“Influenza Pandemic Preparedness For US Hospitals”

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21st Century Epidemics/Pandemics

- SARS pandemic 2002-2003
- Re-emergence of H5N1 HPAI virus 2003
- H1N1 influenza pandemic 2009
- Ebola of 2014 in the West
- MERS in Middle East, to South Korea
- Rika virus in the Americas 2016
Objectives

- History of pandemics
- How and when an influenza pandemic can take place?
- Likely scenario?
- What can we do at a hospital level?
Conclusion of WHO, International Committee Review

- “The world is ill prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public-health emergency.”

Why pandemics are so hard to manage and be prepared for?

- Operational efficiency
- Limited bed surge capacity
- Limited supply of antivirals
- Takes time to produce vaccines
- Relatively rare events
Impediments

- Limitations of scientific knowledge
- Difficulties in decision making under conditions of uncertainty
- Complexities in international cooperation
- Challenges in communication among experts, policymakers and the public
Bird Flu Virus H5N2 Spreading Across U.S.; CDC Warns Doctors to Be Vigilant

by MAGGIE FOX

People exposed to potentially infected ducks, chickens or turkeys should be aware of bird flu. CDC says. PHIL NOBLE / Reuters
History of Pandemics

- Plague of Athens, 430 BC, ¼ pop
- Antonine Plague, 165–180, 5 million
- Plague of Justinian, 541-750, ½ pop
- Black Death, 14th onward, 75 millions
- Third Plague Pandemic, mid 19th century in China, 10 millions
  - San Francisco plague of 1900–1904
History of Influenza

- Hippocrates first described influenza in 412 BC
- The first influenza pandemic was recorded in 1580
- Since then influenza pandemics occurred every 10 to 30 years

Recent Pandemic History

- The "Spanish flu", 1918–1919, 500 millions infected
- The "Asian Flu", 1957–58, 2 millions
- The "Hong Kong Flu", 1968–69, 1 million
- H1N1 Pandemic of 2009- 284,000 deaths
Variable Case Mortality

- U.S. Army camps 5-10% or higher
- British Army in India, white troops was 9.6%, for Indian troops 21.9%.
Variable Case Mortality

- In isolated human populations, the virus killed at even higher rates.
  - In the Fiji islands, it killed 14% of the entire population in 16 days.
- In Labrador and Alaska, it killed at least one-third of the entire native population

A letter from a physician wrote on the 1918 pandemic

- “It is only a matter of a few hours then until death comes [...]. It is horrible. We have been averaging about 100 deaths per day [...]. Pneumonia means in about all cases death [...]. We have lost an outrageous number of Nurses and doctors. It takes special trains to carry away the dead.”
**Recent Pandemic History in US**

- H1N1 2009 to 2010 over 12 months
- 60.8 million cases
- 274,304 hospitalizations
- 12,469 deaths
- Fatality rate at 0.02%

**Unfolding pandemic of H1N1 in 2009**

- Early cases started in Feb/March in Mexico
- As of June 9, 2009, a total of 73 countries had reported more than 26,000 laboratory-confirmed
- By August 2010, virtually all countries report lab-confirmed cases
Why early H1N1 cases so alarming?

- 899 hospitalized patients showed that 58 (6.5%) became critically ill, and of those, 41% died. (2.66% mortality rate)
- Mortality among children, young adults, and pregnant women was much higher than in a typical influenza season
**HPAI H5N1**

- On May 21, 1997, a three-year-old boy died in Hong Kong from a viral infection that turned out to be influenza.
- It took an international team of virologists three months to identify it as H5N1—"bird flu"

**HPAI H5N1**

- Then re-emerged in 2003 with sporadic transmission to more than 700 humans from 15 countries
- Highest rates are in Indonesia, Vietnam and Egypt
- Endemic in six countries
When can a pandemic occur?

1. A new influenza virus subtype must emerge
2. Must infect humans and cause illness
3. Must spread easily and sustainably among humans
Limited, non-sustained human-to-human transmission?

- 2004 in Thailand from child to mother
- 2007
  - China, child to father
  - Indonesia, 8 cases in same family
  - Pakistan, 3 brothers

Why Influenza will always be a threat?

- Socioeconomic and political development
- Indigenous cultures and customs
- Dietary habits
- Mobility of 21st century
Influenza Case Study in Airplanes in 1970s

- 54 people remained on the plane for three hours
- Within 72 hours, nearly 75% of the passengers developed influenza. The source of the infection was a single person on the airplane with influenza
What are other pathways for an influenza pandemic?
Study shows how easily pandemic H5N1 bird flu could evolve
Scientists discovered it took just five genetic mutations for a potentially pandemic strain of H5N1 bird flu virus to emerge

Alok Jha, science correspondent
theguardian.com, Thursday 21 June 2012 14:11 EDT
Jump to comments (35)

U.S. panel defends call not to publish research about hyper-contagious mutant bird flu

REUTERS | February 1, 2012 11:49 AM ET
More from Reuters
The Frightening Conclusion?

- “Re-assortment with mammalian viruses is not needed” for it to evolve to spread through the air
'Appalling irresponsibility': Senior scientists attack Chinese researchers for creating new strains of influenza virus in veterinary laboratory.
How H5N1 influenza is perpetuated?

- Per CDC HPAI H5N1 virus is considered endemic in poultry in six countries (Bangladesh, China, Egypt, India, Indonesia, and Vietnam)
- The disease can be carried without symptoms in wild birds.
CDC explains mix-up with deadly H5N1 avian flu

By Jocelyn Kaiser | 15 August 2014 3:45 pm | Comments

A federal scientist may have accidentally contaminated a relatively benign avian influenza strain with the deadly H5N1 bird flu virus in part because he or she was overworked and rushing to make a lab meeting, according to an internal report released today by the Centers for Disease Control and Prevention (CDC).

In the March incident, CDC sent a sample of low-pathogenicity H9N2 bird flu virus that a lab had unknowingly contaminated with H5N1 to a U.S. Department of Agriculture (USDA) lab, which discovered the mistake when test chickens died. CDC Director Thomas Frieden first disclosed the incident in July at a press conference about other lab accidents. Frieden was especially troubled, he said, because the H5N1 incident was not reported to top CDC leaders for 6 weeks.
Influenza Basics

- Human influenza A and B viruses cause seasonal epidemics
- Influenza B viruses are not divided into subtypes
- Influenza type C infections cause a mild respiratory illness

Influenza Basics

- The Influenza A virus subtypes are labeled according to an
  - \( H \) (hemagglutinin) (H1 to H16)
  - \( N \) (neuraminidase) (N1 to N9)
  - Pandemic potential
Serotypes pathogenic in Humans:

- H1N1, which caused Spanish Flu in 1918, and Swine Flu in 2009
- H2N2, which caused Asian Flu in 1957
- H3N2, which caused Hong Kong Flu in 1968
- H5N1, which caused Bird Flu in 2004
- H7N7, which has unusual zoonotic potential
- H1N2, endemic in humans, pigs and birds
- H9N2
- H7N2
- H7N3
- H10N7
- H7N9

What is striking about the H5N1 outbreak of 2003?

- Predominance of children and young adults
- High mortality rate
- Kills all afflicted poultry livestock
Incubation Period

- Following exposure to infected poultry, 7 days or less, often between 2-5 days
- In clusters of human to human transmission, 3-5 days
Clinical Features of H5N1

- Most gave hx of recent exposure to dead or ill poultry
- Wide range of infection-mild symptoms to life-threatening disease
- Presentation may depend on duration of exposure to virus

Clinical Features of H5N1

- Conjunctivitis only
- Influenza-like illness
- Severe respiratory illness
- Nausea, abdominal pain, diarrhea, vomiting
- Neurologic changes (altered mental status, seizures).
FIG 1: Distribution of sialic acids in human ocular and respiratory tract tissues. Major components of human ocular and respiratory tissues are depicted, with the predominant α2,6- and/or α2,3-linked sugars expressed on epithelial cells identified where known (see references 37 and 38). While these sialic acids are predominantly employed by adhesion and inflammatory cells, additional cellular receptors and the viruses which utilize them are discussed in the text.
Complications?

- Multi-organ failure with renal dysfunction and cardiac compromise
- Pulmonary hemorrhage
- Pneumothorax
- Pancytopenia
- Most deaths due to respiratory failure

Imaging Studies Findings

- Diffuse, multifocal, or patchy infiltrates
- Interstitial infiltrates
- Segmental or lobular consolidation
- Progression to respiratory failure is associated with diffuse bilateral ground glass infiltrates
Who Should Be Tested?

- Recent exposure to dead or ill poultry
- HIGH RISK:
  - Recent travel to H5N1 affected country within 10 days of symptom onset and
  - X-rays confirming pneumonia, ARDS or other severe respiratory illness

Samples

- Should be sent within 3 days of onset of symptoms
- Throat samples better than nasal
- Should be obtained with Dacron tip, not with cotton or calcium alginate tips.
Antigen Tests and PCR

- Commercial rapid tests are less sensitive in detecting influenza A than PCR assays

When to Contact CDC?

- Any + results of H5N1 virus testing.
- should be confirmed immediately at the Influenza Division at CDC
How ready are our hospitals?

What is the likely scenario of an Influenza Pandemic?
ICU Bed Capacity in US?

Our nation has only 105,000 ventilators as of 2005, per NEJM

### Table 1. Number of Episodes of Illness, Healthcare Utilization, and Death Associated with Moderate and Severe Pandemic Influenza Scenarios*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate (1958/68-like)</th>
<th>Severe (1918-like)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness</td>
<td>90 million (30%)</td>
<td>90 million (30%)</td>
</tr>
<tr>
<td>Outpatient medical care</td>
<td>45 million (50%)</td>
<td>45 million (50%)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>885,000</td>
<td>9,900,000</td>
</tr>
<tr>
<td>ICU care</td>
<td>128,750</td>
<td>1,485,000</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>64,875</td>
<td>742,500</td>
</tr>
<tr>
<td>Deaths</td>
<td>209,000</td>
<td>1,903,000</td>
</tr>
</tbody>
</table>

*Estimates based on extrapolation from past pandemics in the United States. Note that these estimates do not include the potential impact of interventions not available during the 20th century pandemics.
Likely Responses

- Panic will grip the nation
- Many health care settings will scurry to meet and plan
- Absenteeism due to illness will spike
“A number of surveys have found that 16%–33% of HCWs may not report to work in the event of an influenza pandemic”

According to CDC on Emerging Diseases Article, “Pandemic (H1N1) 2009 Risk for Frontline Health Care Workers,” Volume 17, Number 6—June 2011
Inpatient setting

- What if patient load surpass bed availability?
- How to house large number of Influenza patients?
- Must have separate housing units for confirmed and yet-to-be confirmed
Call for Ethics Committee

- To decide who meets the criteria for intubation and to be ventilated
- If limited antivirals, prioritize
- Triage those deemed to be
  - Expectant
  - Suspected vs confirmed influenza
What are our defenses?

- National and global Surveillance
- Infection Control
- Pharmacotherapy
- Vaccine
- Social Distancing
National Influenza Surveillance

2. Outpatient Illness Surveillance
3. Mortality Surveillance
4. Hospitalization Surveillance
5. Summary of the Geographic Spread of Influenza
**Bird flu and danger to humans**

Bird flu, or avian flu, has a high mortality rate in humans, but as of yet, cannot be transmitted from person to person.

**Infection with type A virus H5N1**

1. Most virulent bird flu virus; mutates rapidly, altering its genetic material.
2. Humans infected by close contact with live infected poultry.
3. Birds carry virus and excrete it in feces, which dries, becomes pulverized and then can be inhaled or taken in by touch.
4. Humans have no immunity against this virus.

**Symptoms**

- Fatigue
- Fever
- Conjunctivitis
- Sore throat
- Cough
- Muscle aches

**When untreated**

Rapid deterioration; viral pneumonia leading to respiratory distress, kidney failure, multi-organ failure, death.

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Source: World Health Organization Graphic: Julia Schiebe, Morten Lyhne © 2004 KRT
Infection Control
**Why Influenza tend to be more prevalent in colder climates?**

- Transmission of infection was most efficient when the humidity was 20-35%;
- It was blocked at 80% humidity.
Outpatient setting

- Early spot and control dissemination
- Hospital wide enforcement of “proper” use of masks
- Consider humidity of 80% of all waiting areas
### Influenza Treatment

- Tamiflu (oseltamivir) and Relenza (zanamivir)
- Rapivab (Peramivir) in IV only
- Supportive care
- Aggressive bacterial treatment as needed

### Vaccine Production Options

- Egg based
- Cell culture
- Recombinant DNA
Public health response?

- Early identification of sources (national and international surveillance)
- Maintain good contact with possible cases
- Systemic culling of infected poultry
- Isolation and treatment of suspected or confirmed cases.

<table>
<thead>
<tr>
<th>Influenza Season</th>
<th>Reference</th>
<th>Study Site(s)</th>
<th>No. of Patients</th>
<th>Adjusted Overall VE (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007-08</td>
<td>Belongia 2011</td>
<td>WI</td>
<td>1914</td>
<td>37</td>
<td>22.49</td>
</tr>
<tr>
<td>2009-10</td>
<td>Griffin 2011</td>
<td>WI, MI, NY, TN</td>
<td>6757</td>
<td>56</td>
<td>23.75</td>
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<tr>
<td>2010-11</td>
<td>Treanor 2011</td>
<td>WI, MI, NY, TN</td>
<td>4757</td>
<td>60</td>
<td>53.66</td>
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<tr>
<td>2011-12</td>
<td>Ohmit 2014</td>
<td>WI, MI, PA, TX, WA</td>
<td>4771</td>
<td>47</td>
<td>36.56</td>
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<tr>
<td>2012-13</td>
<td>McLean 2014</td>
<td>WI, MI, PA, TX, WA</td>
<td>6452</td>
<td>49</td>
<td>43.55</td>
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<tr>
<td>2013-14</td>
<td>Unpublished</td>
<td>WI, MI, PA, TX, WA</td>
<td>5990</td>
<td>51</td>
<td>43.58</td>
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<tr>
<td>2014-15</td>
<td>ACIP presentation, Flannery</td>
<td>WI, MI, PA, TX, WA</td>
<td>9329</td>
<td>23</td>
<td>14.31</td>
</tr>
</tbody>
</table>
Public health response goals

- Goal to contain outbreak as much and early possible
- Massive vaccination campaign to follow
- Prophylaxis with antivirals

Comparison of tools available to fight the next Influenza Pandemic.
<table>
<thead>
<tr>
<th>1918 Spanish Flu</th>
<th>21st Century</th>
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</thead>
<tbody>
<tr>
<td>No antivirals</td>
<td>No antivirals?</td>
</tr>
<tr>
<td>No ventilators</td>
<td>No ventilators</td>
</tr>
<tr>
<td>No antibiotics</td>
<td>No antibiotics?</td>
</tr>
<tr>
<td>1/3 of HCWs died?</td>
<td>1/3 of HCWs will not show up for work</td>
</tr>
<tr>
<td>Majority young 20-40s yrs of age</td>
<td></td>
</tr>
</tbody>
</table>
What are lessons from recent outbreaks?

“We have the Spanish influenza situation well in hand now.”

Dr. John Dill Robertson, Health Commissioner for Chicago
Underestimate of the Pandemic

- Sept 23, 1918, <50 deaths/day
- By October 1, >400 deaths per day
- Two weeks later, at the peak of the epidemic, >2000 per day.
- By early November, approximately 300
SARS 2003 in Toronto

- Of the almost 375 people who contracted SARS in this outbreak,
- 72% were infected in a healthcare setting,
- 45% of these cases were HCWs, including 3 who died

Lesson from “Tale of Two Cities”
Summary

- Influenza viruses are the most adaptable and deadly
- Our defenses are weaker than we hope for
- The key is how well hospitals handle sentinel cases
- Swift public health response