to GARDASIL 9 Using a 2-Dose Regimen in Individuals 9 through 14 Years of Age

Effectiveness of GARDASIL 9 against persistent infection and disease related to vaccine HPV types in 9- through 14-year-old girls and boys who received a 2-dose regimen was inferred from non-inferiority comparison conducted in the PPI population in Study 8 of GMTs following vaccination with GARDASIL 9 among 9- through 14-year-old girls and boys who received a 2-dose regimen (at 0, 6 months or 0, 12 months) with those among 16- through 26-year-old girls and women who received a 3-dose regimen (at 0, 2, 6 months). Anti-HPV GMTs at one month after the last dose among 9- through 14-year-old girls and boys who received 2 doses of GARDASIL 9 were non-inferior to anti-HPV GMTs among 16- through 26-year-old girls and women who received 3 doses of GARDASIL 9 (Table 11).

One month following the last dose of the assigned regimen, between 97.9% and 100% of subjects across all groups became seropositive for antibodies against the 9 vaccine HPV types (Table 11).

In the same study, in girls and boys 9 through 14 years old, GMTs at one month after the last vaccine dose were numerically lower for some vaccine types after a 2-dose schedule than in girls 9 through 14 years old after a 3-dose schedule (HPV types 18, 31, 45, and 52 after 0, 6 months and HPV type 45 after 0, 12 months; Table 11). The clinical relevance of these findings is unknown.

Duration of immunity of a 2-dose schedule of GARDASIL 9 has not been established.

LAB RAFTS!

Table 11: Summary of Anti-HPV cLIA Geometric Mean Titers in the PPI* Population at One Month After the Last Vaccine Dose Among Subjects Who Received 2 Doses[†] or 3 Doses[‡] of GARDASIL 9 (Study 8)

Population (Regimen)	N	n	GMT mMU ³ /mL	GMT Ratio relative to 3- dose regimen in 16- through 26-year-old girls and women (95% CI)
Anti-HPV 6				
9- to 14-year-old girls (0, 6) [†]	301	258	1657.9	2.15 (1.83, 2.53) [§]
9- to 14-year-old boys (0, 6) [†]	301	263	1557.4	2.02 (1.73, 2.36) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	257	2678.8	3.47 (2.93, 4.11) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	254	1496.1	1.94 (1.65, 2.29) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	238	770.9	1
Anti-HPV 11				
9- to 14-year-old girls (0, 6) [†]	301	258	1388.9	2.39 (2.03, 2.82) [§]
9- to 14-year-old boys (0, 6) [†]	301	264	1423.9	2.45 (2.09, 2.88) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	257	2941.8	5.07 (4.32, 5.94) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	254	1306.3	2.25 (1.90, 2.66) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	238	580.5	1
Anti-HPV 16				
9- to 14-year-old girls (0, 6) [†]	301	272	8004.9	2.54 (2.14, 3.00) [§]
9- to 14-year-old boys (0, 6) [†]	301	273	8474.8	2.69 (2.29, 3.15) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	264	14329.3	4.54 (3.84, 5.37) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	269	6996.0	2.22 (1.89, 2.61) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	249	3154.0	1
Anti-HPV 18				
9- to 14-year-old girls (0, 6) [†]	301	272	1872.8	2.46 (2.05, 2.96) [§]
9- to 14-year-old boys (0, 6) [†]	301	272	1860.9	2.44 (2.04, 2.92) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	266	2810.4	3.69 (3.06, 4.45) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	270	2049.3	2.69 (2.24, 3.24) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	267	761.5	1
Anti-HPV 31				
9- to 14-year-old girls (0, 6) [†]	301	272	1436.3	2.51 (2.10, 3.00) [§]
9- to 14-year-old boys (0, 6) [†]	301	271	1498.2	2.62 (2.20, 3.12) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	268	2117.5	3.70 (3.08, 4.45) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	271	1748.3	3.06 (2.54, 3.67) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	264	572.1	1
Anti-HPV 33				
9- to 14-year-old girls (0, 6) [†]	301	273	1030.0	2.96 (2.50, 3.50) [§]
9- to 14-year-old boys (0, 6) [†]	301	271	1040.0	2.99 (2.55, 3.50) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	269	2197.5	6.31 (5.36, 7.43) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	275	796.4	2.29 (1.95, 2.68) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	279	348.1	1
Anti-HPV 45				
9- to 14-year-old girls (0, 6) [†]	301	274	357.6	1.67 (1.38, 2.03) [§]
9- to 14-year-old boys (0, 6) [†]	301	273	352.3	1.65 (1.37, 1.99) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	268	417.7	1.96 (1.61, 2.37) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	275	661.7	3.10 (2.54, 3.77) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	280	213.6	1
Anti-HPV 52				
9- to 14-year-old girls (0, 6) [†]	301	272	581.1	1.60 (1.36, 1.87) [§]
9- to 14-year-old boys (0, 6) [†]	301	273	640.4	1.76 (1.51, 2.05) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	268	1123.4	3.08 (2.64, 3.61) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	275	909.9	2.50 (2.12, 2.95) [†]
16- to 26-year-old women (0, 2, 6) [†]	314	271	364.2	1
Anti-HPV 58				
9- to 14-year-old girls (0, 6) [†]	301	270	1251.2	2.55 (2.15, 3.01) [§]
9- to 14-year-old boys (0, 6) [†]	301	270	1325.7	2.70 (2.30, 3.16) [§]
9- to 14-year-old girls and boys (0, 12) [†]	300	265	2444.6	4.98 (4.23, 5.86) [§]
9- to 14-year-old girls (0, 2, 6) [†]	300	273	1229.3	2.50 (2.11, 2.97) [†]

16 HOW SUPPLIED/STORAGE AND HANDLING

GARDASIL 9 is supplied in vials and syringes.

Carton of ten 0.5-mL single-dose vials. NDC 0006-4119-03

Carton of ten 0.5-mL single-dose prefilled Luer Lock syringes with tip caps. NDC 0006-4121-02

Store refrigerated at 2 to 8°C (36 to 46°F). Do not freeze. Protect from light.

GARDASIL 9 should be administered as soon as possible after being removed from refrigeration. GARDASIL 9 can be administered provided total (cumulative multiple excursion) time out of refrigeration (at temperatures between 8°C and 25°C) does not exceed 72 hours. Cumulative multiple excursions between 0°C and 2°C are also permitted as long as the total time between 0°C and 2°C does not exceed 72 hours. These are not, however, recommendations for storage.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Inform the patient, parent, or guardian:

- Vaccination does not eliminate the necessity for women to continue to undergo recommended cervical cancer screening. Women who receive GARDASIL 9 should continue to undergo cervical cancer screening per standard of care.
- Recipients of GARDASIL 9 should not discontinue anal cancer screening if it has been recommended by a health care provider.
- GARDASIL 9 has not been demonstrated to provide protection against disease from vaccine and non-vaccine HPV types to which a person has previously been exposed through sexual activity.
- Since syncope has been reported following HPV vaccination sometimes resulting in falling with injury, observation for 15 minutes after administration is recommended.
- Vaccine information is required to be given with each vaccination to the patient, parent, or guardian.
- Provide information regarding benefits and risks associated with vaccination.
- Safety and effectiveness of GARDASIL 9 have not been established in pregnant women. A pregnancy registry is available. Women exposed to GARDASIL 9 around the time of conception or during pregnancy are encouraged to register by calling 1-800-986-8999. [See *Use in Specific Populations* (8.1).]
- It is important to complete the full vaccination series unless contraindicated.
- Report any adverse reactions to their health care provider.

Manuf. and Dist. by: Merck Sharp & Dohme Corp., a subsidiary of
 **MERCK & CO., INC.**, Whitehouse Station, NJ 08889, USA

For patent information: www.merck.com/product/patent/home.html

The trademarks depicted herein are owned by their respective companies.

Copyright © 2006-2018 Merck Sharp & Dohme Corp., a subsidiary of **Merck & Co., Inc.**
All rights reserved.

uspi-v503-i-1810r008

OPT IN TO RECEIVE YOUR DAILY NEWS EMAIL HOT OFF THE PRESS

0.
Subscribe (https://www.facebook.com/AustralianNationalReview)
Twitter (https://twitter.com/ANRNews)

[HTTPS://AUSTRALIANNATIONALREVIEW.COM](https://australiannationalreview.com)

[Home \(https://australiannationalreview.com/\)](https://australiannationalreview.com/)

[Will you help us remain a force for good and save the free press in these difficult times? \(https://australiannationalreview.com/donate/\)](https://australiannationalreview.com/donate/)

[Business \(https://australiannationalreview.com/category/business/\)](https://australiannationalreview.com/category/business/)

[Finance \(https://australiannationalreview.com/category/finance/\)](https://australiannationalreview.com/category/finance/)

[Property \(https://australiannationalreview.com/category/property/\)](https://australiannationalreview.com/category/property/)

[State of Affairs \(https://australiannationalreview.com/category/state-of-affairs/\)](https://australiannationalreview.com/category/state-of-affairs/)

[Lifestyle \(https://australiannationalreview.com/category/lifestyle/\)](https://australiannationalreview.com/category/lifestyle/)



COMMENTARY

Lead Developer Of HPV Vaccines Comes Clean, Warns Parents & Young Girls It's All A Giant Deadly

Walmart.com | Save

Scam

By Secretsofthefed.com - January 21, 2018

Shop Walmart.com
for Every Day Low
Prices. Free
Shipping

Lead Developer Of HPV Vaccines Comes Clean, Warns Parents & Young Girls It's All A Giant Deadly Scam

www.walmart.com

Shares

3
SHARES

Dr. Diane Harper was a leading expert responsible for the Phase II and Phase III safety and effectiveness studies which secured the approval of the human papilloma virus (HPV) vaccines, Gardasil™ and Cervarix™. Dr. Harper also authored many of the published, scholarly papers about the vaccines. She is now the latest in a long string of experts who are pressing the red alert button on the devastating consequences and irrelevancy of these vaccines. Dr. Harper made her surprising confession at the 4th International Conference on Vaccination which took place in Reston,

Her speech, which was originally intended to promote the f the vaccines, took a 180-degree turn when she chose instead to conscience about the deadly vaccines so she "could sleep at night . The following is an excerpt from a story by Sarah Cain (<http://southweb.org/lifewise/the-lead-vaccine-developer-comes-clean-so-she-can-sleep-at-night-gardasil-and-cervarix-dont-work-are-dangerous-and-werent-tested/>):

"Dr. Harper explained in her presentation that the cervical cancer risk in the U.S. is already extremely low, and that vaccinations are unlikely to have any effect upon

the rate of cervical cancer in the United States. In fact, 70% of all HPV infections resolve themselves without treatment in a year, and the number rises to well over 90% in two years. Harper also mentioned the safety angle. All trials of the vaccines were done on children aged 15 and above, despite them currently being marketed for 9-year-olds. So far, 15,037 girls have reported adverse side effects from Gardasil™ alone to the Vaccine Adverse Event Reporting System (VAERS), and this number only reflects parents who underwent the hurdles required for reporting adverse reactions. At the time of writing, 44 girls are officially known to have died from these vaccines. The reported side effects include Guillian Barré Syndrome (paralysis lasting for years, or permanently — sometimes eventually causing suffocation), lupus, seizures, blood clots, and brain inflammation. Parents are usually not made aware of these risks. Dr. Harper, the vaccine developer, claimed that she was speaking out, so that she might finally be able to sleep at night. 'About eight in every ten women who have been sexually active will have HPV at some stage of their life,' Harper says. 'Normally there are no symptoms, and in 98 per cent of cases it clears itself. But in those cases where it doesn't, and isn't treated, it can lead to pre-cancerous cells which may develop into cervical cancer.'"

Although these two vaccines are marketed as protection against cervical cancer, this claim is purely hypothetical. Studies have proven "there is no demonstrated relationship between the condition being vaccinated for and the rare cancers that the vaccine might prevent, but it is marketed to do that nonetheless. In fact, there is no actual evidence that the vaccine can prevent any cancer. From the manufacturers own admissions, the vaccine only works on 4 strains out of 40 for a specific venereal disease that dies on its own in a relatively short period, so the chance of it actually helping an individual is about about the same as the chance of her being struck by a meteorite."

CONTINUE > ([HTTPS://AUSTRALIANNATIONALREVIEW.COM/2018/01/21/LEAD-DEVELOPER-OF-HPV-VACCINES-COMES-CLEAN-WARNS-PARENTS-YOUNG-GIRLS-ITS-ALL-A-GIANT-DEADLY-SCAM/2/](https://australiannationalreview.com/2018/01/21/lead-developer-of-hpv-vaccines-comes-clean-warns-parents-young-girls-its-all-a-giant-deadly-scam/2/))

0 Comments

Sort by Oldest

Add a comment...

Facebook Comments Plugin

- [Information](#)
- [Security Systems](#)
- [Home](#)
- [Categories](#)
- [Children](#)
- [Aaron](#)
- [Active](#)
- [Addiction](#)
- [Security Systems](#)
- [Home](#)
- [Categories](#)
- [Children](#)
- [Aaron](#)
- [Active](#)
- [Addiction Treatment](#)
- [Adn](#)

CATEGORIES

[Home \(https://australiannationalreview.com/\)](https://australiannationalreview.com/)

[Will you help us remain a force for good and save the free press in these difficult times? \(https://australiannationalreview.com/donate/\)](https://australiannationalreview.com/donate/)

[Business \(https://australiannationalreview.com/category/business/\)](https://australiannationalreview.com/category/business/)

[Finance \(https://australiannationalreview.com/category/finance/\)](https://australiannationalreview.com/category/finance/)

[Property \(https://australiannationalreview.com/category/property/\)](https://australiannationalreview.com/category/property/)

[State of Affairs \(https://australiannationalreview.com/category/state-of-affairs/\)](https://australiannationalreview.com/category/state-of-affairs/)

[Lifestyle \(https://australiannationalreview.com/category/lifestyle/\)](https://australiannationalreview.com/category/lifestyle/)

INFORMATION

[Home \(https://australiannationalreview.com/\)](https://australiannationalreview.com/)

[About \(https://australiannationalreview.com/about-us/\)](https://australiannationalreview.com/about-us/)

RECENT POST

[CDC Finally Admits What Anti-vaxxers Say About The MMR Vaccine](#)

By - December 16, 2018

[\(https://australiannationalreview.com/2018/12/16/cdc-finally-admits-what-anti-vaxxers-say-about-the-mmr-vaccine/\)](https://australiannationalreview.com/2018/12/16/cdc-finally-admits-what-anti-vaxxers-say-about-the-mmr-vaccine/)

[WikiLeaks Founder Julian Assange Examined By Doctors As MSM And Democrats Push Fake News Story On Meeting With Paul Manafort](#)

By - December 16, 2018

[\(https://australiannationalreview.com/2018/12/16/wikileaks-founder-julian-assange-examined-by-doctors-as-msm-and-democrats-push-fake-news-story-on-meeting-with-paul-manafort/\)](https://australiannationalreview.com/2018/12/16/wikileaks-founder-julian-assange-examined-by-doctors-as-msm-and-democrats-push-fake-news-story-on-meeting-with-paul-manafort/)

SUBSCRIBE

OPT IN TO RECEIVE YOUR DAILY NEWS EMAIL HOT OFF THE PRESS

0

SUBMIT

f [\(https://www.facebook.com/AustralianNationalReview/\)](https://www.facebook.com/AustralianNationalReview/) **t** [_ \(https://twitter.com/ANRNews\)](https://twitter.com/ANRNews)

Copyright © 2018 Australian National Review.



Download

Share

Export

Vaccine

Volume 34, Issue 15, 4 April 2016, Pages 1800-1805

Adverse events following HPV vaccination, Alberta 2006–2014

Xianfang C. Liu ^a✉, Christopher A. Bell ^b✉, Kimberley A. Simmonds ^b✉, Lawrence W. Svenson ^{a, b, c}✉, Margaret L. Russell ^a✉

Show more

<https://doi.org/10.1016/j.vaccine.2016.02.040>

Get rights and content

Under a Creative Commons license

open access

Highlights

- Reported adverse events (HPV vaccination) were examined for Alberta for June 2006–November 2014.

- Emergency department (ED) visits and hospitalizations within 42 days were also examined.

- Data include females aged 12–19 years

Register to receive personalized recommendations based on your recent signed-in activity ^x

- Venous thromboses and hospitalizations were examined

Register for free

- AEFI rates were low and consistent with types of event seen elsewhere.

Abstract

Background

In Canada, private purchase of human papilloma virus (HPV) vaccines has been possible since 2006. In Alberta, Canada, a publicly funded quadrivalent HPV vaccine program began in the 2008/2009 school year. There have been concerns about adverse events, including venous thromboembolism (VTE) associated with HPV vaccines. We describe the frequencies of adverse events following HPV vaccination among Alberta females aged 9 years or older and look at VTE following HPV vaccination.

Methods

We used the Alberta Immunization and Adverse Reaction to Immunization (Imm/ARI) repository (publicly funded vaccine), the population-based Pharmaceutical Information Network (PIN) information system (dispensing of a vaccine), and the Alberta Morbidity and Ambulatory Care Abstract reporting system (MACAR) for June 1, 2006–November 19, 2014. Deterministic data linkage used unique personal identifiers. We identified all reported adverse events following immunization (AEFI) and all emergency department (ED) utilization or hospitalizations within 42 days of immunization. We calculated the frequency of AEFI by type, rates per 100,000 doses of HPV vaccine administered and the frequencies of ICD-10-CA codes for hospitalizations and emergency department visits.

Results

Over the period 195,270 females received 528,913 doses of HPV vaccine. Of those receiving at least one dose, 192 reported one or more AEFI events (198 AEFI events), i.e., 37.4/100,000 doses administered (95% CI 32.5–43.0). None were consistent with VTE. Of the women who received HPV vaccine 958 were hospitalized and 19,351 had an ED visit within 42 days of immunization. Four women who had an ED visit and hospitalization event were diagnosed with VTE. Three of these had other diagnoses known to be associated with VTE; the fourth woman had VTE among ED diagnoses but not among those for the hospitalization.

Conclusions

Rates of AEFI after HPV immunization in Alberta are low and consistent with types of events seen elsewhere.



Abbreviations

WHO, World Health Organization; HPV, human papillomavirus; qHPV, quadrivalent human papillomavirus; bHPV, bivalent human papillomavirus; NACI, National Advisory Committee on Immunization; AEFI, Adverse Events Following Immunization; VTE, venous thromboembolic events; ULI, unique personal identifier; Imm/ARI, immunization and adverse reaction to immunization; PIN, Pharmaceutical Information Network; ED, Emergency Department; MACAR, (Alberta) Morbidity and Ambulatory Care Abstract Reporting; ICD-10-CA, International Classification of Diseases, 10th Revision-Canadian Adaptation

Keywords

*Papillomavirus vaccines/ae [adverse effects]; *Vaccination/ae [adverse effects]; Population surveillance; Humans; Alberta; HPV vaccination; Canada; *Product surveillance; Postmarketing

1. Introduction

The World Health Organization (WHO) recommends the human papillomavirus (HPV) vaccine for prevention of cervical cancer and other HPV-related diseases [1]. Quadrivalent HPV (qHPV) vaccine was authorized and became available for private purchase in Canada in 2006 for females aged 9–26 years. This authorization was expanded to include females aged 9–45 years in 2011. Bivalent HPV (bHPV) vaccine was also authorized for use among females aged 10–25 years in 2010. Canada's National Advisory Committee on Immunization (NACI) has recommended both vaccines in females aged 9–26 years of age [2]. Both vaccines were initially administered in a three-dose series; however NACI now recommends a two-dose series for immunocompetent persons aged 9–14 years [2].

In Alberta, the publicly funded routine childhood and adolescent vaccines are administered exclusively by public health nurses. Alberta began to deliver a publicly funded three-dose qHPV vaccine series in the 2008/09 school year for females in grade 5, most of whom were aged 10–11 years [3]. A catch-up program was implemented from 2009/10 to 2011/12 for females in grade 9 (most of whom were aged 14–15 years). Both qHPV and bHPV vaccines

are also available for private purchase through pharmacies.

The monitoring of adverse events following immunization (AEFI) contributes to vaccine safety surveillance and is an important component of all vaccination programs. Vaccine safety is monitored by passive surveillance in Alberta. There have been community concerns that HPV vaccines may be associated with adverse events. Venous thromboembolic events (VTE) are a particular concern, as some were reported to occur following HPV immunization in the United States [4]. The objective of this study is to describe the frequencies of adverse events among females aged 9 years or older that occurred following HPV vaccination including looking specifically at VTE following HPV vaccination.

2. Methods

2.1. Ethics and role of funding source

The study was approved by the University of Calgary Conjoint Health Research Ethics Board (Ethics ID: REB 14-0598). The funding source had no role in study design, collection, analysis or interpretation of data, report writing or publication decision.

2.2. Data source and data extraction

Alberta has a publicly funded universal healthcare system in which >99% of residents are registered [5]. The registration file for this program includes a Person Health Number that serves as a unique personal identifier (ULI) [6] that permits data linkage at the level of the individual across other administrative databases. We used ULI to deterministically link data on vaccination, AEFI, and healthcare utilization.

Alberta's Immunization and Adverse Reaction to Immunization repository (Imm/ARI) contains complete vaccination records, including AEFI, for all publicly funded vaccines that were administered by public health since 2006. Vaccination records prior to 2006 comprise historical data and are entered electronically into Imm/ARI by public health nurses after review of paper vaccination records. The Pharmaceutical Information Network (PIN) contains records of all prescriptions dispensed by pharmacies, whether privately or publicly funded. In the case of HPV vaccine, this would only include privately funded vaccines. It is estimated that PIN captures over 95% of dispensed pharmacologic products [7]. We have assumed that all vaccine dispensed according to PIN was actually administered to the purchaser as the cost to purchaser of HPV vaccine is about \$150/dose [8]. Both Imm/ARI

and PIN contain information on the patient, vaccine, dose, and date that vaccine was administered/dispensed [9].

In Alberta, AEFI surveillance is a passive reporting system. Individuals who experience an AEFI report to their vaccine provider, who completes a provincial AEFI reporting form; the data are entered into Imm/ARI [10]; Alberta Health then reports AEFI to the Public Health Agency of Canada. The provincial AEFI reporting form consists of a close ended checklist of types of adverse events, accompanied by an open ended text field into which a description of event is to be entered as well as an open ended comment section. The reporting form also collects time of onset following immunization, outcome, hospitalization dates, patient identifiers, vaccine antigens, vaccination date, and dose number. Alberta policy is that providers should “Report events that do not meet specific case definitions but are felt to be significant (i.e., serious or unusual) under [checkbox] Other Severe or Unusual Events... When an AEFI is:

- Serious (death, hospitalization, congenital abnormality, residual abnormality, life threatening), unexpected (in terms of type or frequency),
- Of concern (to the vaccinee, his/her caregiver(s) or AEFI reporter).”

AEFI's that meet any of these criteria should be reported regardless of consistency with time period of occurrence for the event or the case definition of any such event. VTE cases are captured by the checkbox ‘other unusual events’ on the AEFI reporting form. Event codes and text descriptions on all AEFI reports are reviewed by trained nurses and coded into Imm/ARI. Information related to hospitalizations and emergency department (ED) visits are captured in the Alberta Morbidity and Ambulatory Care Abstract Reporting (MACAR) system, including dates of admission and discharge, and ICD-10-CA (International Classification of Diseases, 10th Revision-Canadian Adaptation) codes for diagnoses.

We extracted data on vaccinations, AEFI reports, hospitalizations and ED visits (within 42 days of vaccination) [4], [11] for all females for whom an HPV dispense or vaccination event was recorded over June 1, 2006–November 19, 2014, using ULI to link records for unique individuals.

2.3. Data analysis

We counted the number of females who received one or more doses of HPV vaccine by number of doses received and age at first dose. We described the frequencies of occurrence

of AEFIs by type of AEFI, and dose number associated with the AEFI. We calculated rates of AEFI per 100,000 doses of HPV vaccine dispensed/administered by dividing counts of AEFIs by the number of vaccine doses received among the population of interest over the period. We described hospitalizations within 42 days of HPV vaccinations by ICD-10-CA diagnostic codes for the most responsible diagnoses for all hospitalizations within 42 days of immunization. "Most responsible diagnosis" is recorded by the health care provider at discharge, using general coding standards that define the most responsible diagnostic ICD code as that responsible for the greatest portion of the length of stay or greatest use of resources [12]. A hospitalization event is defined as a hospital visit where a person was admitted and discharged from a hospital. Some hospitalization events were recorded twice because the person had one hospital visit that was temporally associated with receipt of two different vaccine doses (e.g., was hospitalized within 42 days of receiving both dose 1 and dose 2). For these, we removed the duplicate event and counted it as a single hospitalization event. For each person, we assumed that a transfer from one hospital to another had occurred if the date of discharge from the first hospital was the same as the date of admission to a second hospital. We counted each hospital transfer as a separate event. However, for the purpose of describing the frequency of the most responsible diagnoses (the diagnosis that contributed the greatest to length of stay) for such persons, we counted each most responsible diagnosis if they differed between hospitalization events. We operationally defined 'serious' AEFI as those that resulted in hospitalization and counted the number of 'serious' AEFI. We linked hospitalizations and ED visits to identify those who reported both events within 42 days of vaccination. Data analyses were conducted using SAS 9.3 (SAS Institute Inc., Cary, NC 2011).

2.4. AEFI review to identify VTE

One investigator (MLR), a physician, reviewed all text descriptions for AEFIs coded as 'other unusual events' for evidence that the AEFI might have been VTE.

2.5. Identification of VTE not captured by AEFI reports

In order to maximize the chances of finding a VTE that was not captured by an AEFI report within Imm/ARI, we identified within MACAR all females who were hospitalized or visited the ED within 42 days of vaccination by deterministically linking Imm/ARI, PIN and MACAR using the ULI. Our definition of VTE for this study was the occurrence of an ICD-10-CA diagnostic code of I80.x or I82.x in any of the potential diagnostic code fields (25) for a hospitalization or ED (10) visit. For any woman who had such an ICD-10-CA code for a hospitalization or ED visit, one investigator (MLR) reviewed all ICD codes for that event to

assess if they were consistent with any other condition for which VTE is known to occur as per Spencer and colleagues [13].

3. Results

3.1. Source population

As can be seen from Table 1, from June 1, 2006 to November 19, 2014, 195,270 females received one or more doses of HPV vaccine. They received a total of 528,913 publicly and privately funded doses of vaccine over the study period. Nearly all of the vaccine was qHPV (99.2% of doses). The majority of women received three doses of HPV vaccine (82.4%), while a smaller proportion received only two doses (9.9%) or only one dose (6.4%). Most were aged 9–14 years (79.5%) when their first dose of HPV vaccine was received, followed by age groups 15–19 years (10.0%), 20–24 years (5.9%), or 25–29 years (2.7%).

Table 1. Distribution of HPV vaccine by numbers of women aged 9+ years immunized, by attributes of recipients and vaccine.

Characteristic	Number of women (%)	
<i>N</i> women immunized	195,270 (100)	
Number of doses received per individual		
	1	12,473 (6.4)
	2	19,280 (9.9)
	3	160,950 (82.4)
	4+	2567 (0.1)
Age (years) at which first dose of vaccine received		
	9–14	155,300 (79.5)
	15–19	19,483 (10.0)
	20–24	11,551 (5.9)
	25–29	5351 (2.7)
	30–34	1725 (0.9)

35–39 874 (0.4)

40–44 583 (0.3)

45+ 403 (0.2)

Type of vaccine funding

Public 164,743 (84.4)

Private 29,025 (14.9)

Mixed^a 1502 (0.8)**Total number of doses dispensed/administered**

528,913 (100)

Type of vaccine dispensed/administered

qHPV 524,645 (99.2)

bHPV 4193 (0.8)

Unknown 75 (<0.1)

a

Mixed funding: some doses were publicly funded, some were privately purchased.

3.2. Frequency of occurrence of AEFI & serious AEFI events

Of the 195,270 women who received HPV vaccine, 192 (<0.1%) reported one or more AEFI events (198 AEFI events). Of the 192, 186 reported one AEFI event, while six reported two different AEFI events. All AEFI events occurred after receipt of the qHPV vaccine. Six persons who experienced an AEFI had received one or more vaccines in addition to HPV on the same day as they received HPV vaccine. Table 2 displays the frequency of occurrence of types of AEFI by dose of HPV vaccine in series received that corresponded to the AEFI event. Among the 198 events, the most commonly reported events were allergic reaction ($n = 90$), other unusual events ($n = 34$), other rash ($n = 32$), and pain and/or swelling ($n = 23$) (Table 2). Most AEFI events occurred after receipt of the first dose of vaccine ($n = 117$), followed by second ($n = 55$) and third ($n = 25$) doses. Review of the text fields for 'other unusual events' found none of these events to be consistent with VTE.

Table 2. Distribution of types of AEFI by dose of vaccine for which AEFI event reported.^a

	Number of doses of HPV vaccine received at time of occurrence of AEFI				N persons
	1	2	3	5	
Allergic reaction	54	32	4	0	90
Other unusual events	20	10	4	0	34
Other rash	23	3	6	0	32
Pain and/or swelling	12	5	5	1	23
Fever	1	2	1	0	4
Severe diarrhea	1	2	1	0	4
Anaphylaxis	2	0	1	0	3
Adenopathy	1	1	0	0	2
Convulsion/seizure	1	0	1	0	2
Anesthesia/paraesthesia	1	0	0	0	1
Arthralgia/arthritis	0	0	1	0	1
Erythema multiforme	0	0	1	0	1
Sterile abscess	1	0	0	0	1
Total	117	55	25	1	198

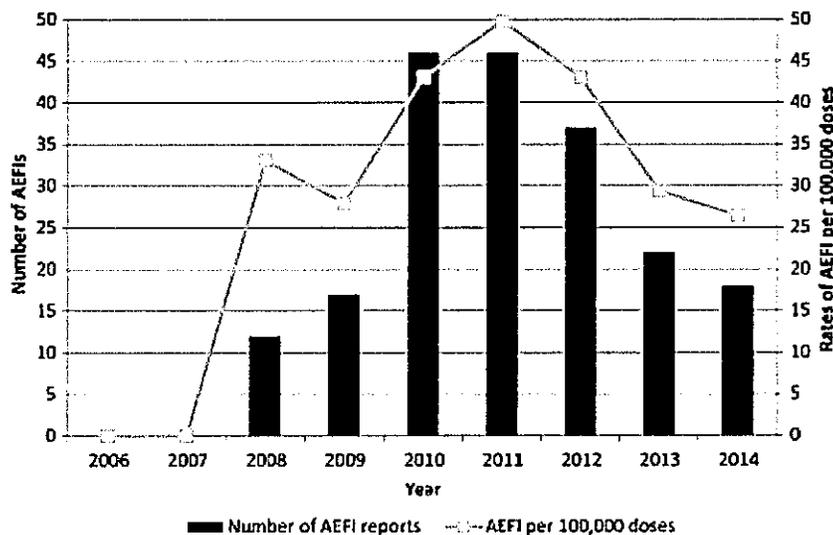
a

Six of the 192 persons who experienced an AEFI had an AEFI on two occasions.

Of the 192 persons reporting AEFI events, five had a serious AEFI, (all classified as 'serious' because of hospitalization); however only 4 of them were hospitalized within 42 days of immunization. The fifth person was hospitalized on day 110, well outside of the 42 day window.

3.3. Rate of occurrence & outcome of AEFI events

Over the study period, the rate of AEFI events was 37.4 per 100,000 doses of HPV vaccine administered (95% CI: 32.5–43.0). The rate varied over time: no events were reported for 2006 or 2007, however only about 5000 doses of vaccine were dispensed in those years (data not shown). For the period January 1, 2008–November 19, 2014, the rate was 37.7 per 100,000 doses (95% CI: 32.8–43.3). AEFI rates varied over time, peaking in 2011 (Fig. 1).



[Download full-size image](#)

Fig. 1. Numbers of AEFI and AEFI rates/100,000 doses dispensed 2006–2014.

Of the 198 AEFI events, the outcomes were known for 171, all of which were full recovery.

3.4. Hospitalization within 42 days of vaccination

Among the 195,270 females who received HPV vaccine, 958 were hospitalized (1053 hospitalization events) within 42 days of immunization; however only 4 of those hospitalized had a reported AEFI (see above). Of the 958 who were hospitalized, most (861, 89.8%) had only one hospitalization event within 42 days of immunization. The large majority of those hospitalized were aged 9–14 years (66.0%) or 15–19 years (22.0%). The proportion of hospitalizations that occurred on the same day as vaccination was 0.7%, 34.6% within 1–14 days, 32.8% within 15–28 days, and 31.9% within 29–42 days (data not shown).

Thirty-two women had hospital transfers. Thirty-one women had one hospital transfer and one woman had two transfers, resulting in 69 hospitalization events. Of these, six transfers (12 events) had the same most responsible diagnosis. Fourteen women had multiple

hospitalization records because they received two doses of HPV vaccine within 42 days, and thus both doses were temporally associated with the hospitalization. Fifty-two persons had more than one hospitalization event because they were hospitalized on separate occasions (i.e., these were not hospital transfers). From the 1053 hospitalization events, after accounting for transfers, we counted 1047 most responsible diagnoses.

The frequencies of the 1047 most responsible diagnoses are shown in Table 3. Mental, behavioral and neurodevelopmental disorders (19.4%) were the most frequently coded most responsible diagnoses, followed by diseases of the digestive system (15.8%), and injury, poisoning and certain other consequences of external causes (13.8%).

Table 3. Frequency of most responsible diagnoses among women hospitalized within 42 days of immunization.

ICD 10 Chapter codes	Count (%)
Certain infectious and parasitic diseases (A00-B99)	29 (2.8)
Neoplasms (C00-D49)	22 (2.1)
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)	12 (1.1)
Endocrine, nutritional and metabolic diseases (E00-E89)	35 (3.3)
Mental, Behavioral and Neurodevelopmental disorders (F01-F99)	204 (19.4)
Diseases of the nervous system (G00-G99)	35 (3.3)
Diseases of the eye and adnexa (H00-H59)	4 (0.4)
Diseases of the ear and mastoid process (H60-H95)	8 (0.8)
Diseases of the circulatory system (I00-I99)	15 (1.4)
Diseases of the respiratory system (J00-J99)	104 (9.9)
Diseases of the digestive system (K00-K95)	165 (15.8)

Diseases of the skin and subcutaneous tissue (L00-L99)	8 (0.8)
Diseases of the musculoskeletal system and connective tissue (M00-M99)	73 (7.0)
Diseases of the genitourinary system (N00-N99)	54 (5.2)
Pregnancy, childbirth and the puerperium (O00-O9A)	8 (0.8)
Certain conditions originating in the perinatal period (P00-P96)	1 (0.1)
Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	19 (1.8)
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99)	66 (6.3)
Injury, poisoning and certain other consequences of external causes (S00-T88)	144 (13.8)
External causes of morbidity (V00-Y99)	0 (0)
Factors influencing health status and contact with health services (Z00-Z99)	41 (3.9)
Total	1047 (100)

3.5. Identification of VTE among those hospitalized

In addition to assessing frequencies of the most responsible diagnoses we examined all ICD-10-CA diagnostic codes (in any of the fields possible for hospitalizations) for codes corresponding to our case definition of VTE. There were three women who had such codes. The first had a most responsible diagnosis of Z50.1 (other physical therapy), and an I80.2 other diagnosis. She was 26 years of age and received the first dose of HPV vaccine 23 days prior to hospitalization. The other ICD-10-CA codes were consistent with having incurred an injury.

The second, aged 11 years, had a most responsible diagnosis of R07.4 (chest pain unspecified), and an I80.1 other diagnosis. She had received the third dose of HPV vaccine 14 days prior to hospitalization. The other ICD-10-CA codes for this hospitalization indicated the presence of a congenital heart defect known to be associated with VTE.

The third was hospitalized for most responsible diagnosis of I80.2 (phlebitis and thrombophlebitis of other deep vessels of lower extremities). She was 14 years of age and

received the third dose of HPV vaccine 11 days prior to hospitalization. Review of the other ICD 10 codes for this hospitalization indicated that the VTE was classified as a complication of other diagnoses (sepsis) that caused the hospitalization.

Two of these three persons had received one or more vaccines in addition to HPV on the same days as they received HPV vaccine. None of those hospitalized with a VTE diagnosis died.

3.6. ED visits within 42 days of immunization

Among those who received HPV vaccine, 19,351 had an ED visit within 42 days of immunization (26,849 events). Of these, 713 also had a hospitalization within 42 days. Among those with an ED visit and hospitalization event, 4 were diagnosed with VTE (including the 3 hospitalized with a VTE diagnosis described above). One person visited the ED and was diagnosed with VTE, but did not have any ICD-10-CA codes consistent with VTE among the discharge diagnoses for the hospitalization.

4. Discussion

In this study, we linked vaccination data with AEFI reports, hospitalization records, and ED visit records, at a population-level, to describe AEFI type as well as to identify VTEs that may be related to HPV vaccination among women aged 9 years or older. We found an AEFI rate (37.4/100,000 doses) that was substantially less than that from reports from the American Vaccine Adverse Event Reporting System (VAERS) (53.9/100,000 doses) [14]. The most common types of adverse events that we observed (e.g., allergic reactions, 'other unusual events', rash) were similar to those found from analysis of the VAERS data [14] and similar to those seen in the province of Ontario [15]. Our results are consistent with other large post-licensure safety and surveillance studies that found that HPV vaccines are safe [11], [16].

While we observed three cases of VTE among those hospitalized within 42 days of immunization, all three had other health conditions known to be associated with VTE. While one additional person had an ED visit with a VTE code, this code was not among the discharge diagnoses for the immediately following hospitalization. We think it likely that the VTE diagnosis from the ED visit was a tentative diagnosis that was not substantiated by further investigations during hospitalization. While Gee and colleagues [4] noted an association with VTE after HPV immunization, this association was not statistically significant, only five confirmed cases were observed and all of those cases had other known

risk factors for VTE. Other investigators have found no association between HPV vaccination and the occurrence of VTE [11], [16], [17], [18].

In Alberta, AEFI events are reportable if they meet case definitions outlined by Alberta Health [10]. AEFI reports are reviewed by public health nurses who ensure AEFIs meet case definitions and enter the data into Imm/ARI. We found a higher rate of AEFI events (37.4/100,000) than that reported for the Ontario schoolgirl HPV immunization program over 2007–2011 (19.2/100,000 doses dispensed) [15]. These differences are almost certainly due to the use of stricter guidelines for the classification of AEFI in Ontario. Harris and colleagues identified 213 qHPV AEFI reports for Ontario, of whom only the 133 classified as 'confirmed' were used in their analyses. If all 213 reports had been used, the Ontario rate of AEFI would have been 30.7/100,000; a rate much closer to that which we observed. However, as was also seen in Ontario, AEFI rates varied by year. Passive surveillance data may be affected by numerous factors, including "biased reporting, underreporting and the inability to determine whether a vaccine caused the adverse event in any individual report" [19]. Changes in reporting may result from changes in the reporting practices of healthcare personnel, or by community concerns (resulting in increased reporting to healthcare personnel) [20], [21]. It is possible that the 2011 publication of the report of Gee and colleagues [4] might have affected reporting rates elsewhere, including in Ontario and in Alberta. However it is also possible that a longer follow-up time for HPV immunizations administered in the earlier years of the study period may also have contributed to the observed pattern of reporting.

The strengths of this study included capturing women who had received either publicly funded or privately purchased HPV vaccines. Similarly, in addition to the passively reported AEFI data, our design overcame the limitations of passive reporting in our search for VTE by accessing the records of all hospitalizations for the entire population of women immunized regardless of types of vaccine received or modes of vaccine funding. However, our study also has limitations. Residents of Alberta who were hospitalized within Alberta but immunized out of province would not have been captured. Similarly, those who were immunized within Alberta but hospitalized out of province would not have been captured. We do not know how many women this would be, but posit that the numbers are small. We did not validate the ICD codes for hospitalizations or emergency department visits by chart review. As the predictive value of ICD codes for VTE is variable [17] this may have led to misclassification of outcome. Even in the absence of misclassification, it is possible that VTE identified during hospitalization might have had symptom onset prior to hospitalization.

Finally, the women in our study received 528,913 doses of vaccine: thus AEFI that occur very rarely but which are truly associated with immunization with HPV vaccine would not be detected.

5. Conclusion

Adverse events following HPV immunization in Alberta are low, consistent with those seen elsewhere, and consistent in the types of event seen elsewhere.

Authors' contribution

XCL participated in data analysis, data interpretation and drafted the manuscript. CAB participated in study conceptualization, study design, acquired the data and participated in data analysis, data interpretation and drafting the manuscript. KAS participated in study conceptualization, study design, data interpretation and drafting the manuscript. MLR participated in study conceptualization, study design, data interpretation and drafting the manuscript. LWS participated in study conceptualization, study design, data interpretation and drafting the manuscript. All authors critically reviewed the manuscript.

Acknowledgement

The study was funded by a research agreement with the Alberta Ministry of Health (RSO 1026380).

Conflicts of interest: None of the authors have any competing interests.

Recommended articles Citing articles (10)

References

- [1] World Health Organization
Human papillomavirus vaccines: WHO position paper, October 2014
Wkly Epidemiol Rec. 43 (89) (2014), pp. 465-492
[View Record in Scopus](#) [Google Scholar](#)
- [2] National Advisory Committee on Immunization
Update on the recommended Human Papillomavirus (HPV) vaccine immunization schedule
Public Health Agency of Canada (2015)

- Available from: http://www.phac-aspc.gc.ca/naci-ccni/acs-dcc/2015/hpv-vph_0215-eng.php [cited October 19, 2015]
Google Scholar
- [3] Government of Alberta
Government approves vaccine program to protect girls from cancer
(2008)
Available from: <http://alberta.ca/release.cfm?xID=237617ED835A4-93CA-9697-D24EF32FB5CC5196>
[cited October 19, 2015]
Google Scholar
- [4] J. Gee, A. Naleway, I. Shui, J. Baggs, R. Yin, R. Li, *et al.*
Monitoring the safety of quadrivalent human papillomavirus vaccine: findings from the Vaccine Safety Datalink
Vaccine, 29 (46) (2011), pp. 8279-8284
Article  Download PDF View Record in Scopus Google Scholar
- [5] Government of Alberta
Alberta Health Care Insurance Plan Statistical Supplement 2013/2014
(2015)
Available from: <http://www.health.alberta.ca/documents/AHCIP-Stats-Supplement-14.pdf> [December 17, 2015]
Google Scholar
- [6] X. Liu, K. Simmonds, M. Russell, L. Svenson
Herpes zoster vaccine (HZV): utilization and coverage 2009–2013, Alberta, Canada
BMC Public Health, 14 (1) (2014), p. 1098
CrossRef View Record in Scopus Google Scholar
- [7] Alberta Health
Overview of administrative health datasets
(2015)
Available from: <http://www.health.alberta.ca/documents/Research-Health-Datasets.pdf> [December 17, 2015]
Google Scholar
- [8] Alberta Health Services
Cervical cancer: about HPV and the HPV vaccine
(2012)
Available from: <http://www.screeningforlife.ca/cervicalscreening/about-hpv-a-hpv-vaccine> [cited June 3,

2015]

Google Scholar

- [9] Alberta Health
An overview of Alberta's Electronic Health Record Information System
(2015)
Available from: http://www.albertanetcare.ca/documents/An_Overview_of_Albertas_ERHIS.pdf [October 19, 2015]
Google Scholar
- [10] Government of Alberta
Adverse events following immunization (AEFI) policy for Alberta Immunization Providers
(2015)
Available from: <http://www.health.alberta.ca/documents/AIP-AEFI-Policy-2015.pdf> [October 19, 2015]
Google Scholar
- [11] N. Scheller, B. Pasternak, H. Svanström, A. Hviid
Quadrivalent human papillomavirus vaccine and the risk of venous thromboembolism
JAMA, 312 (2) (2014), pp. 187-188
CrossRef View Record in Scopus Google Scholar
- [12] Canadian Institute for Health Information
Canadian coding standards for version 2012 ICD-10-CA and CCI
CIHI, Ottawa, ON (2012)
Revised September 2012
Google Scholar
- [13] F.A. Spencer, C. Emery, D. Lessard, F. Anderson, S. Emani, J. Aragam, *et al.*
The Worcester Venous Thromboembolism Study
J Gen Intern Med, 21 (7) (2006), pp. 722-727
CrossRef View Record in Scopus Google Scholar
- [14] B.A. Slade, L. Leidei, C. Vellozzi, E.J. Woo, W. Hua, A. Sutherland, *et al.*
Postlicensure safety surveillance for quadrivalent human papillomavirus recombinant vaccine
JAMA, 302 (7) (2009), pp. 750-757
CrossRef View Record in Scopus Google Scholar
- [15] T. Harris, D.M. Williams, J. Fediurek, T. Scott, S.L. Deeks
Adverse events following immunization in Ontario's female school-based HPV program
Vaccine, 32 (9) (2014), pp. 1061-1066

Article  Download PDF View Record in Scopus Google Scholar

- [16] L. Arnheim-Dahlström, B. Pasternak, H. Svanström, P. Sparén, A. Hviid
Autoimmune, neurological, and venous thromboembolic adverse events after immunisation of adolescent girls with quadrivalent human papillomavirus vaccine in Denmark and Sweden: cohort study

BMJ, 347 (2013)

Google Scholar

- [17] A.L. Naleway, B. Crane, N. Smith, M.F. Daley, J. Donahue, J. Gee, *et al.*
Absence of venous thromboembolism risk following quadrivalent human papillomavirus vaccination, Vaccine Safety Datalink, 2008–2011

Vaccine, 34 (1) (2016), pp. 167-171

Article  Download PDF View Record in Scopus Google Scholar

- [18] W.K. Yih, S.K. Greene, L. Zichittella, M. Kulldorff, M.A. Baker, J.L.O. de Jong, *et al.*
Evaluation of the risk of venous thromboembolism after quadrivalent human papillomavirus vaccination among US females

Vaccine, 34 (1) (2016), pp. 172-178

Article  Download PDF View Record in Scopus Google Scholar

- [19] F. Varricchio, J. Iskander, F. Destefano, R. Ball, R. Pless, M.M. Braun, *et al.*
Understanding vaccine safety information from the Vaccine Adverse Event Reporting System

Pediatr Infect Dis J. 23 (4) (2004), pp. 287-294

CrossRef View Record in Scopus Google Scholar

- [20] J.M. Eberth, K.N. Kline, D.A. Moskowitz, J.R. Montealegre, M.E. Scheurer
The role of media and the Internet on vaccine adverse event reporting: a case study of human papillomavirus vaccination

J Adolesc Health, 54 (3) (2014), pp. 289-295

Article  Download PDF View Record in Scopus Google Scholar

- [21] M.J. Goodman, J. Nordin
Vaccine adverse event reporting system reporting source: a possible source of bias in longitudinal studies

Pediatrics, 117 (2) (2006), pp. 387-390

CrossRef View Record in Scopus Google Scholar

ELSEVIER

[About ScienceDirect](#) [Remote access](#) [Shopping cart](#) [Contact and support](#)
[Terms and conditions](#) [Privacy policy](#)

We use cookies to help provide and enhance our service and tailor content and ads. By continuing you agree to the use of cookies.

Copyright © 2018 Elsevier B.V. or its licensors or contributors. ScienceDirect® is a registered trademark of Elsevier B.V.

 **RELX Group™**

Advertisements

**RULES
OF
MODERN
INVESTING™**

REPORT THIS AD



WELLNESS AND EQUALITY

News, commentary, and advice to improve your health.

How Much Money Do Pediatricians Really Make From Vaccines?

If you want to be sure your pediatrician has your child's best interest, this is mandatory reading. Pediatricians around the country have begun refusing to accept families who opt out of some or all vaccines. Thanks to a tip sent to *Wellness & Equality* by a reader, now we know why.

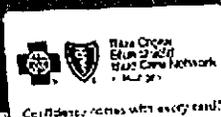
When my friend's child suffered a life-threatening reaction to a vaccine a week after her first birthday, my friend assumed her pediatrician would write her a medical exemption from future vaccines. Shortly after receiving a routine set of vaccines, the happy, vibrant one-year-old spiked a 106 degree fever, began having seizures, and was hospitalized. When the unexplained "illness" passed after a week in the hospital, the little girl had lost her ability to walk. My friend describes

how her daughter, who had learned to walk several months earlier at 9 months, suddenly “stumbled around like a drunk person” for weeks following the vaccines. My friend met with a team of pediatricians, neurologists, and naturopathic doctors, and they agreed: Her daughter had suffered a brain injury caused by a reaction to one of the vaccines. Hoping the injury would be temporary and that she might recover and ease her brain inflammation if they could help her small body quickly eliminate the vaccine additives that caused the reaction, my friend’s daughter underwent an intensive detoxification program overseen by a nutritionalist. Slowly, her daughter relearned to walk.

My friend is a practicing attorney who graduated from a Top 10 college. The evidence was overwhelming that her daughter’s reaction had been caused by vaccines, she told me.

But a few months later, when she took her daughter back into the pediatrician for a visit, *he wanted to vaccinate her daughter again*. She was baffled. Why?

After a reader sent us a link to a PDF file of Blue Cross Blue Shield’s Physician Incentive Program available online, *Wellness & Equality* learned that insurance companies pay pediatricians massive bonuses based on the *percentage* of children who are *fully* vaccinated by age 2.



HEALTH CARE OUTCOMES: PREVENTIVE HEALTH

CHILDHOOD IMMUNIZATIONS – COMBO 10

Product lines	BCN Commercial
Source	HEDIS
Description	<p>The percentage of children 2 years of age who meet the combination 10 criteria on or before their second birthday:</p> <ul style="list-style-type: none"> • (4) DTaP* vaccinations • (3) IPV* vaccinations • (1) MMR vaccination • (1) VZV vaccination • (3) HiB* vaccinations • (3) Hepatitis B vaccinations • (4) PCV* vaccinations • (1) HepA vaccination • (2 or 3) RV* vaccinations • (2) Influenza** vaccinations <p>*Vaccinations administered prior to 42 days after birth are not counted as a numerator hit. **Vaccinations administered prior to 180 days after birth are not counted as a numerator hit.</p>
Continuous enrollment	Must be continuously enrolled 12 months prior to child's second birthday
Age criteria	Children who turn 2 years of age during 2016
Exclusionary criteria	Children who are documented with an anaphylactic reaction to the vaccine or its components
Numerator	The number of children who completed vaccinations as defined above
Denominator	The eligible population
Level of measure	Provider level
Target: COMM	63%
Payout: COMM	\$400 per Combo 10 completed for each eligible member

So how much money do doctors really make from vaccines? The average American pediatrician has 1546 patients, though some pediatricians see many more. The vast majority of those patients are very young, perhaps because children transition to a family physician or stop visiting the doctor at all as they grow up. As they table above explains, Blue Cross Blue Shield pays pediatricians \$400 per fully vaccinated child. If your pediatrician has just 100 fully-vaccinated patients turning 2 this year, that's \$40,000. Yes, Blue Cross Blue Shield pays your doctor a \$40,000 bonus for fully vaccinating 100 patients under the age of 2. If your doctor manages to fully vaccinate 200 patients, that bonus jumps to \$80,000.

But here's the catch: **Under Blue Cross Blue Shield's rules, pediatricians lose the whole bonus unless at least 63% of patients are fully vaccinated, and that includes the flu vaccine. So it's not just \$400 on your child's head—it could be the whole bonus.** To your doctor, your decision to vaccinate your child might be worth \$40,000, or much more, depending on the size of his or her practice.

If your pediatrician recommends that your child under the age of 2 receive the flu vaccine—even though the flu vaccine has *never* been studied in very young children and evidence suggests that the flu vaccine actually weakens a person's immune system over the long term—ask yourself: **Is my doctor more concerned with selling me vaccines to keep my child healthy or to send his child to private school?**

Sources:

[The Physician Alliance Blue Cross Blue Shield Incentive Program](#) *[Please read our update below to find out how you can access the pamphlet.]*

Update 4/30/2017: After Wellness & Equality published this article, Blue Cross Blue Shield locked online access to their incentive program and then removed the page altogether. Clearly this incentive program was never intended to be public knowledge and created a bit of PR issue for them. Fortunately, another website managed to save the entire BCBS incentive program booklet and has published it in entirety online... You can read it here: [Blue Cross Blue Shield Physician Incentive Program](#)

[Getting A Flu Shot Every Year? More May Not Be Better](#)

[Distribution of Pediatric Practice: Size, Age, Sex](#)

I Toni submit this testimony now as I am opposing HAR 11-157 we do not want more shots until you can prove you have tested them and there safe.

Violation of Civil Rights,

Violation of Privacy or Security of Health Information (HIPAA)

This bill is not specifically about mandatory immunizations YET we know that's next it's coming. we're going to block it. This HAR -157 is a wolf in sheep's clothing.

The DOH is in violation of our trust because you did not do a benefit vs risk analysis. You are supporting the mass profits of the massive pharmaceutical company's run-away train. I want to ask you DOH " how can we stop more and mandatory vaccinations" _____?

Last year you proposed mandatory forced .immunizations SB-2316 Bill & it got tabled. because people testified against it.

They DOH said they would create education materials for parents of all students. For the good of immunizations.
. So obviously there was no proof found to show no harm.

The trend today is more and more people do not immunize because they see the results of damaged children and death. 50,000. In Texas opt out. Over 20% of Hawaii children do not immunize 40,000.00

I am a Anti- Vaxxer for 30 years because of the toxic nature of the shots, philosophical, moral, medical danger and religious beliefs. I represent thousands of un-immunized people. We will never immunize. No matter what

Dear DOH is there any one here today from the head of DOH that's really listening?

It's your job to keep the public safe. And to enhance health. Then Help protect us it's your job do it

Yet the FDA, AMA, CDC have run amuck (the woods transcripts show CDC covered up tests that proved harm from vaccines.) Yet the Pharmaceutical companies govern themselves making billions on more and more mandatory shots at as much as 350.00 ea.

With no proven testing, toxic ingredients, and no accountability.

We rise up and say no more !!!

Kauai branch Toni Torre e-mailed me to assure me that this is not about making vaccines being made mandatory. Oh Really

Yet 3 states just passed it CA. WV. Mississippi

All are pushing for it though 8 states stopped it by standing up against it

and that's what we are doing here today, we want to protect our basic human, constitutional rights. And put an end to the travesty of toxic shots into humanity.

President Trump has recently commissioned Robert Kennedy Jr. to study the immunizations and see what's really going on here.

With the push from the billions of \$ made by the Pharmaceutical co.'s The trend is Many states & countries like Argentina have mandated vaccines with no exceptions.

Here is What We on Kauai want to Input :

Stop injuring children, get the toxic ingredients out.
prove the shots are safe. Require the testing

Stop the bullying and using coercion to force people to do it.
Stop denying that when a child is injured that it's not because of the vaccine and by the way we believe the mother.

We rise up!

We are requesting that congress repeal the 1986 national childhood vaccine injury act and instead hold pharmaceutical manufacturers liable for all injuries caused by their vaccinations.

We rise up

We request that all vaccines be classified as pharmaceutical drugs and tested accordingly publicly this is not being done now

We rise up!

Our medical records kept private according to Hipaa rights

rise up We

We request that they take out the toxic ingredients that are in the shots now prove there safe before adding anymore.

We Rise up

Stop mandating how we choose to live our lives and what medical treatments and procedures we have to do. What's next?

Where there is a risk there must be a choice.

We rise up

We Rise up

+We Rise up

March, 2017

Vaccine Dangers: Examine The Evidence

Scientific evidence published in recent years shows that vaccines have great potential for causing brain and immune system injury. The emerging understanding of vaccine injury mechanisms is only just beginning to be explored in human studies.

New scientific evidence strongly suggests that vaccines are at least partly responsible for the alarming increase in neurological and immune system disorders in children, including autism. The scientific evidence frequently cited as proof that vaccines do not cause autism is limited to the MMR vaccine and the preservative thimerosal. The MMR and thimerosal studies are not relevant to the emerging body of compelling science presented below.

Vaccine injury is a vast and complex topic. This document focuses on the three critical issues related to vaccine dangers: Healthy user bias, aluminum adjuvant toxicity, and immune activation injury.

The American Academy of Pediatrics (AAP) circulates a list of 42 studies as evidence that vaccines are safe and do not cause autism or neurological disorders. The AAP's list and associated arguments are flawed in these ways:

1) 25 of the 42 studies look only at the MMR or the measles vaccine. The AAP refers to these studies as evidence that no vaccine causes autism. This is illogical, unscientific, and a misuse of the science. Studies of MMR cannot be used as evidence of safety for other vaccines. Every vaccine contains different ingredients. For example, the MMR vaccine does not contain aluminum adjuvant, a dangerous ingredient proven to cause brain inflammation and cognitive and behavioral deficits in animals at the same dosages given to human infants.

2) The MMR-autism and other vaccine studies are susceptible to healthy user bias, a type of selection bias that conceals evidence of harm. Healthy user bias is a systematic source of error. It may affect all the MMR-autism studies and none adequately control for it. Healthy user bias renders many studies of vaccine safety incapable of actually establishing safety.

3) None of the studies listed by the AAP include a fully-unvaccinated control group.

4) None of the studies listed by the AAP support the safety of aluminum adjuvant.

5) None of the studies listed by the AAP provide evidence that vaccines do not cause immune activation injury.

6) Two studies (Smith 2010 and DeStefano 2013) purport to show that general vaccine exposure (number of vaccines or vaccine antigens) is not associated with neurological disorders. These studies are fatally flawed because they do not include an unvaccinated control group.

Smith 2010 for example includes an analysis comparing groups that received 10.1 and 11.8 vaccines. Such a small difference in exposure is not able to detect adverse effects. Hence, it cannot be used as evidence of safety.

DeStefano 2013 focuses on number of antigens, but there is no evidence the number of antigens is a rational metric for vaccine risk. It's the aluminum adjuvant that creates the danger, but adjuvant exposure is not considered in this study. Also, this study has no unvaccinated controls. The DeStefano 2013 study is essentially meaningless.

Below is a list of studies that raise serious concerns about vaccine safety. The issues of healthy user bias, aluminum adjuvant toxicity and immune activation injury have been almost completely overlooked by the medical community.

Citation List Provided by VaccinePapers.org

Contact: 

Healthy User Bias (HUB)

Healthy user bias is a type of selection bias that is particularly relevant to vaccine safety research. HUB is created when people with health problems avoid vaccination, or when healthy people choose vaccination. When this occurs, the vaccinated have better baseline health, which is erroneously credited to the vaccine.

Vaccine safety studies typically use administrative data (data collected by government agencies, HMOs and insurance companies), and HUB is present in this type of data. With administrative data, researchers can not control who receives the vaccine and who does not. HUB creates the appearance that vaccines have dramatic, diverse and implausible beneficial effects. For example, HUB is likely responsible for the dramatic low mortality associated with use of the influenza vaccine.

HUB is universally acknowledged as a problem (even by Dr Offit!), but is rarely addressed in vaccine research. Vaccine safety studies almost never attempt to control for this potent source of error. HUB can be strong enough to reverse a study outcome, making very dangerous vaccines appear to be safe or powerfully beneficial.

Citation	Summary	Citation Quotes
Confounding in Studies of Adverse Reactions to Vaccines Fine et al., American Journal of Epidemiology, Vol. 136, 1992	<p>CDC researchers review healthy user bias, and show that this bias may explain why the studies of SIDS fail to consistently observe an association with vaccines.</p> <p>Calculations show that HUB can reverse study outcomes and make very dangerous vaccines appear safe. HUB can have a 5-10-fold impact on relative risk (RR). HUB can cause a true RR of 5 to become 1 or even less. HUB is a powerful bias that can completely conceal adverse effects of a vaccine.</p>	<p>“Confounding...is a general problem for studies of adverse reactions to prophylactic interventions, as they may be withheld from some individuals precisely because they are already at high risk of the adverse event.”</p> <p>“If [epidemiological vaccine] studies are to prove useful, they must include strenuous efforts to control for such factors [i.e. HUB] in their design, analysis, and interpretation.”</p> <p>“The magnitude of such confounding effects may be considerable.”</p>
Mortality Reduction with Influenza Vaccine in Patients with Pneumonia Outside “Flu” Season Eurich et al., AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, Vol. 178, 2008.	<p>This study looked at health outcomes in flu vaccine users when flu is <u>not</u> circulating (in the summer). Vaccinated subjects had far better health outcomes than unvaccinated controls, which cannot be caused by the vaccine.</p> <p>This result is likely due to the fact that the people in this study who chose vaccination were healthier to start with and had greater “health seeking” behavior. This is healthy user bias at work.</p>	<p>“The 51% reduction in mortality with vaccination initially observed in patients with pneumonia who did not have influenza was most likely a result of confounding.”</p> <p>“...studies that have restricted their analyses to the influenza season have overestimated the potential mortality benefit of vaccination.”</p> <p>“...our results empirically demonstrate that the mortality benefits of influenza vaccination may have been largely overestimated.”</p>

<p>Healthy User and Related Biases in Observational Studies of Preventative Interventions: A Primer for Physicians</p> <p>Shrank et al., Journal of General Internal Medicine, Vol. 26, 2011.</p>	<p>This review considers a variety of evidence that non-randomized studies of preventative interventions (including vaccines) can be severely affected by healthy user bias (and related biases), it cites a strong effect of adherence in predicting health outcomes in the placebo arm of a drug trial.</p>	<p>“Clinicians should be skeptical when interpreting results of observational studies of preventive services that have not accounted for healthy user and related biases.”</p> <p>“Another topic of recent debate is the magnitude of the benefit of influenza vaccination on mortality among elderly patients. Observational studies have typically reported 40%–50% reductions in all-cause mortality.^{14,15} However, the observation that influenza vaccination appears to protect patients against mortality prior to the start of the flu season has cast doubt on these findings,¹⁶ as have results indicating that improved statistical adjustment greatly reduces the apparent benefit.¹⁷”</p>
<p>The Introduction of Diphtheria-Tetanus-Pertussis and Oral Polio Vaccine Among Young Infants in an Urban African Community: A Natural Experiment</p> <p>Mogensen et al. EbioMedicine, January 31, 2017</p>	<p>The study has a clever design that eliminates healthy user bias. This study compared mortality among children receiving the DTP vaccine at older or younger ages. Variation of age at vaccination occurred because of infrequent (quarterly) vaccine clinic scheduling, and so is effectively random. Timing of vaccines is unrelated to child health. The study found a 5X higher mortality associated with the DTP vaccine.</p>	<p>“...the “unvaccinated” children in these [prior DTP vaccine] studies have usually been frail children too sick or malnourished to get vaccinated, and the studies may therefore have underestimated the negative effect of DTP.”</p> <p>“When unvaccinated controls were normal children who had not yet been eligible for vaccination, mortality was 5 times higher for DTP-vaccinated children.”</p> <p>“The negative effect of DTP was much worse in this natural experiment than has been reported in previous studies of DTP. This is presumably due to the “unvaccinated” control children in previous studies having been a frail subgroup too frail to get vaccinated.”</p>

Aluminum Adjuvant Toxicity

Most vaccines contain aluminum adjuvant, an ingredient necessary for inducing immunity. Al adjuvant comprises particles which are transported around the body by macrophages. Al adjuvant particles travel into the brain and other sensitive organs, where they cause chronic inflammation. Recent animal studies show that Al adjuvant can cause brain injury and behavioral disorders at dosages infants receive from vaccines (the same mcg/kg body weight). Al adjuvant causes microglial activation in the brain. Aluminum induces IL-6 expression in the brain; elevated IL-6 causes autism.

The CDC's case for Al adjuvant safety is based on two false claims: 1) that mice or rats ingesting 26 mg/kg/day Al do not experience adverse effects, and 2) that Al adjuvant particles have zero toxicity while in particulate form. These errors are fundamental to the fatally flawed Mitkus 2011 study used to defend aluminum adjuvant safety and cited by the CDC. Claims of Al adjuvant safety are indefensible in view of recent science on aluminum adjuvant kinetics and toxicity.

Citation	Summary	Quotes
<p>Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective low dose neurotoxicity</p> <p>Crepeaux et al., Toxicology, Vol. 375, 2016.</p>	<p>Shows that Al adjuvant at dosage of 200mcg/kg is transported into the brain, where it causes microglial activation (inflammation), and a 50-fold increase in brain aluminum concentration. Al adjuvant also caused behavioral abnormalities.</p>	<p>"In the context of massive development of vaccine-based strategies worldwide, the present study may suggest that aluminium adjuvant toxicokinetics and safety require reevaluation."</p>
<p>Neuroprotective Effect of Nanodiamond in Alzheimer's Disease Rat Model: a Pivotal Role for Modulating NF-κB and STAT3 Signaling</p> <p>Alawdi et al., Mol Neurobiol, Vol 2016.</p>	<p>Ingestion of 3.4 mg/kg/day Al caused cognitive impairment and a 4-fold increase of IL-6 in the brain. IL-6 causes autism. This is one of several studies disproving the foundation of the Mitkus 2011 analysis: that animals ingesting 26mg/kg/day Al do not experience adverse effects.</p>	<p>"The results also showed that aluminum administration increased the hippocampus pro-inflammatory cytokines TNF-α by 3.8-fold, IL-6 by 4-fold...compared to the normal control group."</p>
<p>Slow CCL2-dependent translocation of biopersistent particles from muscle to brain</p> <p>Khan et al. BMC Medicine, Vol. 11, 2013</p>	<p>Mice were injected intramuscularly with aluminum adjuvant, which was detected in the brain 1 year later, in particulate form. Transport into the brain is accelerated by the inflammatory chemokine CCL2 (also known as MCP-1). CCL2/MCP-1 is consistently elevated in autism and is induced by some vaccines. Transport effect of CCL2/MCP-1 indicates that macrophages are responsible for transporting the adjuvant particles.</p>	<p>"Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection." "...alum has high neurotoxic potential, and planning administration of continuously escalating doses of this poorly biodegradable adjuvant in the population should be carefully evaluated by regulatory agencies since the compound may be insidiously unsafe."</p>

<p>Aluminium-induced electrophysiological, biochemical and cognitive modifications in the hippocampus of aging rats</p> <p>Sethi et al., NeuroToxicology, Vol. 29, 2008</p>	<p>Rats ingested 5.6 mg/kg/day Al, which caused cognitive impairment and numerous adverse effects. This is one of several studies disproving the foundation of the Mitkus 2011 analysis: that animals ingesting 26mg/kg/day Al do not experience adverse effects.</p>	<p>“...aluminium intake impairs spatial learning abilities and increases anxiety by modifying brain functions at electrophysiological, biochemical and structural levels. We have also observed the magnitude of aluminium inflicted neurotoxicity was significantly higher in younger rats in comparison to older rats.”</p>
<p>Curcumin attenuates aluminium-induced functional neurotoxicity in rats</p> <p>Sethi et al. Pharmacology, Biochemistry, and Behavior, Vol. 93, 2009.</p>	<p>Rats ingested 5.6 mg/kg/day Al, which caused behavioral abnormalities and neurotoxicity. This is one of several studies disproving the foundation of the Mitkus 2011 analysis: that animals ingesting 26mg/kg/day Al do not experience adverse effects.</p>	<p>“...aluminium enhances neurotoxicity by inflicting damage at sub-cellular structures. In accordance to previous reports we observed increased vacuolation, swollen mitochondria, and hyper-electron dense cells in Al-toxicated young and old rats compared to age-matched controls.”</p>
<p>Administration of aluminium to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes</p> <p>Shaw et al. Journal of Inorganic Biochemistry, Vol. 128, 2013.</p>	<p>Mice were injected subcutaneously with a total of 550 mcg/kg Al adjuvant over the first 3 weeks of life. This dosage is approximately equal to the dosage received by infants according to the CDC vaccine schedule. Al adjuvant caused behavioral abnormalities and abnormal weight gain.</p>	<p>“...our current results are consistent with the existing evidence on the toxicology and pharmacokinetics of Al adjuvants which altogether strongly implicate these compounds as contributors to the rising prevalence of neurobehavioural disorders in children.”</p>
<p>Aluminum hydroxide injections lead to motor deficits and motor neuron degeneration</p> <p>Shaw et al. Journal of Inorganic Biochemistry, Vol. 103, 2009.</p>	<p>Mice were injected with a total of 300mcg/kg Al adjuvant. The mice displayed pathological behavioral abnormalities and impaired learning and memory. The Al adjuvant caused brain inflammation and tau protein accumulation (associated with alzheimers disease). Aluminum was detected in the brain.</p>	<p>“...current results and our previous study have demonstrated significant behavioural and neuropathological outcomes with aluminum hydroxide.”</p>

<p>Aluminum Adjuvant Linked to Gulf War Illness Induces Motor Neuron Death in Mice</p> <p>Petrik et al, Nanomolecular Medicine, Vol. 9, 2007.</p>	<p>Mice were injected with a total of 100mcg/kg Al adjuvant. The adjuvant caused impaired neuromuscular function, inflammation and apoptosis in the nervous system, and death of motor neurons in the spinal cord. Squalene (an adjuvant) did not produce these effects.</p>	<p>“Aluminum hydroxide induced both behavioral and motor deficits, and the increased presence of apoptotic neurons and in various regions of the central nervous system with significant motor neuron loss in the lumbar spinal cord.”</p> <p>“...the continued use of aluminum adjuvants in various vaccines for the general public may have widespread health implications.”</p>
--	--	--

Immune Activation Injury

It is generally accepted that immune activation during early development causes brain injury and mental illnesses, including autism and schizophrenia. Specifically, the brain injury is caused by cytokines; autism is caused by elevated interleukin-6 (IL-6) and interleukin-17a (IL-17). Immune activation experiments have been replicated in monkeys. Hundreds of studies have been published on the phenomenon. Adjuvant and vaccine adverse reactions induce cytokines (including IL-6) in the brain. An important study (Li et al. 2015) demonstrated that the hepatitis B vaccine adversely affects brain development by an immune activation mechanism, thereby demonstrating that vaccines can impact brain development via immune activation.

Dr Paul Patterson, a pioneering immune activation and autism researcher at Caltech, wrote this in 2006:

“Should we really be promoting universal maternal vaccination? The flu vaccine has been recommended routinely to pregnant women in the United States since 1957. The official policy of the CDC states that “administration of vaccines to women seeking prenatal care is an opportunity for preventative intervention that should not be wasted.” Now you might say, “Well, of course, you don’t want to get the flu if you’re pregnant!” But remember that double-stranded RNA experiment—we activated the immune system, and it caused all these downstream effects on the fetus. And what does a vaccination do? It activates the immune system. That’s the *point* of vaccination.

I think that universal vaccination of pregnant women could get us into a whole new set of problems.”

--“Pregnancy, Immunity, Schizophrenia and Autism”, Engineering & Science (A CalTech magazine), No. 3, 2006.

Citation	Summary	Quotes
<p>Neonatal vaccination with bacillus Calmette–Guérin and hepatitis B vaccines modulates hippocampal synaptic plasticity in rats</p> <p>Li et al., Journal of Neuroimmunology, Vol. 288, 2015.</p>	<p>Rats given BCG or Hep B vaccines showed long-term changes in brain development. Hep B vaccine caused adverse changes in neuron function, and induced IL-6 in the brain. Also shows that vaccines affect brain development by an immune activation mechanism, and can cause chronic brain inflammation. Also shows that vaccines can interact via effects on immune function. <u>This study establishes that vaccines can cause immune activation injury.</u></p>	<p>“Our work highlights a critical role of neonatal vaccination in synaptic plasticity...which suggests the necessity of further studies on the association of vaccination with brain development”</p> <p>“Immune activation early in life can significantly affect the development of neural processes.”</p>
<p>Maternal immune activation yields offspring displaying mouse versions of the three core symptoms of autism</p> <p>Malkova et al., Brain, Behavior and Immunity, Vol. 26, 2012</p>	<p>Mice exposed to immune activation in utero displayed abnormal behavior characteristic of autism at maturity. Mice displayed abnormal communication, social interaction and repetitive behavior, the three defining characteristics of autism.</p>	<p>“Maternal immune activation (MIA) yields male offspring with deficient social and communicative behavior, as well as high levels of repetitive behaviors, all of which are hallmarks of autism.”</p>
<p>Maternal Immune Activation Alters Fetal Brain Development through Interleukin-6</p> <p>Smith et al., J. Neurosci, 2007</p>	<p>This study was the first to show that the cytokine interleukin-6 (IL-6) causes autistic behavior in an animal model of autism.</p>	<p>“The data identify interleukin-6 (IL-6) as a key mediator of the effects of maternal immune activation on fetal brain development.”</p>

<p>Brain IL-6 elevation causes neuronal circuitry imbalances and mediates autism-like behaviors</p> <p>Wei et al., Biochimica et Biophysica Acta, Vol. 1822, 2012</p>	<p>Shows that chronic exposure of the brain to IL-6, <u>beginning after birth</u>, causes autistic behavioral abnormalities. IL-6 also created an excess of excitatory synapses, and a deficit of inhibitory synapses. This may explain hypersensitivity to lights and sounds in autism.</p>	<p>“IL-6 elevation in the brain could mediate autistic-like behaviors, possibly through the imbalances of neural circuitry and impairments of synaptic plasticity.”</p> <p>“IL-6 elevation resulted in increased excitatory synaptic formation and a decreased number of inhibitory synapses.”</p>
<p>Activation of the Maternal Immune System During Pregnancy Alters Behavioral Development of Rhesus Monkey Offspring</p> <p>Bauman et al., Biol Psychiatry, Vol. 75, 2014.</p>	<p>This study describes effects of maternal immune activation (MIA) in monkeys. MIA caused autistic behavioral abnormalities: social and communicative behavior deficits, and an increase in repetitive behavior. Findings match those observed in mice.</p>	<p>“In this rhesus monkey model, MIA yields offspring with abnormal repetitive behaviors, communication, and social interactions. These results extended the findings in rodent MIA models to more human-like behaviors resembling those in both autism and schizophrenia.”</p>
<p>Maternal Immune Activation in Nonhuman Primates Alters Social Attention in Juvenile Offspring</p> <p>Machado et al., Biol Psychiatry, Vol. 77, 2015</p>	<p>This study reports that MIA causes abnormal visual scanning behavior in monkeys. Immune activation caused reduced visual scanning of images of faces and eyes. This is a characteristic of human autism. Human autistics avoid looking at faces and eyes.</p>	<p>“The use of noninvasive eye tracking extends the findings from rodent MIA models to more human-like behaviors resembling those in both autism spectrum disorder and schizophrenia.”</p>
<p>Acquired Reversible Autistic Syndrome in Acute Encephalopathic Illness in Children</p> <p>Arch Neurol, Vol. 38, 1981</p>	<p>Describes 3 cases of sudden onset autism caused by infection and inflammation in the brain. Cases were 5, 7, and 11 years of age. This and similar case reports demonstrate that immune activation can cause autism in older children. This shows that the developing brain is sensitive to immune activation postnatally.</p>	<p>“...striking autistic features developed in previously normal children in the course of an acute encephalopathic illness...”</p> <p>“Cases are...reversible autistic syndrome...affording some insight into the neurological substrate of that syndrome.”</p>
<p>Impaired synaptic development in a maternal immune activation mouse model of neurodevelopmental disorders</p> <p>Coiro, et al. Brain, Behavior, and Immunity, Vol. 50, 2015.</p>	<p>Behavioral abnormalities induced by MIA are blocked by an anti-inflammatory drug given <u>postnatally</u>. This demonstrates that the brain is impacted by inflammation <u>in the postnatal period</u> (when vaccines are given).</p>	<p>“Our results suggest that a possible altered inflammatory state associated with maternal immune activation results in impaired synaptic development that persists into adulthood but which can be prevented with early anti-inflammatory treatment.”</p>

<p>Postnatal systemic inflammation exacerbates impairment of hippocampal synaptic plasticity in an animal seizure model</p> <p>Chen et al., Neuroimmunomodulation, Vol. 20, 2013.</p>	<p><u>Postnatal</u> immune activation increased seizure susceptibility in rats. Other adverse brain effects were also reported. The postnatal timing is important because some vaccine advocates erroneously argue that the brain can only be injured during gestation.</p>	<p>“Central nervous system inflammation during critical stages of childhood development could disrupt the balance needed for neurophysiological actions of immune processes, producing direct, pernicious effects on memory, neural plasticity and neurogenesis into adulthood.”</p>
<p>Maternal immune activation promotes hippocampal kindling epileptogenesis in mice</p> <p>Pineda et al., Ann Neurol, Vol. 74, 2013.</p>	<p>This study replicated the finding that IL-6 causes autism. It also shows that the cytokine combination IL-6 + IL-1B causes epilepsy. This explains the association between autism and seizure disorder.</p>	<p>“In addition to confirming previously established critical role of IL-6 in the development of autism-like behavior following MIA, the present study shows that concurrent involvement of IL-6 and IL-1β is required for priming the offspring for epilepsy. These data shed light on mechanisms of comorbidity between autism and epilepsy.” “IL-6 is necessary and sufficient for causing autism in the offspring.”</p>
<p>The maternal interleukin-17a pathway in mice promotes autismlike phenotypes in offspring</p> <p>Choi et al., Science, Vol. 351, 2016.</p>	<p>Shows that IL-6 causes autism by inducing the cytokine IL-17a.</p> <p>IL-6 and IL-17a are closely connected in a feedback loop. IL-6 induces IL-17a, and vice versa.</p> <p>Vitamin D reduces IL-17a production, which perhaps explains why vitamin D reduces autism severity and prevents autism.</p>	<p>“...in agreement with previous reports IL-6 injection into pregnant wild type (WT) mothers was sufficient to produce MIA-associated behavioral phenotypes.” “...IL-6 injections into WT mothers were sufficient to induce IL-17a levels comparable to those of poly(I:C)-injected WT mothers.” Note: Wild type=not genetically engineered.</p>
<p>Serum and CSF levels of cytokines in acute encephalopathy following prolonged febrile seizures</p> <p>Ichiyama et al., Brain and Development, Vol. 30, 2008.</p>	<p>Shows that febrile seizures strongly induce IL-6 in cerebrospinal fluid (CSF). IL-6 increase is comparable to levels that cause autistic behavioral abnormalities in animal studies. Vaccines cause seizures. <u>Seizures always cause an IL-6 surge in the brain.</u> Febrile seizures in infants are associated with regressive autism.</p>	<p>“CSF IL-6 levels were significantly higher in...febrile seizure compared with control subjects.”</p>

<p>Risk Factors for Autistic Regression: Results of an Ambispective Cohort Study</p> <p>Zhang et al., Journal of Child Neurology, Vol. 27, 2012.</p>	<p>Shows that febrile seizure is associated with regressive autism. Odds ratio (OR) =3.53, which is comparable to the OR for family history of autism (OR=3.62). The finding is expected because febrile seizures always induces IL-6 in the brain.</p>	<p>“...febrile seizures were associated with a significantly increased risk of regression.”</p>
<p>Brain IL-6 and Autism</p> <p>Wei et al., Neuroscience, Vol. 252, 2013.</p>	<p>Reviews the evidence that autism is caused by elevated IL-6 in the brain. Autistic behavioral abnormalities are caused by either acute or chronic IL-6 elevation. Aluminum causes chronic IL-6 elevation in the brain.</p>	<p>“All these evidences suggest that brain IL-6 may play an important role in the development of autism.” “Many studies show IL-6 dysregulation in individuals with autism...”</p>
<p>Maternal immune activation in late gestation increases neuroinflammation and aggravates experimental autoimmune encephalomyelitis in the offspring</p> <p>Zager et al. Brain, Behavior, and Immunity, Vol. 43, 2015.</p>	<p>MIA increased the severity of multiple sclerosis (MS) in a mouse model. Susceptibility to MS was tested at maturity (60 days of age). So the results suggest that early life immune activation increases disease risk long term, perhaps for a lifetime.</p>	<p>“...maternal immune activation during mice late gestation influences the development of offspring’s immune system, an effect that persists until adulthood. Specifically, the offspring...showed aggravated clinical manifestations and immune responses during the course of EAE.” Note: EAE= multiple sclerosis.</p>
<p>The microbiota modulates gut physiology and behavioral abnormalities associated with autism</p> <p>Hsiao et al. Cell, Vol. 155, 2013.</p>	<p>MIA caused adverse changes to the gastrointestinal microbiome. Neurotoxic substances produced by a pathogenic microbiome caused autistic behavioral abnormalities. Administering the beneficial, anti-inflammatory probiotic B. Fragilis completely alleviated some of the behavioral abnormalities. This study supports Dr Wakefield’s 1998 hypothesis that vaccines cause autism by triggering an inflammatory gastrointestinal disorder.</p>	<p>“...these findings support a gut-microbiome-brain connection in autism and identify a potential probiotic therapy for gastrointestinal and behavioral symptoms of autism.” “Remarkably, <i>B. fragilis</i> treatment ameliorates abnormal communicative, stereotyped, sensorimotor and anxiety-like behaviors in MIA offspring, supporting emerging evidence for a gut-brain link in autism.”</p>

<p>Association Between Influenza Infection and Vaccination During Pregnancy and Risk of Autism Spectrum Disorder</p> <p>Zerbo et al. JAMA Pediatrics, Vol. 171, 2017.</p>	<p>This is perhaps the first human study looking for immune activation brain injury by vaccination. The authors inappropriately used a bonferroni correction to discount a significant association between 1st-trimester influenza vaccination and autism. Hazard ratio was 1.2, equivalent to about 4 autism cases per 1000 vaccinations. This represents a severely inverted risk/benefit, since 1000 vaccinations should be expected to prevent about 10-20 influenza illnesses, and cause a comparable number of non-influenza illnesses.</p>	<p>“If influenza vaccination during the first trimester of pregnancy causes ASD, our results suggest that it would amount to 4 additional ASD cases for every 1000 women vaccinated. Our finding of a possible association between maternal influenza vaccination in the first trimester and increased ASD risk parallels previous studies reporting an association between maternal viral infection or fever and increased ASD risk in the first trimester.”</p>
--	---	---

First Peer-Reviewed Study of Vaccinated versus Unvaccinated Children (Censored by an International Scientific Journal) Now Public



By Kevin Barry

Today, a groundbreaking new study of the overall health of vaccinated and unvaccinated children has been released to the public for the first time. The critically important new pilot study has been posted on line.

The paper was leaked to journalist and author [James Grundvig, who published an article describing aspects of the study on Medium](#) on February 22, 2017. Grundvig describes how the paper was leaked to him (and others?), and he describes how he authenticated it with the study's author and with the journal which censored it.

I will list a few of the many reasons why this paper is critically important at this time.

1. The #RFKcommission.

This study provides numerous clues for potential future research. It may help serve as a blueprint for the RFK Commission in the United States and for other countries.

2. President Trump

President Trump is the first President to show any interest at all in vaccine safety. This study reaffirms that President Trump's concerns about vaccine safety are legitimate, and may help him stand firm in forming the #RFKcommission.

3. Existing vaccine rights are under attack in 30 states.

Vaccine exemption attacks and vaccine mandate [increases in 30 state capitals in 2017](#).

Parent advocates nationwide can add the findings of this study to their arsenal when protecting their and their children's existing rights from the [trillion dollar Pharmaceutical industry in state capitals](#).

4. Informed consent

The [international bioethics standard for preventative medical is informed consent](#). Comparing total health outcomes between vaccinated and unvaccinated populations are an important piece of information to weigh when considering consent.

5. Censorship or self-censorship?

Is submitting papers dealing with vaccine safety to the "peer review" process of scientific journals, after years of rejection, a form of self-censorship?

The paper released today was scheduled to be published in November 2016. Had it been published in the journal it would have been "peer reviewed".

Speaking for the 7,484,325,473 billion people on the planet who were NOT peer reviewers of this paper,

it's absurd that this paper is legitimate if the 3 reviewers bosses don't get spooked, and not legitimate if they do get spooked. I hope the 3 peer reviewers - Amit, Kelly and Linda - would agree that their bosses shouldn't block important information from the other 7 billion of us.

I've read numerous beautiful tributes to brilliant, wonderful and fearless Dan Olmsted on Age of Autism over the past month. I'm not nearly as talented a writer as those who have honored Dan on these pages. I didn't know how I could help honor him ... until now. Dan tried for more than a decade to get a vaccinated vs. unvaccinated study done, and he pioneered the concept with his series on the Amish.

Please help guide us Dan, and thank you for your dedication to all of our children.



First Study of Vaccinated versus Unvaccinated Children - Censored by an International Scientific Journal - Now Public Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports, was censored by the journal *Frontiers in Public Health*.

Key Study Findings

Background: The long-term health outcomes of the routine vaccination program remain unknown. Studies have been recommended by the Institute of Medicine to address this question.

Specific Aims: To compare vaccinated and unvaccinated children on a broad range of health outcomes, and to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors.

Design and Methods: A cross-sectional survey of mothers of children educated at home. Homeschool organizations in four states (Florida, Louisiana, Mississippi, and Oregon) were asked to forward an email to their members, requesting mothers to complete an anonymous online questionnaire on the vaccination status and health outcomes of their biological children ages 6 to 12. A total of 415 mothers provided data on 666 children, of which 261 (39%) were unvaccinated. The collected data included pregnancy experiences and birth histories as well as acute and chronic conditions, medications, and the use of health services.

Results: Vaccinated children were significantly less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but significantly more likely to have been diagnosed with other infections, allergies and NDDs (defined as Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and/or a learning disability).

Chronic Illness Detail:

- Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following chronic illnesses:
 - 7-fold higher odds of any neurodevelopmental disorder (i.e., learning disability, ADHD, or ASD)
 - 2-fold increase in Autism Spectrum Disorder ("ASD")
 - 2-fold increase in ADHD
 - 2-fold increase in learning disabilities
 - 1-fold increase in allergic rhinitis

- 9-fold increase in other allergies
- 9-fold increase in eczema/atopic dermatitis
- 4-fold increase in any chronic illness
- No significant differences were observed with regard to cancer, chronic fatigue, conduct disorder, Crohn's disease, depression, Types 1 or 2 diabetes, encephalopathy, epilepsy, hearing loss, high blood pressure, inflammatory bowel disease, juvenile rheumatoid arthritis, obesity, seizures, and Tourette's syndrome. However, larger samples would be needed to detect group differences in these less common conditions.

Acute Illness Detail:

- Vaccinated children were significantly less likely than unvaccinated children to have had chickenpox or whooping cough ($p < 0.001$).
- Vaccinated children had a 3.8-fold increased odds of middle ear infections and a 5.9-fold increased odds of being diagnosed with pneumonia compared to unvaccinated children.
- No significant differences were seen between the two groups with regard to Hepatitis A or B, high fever in the past 6 months, measles, mumps, meningitis (viral or bacterial), influenza, or rotavirus.

Vaccination, Preterm Birth and Neurodevelopmental Disorders (NDDs):

In regression analyses, vaccination was associated with a significant 3.1-fold increased odds of neurodevelopmental disorders (combining the diagnoses of ASD, ADHD, and learning disability), after controlling for other factors. An important detail emerged regarding a possible synergism between vaccination and preterm birth. In a final adjusted statistical model, vaccination but not preterm birth remained associated with NDD, as defined, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% Confidence Interval: 2.8, 15.5).

* * * * *

Quotes from independent scientists not involved in the study:

"I am delighted to see a properly analyzed study on vaccine safety" said Dr. Lyons-Weiler, CEO and President of the Institute for Pure and Applied Knowledge. "Unlike past studies, which ignored the interaction term, Dr. Mawson and colleagues followed appropriate steps toward interpreting the significance of the interaction between variables. The study reported a significant interaction effect between pre-term birth, and vaccination as a 6.6-fold increase in the risk of neurodevelopmental disorders."

"This study, however, as a survey study, is potentially subject to variation due to responses from well-intended participants. The next logical step would be additional, larger studies that would try to replicate the results using electronic medical health records - by independent investigators not involved in profiting from vaccines", said Dr. Lyons-Weiler.

"This is a long-overdue study involving a fair comparison of vaccinated vs unvaccinated children where the two subpopulations likely don't reflect other biases, due to their being drawn from a common population of home-schooled children", said Dr. Stephanie Seneff, Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory. "The results are alarming, and it leaves no doubt that we need to seriously question whether the benefits of vaccines outweigh the risks. A much larger study to see if the results still hold up is paramount at this point."

Dr. Lyons-Weiler and Dr. Seneff were not involved in the study.

First Study of Vaccinated versus Unvaccinated Children

Now Public Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports, was censored by the journal *Frontiers in Public Health*.

Key Study Findings

Background: The long-term health outcomes of the routine vaccination program remain unknown. Studies have been recommended by the Institute of Medicine to address this question.

Specific Aims: To compare vaccinated and unvaccinated children on a broad range of health outcomes, and to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors.

Design and Methods: A cross-sectional survey of mothers of children educated at home. Homeschool organizations in four states (Florida, Louisiana, Mississippi, and Oregon) were asked to forward an email to their members, requesting mothers to complete an anonymous online questionnaire on the vaccination status and health outcomes of their biological children ages 6 to 12. A total of 415 mothers provided data on 666 children, of which 261 (39%) were unvaccinated. The collected data included pregnancy experiences and birth histories as well as acute and chronic conditions, medications, and the use of health services.

Results: Vaccinated children were significantly less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but significantly more likely to have been diagnosed with other infections, allergies and NDDs (defined as Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and/or a learning disability).

Chronic Illness Detail:

- Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following chronic illnesses:
 - 7-fold higher odds of any neurodevelopmental disorder (i.e., learning disability, ADHD, or ASD)
 - 2-fold increase in Autism Spectrum Disorder (“ASD”)
 - 2-fold increase in ADHD
 - 2-fold increase in learning disabilities
 - 1-fold increase in allergic rhinitis
 - 9-fold increase in other allergies
 - 9-fold increase in eczema/atopic dermatitis
 - 4-fold increase in any chronic illness
 - No significant differences were observed with regard to cancer, chronic fatigue, conduct disorder, Crohn’s disease, depression, Types 1 or 2 diabetes, encephalopathy, epilepsy, hearing loss, high blood pressure, inflammatory bowel disease, juvenile rheumatoid arthritis, obesity, seizures, and Tourette’s syndrome.

However, larger samples would be needed to detect group differences in these less common conditions.

Acute Illness Detail:

- Vaccinated children were significantly less likely than unvaccinated children to have had chickenpox or whooping cough ($p < 0.001$).
- Vaccinated children had a 3.8-fold increased odds of middle ear infections and a 5.9-fold increased odds of being diagnosed with pneumonia compared to unvaccinated children.
- No significant differences were seen between the two groups with regard to Hepatitis A or B, high fever in the past 6 months, measles, mumps, meningitis (viral or bacterial), influenza, or rotavirus.

Vaccination, Preterm Birth and Neurodevelopmental Disorders (NDDs):

In regression analyses, vaccination was associated with a significant 3.1-fold increased odds of neurodevelopmental disorders (combining the diagnoses of ASD, ADHD, and learning disability), after controlling for other factors. An important detail emerged regarding a possible synergism between vaccination and preterm birth. In a final adjusted statistical model, vaccination but not preterm birth remained associated with NDD, as defined, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% Confidence Interval: 2.8, 15.5).

Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports, by Anthony R. Mawson, et al.

* * * * *

Quotes from independent scientists not involved in the study:

"I am delighted to see a properly analyzed study on vaccine safety" said Dr. Lyons-Weiler, CEO and President of the Institute for Pure and Applied Knowledge. "Unlike past studies, which ignored the interaction term, Dr. Mawson and colleagues followed appropriate steps toward interpreting the significance of the interaction between variables. The study reported a significant interaction effect between pre-term birth, and vaccination as a 6.6-fold increase in the risk of neurodevelopmental disorders."

"This study, however, as a survey study, is potentially subject to variation due to responses from well-intended participants. The next logical step would be additional, larger studies that would try to replicate the results using electronic medical health records - by independent investigators not involved in profiting from vaccines", said Dr. Lyons-Weiler.

"This is a long-overdue study involving a fair comparison of vaccinated vs unvaccinated children where the two subpopulations likely don't reflect other biases, due to their being drawn from a

common population of home-schooled children”, said Dr. Stephanie Seneff, Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory. “The results are alarming, and it leaves no doubt that we need to seriously question whether the benefits of vaccines outweigh the risks. A much larger study to see if the results still hold up is paramount at this point.”

Dr. Lyons-Weiler and Dr. Seneff were not involved in the study.

First Study of Vaccinated vs. Unvaccinated Children Is Now Public

Vaccination and Health Outcomes: A Survey of 6- to 12-year-old Vaccinated and Unvaccinated Children based on Mothers' Reports

By Kevin Barry

Key Study Findings

Background: The long-term health outcomes of the routine vaccination program remain unknown. Studies have been recommended by the Institute of Medicine to address this question.

Specific Aims: To compare vaccinated and unvaccinated children on a broad range of health outcomes, and to determine whether an association found between vaccination and neurodevelopmental disorders (NDD), if any, remained significant after adjustment for other measured factors.

Design and Methods: A cross-sectional survey of mothers of children educated at home. Homeschool organizations in four states (Florida, Louisiana, Mississippi, and Oregon) were asked to forward an email to their members, requesting mothers to complete an anonymous online questionnaire on the vaccination status and health outcomes of their biological children ages 6 to 12. A total of 415 mothers provided data on 666 children, of which 261 (39%) were unvaccinated. The collected data included pregnancy experiences and birth histories as well as acute and chronic conditions, medications, and the use of health services.

Results: Vaccinated children were significantly less likely than the unvaccinated to have been diagnosed with chickenpox and pertussis, but significantly more likely to have been diagnosed with other infections, allergies and NDDs (defined as Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and/or a learning disability).

Chronic Illness Detail:

- Vaccinated children were significantly more likely than the unvaccinated to have been diagnosed with the following chronic illnesses:
 - 3.7-fold higher odds of any neurodevelopmental disorder (i.e., learning disability, ADHD, or ASD)
 - 4.2-fold increase in Autism Spectrum Disorder (“ASD”)
 - 4.2-fold increase in ADHD
 - 5.2-fold increase in learning disabilities
 - 30.1-fold increase in allergic rhinitis
 - 3.9-fold increase in other allergies
 - 2.9-fold increase in eczema/atopic dermatitis
 - 2.4-fold increase in any chronic illness
 - No significant differences were observed with regard to cancer, chronic fatigue, conduct disorder, Crohn’s disease, depression, Types 1 or 2 diabetes,

encephalopathy, epilepsy, hearing loss, high blood pressure, inflammatory bowel disease, juvenile rheumatoid arthritis, obesity, seizures, and Tourette's syndrome. However, larger samples would be needed to detect group differences in these less common conditions.

Acute Illness Detail:

- Vaccinated children were significantly less likely than unvaccinated children to have had chickenpox or whooping cough ($p < 0.001$).
- Vaccinated children had a 3.8-fold increased odds of middle ear infections and a 5.9-fold increased odds of being diagnosed with pneumonia compared to unvaccinated children.
- No significant differences were seen between the two groups with regard to Hepatitis A or B, high fever in the past 6 months, measles, mumps, meningitis (viral or bacterial), influenza, or rotavirus.

Vaccination, Preterm Birth and Neurodevelopmental Disorders (NDDs):

In regression analyses, vaccination was associated with a significant 3.1-fold increased odds of neurodevelopmental disorders (combining the diagnoses of ASD, ADHD, and learning disability), after controlling for other factors. An important detail emerged regarding a possible synergism between vaccination and preterm birth. In a final adjusted statistical model, vaccination but not preterm birth remained associated with NDD, as defined, while the interaction of preterm birth and vaccination was associated with a 6.6-fold increased odds of NDD (95% Confidence Interval: 2.8, 15.5).

* * * * *

Quotes from independent scientists not involved in the study:

"I am delighted to see a properly analyzed study on vaccine safety" said Dr. Lyons-Weiler, CEO and President of the Institute for Pure and Applied Knowledge. "Unlike past studies, which ignored the interaction term, Dr. Mawson and colleagues followed appropriate steps toward interpreting the significance of the interaction between variables. The study reported a significant interaction effect between pre-term birth, and vaccination as a 6.6-fold increase in the risk of neurodevelopmental disorders."

"This study, however, as a survey study, is potentially subject to variation due to responses from well-intended participants. The next logical step would be additional, larger studies that would try to replicate the results using electronic medical health records - by independent investigators not involved in profiting from vaccines", said Dr. Lyons-Weiler.

"This is a long-overdue study involving a fair comparison of vaccinated vs unvaccinated children where the two subpopulations likely don't reflect other biases, due to their being drawn from a common population of home-schooled children", said Dr. Stephanie Seneff, Senior Research Scientist at the MIT Computer Science and Artificial Intelligence Laboratory. "The results are alarming, and it leaves no doubt that we need to seriously question whether the benefits of vaccines outweigh the risks. A much larger study to see if the results still hold up is paramount at this point."

*Dr. Lyons-Weiler and Dr. Seneff were not involved in the study.

Lead Developer of HPV Vaccines Comes Clean, Warns Parents & Young Girls It's All A Giant Deadly Scam

Dr. Diane Harper was a leading expert responsible for the Phase II and Phase III safety and effectiveness studies which secured the approval of the human papilloma virus (HPV) vaccines, Gardasil™ and Cervarix™. Dr. Harper also authored many of the published, scholarly papers about the vaccines. She is now the latest in a long string of experts who are pressing the red alert button on the devastating consequences and irrelevancy of these vaccines. Dr. Harper made her surprising confession at the 4th International Conference on Vaccination which took place in Reston, Virginia. Her speech, which was originally intended to promote the benefits of the vaccines, took a 180-degree turn when she chose instead to clean her conscience about the deadly vaccines so she “could sleep at night”. The following is an excerpt from a story by Sarah Cain:

“Dr. Harper explained in her presentation that the cervical cancer risk in the U.S. is already extremely low, and that vaccinations are unlikely to have any effect upon the rate of cervical cancer in the United States. In fact, 70% of all HPV infections resolve themselves without treatment in a year, and the number rises to well over 90% in two years. Harper also mentioned the safety angle. All trials of the vaccines were done on children aged 15 and above, despite them currently being marketed for 9-year-olds. So far, 15,037 girls have reported adverse side effects from Gardasil™ alone to the Vaccine Adverse Event Reporting System (VAERS), and this number only reflects parents who underwent the hurdles required for reporting adverse reactions. At the time of writing, 44 girls are officially known to have died from these vaccines. The reported side effects include Guillian Barré Syndrome (paralysis lasting for years, or permanently — sometimes eventually causing suffocation), lupus, seizures, blood clots, and brain inflammation. Parents are usually not made aware of these risks. Dr. Harper, the vaccine developer, claimed that she was speaking out, so that she might finally be able to sleep at night. ‘About eight in every ten women who have been sexually active will have HPV at some stage of their life,’ Harper says. ‘Normally there are no symptoms, and in 98 per cent of cases it clears itself. But in those cases where it doesn’t, and isn’t treated, it can lead to pre-cancerous cells which may develop into cervical cancer.’”

Although these two vaccines are marketed as protection against cervical cancer, this claim is purely hypothetical. Studies have proven “there is no demonstrated relationship between the condition being vaccinated for and the rare cancers that the vaccine might prevent, but it is marketed to do that nonetheless. In fact, there is no actual evidence that the vaccine can prevent any cancer. From the manufacturers own admissions, the vaccine only works on 4 strains out of 40 for a specific venereal disease that dies on its own in a relatively short period, so the chance of it actually helping an individual is about the same as the chance of her being struck by a meteorite.”

UPDATE #1: Since coming forward with the truth about the devastating consequences of the HPV vaccine, Dr. Harper has been victim of a relentless campaign attempting to discredit the validity of her claims. Harper was even misquoted by British tabloid The Sunday Express which printed a false story loaded with fabricated quotations attributed to Harper. In an interview with The Guardian, Harper makes it very clear about what exactly she said in order to protect herself from a potential lawsuit. In an interview with CBS NEWS, Harper clarifies her position, and once again makes it crystal clear just how devastating this vaccine can be: “If we vaccinate 11 year olds and the protection doesn’t last ... we’ve put them at harm from side effects, small but real, for no benefit,” says Dr. Harper. “The benefit to public health is nothing, there is no reduction in cervical cancers, they are just postponed, unless the protection lasts for at least 15 years, and over 70% of all sexually active females of all ages are vaccinated.” She also says that enough serious side effects have been reported after Gardasil use that the vaccine could prove riskier than the cervical cancer it purports to prevent. Cervical cancer is usually entirely curable when detected early through normal Pap screenings.

“The risks of serious adverse events including death reported after Gardasil use in (the JAMA article by CDC’s Dr. Barbara Slade) were 3.4/100,000 doses distributed,” Harper tells CBS NEWS. “The rate of serious adverse events on par with the death rate of cervical cancer. Gardasil has been associated with at least as many serious adverse events as there are deaths from cervical cancer developing each year. Indeed, the risks of vaccination are underreported in Slade’s article, as they are based on a denominator of doses distributed from Merck’s warehouse. Up to a third of those doses may be in refrigerators waiting to be dispensed as the autumn onslaught of vaccine messages is sent home to parents the first day of school. Should the denominator in Dr. Slade’s work be adjusted to account for this, and then divided by three for the number of women who would receive all three doses, the incidence rate of serious adverse events increases up to five fold. How does a parent value that information,” said Harper.

“Parents and women must know that deaths occurred,” Harper tells CBS NEWS. “Not all deaths that have been reported were represented in Dr. Slade’s work, one-third of the death reports were unavailable to the CDC, leaving the parents of the deceased teenagers in despair that the CDC is ignoring the very rare but real occurrences that need not have happened if parents were given information stating that there are real, but small risks of death surrounding the administration of Gardasil.” She also worries that Merck’s aggressive marketing of the vaccine may have given women a false sense of security. “The future expectations women hold because they have received free doses of Gardasil purchased by philanthropic foundations, by public health agencies or covered by insurance is the true threat to cervical cancer in the future. Should women stop Pap screening after vaccination, the cervical cancer rate will actually increase per year. Should women believe this is preventive for all cancers — something never stated, but often inferred by many in the population — a reduction in all health care will compound our current health crisis. Should Gardasil not be effective for more than 15 years, the most costly public health experiment in cancer control will have failed miserably.” Harper notes that her concern for the vaccine’s deadly side effects applies only to women in the Western world. “Of course, in developing countries where there is no safety Pap screening for women repeatedly over their lifetimes, the risks of serious adverse events may be acceptable as the incidence rate of cervical cancer is five to 12 times higher than in the US, dwarfing the risk of death reported after Gardasil.”

UPDATE #2: The National Vaccine Information Center HAS CONFIRMED two virologists, Stephen Krahling and Joan Wlochowski have filed a lawsuit against their former employer and vaccine manufacturer Merck. NVIC writes: “The lawsuit alleges that Merck defrauded the U.S. for over 10 years by overstating the MMR vaccine’s effectiveness. The virologists claim in their lawsuit that they ‘Witnessed firsthand the improper testing and data falsification in which Merck engaged to artificially inflate the vaccine’s efficacy findings.’ NVIC president and co-founder, Barbara Loe Fisher, warns of the disturbingly cozy relationship and overwhelming conflict of interest between federal agencies charged with vaccine safety oversight (such as the Centers for Disease Control) and vaccine manufacturers. Merck’s global vaccine sales total more than \$20 BILLION A YEAR.

As the world’s pharmaceutical giants continue to be driven less by moral accountability and more by profit and shareholder-driven bottom lines, we are going to see more and more products such as this vaccine which are marketed as “essential to one’s survival.” While some vaccines are indeed essential, such as vaccines for polio and measles, the HPV vaccine is a new beast entirely. To learn more about how pharmaceutical giants are putting profits ahead of ethics you need to watch FRONTLINE’s terrifying new documentary “Hunting The Nightmare Bacteria.”

CONCLUSION

Today about 1 in 6 American children suffer from a neurodevelopmental disorder, a large increase compared to decades ago. Vaccines are very likely contributing to this new crisis.

Vaccine advocates are silent about the research on Al adjuvant toxicity and immune activation.

There has never been a study of the entire vaccine schedule, comparing health outcomes with the unvaccinated. Further, vaccine studies almost never use unvaccinated controls, but rather use other vaccines or Al adjuvant as false placebos. Such research is unscientific and cannot establish safety.

A 1986 federal law completely protects vaccine manufacturers from all product liability lawsuits. Consequently, the industry has no incentive to make safe vaccines. Perverse incentives resulting from this law encourage continued production of unsafe vaccines.

Supporting references provided at:

VaccinePapers.org/brochure

“...the existing evidence on the toxicology and pharmacokinetics of Al adjuvants...strongly implicate these compounds as contributors to the rising prevalence of neurobehavioral disorders in children.” [3]

— Dr C.A Shaw (University of British Columbia) et al.

“And what does a vaccination do? It activates the immune system. That’s the point of vaccination... I think that universal vaccination of pregnant women could get us into a whole new set of problems.” (2006)

— Dr Paul Patterson (California Institute of Technology)

“Maternal immune activation yields male offspring with deficient social and communicative behavior, as well as high levels of repetitive behaviors, all of which are hallmarks of autism.” [6]

— Dr Paul Patterson (California Institute of Technology) et al.

“Interleukin-6 is necessary and sufficient for producing autism in the offspring...” [7]

— Dr Eduardo Pineda (David Geffen School of Medicine, UCLA) et al.

OBJECTIONS ANSWERED

What about the studies showing vaccines do not cause autism?

They look only at MMR, which does not contain Al and is given at older ages when the brain is less sensitive to immune activation. Also, MMR-autism studies ignore healthy user bias, created when parents do not give MMR to children with neurological damage caused by prior vaccines [11].

But aluminum has been used in vaccines for over 80 years.

TRUE. But it has not been studied for safety, until recently. Al dosage from vaccines increased dramatically in the last 25 years, in parallel with childhood neurodevelopmental disorders.

Aluminum is everywhere and ingested constantly. It cannot be harmful.

99.7% of ingested aluminum is not absorbed. The absorbed 0.3% comprises dissolved ions, which are rapidly eliminated in urine. Al adjuvant comprises low-solubility Al nanoparticles, which cannot be eliminated in urine and are far more harmful than soluble Al.

But immune activation studies are based on prenatal immune activation, not postnatal.

Most, but not all immune activation studies use prenatal exposure [8]. For years after birth the human brain remains sensitive to immune activation. Consequently, postnatal immune activation can damage the brain just like prenatal can. Also, the CDC recklessly promotes multiple vaccines for pregnant women, causing prenatal exposure.

Are there ways to prevent damage from aluminum and immune activation?

YES. The nutrient silica removes Al from the body. Taurine and curcumin reduce Al neurotoxicity [5]. Vitamin D regulates immune activation, and has been observed to reverse autism [12].

REFERENCES

- 1 Petrik et al. 2007 “Aluminum Adjuvant Linked to Gulf War Illness Induces Motor Neuron Death in Mice”, *NeuroMolecular Medicine* 9. PMID:17114826
- 2 Shaw et al. 2009 “Aluminum Hydroxide Injections Lead to Motor Deficits and Motor Neuron Degeneration”, *J. Inorg. Biochem.* PMID:19740540.
- 3 Shaw et al. 2013 “Administration of aluminum to neonatal mice in vaccine-relevant amounts is associated with adverse long term neurological outcomes”, *J. Inorg. Biochem.* PMID: 23932735
- 4 Khan et al. 2013 “Slow CCL2-dependent translocation of biopersistent particles from muscle to brain”, *BMC Medicine* 11. PMID: 23557144
- 5 Sethi et al. 2009 “Curcumin Attenuates Aluminum-Induced Functional Neurotoxicity in Rats”, *Pharmacol Biochem Behav.* 93. PMID: 22326555
- 6 Bilkei-Gorzo 1993 “Neurotoxic Effect of Enteral Aluminum”, *Food Chem Toxicol.* 31. PMID: 8505021
- 7 Kneusel et al. 2014 “Maternal Immune Activation and Abnormal Brain Development Across CNS Disorders”, *Nature ReviewsNeurology*, 10. PMID: 25311587
- 8 Wei et al. 2012 “Brain IL-6 Elevation Causes Neuronal Circuitry Imbalances and Mediates Autism-Like Behaviors”, *Biochim Biophys Acta.* PMID: 22326556
- 9 Malkova et al. 2012 “Maternal Immune Activation Yields Offspring Displaying Mouse Versions of the Three Core Symptoms of Autism”, *Brain Behav Immun.* 26. PMID 22310922
- 10 Pineda et al. 2013 “Maternal Immune Activation Promotes Hippocampal Kindling Epileptogenesis in Mice”, *Ann Neurol.* 74. PMID: 23907982
- 11 See VaccinePapers.org/healthy-user-bias
- 12 Jia et al. 2015 “Core Symptoms of Autism Improved After Vitamin D Supplementation”, *Pediatrics* 135. PMID: 2551123

Vaccines and the Brain

The most important science is being ignored.



Powerful scientific evidence shows 2 ways vaccines cause brain damage.

1 Aluminum Adjuvant Toxicity

Vaccines contain neurotoxic amounts of aluminum, which can cause brain damage.

2 Immune System Activation

A developing brain can be damaged when the immune system is activated by a vaccine. Immune activation has been researched extensively and is proven to cause autism and other brain damage.

VaccinePapers.org

Aluminum Adjuvant

Aluminum (Al) adjuvant is a vaccine ingredient used for stimulating the immune system. It is used in many vaccines. Infants in the USA receive dosages of Al adjuvant that cause brain damage in animal experiments. The dosages of Al adjuvant received according to the CDC vaccine schedule are:*

CDC VACCINE SCHEDULE

Aluminum		
Birth	74 mcg/kg	(1 vaccine with 250 mcg, 3.4 kg infant)
2 months	245 mcg/kg	(6 vaccines with 1225 mcg, 5 kg infant)
4 months	150 mcg/kg	(5 vaccines with 975 mcg, 6.5 kg infant)
6 months	153 mcg/kg	(7 vaccines with 1225 mcg, 8 kg infant)
TOTAL	622mcg/kg	3675 mcg aluminum

In scientific experiments, dosages of 100mcg/kg, 300mcg/kg, and 550mcg/kg Al adjuvant cause neuron death, muscle weakness, learning and memory impairment, and pathological behavior changes in animals.

**Aluminum dosage varies by vaccine manufacturer and infant weight. Chart shows maximum possible dosages for average-weight infants. Charts and graphs below redrawn from originals*

FOR FURTHER READING: VaccinePapers.org

Dosage of 550mcg/kg also caused excessive weight gain (a sign of metabolic disorder). All 3 dosages (100, 300 and 550mcg/kg) also caused numerous signs of nerve damage (observable by microscopy and biochemical changes) and/or abnormal anxious behavior.

All these results together are conclusive evidence of brain damage caused by the same dosages (mcg/kg) human infants receive according to the US vaccine schedule.

Vaccine advocates argue that injected Al adjuvant is safe, based on studies of ingested Al salts. This is unscientific because ingesting Al salts and injecting Al nanoparticles present very different risks. Both the route of administration and the chemical forms are different.

Recent experiments prove that Al adjuvant is transported into the brain by white blood cells [4]. This explains why injected Al adjuvant can be more dangerous to the brain than ingested Al salts.

Vaccine advocates like Paul Offit make false statements about Al toxicity studies. The studies show that ingested Al is harmful at dosages less than half of what advocates claim to be safe [5, 6].

Immune Activation

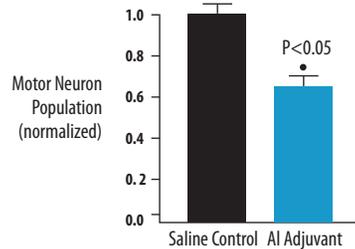
In early life, the brain and immune system develop together. Communication chemicals ("cytokines") used by the immune system also guide brain development. Immune activation causes surges in cytokine production; cytokine surges during brain development cause permanent brain damage and mental illnesses. The brain-damaging effects of immune activation have been studied extensively. The science is high quality and there is a lot of it [7]. It is well-known that vaccines cause immune activation and can cause surges of many different cytokines.

Research has identified interleukin-6 (IL-6) as the specific cytokine responsible for autism; IL-6 is stimulated by vaccine adverse reactions (fever, seizures). IL-6 causes all three autism traits (social impairment, speech impairment and compulsive behavior), and damage to specific brain structures (e.g., the cerebellum) known to be damaged in human autism. Both prenatal and postnatal surges of IL-6 can cause autism [8, 9].

Immune activation during brain development has also been shown to cause schizophrenia, seizure disorders [10], and ADHD.

Motor Neuron Death

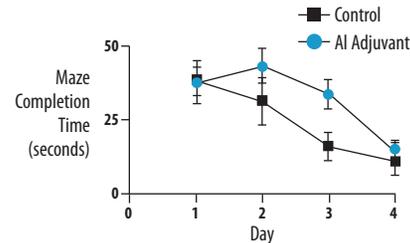
100mcg/kg



100mcg/kg Al adjuvant destroyed about 35% of motor neurons in mice in the lower (lumbar) spine [1].

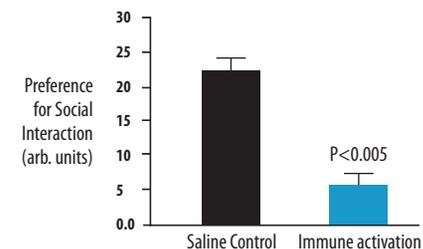
Learning & Memory Impairment

300mcg/kg



300mcg/kg Al adjuvant impaired learning and memory in mice. Impairment is significant with P=0.0389 [2].

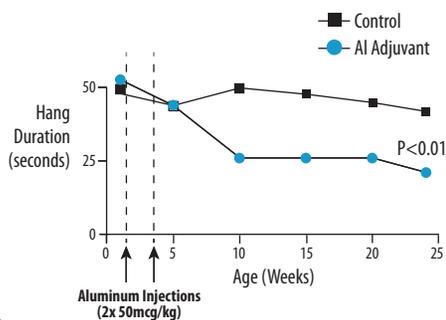
Social Behavior Impairment



Immune activation caused mice to associate with inanimate objects instead of other mice [6].

Muscle Strength Reduction

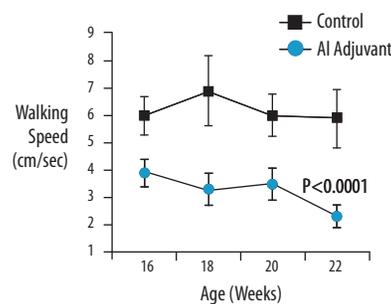
100mcg/kg



100mcg/kg Al adjuvant reduced neuromuscular strength, as measured by the duration mice can hang on a wire mesh [1].

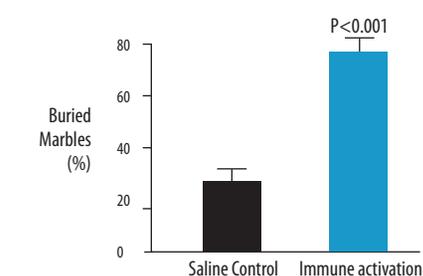
Movement Impairment

550mcg/kg



550mcg/kg Al adjuvant caused a 50% reduction in walking speed (a sign of neurological damage) in male mice. Many other adverse changes were also observed. Al adjuvant injected at ages 0-3 weeks [3].

Compulsive Behavior Increase



Immune activation caused high levels of repetitive/compulsive behavior in mice (marble burying in this experiment) [6].