Re-emerging & Emerging Infectious Diseases: Dengue & Zika

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Fight the Bite
Prevent · Prepare · Protect

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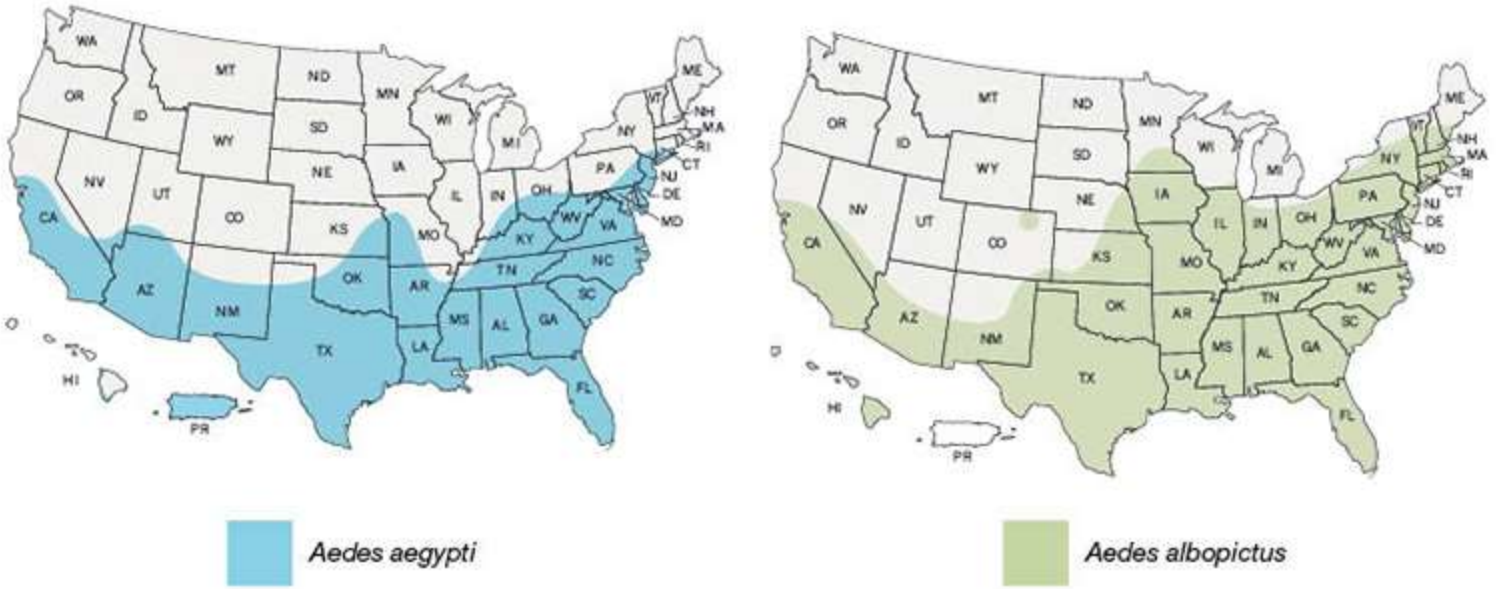
Disclosures

- I have no financial relationships related to this presentation.
- I will not be speaking about any specific commercial product, device, or medication.
- I will not be speaking of any off label use of medications or devices.

Mosquitoes of Concern: *Aedes (Stegomyia)*

- Day biters
- Most competent and ideal mosquito vector, *Aedes aegypti*
  - Females bloodfeed primarily on humans to produce eggs
  - Tropical and subtropical
- *Aedes albopictus*, found statewide; may be considered maintenance vector
  - Opportunistic, aggressive biter (females) with wide host range (man, domestic, and wild animals)
  - Subtropical but expanding into temperate climates

ESTIMATED POTENTIAL Range of *Aedes aegypti* and *albopictus* in the United States, 2016



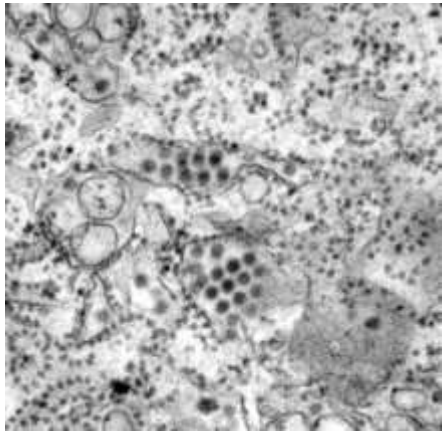
http://www.cdc.gov/zika/vector/range.html

The Foe We Know

Dengue

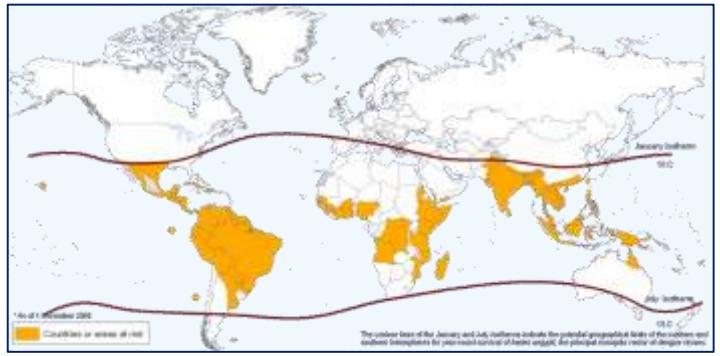
Dengue Virus

- Flavivirus
- Four antigenically distinct serotypes: 1, 2, 3, 4
- Each produces closely similar clinical syndrome



Dengue Epidemiology

- Spread via mobile, viremic humans and rapid rise in urban mosquito populations
  - Unplanned urban overpopulation
  - International travel
  - Poor vector management



- Major global health threat per WHO; rapidly re-emerged, past 20 yrs

World Health Organization (WHO). Dengue and dengue hemorrhagic fever. Fact Sheet No. 117. March 2009. http://www.who.int/mediacentre/factsheets/fs117/en/index.html

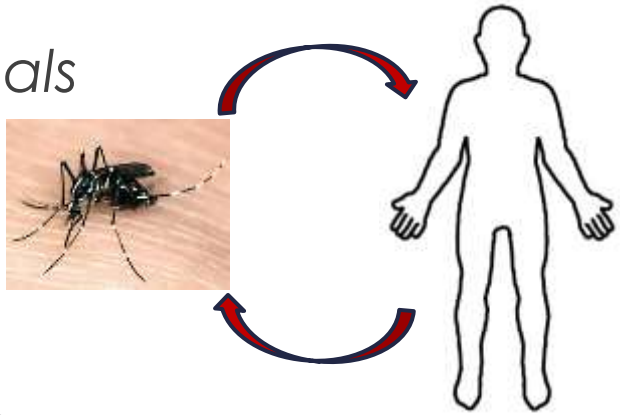
Origin of Imported Dengue Cases in Hawaii, 2011–2015

Year	No. of Cases	Import Countries
2011	7	Philippines, Bangladesh, Guatemala, Thailand, Puerto Rico
2012	7	Philippines, Singapore, Costa Rica, Haiti, Indonesia
2013	10	Philippines, Puerto Rico, Indonesia, Brazil, Kiribati
2014	14	French Polynesia, Indonesia, Thailand, Philippines, American Samoa, Fiji, Tonga, Japan
2015	16	Philippines, Brazil, French Polynesia, Indonesia, Burma, Cambodia, Thailand, American Samoa

Unpublished Hawaii Department of Health data.

Dengue Epidemiology

- Reservoir:
  - Humans
  - Subhuman primates susceptible, *but not other animals*
- Extrinsic incubation in mosquitoes
  - 8–12 days
  - Infected for remainder of lifespan (days–a few wks)
- Intrinsic incubation in humans: usually 4–7 days (range, 2–15)



Clinical Features—Dengue Fever

- Usually chills, red mottling, facial flushing → then fever
- Rash typically from day 3 (duration 1–5 days)
- Some with severe muscle/bone aches (*breakbone fever*)
- ~10% with minor bleeding symptoms (e.g., nose bleed, blood dots, bruising)
- 3–10 days duration; recovery complete in 7–10 days

Clinical Features—Severe Dengue

- Severe dengue (dengue hemorrhagic fever) may develop ~day 3–7 of illness, when seeming to improve
- Shock occurs with circulatory failure from "leaky vessels"—time limited, usually 24–48 hrs

Differential Diagnosis of Dengue

- Leptospirosis
- Murine typhus
- Chikungunya*
- Zika*
- Viral hepatitis
- Influenza
- Measles
- Bacterial sepsis/Septic shock
- Meningococcemia
- Lymphocytic choriomeningitis
- West Nile Fever
- Malaria
- Yellow fever

Diagnosis

- High index of suspicion
- Clinical + epi + general lab findings = *dengue-like* disease
- Diagnosis requires lab confirmation via virus isolation or detecting dengue-specific antibodies (Abs)
  - *RT-PCR, collect within 5 days of symptom onset
  - *IgM (MAC-ELISA), specimen should be ≥6 days after onset
  - Plaque reduction neutralization test (PRNT)—considered "gold standard" to characterize and quantify circulating levels of anti-DENV neutralizing Ab
- Abs may cross-react with other flaviviruses

*Available at State Laboratories Division.

Management of Dengue Infection

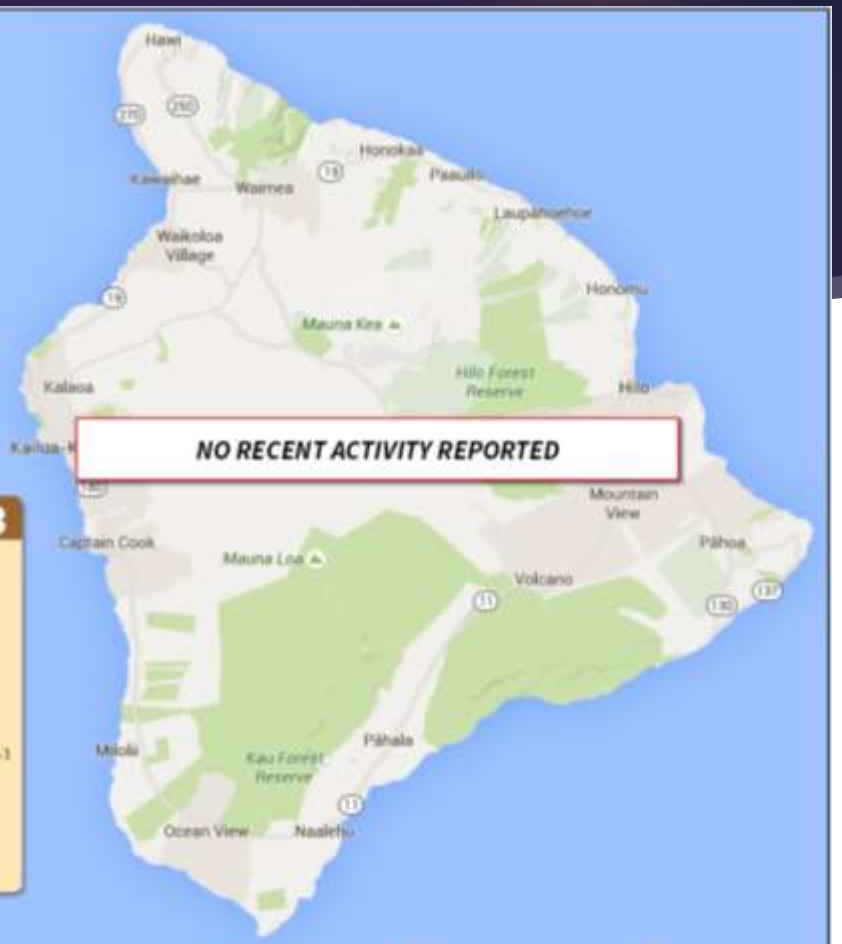
- **URGENTLY NOTIFIABLE**—report any suspect cases to Dept of Health (call **808-586-4586**)
- Avoid mosquito exposure
- Dengue fever usually self-limited—supportive care, no aspirin/NSAIDS/corticosteroids
- Successful severe dengue management depends on early recognition and anticipatory treatment

Hawaii Island Outbreak, 2015–16

- DOH notified Oct 21st regarding positive dengue IgM result
- Investigation initiated
  - Contact physician to obtain medical records and history
  - Find patient to obtain epidemiological history → illness onset 3 wks prior, recovered
- Specimen sent to CDC to verify via PRNT
- Meanwhile, Oct 24th, persons with illness compatible with leptospirosis vs. dengue reported to DOH
  - Specimens routed for testing at State Laboratories Division
  - Oct 28th, confirmed positive for dengue by RT-PCR
- Oct 29th, medical advisory sent to Hawaii healthcare providers; press release distributed

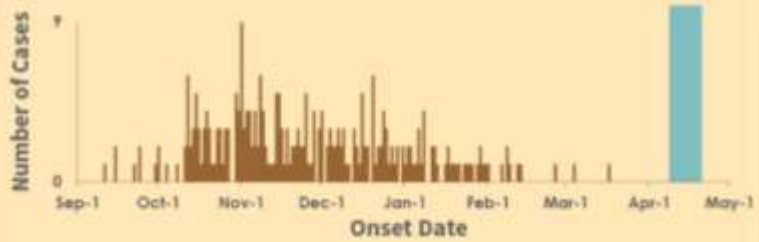
Johnston D, et. al. Notes from the field: outbreak of locally acquired cases of dengue fever—Hawaii, 2015. MMWR, January 2016.

Risk Areas for Potential Dengue Infection Hawaii—2015-2016



As of April 20 2016

Total number of confirmed cases 263



= Cases no longer infectious to mosquitoes
= Cases likely still infectious to mosquitoes
= Illness that began during this time may not yet be reported to/confirmed by HDOH

(HDOH preliminary data - subject to change pending new information)

Map data ©Google

Risk levels for potential dengue infection*: High Risk Moderate Risk Some Risk

*Risk levels of areas where confirmed cases may have contracted dengue fever are determined by the number of confirmed cases with recent onset dates who reported visiting those areas. Individuals should always protect themselves against mosquitoes and mosquito bites island-wide; extra precaution should be taken in areas of risk. For more information on dengue fever and ways to protect yourself from mosquitoes, visit: http://health.hawaii.gov/docd/dengue-outbreak-2015/

Hawaii Island Outbreak, 2015–16

- As of 26 April 2016, 1,907 persons evaluated for dengue infection
- 264 (14%) confirmed with laboratory positive dengue infection
  - 238 Hawaii Island residents (90%), 26 visitors—all from out of state
  - 218 adults (83%), 46 children—under age 18 yrs
  - Onsets of illness ranged from 9 Sept 2015–17 Mar 2016
  - 37 (14%) hospitalized (median stay, 2 days)
  - No cases with severe dengue
- DENV 1 identified as outbreak type
- During outbreak period, identified unrelated imported cases of dengue (16), chikungunya (2), Zika (5)

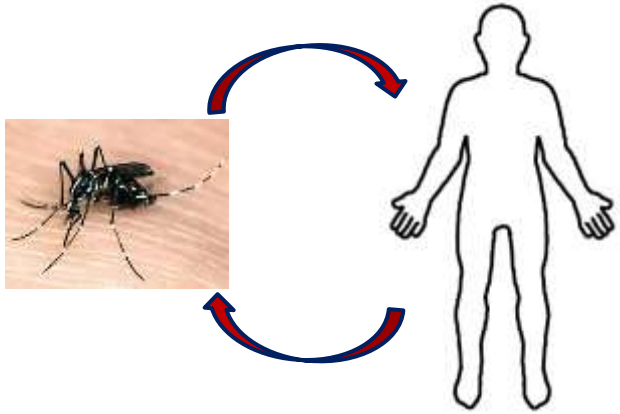
Unpublished Hawaii Department of Health data.

A Mosquito-borne Virus and Congenital Infection?.....and also Sexually Transmissible?

Zika

Zika Virus

- Flavivirus
- Closely related to dengue, WNV, Japanese encephalitis (JEV), and yellow fever (YFV)
- Transmission
  - Primarily anthroponotic
  - Maternal-fetal
  - Sexual
  - Blood transfusion
  - Laboratory exposure



Zika Epidemiology

- First isolated in 1947 in Uganda, rhesus monkey (YFV surveillance)
- 1952, identified in humans in Uganda, Tanzania
- Sporadic human cases in Africa, Southeast Asia
- 2007, first outbreak in Yap Island, FSM*
- 2013–14, large scale outbreak in French Polynesia
- May 2015, first locally-acquired cases in Americas reported in Brazil, subsequently Colombia → across Latin America

*Duffy M, et. al. Zika virus outbreak on Yap Island, Federated State of Micronesia. N Engl J Med, 2009.

Zika Epidemiology

- Incubation period after mosquito bite unclear; likely a few days
- Role of sexual transmission unclear
  - Most reports involve symptomatic male partner, within 3 wks of symptom onset
  - Recent report of symptomatic, acutely ill female to male partner†
  - Unclear whether poses different risk and/or greater risk than mosquito-borne transmission
  - Much still unknown

*Atkinson B, et. al. Detection of Zika virus in semen[letter]. Emerg Infect Dis, 2016.
†Davidson A, et. al. Suspected female-to-male sexual transmission of Zika virus—New York City, 2016. MMWR, 15 July 2016.

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Clinical Features of Zika Infection

- Symptoms usually mild; duration ranges from 2–7 days
- Most commonly reported:
  - Rash
  - Conjunctivitis, mild
  - Arthritis or arthralgia
  - Fever (mild)
- Guillain-Barré syndrome (ascending paralysis) reported
  - In Fr Polynesia, incidence estimated to be 24 per 100,000 Zika infections*
  - In US, usual estimated incidence ~1–2 per 100,000 persons
  - Latin American countries reporting increased number of people with GBS and Zika infection

*Cao-Lormeau V, et. al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet, 2016.

Clinical Features of Zika Infection

- Congenital infection
  - Full spectrum of effects unknown
  - Impact of timing and severity of maternal infection unknown
  - Mechanism of pathogenesis unknown
  - Microcephaly—neonatal head circumference ≥2 SD below mean for newborn's gestational age and sex
  - No evidence congenital infection occurring when maternal infection preceded and resolved pre-conception

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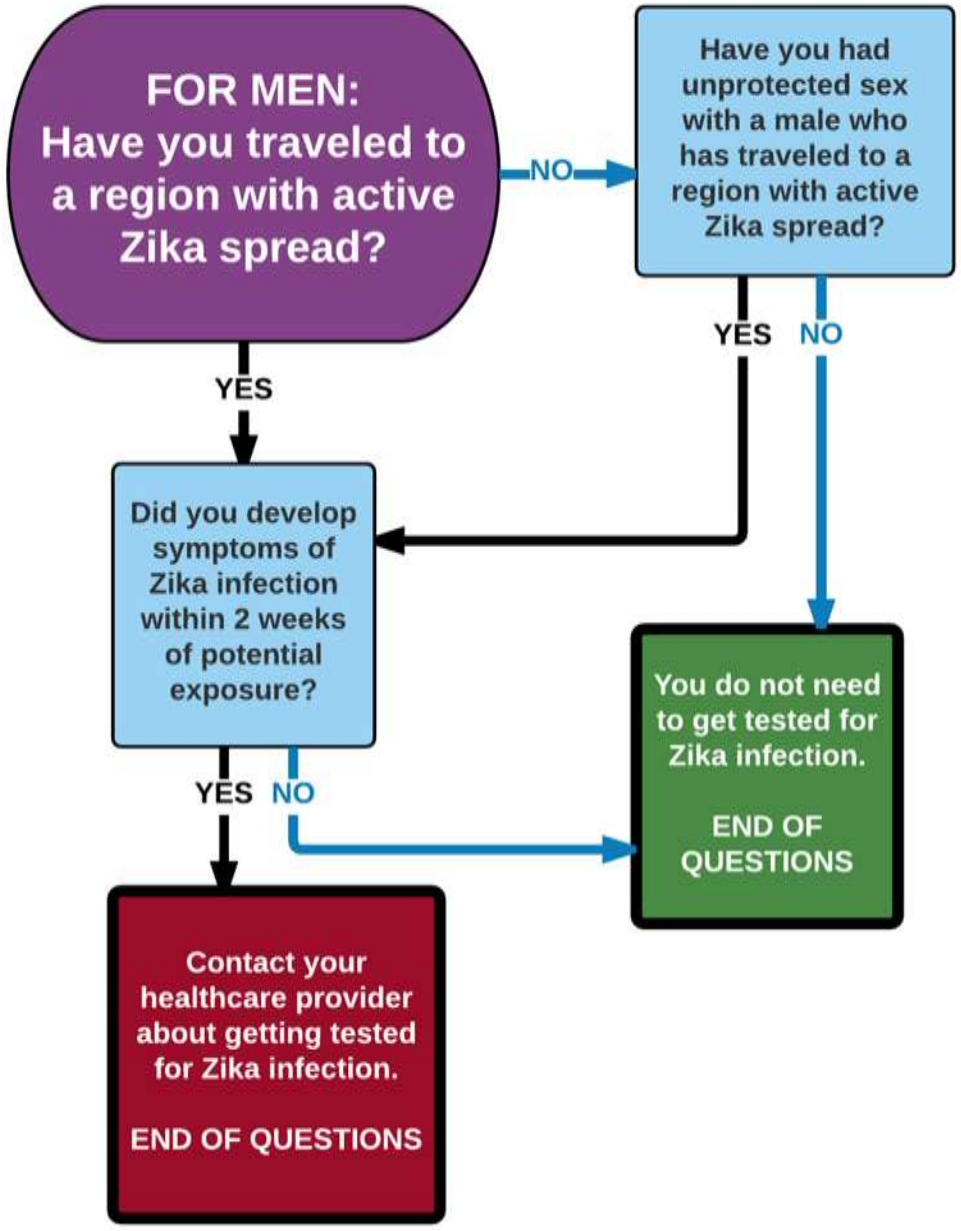
Diagnosis of Zika Infection

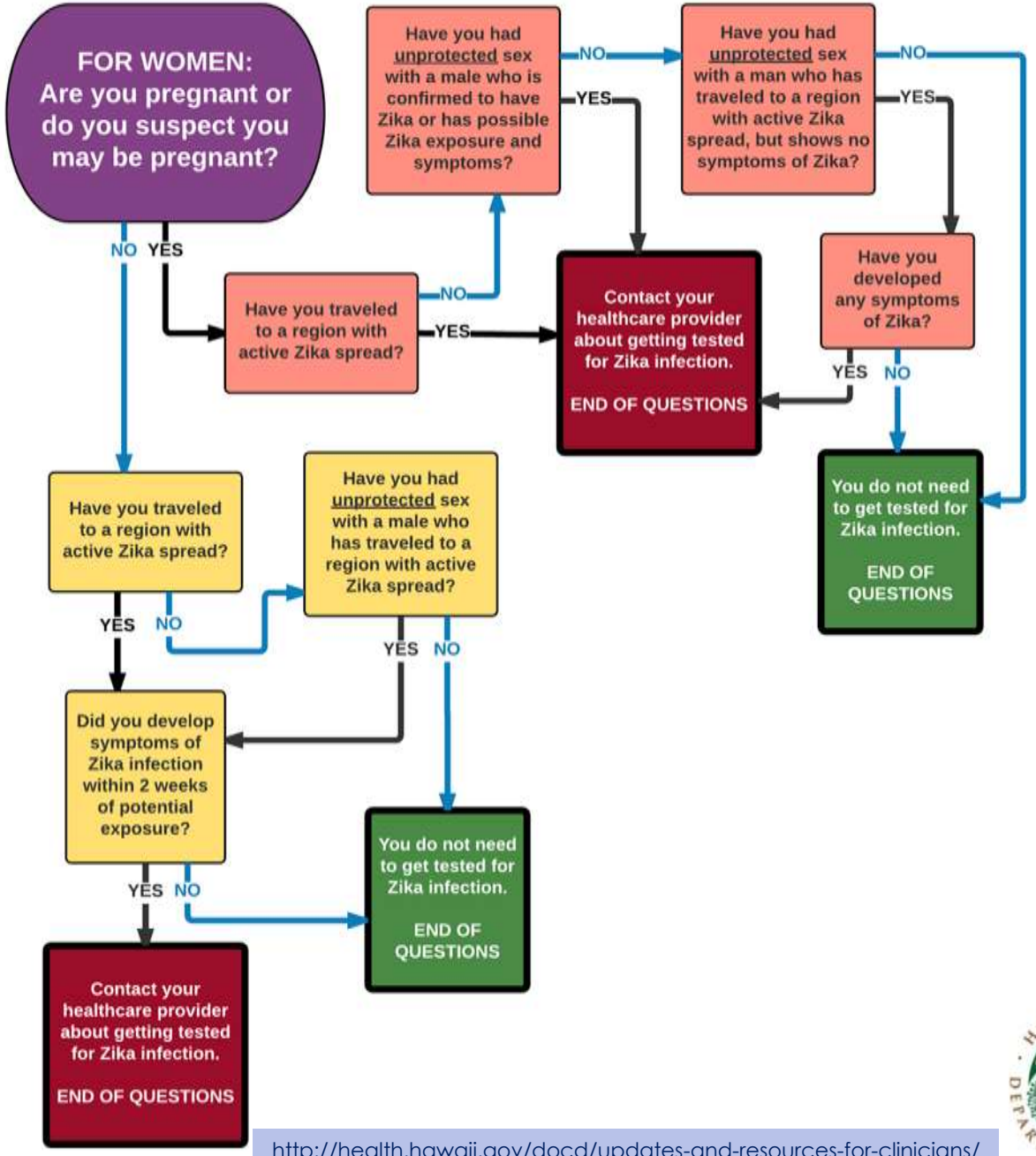
- *RT-PCR for viral RNA if ≤7 days after symptom onset
- *IgM serology if ≥4 days after illness onset—requires further verification
- PRNT for virus-specific neutralizing Abs in paired sera
- Immunohistochemical staining for viral antigens or RT-PCR on fixed tissues (e.g., placenta)
- *Previous infection with or vaccination against flavivirus may compromise results*

*Available at State Laboratories Division.

FOR MEN: SHOULD I GET TESTED FOR ZIKA?



FOR WOMEN: SHOULD I GET TESTED FOR ZIKA?



http://health.hawaii.gov/docd/updates-and-resources-for-clinicians/

Management of Zika Infection

- **URGENTLY NOTIFIABLE**—report any suspect cases to Dept of Health (call **808-586-4586**)
- Avoid mosquito exposure
- Supportive therapy
- Avoid aspirin and NSAIDs until dengue excluded
- Pregnant women with any possible Zika virus exposure
  - Fetal ultrasound
  - Serial ultrasound (~every 3–4wks) if positive or inconclusive Zika test results
  - (-) IgM on serum collected 2–12 wks after known exposure = likely no infection

Prevention of Zika Infection

Pregnant women → NO TRAVEL TO AFFECTED AREAS!*

Pregnant couples, man with possible Zika virus exposure → Use condoms correctly during sex or no sex for duration of pregnancy

*Refer to CDC travel website (http://www.cdc.gov/zika/geo/index.html or http://wwwnc.cdc.gov/travel/page/zika-information).

DOH will work with healthcare providers to monitor infected pregnant women and infants of mothers infected during pregnancy.

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Prevention of Zika Infection

MEN

Confirmed Zika infection OR possible Zika exposure with consistent signs/symptoms → Use condoms correctly during sex or no sex for at least 6 months after illness onset

Possible Zika virus exposure, NO symptoms → Use condoms correctly during sex or no sex for at least 8 weeks after last exposure date

NONPREGNANT WOMEN

Confirmed Zika infection OR possible Zika exposure, *regardless* of symptom history → Ensure partner(s) use condoms correctly during sex or no sex for at least 8 weeks after last exposure date

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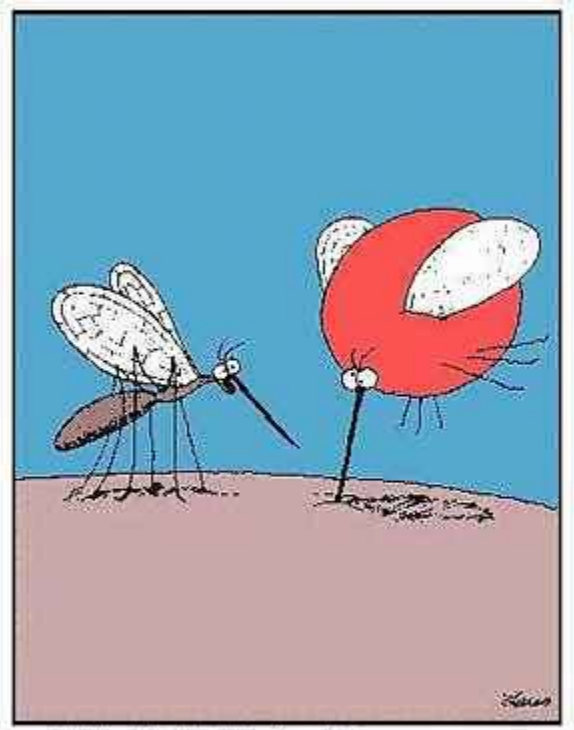
Mosquito Prevention

- Avoid mosquito bites
  - Wear long sleeves/pants when possible
  - Use insect repellant—20–30% DEET
- Mosquito control
  - Eliminate mosquito sources (i.e., standing water) especially around residences and businesses
  - Ensure screens secure and in good repair
- **Infected person should limit any potential exposure to mosquitoes while symptomatic/febrile**

Points to Remember

- *Reportable* in Hawaii under URGENT categorization
- Always obtain *travel history*—specific geographic locations
- Mosquito-borne disease introductions *always* possible in Hawaii
- Controlling and preventing transmission requires interrupting human-mosquito-human cycle at home and abroad



"Pull out, Betty! Pull out! . . . You've hit an artery!"

Mahalo!

http://health.hawaii.gov/docd/dib/disease/mosquito-borne-diseases/