Clinical Outcomes of Influenza Infection

- Asymptomatic
- Symptomatic
  - Respiratory syndrome - mild to severe
  - Involvement of major organs - brain, heart, etc.
  - Death
Factors Influencing the Response to Influenza

- Age
- Pre-existing immunity (some crossover)
- Smoking
- Concurrent other health conditions
- Immunosuppression
- Pregnancy
Virology of Influenza

Subtypes:
A - Causes outbreak
B - Causes outbreaks
C - Does not cause outbreaks
Immunogenic Components of the Influenza Virus

- Surface glycoproteins, 15 hemagglutinins (H₁-H₁₅), nine neuraminidases (N₁-N₉)
- H₁-H₃ and N₁N₂ established in humans
- Influenza characterized by combination of H and N glycoproteins
  - 1912 pandemic - H₁N₁
  - 2004 avian influenza - H₅N₁
- Antigenic mix determines severity of disease
- Human response specific to hemagglutinin and neuraminidase glycoproteins
Spread of H₅N₁ Avian Influenza

- South Korea
- Vietnam
- Japan
- Thailand
- Cambodia
- China & Laos
- Indonesia

December, 2003

January 2004

Feb
Figure 1. Natural hosts of influenza viruses

Figure 2. Origin of antigenic shift and pandemic influenza. The segmented nature of the influenza A genome, which has eight genes, facilitates reassortment; up to 256 gene combinations are possible during coinfection with human and non-human viruses. Antigenic shift can arise when genes encoding at least the haemagglutinin surface glycoprotein are introduced into people, by direct transmission of an avian virus from birds, as occurred with H5N1 virus, or after genetic reassortment in pigs, which support the growth of both avian and human viruses.
<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Signs and symptoms on admission*</th>
<th>Subsequent complications</th>
<th>Initial Investigative findings</th>
<th>Treatment and outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7</td>
<td>Fever, cough, sore throat for 6 days. Dyspnea on day 6; CXR† bilateral interstitial infiltrates.</td>
<td>Respiratory failure on day 10; cardiac failure, pneumothorax, ARDS§, gastrointestinal bleeding.</td>
<td>Leukocytes: 4,100/µL Lymphocytes: 1,440/µL Platelets: 304,000/µL AST*: 120, ALT**: 52</td>
<td>Osestimavir on days 18–22. Died on day 29.</td>
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<tr>
<td>Male</td>
<td>6</td>
<td>Fever, cough, rhinorrhea for 5 days. Dyspnea on day 6; CXR patchy infiltrates in right lower lobe.</td>
<td>Respiratory failure on day 8; hepatitis, ARDS.</td>
<td>Leukocytes: 1,200/µL Lymphocytes: 624/µL Platelets: 89,000/µL AST: 790, ALT: 150 Proteinuria: ≥3</td>
<td>Osestimavir on days 18–20. Died on day 20.</td>
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<tr>
<td>Male</td>
<td>6</td>
<td>Fever, cough, rhinorrhea, sore throat for 4 days. Dyspnea on day 5; CXR multifocal patchy infiltrates.</td>
<td>Respiratory failure on day 6; pneumothorax, ARDS.</td>
<td>Leukocytes: 2,200/µL Lymphocytes: 638/µL Platelets: 150,000/µL AST: 175, ALT: 43</td>
<td>Died on day 18.</td>
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<tr>
<td>Female</td>
<td>58</td>
<td>Fever, cough, sore throat, myalgia for 2 days. Dyspnea on day 2; CXR multifocal patchy infiltrates.</td>
<td>Respiratory failure on day 4; cardiac failure, renal failure, ARDS.</td>
<td>Leukocytes: 5,680/µL Lymphocytes: 454/µL Platelets: 185,000/µL BUN†: 39 mg/dL Creatinine: 2.3 mg/dL</td>
<td>Died on day 8.</td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
<td>Fever, cough, sore throat, myalgia for 4 days. Dyspnea on day 5; CXR multifocal patchy infiltrates.</td>
<td>Respiratory failure on day 5; cardiac failure, renal failure, ARDS.</td>
<td>Leukocytes: 2,900/µL Lymphocytes: 696/µL Platelets: 87,000/µL AST: 280, ALT: 50 BUN: 54 mg/dL Creatinine: 4.6 mg/dL</td>
<td>Osestimavir on days 5–8. Died on day 8.</td>
</tr>
</tbody>
</table>

* No patients had an underlying illness reported.
† Chest radiograph.
§ Acute respiratory distress syndrome.
* Aspartate aminotransferase.
§ Alanine aminotransferase.
†† Blood urea nitrogen.
Intervention Strategies

- Culling (killing of infected flocks)
- Innovative surveillance strategies
  - Identification and analysis of human to human clusters
  - Necessary for vaccine development (Science 304:968-9, 5/2004)
- Vaccination of bird handlers (vaccine being developed)