100 Years Since 1918: Are We Ready for the Next Pandemic?

Daniel B. Jernigan, MD MPH
Director, Influenza Division

Barbara Jester, RN
Pandemic Preparedness Portfolio Manager, Influenza Division

Centers for Disease Control and Prevention
August 29, 2018
Significant Annual Burden of Influenza in Humans

**United States**
- Deaths: 12,000 – 56,000
- Severe Cases: 140,000 – 710,000
- Hospitalizations: 9.2M – 35.6M

**Global**
- Deaths: 291,000 – 646,000
- Hospitalizations: 3M to 5M
- Cases: 1.0 B

Human-adapted viruses can arise from reassortment to cause efficient and sustained transmission.

Four pandemics in last 100 years.
The World in 1918: At War
U.S. Joins War Effort April 6, 1917

- Soldiers, food, ammunition, and money needed for war effort
- Civilian population asked to ration food, gasoline, and fabric\(^1\)
- Army Increases in Numbers
  - 378,000 in April 1917
  - >4.1 million by war’s end\(^2\)
  - Draft age
    - Originally 21-30
    - Expanded to 18-45 in May, 1918

\(^1\)Navarro, 2010; \(^2\)Byerly, 2010
Crowding Facilitated Transmission of Infection

- Industrialization and war response added to urban overcrowding

- Soldiers in crowded camps
  - >100K in tents in US
  - 1917-18 record cold winter
Wartime Movement Aided Transmission of Infection

- Massive troop movement
  - Immunologically-naïve young men, moved from isolated towns to training bases, and then to Europe
  - 10,000 men shipped to France every day in summer 1918

- Unprecedented troop movement allowed infection to move from camp to camp
  - JAMA in Oct 1918 reported:
    - Measles
    - Chronic Bronchitis
    - Scarlet fever
  - Pneumonia was then (and remained until 1936) the leading cause of death in the world
The Dawn of Modern Medicine

- Viruses not discovered yet, no flu treatment or prevention, flu transmission poorly understood
  - Cause of influenza attributed in 1892 by Pfeiffer to be a bacillus – *Haemophilus influenzae*

- Few vaccines:
  - typhoid, cholera, plague

- Only palliative therapies:
  - Aspirin, quinine, opium, ammonium, iodine, turpentine, beef tea
Wartime Shortage of Medical Personnel

- 30% of physicians serving in military\(^1\)
- 9,000 nurses had deployed overseas and thousands more were working in training camps\(^2\)

\(^1\)Byerly, 2010; \(^2\)Keeling, 2010
Public Health Service

- US Public Health Service established in 1789
- When war began in 1917, President Wilson made Public Health Service part of the military

Public Health Services Officer in 1912
The Pandemic Begins
“Spanish” Flu

- Spain was non-combatant in WWI
- Only country to make details of their influenza experience public
- The Allied and Central Nations restricted details of their flu experience to:
  - Avoid enemy knowledge of reduced troop strength
  - Maintain morale in the population
First Published Cases in US
Public Health Reports, April 1918

On March 30, 1918, the occurrence of 18 cases of influenza of severe type, from which 3 deaths resulted, was reported at Haskell, Kans.
Signs and Symptoms

- Classic ILI - fever, cough, sore throat, stuffy nose, myalgia, fatigue
- Pneumonia in 10-20% of pandemic cases in Western world
  - 280,000 pneumonia deaths in healthy young adults
    - Primary viral pneumonia
    - Secondary bacterial pneumonia and empyema
- Extensive organ involvement
- Perioral cyanosis
- Death could occur quickly but typically in 3-10 days

Glezen 1996; Barry 2005; Cunha 2004; Morens 2007; Hsieh 2006; Shanks 2015
Signs and Symptoms of 1918 Pandemic

- ‘Purple Death’ often in 24 hrs
  - “They very rapidly develop the most vicious type of pneumonia that has ever been seen.”
  - “Cyanosis extending from their ears and spreading all over the face”
  - “It takes special trains to carry away the dead. For several days there were no coffins and the bodies piled up something fierce.”
  - “Bodies stacked in the morgue from floor to ceiling like cord wood.”

Healthcare Provider Experiences

- Not uncommon to enter a home and find bodies of deceased alongside those with disease
- Some nurses were literally kidnapped during the pandemic
  - Held by force in some homes where patients were too frightened and desperate to let them leave

Barry, 2005; http://www.influenzaarchive.org/cities/city-stlouis.html#
Effect of Community Mitigation Efforts

- Earlier timing of interventions was associated with lower peak death rates

Interventions included:
  - Closure of schools, churches, dance halls, and theaters
  - Bans on public gatherings

Examples from Philadelphia and St Louis
  - Philadelphia *delayed* implementation of interventions, allowed Liberty Loan Parade in September
  - St Louis implemented multiple measures *early* after first cases identified

The difference of 14 days in response times between the two cities was approximately three to five doubling times for an influenza epidemic
Three Pandemic Waves in Ten Months

- Wave 1
  - Between February and April in North America
  - Between May and July in Europe
  - Spread across globe in less than 6 months (smallpox had taken half a century)

- Wave 2:
  - Fall (September/October)

- Wave 3:
  - Early 1919
Mortality

- Likely caused 50M deaths globally\(^1\)
- \(~675,000\) US deaths
  - 5 times the military losses of WWI
  - Exceeds military losses of WWI + WWII + Korea + Vietnam\(^2\)
- W-shaped mortality curve showing increased rate among young- to middle-aged adults

\(^1\)Chowell & Viboud 2016 and Johnson & Mueller 2002; \(^2\)Patterson & Pyle 1991
Depressed overall average life expectancy by 10 – 12 years
A prominent health official gave a Midwestern official advice on how to prepare for outbreak:

- “Begin by hunting up wood-workers, cabinet makers, and street laborers and set them to making coffins and digging graves”
Global Mortality From the 1918-1920 Pandemic
Approximately 50 Million Deaths

- USA: 675K
- Canada: 50K
- Mexico: 300K
- Brazil: 180K
- Chile: 35K
- Spain: 257K
- Germany: 225K
- England: 200K
- Nigeria: 455K
- S Africa: 300K
- Russia: 450K
- China: 4M
- Japan: 388K
- India: 18.5M
- Indonesia: 1.5M
- Australia: 15K

Evaluation of the Virus
1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

Reconstructing The 1918 Influenza Virus
1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

1951
Hultin unable to grow live 1918 virus in lab

Reconstructing The 1918 Influenza Virus

Taubenberger Science 1997, Tumpey Science 2005
Influenza Division

1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

1951
Hultin unable to grow live 1918 virus in lab

1997
Hultin returns to gravesite for frozen lung tissue

Reconstructing The 1918 Influenza Virus

Taubenberger Science 1997, Tumpey Science 2005
Reconstructing The 1918 Influenza Virus

1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

1951
Hultin unable to grow live 1918 virus in lab

1997
Hultin returns to gravesite for frozen lung tissue

1997
Taubenberger at AFIP begins sequencing the 1918 virus genes

Taubenberger Science 1997, Tumpey Science 2005
Reconstructing The 1918 Influenza Virus

1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

1951
Hultin unable to grow live 1918 virus in lab

1997
Hultin returns to gravesite for frozen lung tissue

Taubenberger at AFIP begins sequencing the 1918 virus genes

2004
Tumpey at CDC rescues 1918 virus in high containment lab

Taubenberger Science 1997, Tumpey Science 2005
Influenza Division

Reconstructing The 1918 Influenza Virus

1951
Johan Hultin at permafrost gravesite, Brevig Mission AK

1951
Hultin unable to grow live 1918 virus in lab

1997
Hultin returns to gravesite for frozen lung tissue

1997
Taubenberger at AFIP begins sequencing the 1918 virus genes

2004
Tumpey at CDC rescues 1918 virus in high containment lab

2005
CDC shows 1918 virus causes severe pneumonia in mice and identifies the genes responsible for high virulence

Taubenberger Science 1997, Tumpey Science 2005
Emerging Influenza Viruses With Pandemic Potential
Increasing Number of Poultry, Pigs, People and Passengers 1965-2015

- Poultry population
- People population (billions)
- Pig population (billions)
- International tourist arrivals (billions)

Number of Poultry and People per Year In Billions

Number of International Arrivals and Pigs per Year In Billions

Increasing Number of Human Cases of Novel Influenza A Infection, 1959-2017

Freidl G, Meijer A, de Bruin E, et al. Euro Surveill. 2014 May 8;19(18); Cumulative cases of H5N1 and H7N9. WHO. Graph includes avian H4, H5, H6, H7, H9, H10 & swine H1, H3 (not pH1N1).
The Percentage of the Global Population Over 65 Years Of Age Is Increasing

Influenza Division

Are We Ready For The Next Severe Influenza Pandemic?
Estimating the Impact of a 1918-Like Pandemic

The diagram illustrates the relationship between the scaled measure of transmissibility and the scaled measure of clinical severity. The 1918 pandemic is depicted in the top right corner, indicating very high severity and transmissibility. Other pandemics, such as 1957, 1968, 2009, 2014-15, and 2017-18, are shown with varying levels of severity and transmissibility. The 2011-12 season is also included, showing a seasonal range within the low severity category.

Adapted from Reed EID 2013
## Estimated Illness, Types of Medical Care, and Deaths from a Moderate to Very Severe Influenza Pandemic

<table>
<thead>
<tr>
<th>Pandemic Severity (based on multiple factors&lt;sup&gt;a&lt;/sup&gt;)</th>
<th>Transmissibility (% of US population&lt;sup&gt;b&lt;/sup&gt; with clinical illness)</th>
<th>Illness</th>
<th>Outpatient medical care</th>
<th>Hospitalization</th>
<th>ICU care</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>20%</td>
<td>64,000,000</td>
<td>32,000,000</td>
<td>800,000</td>
<td>160,000</td>
<td>48,000</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>96,000,000</td>
<td>48,000,000</td>
<td>1,200,000</td>
<td>240,000</td>
<td>72,000</td>
</tr>
<tr>
<td>Severe</td>
<td>20%</td>
<td>64,000,000</td>
<td>32,000,000</td>
<td>3,800,000</td>
<td>1,200,000</td>
<td>510,000</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>96,000,000</td>
<td>48,000,000</td>
<td>5,800,000</td>
<td>1,700,000</td>
<td>770,000</td>
</tr>
<tr>
<td>Very Severe</td>
<td>20%</td>
<td>64,000,000</td>
<td>32,000,000</td>
<td>7,700,000</td>
<td>2,300,000</td>
<td>1,300,000</td>
</tr>
<tr>
<td></td>
<td>30%</td>
<td>96,000,000</td>
<td>48,000,000</td>
<td>11,500,000</td>
<td>3,500,000</td>
<td>1,930,000</td>
</tr>
</tbody>
</table>


<sup>b</sup> 2015 US Population estimate used for calculation.
If a 1918-Like Pandemic Occurred Today

- Potential disruption of transportation and supply chains

- Potential disruption of healthcare services

- Potential high economic costs
  - $181B-$570B estimated for moderate to severe influenza pandemic
  - SARS cost $30 billion in only 4 months
Surveillance Readiness

**Strengths**

- WHO Global Influenza Surveillance and Response System (GISRS)
  - 144 laboratories for virus monitoring in 113 countries
  - >400K tests reported in FluNet per year
- Next-generation sequencing of all flu viruses sent to CDC and shared with accessible public database
  - Developing field-deployable “NGS in a backpack”
- CDC supports >30 countries for surveillance and novel flu detection

**Gaps**

- ‘Data Deserts’ in Africa and Southern Hemisphere
- Inadequate surveillance in birds and swine
- Specimen sharing is too slow and complicated
Diagnostic Readiness

▪ **Strengths**
  - Global distribution of free testing materials via IRR
  - CDC PCR tests detect H1, H3, B’s, H5, H7 given to >140 labs globally
  - Greatly improved commercial flu assays for fast PCR results

▪ **Gaps**
  - Limited flu testing and poor lab capacity in developing nations
  - Difficult and slow to confirm novel flu
  - Simple, reliable, OTC tests not available
Therapeutic and Clinical Readiness

- **Strengths**
  - **Antivirals**
    - Increased availability of antivirals and new monoclonal antibody (mAb) therapies in pipeline
    - FluOnCall for use in a pandemic
  - **Clinical Care**
    - After SARS/MERS/Ebola, new facilities built for treating patients with emerging infections with high fatalities

- **Gaps**
  - Need better performing antiviral treatment with:
    - Benefit in severe, hospitalized influenza infection
    - Greater availability and lower cost
  - Need reusable respiratory protective devices
  - Ventilatory and clinical support capacity is insufficient in most of globe for a severe pandemic
Respiratory Protective Devices

- The amount of RPD’s needed for healthcare worker protection during an influenza pandemic far exceeds the amount of product available.

- Estimates:
  - Reusable RPDs: 1.62 Million
  - N95: 3,506 Million
  - Facemask: 438 Million

![Graph showing the comparison between the need for RPDs and the market supply during different influenza pandemics.](image)
Vaccine Readiness

**Strengths**

- New vaccine technologies available
  - Synthetic biology for making vaccine viruses
  - Cell-grown vaccines
  - Recombinant protein vaccines
- Improved virologic forecasting
- More manufacturing capacity available
  - WHO Global Action Plan
- New programs for introducing vaccine for low- & mid-income countries

**Gaps**

- Takes too long to have vaccine available for pandemic response
- Need better current vaccines as we work toward a truly “universal” vaccine
Preparedness Planning and Response

- **Strengths**
  - International Health Regulations since 2005 for greater awareness and response
  - WHO Pandemic Influenza Preparedness (PIP) Framework
    - Support for improving surveillance and equitable response during an influenza pandemic
    - 400 M vaccine doses anticipated for next pandemic
  - Response Tools are Available
    - Pandemic Risk Assessments
    - Pandemic Severity Assessments
    - Pandemic preparedness resources

- **Gaps**
  - Most countries do not have robust pandemic plans and very few exercise response efforts
  - Only 1/3 of countries ready for response based on IHR review
1918 and Now
Conclusions

- Seasonal influenza causes a significant burden each year, but the 1918 pandemic was exceptionally severe
  - A similar pandemic today could cause tremendous illness, death, and cost

- Number of detected emerging novel influenza viruses is increasing, necessitating ongoing laboratory surveillance and risk assessments

- Efforts to improve pandemic readiness and response are underway, however, many gaps remain

- Are we ready in 2018 for a severe influenza pandemic?
  - Better than we were, but not where we need to be.
Thank You
Dan Jernigan, MD  MPH
DJernigan@cdc.gov

WHO
B Jester
J Katz
D Wentworth
T Tumpey
X Xu
J Barnes
B Garten
L Gubareva
T Davis
L Chen
S Lindstrom
M Levine
I York
T Maines
S Sambhara

GISRS
V Dugan
D Iuliano
E Azziz-Baumgartner
J Bresee
S Olsen
A Fry
C Reed
L Brammer
B Flannery
M Biggerstaff
A Budd
B Neuhaus
E Eisenberg
S Shepard