Epidemiology of Seasonal and Pandemic Influenza in the U.S.

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Seasonal Influenza (U.S.)

- Annual winter epidemics
  - Caused by influenza A and B viruses
  - Peak activity November - March
  - Severity varies year-to-year
  - Estimated 5-20% of U.S. population ill
  - Influenza A (H3N2) epidemics more severe than A (H1N1) or B

- Impact
  - School and work absenteeism
  - Outpatient, emergency room visits
  - Hospitalizations, deaths
  - Overwhelmed medical systems
Point mutations in the hemagglutinin gene of influenza viruses cause minor antigenic changes to hemagglutinin protein

- Gradual, continuous process
- Immunity against one strain may be limited
- Vaccine strains must be updated each year
  - 6-8 month process

Antigenic “Drift” causes seasonal epidemics
Some Reasons Why Influenza is a Major Public Health Problem Each Year

• Certain groups can develop severe secondary complications after influenza virus infection
  • Exacerbation of chronic underlying medical conditions (e.g. cardiac and lung disease)
  • Invasive bacterial infections (e.g. pneumonia)
  • Rare complications (e.g. myocarditis, encephalopathy)

• Complications can result in hospitalization/death
Influenza - Attributable Hospitalizations (U.S.)

Average of >200,000 influenza-related hospitalizations/year

- Estimated by modeling studies using retrospective data and influenza surveillance data

Children:

- High rates in young children <2 years
- Children 2-5 years next highest
- High rates for children with chronic high-risk conditions

Adults:

- Highest rates in persons ≥65 years
- High rates in persons with chronic illness

Neuzil KM et al., NEJM 2000;342:225-231; Thompson WW et al., JAMA 2004;292:1333-1340;
Neuzil KM et al. JID 2002;185:147-152
Influenza-Associated Hospitalizations By Age Group, 1979-2001, U.S.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Hospitalizations per 100,000 Person Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 Yrs</td>
<td>115</td>
</tr>
<tr>
<td>5-49 Yrs</td>
<td>22</td>
</tr>
<tr>
<td>50-64 Yrs</td>
<td>90</td>
</tr>
<tr>
<td>&gt;65 Yrs</td>
<td>472</td>
</tr>
</tbody>
</table>
NVSN Influenza Laboratory-Confirmed Cumulative Hospitalization Rates for Children 0 - 4 Years, 2007-08 and Previous 4 Seasons

Population-Based Rate per 10,000 Children

2007-2008 Influenza Season 2 Week Reporting Period

- 2003-2004
- 2004-2005
- 2005-2006
- 2006-2007
- 2007-2008
EIP Influenza Laboratory-Confirmed Cumulative Hospitalization Rates for Children Aged 0-4 and 5-17 yrs, 2007-2008 and Previous 4 Seasons
Influenza-associated Mortality, U.S.

• Estimated average of
  • ~36,000 influenza-attributable deaths/year (all ages)
  • Highest mortality rates:
    • Persons ≥65 years
    • Persons with chronic pulmonary and cardiac disease; other chronic conditions

• Mortality data are limited for children
  • Estimated average of 92 influenza-related deaths among children aged <5 years annually
  • 46 - 153 pediatric influenza-associated deaths reported to CDC/season (2003-08)

Influenza-Associated Deaths By Age Group, 1979-2001*

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Respiratory &amp; Circulatory Deaths per 100,000 Person Years **</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 Yr</td>
<td>0.6</td>
</tr>
<tr>
<td>1-4 Yrs</td>
<td>0.4</td>
</tr>
<tr>
<td>5-49 Yrs</td>
<td>0.5</td>
</tr>
<tr>
<td>50-64 Yrs</td>
<td>7.5</td>
</tr>
<tr>
<td>&gt;65 Yrs</td>
<td>98.3</td>
</tr>
</tbody>
</table>

*Thompson WW et al. JAMA 2003
Individuals at Increased Risk for Hospitalizations and Death, U.S.

- Elderly ≥65 years
- Young Infants
- Persons with chronic medical conditions
  - Heart or lung disease, including asthma
  - Metabolic disease, including diabetes
  - HIV/AIDs, other immunosuppression
  - Conditions that can compromise respiratory function or the handling of respiratory secretions
- Pregnant women
- Nursing home residents
Pandemic Influenza Concerns

• Human infections with novel influenza A virus subtypes
  • Low pathogenic (LPAI), highly pathogenic avian influenza (HPAI) viruses
  • HPAI H5N1 viruses
  • LPAI H7N2, H7N3, H7N7, H9N2 viruses
  • Most significant threat: HPAI H5N1 viruses
    • Evolving strains in different clades and subclades
    • Circulating among poultry and wild birds in many countries
    • Primarily a rare zoonotic disease in humans
    • High mortality
Global Epidemiology of H5N1 Cases

- 20 confirmed H5N1 cases (35% fatal) {1997 - February 2003}
- 387 confirmed H5N1 cases (245 deaths) reported to WHO from 15 countries that occurred since November 2003*
- Case fatality proportion: 63%
- Surveillance for human H5N1 cases has focused upon severe respiratory disease (pneumonia)

*Reported to WHO as of September 10, 2008
Epidemiology of H5N1 cases 2003-08

- Infrequent, sporadic cases among previously healthy children, young adults, some seasonality
  - Primary risk factor: direct or close contact with sick/dead poultry
  - Occasional clusters of cases among blood-related family members
    - Most clusters: 2-3 cases; Largest: 7 confirmed cases
    - Most clusters linked to poultry exposures (avian-to-human)
  - Limited, non-sustained human-to-human transmission likely occurred in some clusters
    - 3rd generation spread likely in 2 clusters
    - No evidence of sustained human-to-human spread (WHO Pandemic Alert Period, Phase 3)
Antigenic “shift” causes pandemics

Emergence of a new human influenza A virus subtype (new HA subtype) through:
  • Genetic reassortment (human and animal viruses)
  • Direct animal (poultry) to human transmission

A pandemic can occur if:
  • Efficient and sustained virus transmission occurs among humans (sustained person-to-person spread)

A pandemic can result in:
  • Widespread morbidity and mortality worldwide
  • High proportion of deaths among young adults
  ➢ Little or no immunity to the pandemic virus worldwide
Estimated Impact of Influenza Pandemics

1918-19 Spanish Flu (H1N1)
• 20-100 million estimated deaths worldwide
• >600,000 U.S. deaths
• Estimated mortality = 2%

1957-58 Asian Flu (H2N2)
• 70,000 excess U.S. deaths

1968-69 Hong Kong Flu (H3N2)
• 34,000 excess U.S. deaths
Why Worry About Avian Influenza Viruses?

1918-19 Spanish Flu (H1N1)
- 20-100 million estimated deaths worldwide
  - Direct mutation from avian influenza A virus

1957-58 Asian Flu (H2N2)
- 70,000 excess U.S. deaths
  - Reassortment between human and low pathogenic avian influenza A virus genes (HA, NA, PB1)

1968-69 Hong Kong Flu (H3N2)
- 34,000 excess U.S. deaths
  - Reassortment between human and low pathogenic avian influenza A virus genes (HA, PB1)
Emergence of Influenza A Viruses in Humans

- H1N1 (Spanish Influenza) 1918
- H2N2 (Asian Influenza) 1957
- H3N2 (Hong Kong Influenza) 1968
- H1N1 (Russian Influenza) 1977

Influenza A reservoir

Ag drift

Ag shift

CDC
Pneumonia and Influenza Mortality by Age in Certain Years

Deaths per 100,000 Population

Age

1892-MA
1918-US Reg Area
1936-US
1957-US

CDC
U.S. Impact Estimates for the Next Influenza Pandemic

Deaths: 89-207,000
Hospitalizations: 314-733,000
Outpatient care: 18-42 m
Total infected: 43-100 m

Health related economic impact
Estimated: $71 to $166 billion

Pandemic Severity Index

Case Fatality Ratio

- >2.0% Category 5 >1,800,000
- 1.0 - <2.0% Category 4 900,000 - <1,800,000
- 0.5 - <1.0% Category 3 450,000 - <900,000
- 0.1% - <0.5% Category 2 90,000 - <450,000
- <0.1% Category 1 <90,000

Projected Number of Deaths
US Population, 2006

1918

1957, 1968

*Assumes 30% illness rate and unmitigated pandemic without interventions

CDC
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
<th>Category 4</th>
<th>Category 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case Fatality Ratio (percentage)</td>
<td>&lt;0.1</td>
<td>0.1 - &lt;0.5</td>
<td>0.5 - &lt;1.0</td>
<td>1.0 - &lt;2.0</td>
<td>≥ 2.0</td>
</tr>
<tr>
<td>Excess Death Rate (per 100,000)</td>
<td>&lt;30</td>
<td>30 - &lt;150</td>
<td>150 - &lt;300</td>
<td>300 - &lt;600</td>
<td>≥ 600</td>
</tr>
<tr>
<td>Illness Rate (percentage of the population)</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
<td>20 - 40</td>
</tr>
<tr>
<td>Potential Number of Deaths (based on 2006 U.S. population)</td>
<td>&lt;90,000</td>
<td>90,000-&lt;450,000</td>
<td>450,000-&lt;900,000</td>
<td>900,000-&lt;1.8 million</td>
<td>≥1.8 million</td>
</tr>
<tr>
<td>20th Century U.S. Experience</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1918 Pandemic</td>
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<tr>
<td>Seasonal Influenza (Illness rate 5-20%)</td>
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### Estimated U.S. Impact of the next Influenza Pandemic

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<thead>
<tr>
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<th>Moderate (1957-like)</th>
<th>Severe (1918-like)</th>
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<tbody>
<tr>
<td><strong>Illness</strong></td>
<td>90 million (30%)</td>
<td>90 million (30%)</td>
</tr>
<tr>
<td><strong>Outpatient medical care</strong></td>
<td>45 million (50%)</td>
<td>45 million (50%)</td>
</tr>
<tr>
<td><strong>Hospitalization</strong></td>
<td>865,000</td>
<td>9,900,000</td>
</tr>
<tr>
<td><strong>ICU care</strong></td>
<td>128,750</td>
<td>1,485,000</td>
</tr>
<tr>
<td><strong>Mechanical ventilation</strong></td>
<td>64,875</td>
<td>745,500</td>
</tr>
<tr>
<td><strong>Deaths</strong></td>
<td>209,000</td>
<td>1,903,000</td>
</tr>
</tbody>
</table>
Summary

- Annual seasonal influenza epidemics of variable severity result in an average of >200,000 hospitalizations and >36,000 deaths from complications of influenza in the U.S.
  - Hospitalization and death rates are highest in elderly and those with certain chronic medical conditions
- Rare influenza pandemics can cause high very high morbidity and mortality worldwide