Avian Influenza: State, National and Worldwide View

New York State Department of Health
June 22, 2005
Topics

- Influenza Disease in Humans
- Avian Influenza
- Pandemic Influenza
- Planning for Pandemic Influenza
- Pandemic Response Components
  - Surveillance
  - Vaccination
  - Antiviral drug use
  - Maintaining quality medical care
  - Public health interventions
Influenza

- Acute, febrile respiratory illness affecting nose, throat, bronchial tubes and lungs
- Epidemics caused by influenza viruses A and B
- Occurs worldwide, causing considerable morbidity and mortality each year
Influenza Virus Types

• **Type A** - moderate to severe illness
  - all age groups
  - humans and other animals

• **Type B** - milder epidemics
  - humans only
  - primarily affects children

• **Type C** - rarely reported in humans
  - no epidemics
Influenza A Viruses

Subtyped based on surface glycoproteins:
  • 16 hemagglutinins (HA) and 9 neuraminidases (NA)
  • current human subtypes: H1N1, H3N2, H1N2
Symptoms

• Fever, muscle aches, headache, lack of energy, dry cough, sore throat, possibly runny nose

• Fever and body aches for 3-5 days

• Cough and lack of energy- 2 weeks

• Symptoms similar to adenovirus, RSV, rhinovirus, parainfluenza, legionellosis, etc,
Transmission

• Typical incubation: 2 days
  Range: 1-4 days

• Viral shedding
  – Can begin 1 day before symptom onset
  – Peak shedding first 3 days of illness
    • Correlates with temperature
  – Subsides usually by 5-7\textsuperscript{th} day in adults
    • can be 10+ days in children
Transmission

• Limited studies, varying interpretations
• Contact, droplet, and droplet nuclei (airborne) transmission may all occur
  – Relative contribution of each unclear
  – Droplet thought most important
    • Generated via coughing, sneezing, talking
Public Health Importance of Influenza

• Annual epidemics and potential for pandemics

• >36,000 deaths in US per epidemic (MVA - 40,000 deaths yearly)

• Over 85% of mortality is in persons aged 65 and older

• Attack rates of 5-20% in general population

• Nursing home attack rates of 60%
Avian Influenza
Influenza A Natural History

- Influenza A viruses found in:
  - Ducks, chickens, pigs, whales, horses, seals

- Wild birds, especially waterfowl, are reservoirs of all known influenza A subtypes

- Carry virus in intestines and shed via saliva, nasal secretions, and feces

- Fecal-oral most common transmission between birds
Natural Reservoir for New Human Influenza A Virus Subtypes: Waterfowl (Aquatic Ducks)

Avian Influenza A Viruses
H1 - H15
N1 - N9

Human Influenza A Viruses
H1 - H3

CDC
Timeline of Emergence of Influenza A Viruses in Humans

- **1918**: Spanish Influenza
- **1957**: Asian Influenza
- **1968**: Russian Influenza
- **1977**: Avian Influenza
- **1997**: Hong Kong Influenza
- **1998/9**: Avian Influenza
- **2003**: Avian Influenza
Current H5N1 Outbreak, Dec 03 – June 05

- Thailand, Vietnam, Cambodia, Malaysia, Indonesia, China
- Endemic infection of poultry
- Poultry/bird exposure
- **No sustained** person-to-person transmission identified
- **No influenza A viruses with human and avian genes have been detected**
H5N1 Cases and Deaths, Dec. 26, 2003, to June 8, 2005

<table>
<thead>
<tr>
<th>Country</th>
<th>H5N1 Cases</th>
<th>Deaths</th>
<th>Case Fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>17</td>
<td>12</td>
<td>71%</td>
</tr>
<tr>
<td>Vietnam</td>
<td>79</td>
<td>38</td>
<td>48%</td>
</tr>
<tr>
<td>Cambodia</td>
<td>4</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>54</td>
<td>54%</td>
</tr>
</tbody>
</table>
CDC Recommendations for Avian Influenza

• Guidelines issued Feb 4, 2005
  www.cdc.gov/flu/avian/professional/han020405.htm

• Enhanced surveillance efforts by state and local health departments, hospitals, and clinicians of suspected avian influenza human cases
  – Obtain Travel History
  – Exposure History
Effect of Travel and Missed Cases: The SARS Example

Guangdong Province, China

Hong Kong SAR
95 HCW

>100 close contacts

Hotel M Hong Kong

Hong Kong SAR
95 HCW

Vietnam
37 HCW

21 close contacts

Singapore
34 HCW

37 close contacts

United States
1 HCW

Canada
18 HCW

11 close contacts

Ireland
0 HCW

Canada
18 HCW

United States
1 HCW

Ireland
0 HCW

Effect of Travel and Missed Cases: The SARS Example
Pandemic Influenza
Pandemics

• Result from the emergence of a new virus to which the overall population possesses no immunity

• Most severe occur with changes in both surface proteins

• Asia the source of many outbreaks
  – Viruses can be isolated at any time of year
  – Swine, birds and humans live under the same roof, providing opportunity for admixing
How Influenza Viruses Change

• **Antigenic Drift:**
  – Small changes in virus over time
  – New strains appear and replace older strains
  – May not be recognized by antibodies to older strains

• **Antigenic Shift:**
  – Abrupt, major change (reassortment)
  – Results in novel strain or new subtype
  – Can cause pandemic influenza
Antigenic “Shift” Pandemic

Avian virus

Quail/HK/G1/97 (H9N2)

A/HK156/97 (H5N1)

Avian reassortant virus

Teal/HK/W312/97 (H6N1)

Reassortment in humans

Goose/Guangdong/1/96 (H5N1)

Reassortment in swine

Avian-human pandemic reassortant virus

Model of the emergence of a pandemic influenza virus
Influenza Pandemics 20th Century

1918: “Spanish Flu” A(H1N1)
- 20-40 m deaths
- 675,000 US deaths

1957: “Asian Flu” A(H2N2)
- 1-4 m deaths
- 70,000 US deaths

1968: “Hong Kong Flu” A(H3N2)
- 1-4 m deaths
- 34,000 US deaths

Credit: US National Museum of Health and Medicine
# Flu Pandemics: A Comparison

<table>
<thead>
<tr>
<th>YEAR</th>
<th>1918</th>
<th>2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>World Population</td>
<td>1.8 Billion</td>
<td>5.9 Billion</td>
</tr>
<tr>
<td>Primary Mode of</td>
<td>Troopships, Railroad</td>
<td>Jet Aircraft,</td>
</tr>
<tr>
<td>Transportation</td>
<td></td>
<td>automobile</td>
</tr>
<tr>
<td>Time for Virus to</td>
<td>4 months</td>
<td>4 days</td>
</tr>
<tr>
<td>Circle the Globe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estimated Dead</td>
<td>20+Million</td>
<td>60 Million?</td>
</tr>
<tr>
<td>Worldwide</td>
<td></td>
<td></td>
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Pandemic Planning and Preparedness
WHO Pandemic Preparedness Plan


- Recognition of endemic animal infection with an influenza virus subtype that has repeatedly caused disease in humans

- SARS experience highlights opportunity if not to contain a pandemic, potentially to “buy time”
## New WHO Pandemic Phases

<table>
<thead>
<tr>
<th>Interpandemic period</th>
<th>Phase 1: No new influenza virus subtypes in human; subtype that has caused human infection may be present in animals</th>
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<tbody>
<tr>
<td></td>
<td><strong>Phase 2:</strong> As above, but circulating animal subtype poses substantial risk of human disease</td>
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<tr>
<td>Pandemic alert period</td>
<td><strong>Phase 3:</strong> Human infection w/ new subtype, no human-to-human (HTH) spread, or rare spread to close contact</td>
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<td></td>
<td><strong>Phase 4:</strong> Small clusters w/ limited HTH transmission, highly localized spread, suggesting virus not well adapted to human</td>
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<td></td>
<td><strong>Phase 5:</strong> Larger clusters, but HTH spread still localized, virus increasingly better adapted to humans, but not yet fully transmissible</td>
</tr>
<tr>
<td>Pandemic period</td>
<td>Increased and sustained transmission in general population</td>
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U.S. Pandemic Influenza Preparedness Activities, 1

• Enhanced surveillance
  – CDC cooperative agreements for surveillance in Asia and support for WHO surveillance activities

• Vaccine security and supply
  – HHS funding to assure year-round egg availability and promote expansion and diversification of U.S. influenza vaccine production
  – NIH testing pilot lots of H5N1 vaccine
  – Small H5N1 vaccine stockpile obtained
  – Research on antigen-sparing strategies
U.S. Pandemic Influenza Preparedness Activities, 2

• Antiviral drugs
  – Establishment of a stockpile

• State/local preparedness
  – CDC BT support for State planning activities
  – HRSA funding for health care system preparedness
  – Technical support and tabletop exercises to practice State/local plans
HHS Pandemic Influenza Preparedness and Response Plan

- Description of Federal level activities
  - Coordination (command and control)
  - Actions of HHS agencies
- Legal authorities for pandemic response actions
- Description of current infrastructures & technologies
- Guidance on strategies for response actions and supporting rationales
- Table of specific Federal actions by pandemic phase
What is **Not** in the Federal Pandemic Influenza Plan

- Decisions on pandemic vaccine purchase or distribution
- Definition of priority groups for vaccination
- Resolution of indemnification & liability issues
- Specific instructions & materials
  - Who provides essential community services
  - How to run a mass vaccination clinic
  - Education and communications materials
Ongoing National Pandemic Influenza Planning Activities

• Revise (“finalize”) HHS plan
  – NVAC Pandemic Influenza Working Group to address outstanding issues
    • Members include representatives of public & private sector stakeholders, and ethicists
    • Develop options/recommendations on vaccine purchase, vaccine priority groups (jointly with ACIP), and antiviral priority groups & strategies.

• CDC guidance document for health care partners
New York State Pandemic Planning

• Major Sections of State Plan (in draft)
  – Command and Control Procedures
  – Surveillance and Laboratory Testing
  – Vaccine and Antiviral Delivery
  – Emergency Response
  – Communications

• Activities by phases of a flu pandemic, for state DOH, LHDs, and providers

• Once draft completed, provide to local health departments, and providers for comments
Command and Control

- Outline roles, command structure, and decision-making process

- Ensure incorporation of pandemic plan with Department’s overall emergency response plan

- Ensure legal issues are identified and addressed

- Ensure key stakeholders are informed about necessary infrastructure and resources needed to respond
Surveillance and Laboratory Testing

- Update surveillance guidelines for local health departments
- Develop plans for isolation, quarantine and contact tracing
- Address and plan for epidemiologic surge capacity
- Address and plan for laboratory surge capacity
- Develop laboratory testing algorithms
Vaccine and Antiviral Delivery

- Outline process for prioritization of vaccine and/or antivirals
- Outline process for vaccine and antiviral acquisition and delivery
- Develop data management system to track supplies, distribution and use
- Develop plan for conducting mass vaccination clinics
- Develop system for tracking adverse events to vaccination
Health Care and Emergency Response

- Address hospital surge capacity issues
- Address roles of triage centers, volunteers, home care
- Develop hospital employee health guidance
- Develop infection control guidelines
- Address mass mortality issues
- Develop system for tracking hospital resources
Communications

- During the pre-pandemic phase, develop social marketing strategies for risk reduction behaviors (e.g., handwashing, respiratory etiquette)
- Develop pre-pandemic communications products to expedite delivery of information during a pandemic
- Develop communications plan with “one-voice response” key messages
- Develop communication strategies that will address the “worried well”
- Identify spokesperson(s)
- Produce scripts and Q&A’s for a public call center
Pandemic Response Components
Pandemic Response Components

- Pandemic influenza disease
- Interventions to decrease transmission
- Provide quality medical care
  - Infection control in medical & long term care settings
  - Maintain essential community services/emergency response activities
- Antiviral treatment & prophylaxis
- Vaccination
Enhanced Surveillance Activities in New York State, 2004-05

• Emergency influenza reporting regulations implemented in December 2004:
  • Hospitalized patients diagnosed with laboratory-confirmed influenza
  • Laboratory-confirmed influenza
  • Influenza-associated pediatric deaths
Hospitalized Patients with Laboratory Confirmed Influenza A, B, or Unspecified
Rapid Antigen Testing or Culture Confirmed
(Week ending Sunday, Dec 5 2004 11:59PM)
Patients Hospitalized with Laboratory-Confirmed Influenza Reported on HERDS, 2004-2005

Week Ending

Number of Hospitalizations

4- Dec 18
11- Dec 29
18- Dec 76
25- Dec 232
1- Jan 444
8- Jan 423
15- Jan 314
22- Jan 260
29- Jan 212
5- Feb 262
12- Feb 277
19- Feb 192
26- Feb 172
3- Mar 101
10- Mar 88
17- Mar 66
24- Mar 62
1- Apr 50
8- Apr 27
15- Apr 15
22- Apr 9
Positive Influenza Laboratory Results
Reported on ECLRS, 2004-2005
Vaccine Planning

- When will vaccine first become available?
- Who will own and distribute it?
- What type of guidance will there be regarding how to use it?
Pandemic Vaccine Supply

• Assumptions
  – Imported vaccine will not be available
  – Two doses (15 ug) will be needed for protection
  – 4-8 months until first vaccine doses available

• U.S. manufacturing capacity
  – Only Sanofi has a completely domestic supply chain
  – Estimated production sufficient to deliver ~5 million monovalent doses/week

• Implication – less than 1% of the population may be protected per week
Priority Groups for Pandemic Vaccine

• Base definition of priority groups on pandemic response goals
  – Reduce health impacts – Maintain quality healthcare system and protect those at highest risk
  – Reduce social and economic impacts – Maintain essential community services

• Role of national plan in defining priority groups
  – Need for national guidance vs state-by-state decisions re: target groups generally and specific priorities within groups
## Potential Vaccine Target Groups and Population

<table>
<thead>
<tr>
<th>Group</th>
<th>Population</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health care workers</td>
<td>12.6 M</td>
<td>4.4%</td>
</tr>
<tr>
<td>Hospital HCW</td>
<td>5.1 M</td>
<td>1.8%</td>
</tr>
<tr>
<td>Outpatient</td>
<td>7.5 M</td>
<td>2.6%</td>
</tr>
<tr>
<td>Public safety workers</td>
<td>3.0 M</td>
<td>1.0%</td>
</tr>
<tr>
<td>High risk outpatients</td>
<td>83.0 M</td>
<td>28.9%</td>
</tr>
<tr>
<td>LTCF residents</td>
<td>3.1 M</td>
<td>1.1%</td>
</tr>
<tr>
<td>Essential community service</td>
<td>8.7 M</td>
<td>3.0%</td>
</tr>
</tbody>
</table>
Antiviral Planning

• Will any public sector supply be available and if so, how much?

• What guidance is there regarding how best to use it?
Influenza Antivirals and Impacts

- Adamantanes – amantadine & rimantadine
  - Effective as prophylaxis
  - H5N1 strain is resistant & resistance develops rapidly if used for treatment
  - No studies document impact on complications
  - Adverse events (neurological and GI) common

- Neuraminidase inhibitors – oseltamivir & zanamivir
  - Effective as prophylaxis and treatment
  - Resistance uncommon
  - Few adverse events
Pandemic Antiviral Supply

- Antivirals in the Strategic National Stockpile
  - Oseltamivir (~2 million courses)
  - Rimantadine (~5 million courses)

- Antivirals in the private sector
  - ~1-1.5 million oseltamivir courses, pre-influenza season
  - Amantadine and rimantadine widely available

- Oseltamivir production
  - Currently from single facility in Switzerland
  - U.S. supply chain being established
Potential Uses of Antiviral Drugs in an Influenza Pandemic

• Containment of an initial outbreak
  – Donate portion of U.S. supply to support international intervention (e.g., in SE Asia)

• Slow spread following introduction of initial cases into the U.S.
  – Treatment of cases and prophylaxis of contacts

• Prophylaxis to prevent infection in target groups

• Treatment of cases
Summary of Antiviral Drug Strategies

• With limited antiviral supply, treatment is the best strategy to prevent adverse health outcomes – especially if delivered early

• Ability to maintain essential services with a treatment strategy is unclear
  – Effectiveness related to pandemic severity, ability to implement early, and ability to tolerate some work loss

• Prophylaxis reasonable in defined settings
  – Small high risk or critical service groups
  – Institutional settings – post-exposure prophylaxis
Medical Care during an Influenza Pandemic

• Surge capacity of the hospital system is limited

• Challenges:
  – Magnitude and duration
  – Staff shortages
  – Limited ability to call in external resources
Avian influenza isolation unit, Tropical Diseases Hospital, Ho Chi Minh City, Vietnam, February 2004
FluSurge

• CDC software to estimate the impact of an influenza pandemic on hospitals

• Provides hospital administrators and public health officials estimates of the surge in hospitalization during an influenza pandemic.

• Compares the number of persons:
  • hospitalized
  • requiring ICU care
  • requiring ventilator support

with existing hospital capacity.
Results: Worst Case Scenario

- At the peak of the most drastic scenario of a pandemic influenza outbreak (i.e. 35% attack rate, 6 week duration), New York State (excluding New York City) can expect a maximum of:
  - 14,916 influenza-related hospital admissions per week
  - 3,728 influenza-related deaths per week
    - 2,609 deaths in the hospital

- Influenza patients will most likely utilize:
  - 63% of hospital bed capacity
  - 125% of intensive care capacity
  - 65% of hospital ventilator capacity.
Results:
“Least Worst” Case Scenario

• At the peak of the least dramatic scenario of a pandemic influenza outbreak (i.e. 15% attack rate, 12 week duration), New York State (excluding New York City) can expect a minimum of:
  – 1,395 influenza-related hospital admissions per week
  – 409 influenza-related deaths per week
    • 286 deaths in the hospital per week

• Influenza patients will most likely utilize:
  – 19% of hospital bed capacity
  – 38% of intensive care capacity
  – 20% of hospital ventilator capacity.
Other Control Measures
Interventions Other Than Vaccine or Antiviral Drugs

• Slow spread of virus between countries
  – Travel recommendations

• Reduce infectious and susceptible individuals in populations
  – Isolation of ill persons
  – Quarantine of exposed persons
  – Contact tracing
  – Cancellation of events (school, meetings etc)

• Steps to reduce individual exposure to virus
  – Masks
  – Hand washing
YOUR HEALTH IS IN YOUR HANDS

HELP STOP THE SPREAD OF GERMS That Cause Colds, Flu, and Other Respiratory Diseases.

Always WASH YOUR HANDS WITH SOAP AND HOT WATER, Or USE A WATERLESS HAND CLEANSER After:

- Blowing your nose or coughing
- Using the bathroom
- Before and after eating
- After being in contact with or being near someone who is ill

FIND OUT MORE AT: www.health.state.ny.us
Conclusions: Planning for Uncertainty

• Many unknowns about the next pandemic
  – When and how bad? Risk groups? Vaccine & drug supply?

• Need for specificity – Need for flexibility
  – Plan for health care surge capacity
  – Identify strata within occupational groups for antiviral drugs and vaccine
  – Identify and draft materials to support a response – algorithms, forms, software, educational materials, etc.
  – Consider alternatives and conduct exercises
Acknowledgements

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  - Centers for Disease Control and Prevention
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