Influenza Structure: The Basics

- Different kinds of influenza viruses infect humans and animals; they are divided into types A and B:
  - **Type A**- moderate to severe illness, all age groups in humans, **AND** other animals  
  - **Type B**- milder illness, humans only, primarily affects children

- **Influenza A viruses infect a variety of species besides humans:**
  - Pigs, poultry and birds, horses, marine mammals
  - The natural hosts of influenza A viruses are waterfowl (e.g., ducks)
    - Infected birds shed virus in their feces and respiratory secretions
Influenza A Structure

• Influenza A viruses can be subtyped into different strains, based on two types of surface markers:
  – Hemagglutinin (H) surface proteins
  – Neuraminidase (N) surface proteins

Antibodies to fight off influenza are actually antibodies to these surface proteins.
The Pandemic Influenza Cycle

- Recognized global outbreaks of influenza since the 1500’s
- Historical cycles of 10 to 40 years
- Rapid transmission with worldwide outbreaks of new strains of influenza Type A; multiple waves of disease over a 2 year period.
- Occurrence of cases outside the usual season.
- High attack rate for all age groups.
- High mortality rates, esp. for young adults.
- Last pandemic was in 1968-69, a mild one (35 years ago)
How do These New Strains of Influenza Type A Virus Develop? (Theories)

- Two influenza A viruses can combine in one host cell (either human, pig, or bird) and create a new “novel” virus that can be transmitted to humans.

- An influenza virus that previously only infected birds/animals changes, so that it can directly infect humans.

- Either of these situations can create a virus which no one alive on the planet has seen before, and therefore to which no one has immunity.
Mechanisms of Antigenic Shift

- **DIRECT - 1918**
  - Non-human virus
  - Human virus
- **1957, 1968**
  - Reassortant Virus – 1957, 1968
Global Status of Current Pandemic Threat

• World Health Organization (WHO) defines 3 major periods (broken into 6 phases) of increasing human infection with new flu virus:
  – Interpandemic (no human infection)
  – Pandemic Alert (limited human infection)
  – Pandemic (widespread human infection)

• We are at Pandemic Alert

• Isolated human infections with a novel influenza strain [H5N1] with no (or rare) person-to-person transmission.
Will H5N1 become the next pandemic?

- Impossible to know if or when it may become a pandemic
- H5N1 disease activity is unprecedented
  - Infections in other mammals and humans
  - Persistent outbreaks in Asian poultry
  - Birds are spreading H5N1 to new locations
- Risk to people exists as long as H5N1 influenza continues to infect birds with human contact
- If not H5N1 Influenza A, then another “novel” strain of Influenza A will come along at some point
- The prudent time to plan is now
HHS Assumptions: The Objectives of Pandemic Planning and Response

- **Primary objective**: Minimize sickness and death
- **Secondary objectives**: Preserve functional society, Minimize economic disruption

• There is not complete consensus on the proper order of these assumptions!
Assumptions about Disease Transmission (1)

- No one is immune to the virus; **30% of the population will become ill**
- Most will become ill 2 days (range 1-10) after exposure to the virus
- People may be contagious up to 24 hours before they know they are sick
- People are most contagious the first 2 days of they are sick
  - Sick children are more contagious than adults
- **On average, each ill person can infect 2 or 3 others (if no precautions are taken)**
Assumptions about Disease Transmission (2)

• Pandemics move through community in waves
• Each wave in a community will last 6-8 weeks
• There will be at least 2 “waves” of pandemic disease, likely separated by several months
• The entire pandemic period (all waves) will last about 18 months to 2 years
• Disease may break out in multiple locations simultaneously, or in isolated pockets
Hospital and Business Assumptions (during entire pandemic period):

- **Hospital demands**
  - Estimate $\geq 25\%$ more patients than normal needing hospitalization during the 6-8 weeks of a local pandemic wave

- **Absenteeism**
  - During a 6-8 week wave, at any one time, $\sim 40\%$ of employees may be absent because of illness, fear or to care for a family member

- **Death**
  - Overall mortality estimates: $0.2\%$ to $2\%$ of all clinically ill patients
Medical Burden in Tennessee (pop. 6 million) (HHS Plan Estimates)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate</th>
<th>Severe*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illness (30%)</td>
<td>1.8 million</td>
<td>1.8 million</td>
</tr>
<tr>
<td>Outpatient Care</td>
<td>900,000</td>
<td>900,000</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>17,300</td>
<td>198,000</td>
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<tr>
<td>ICU Care</td>
<td>2,575</td>
<td>29,700</td>
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<tr>
<td>Mechanical Ventilation</td>
<td>1,300</td>
<td>14,850</td>
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<tr>
<td>Deaths</td>
<td>4,180 (0.2%)</td>
<td>38,060 (2%)</td>
</tr>
</tbody>
</table>

*HHS recommends that states plan for severe scenario
Vaccine and Antivirals:

- **Pandemic influenza vaccine**
  - Currently: Research and limited production
  - Probably no one would have vaccine for the first 4 to 6 months of the pandemic
  - 2 doses needed for protection
  - HHS Priority groups

- **Antiviral drugs**
  - Limited production
  - Federal/State stockpiles
  - HHS Priority groups
Estimated Current US Annual Domestic Production of Pandemic Influenza Vaccine: Supply, Capacity, and Need

A: Current stockpile
B: Stockpile with current production
C: Current annual domestic capacity
   - Assumes all capacity dedicated to pandemic vaccine
   - Assumes NO annual influenza vaccine
D: National need

*2 doses/person

People vaccinated* (Millions)

- 0.17
- 1.8
- 14
- 300

*2 doses/person
HHS vaccine priority groups eligible over one year of production at current capacity*
(Populations are national estimates)

1a. Military (up to 1.5 million persons)

1. Vaccine manufacturers (~40,000 persons)

2. Healthcare workers with direct patient care (8-9 million persons)

3. Persons as highest risk for complications (~26 million persons)

*Current capacity = 14 million persons per year of production
**TAMIFLU**

- Anti-viral agent

- One of main ingredients is a chemical compound called shikimic acid

- Shikimic Acid is found in the seed pod of star anise, a fruit grown in only four provinces in China (used in cooking and herbal medicines)

- Might be used to limit the first human outbreak
HHS antiviral priority groups eligible with current national stockpile*

1a. Military (as needed)
1. Patients admitted to hospitals (est. 10 million)

* Current stockpile: 4.3 million courses
Resources will be limited…

• Part of the community response will be educational: we can’t depend on influenza vaccine and antiviral agents to deal with the problem.

• **Self protection** and **self help** will be much more important tools to use during the pandemic… more on this later.