

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.

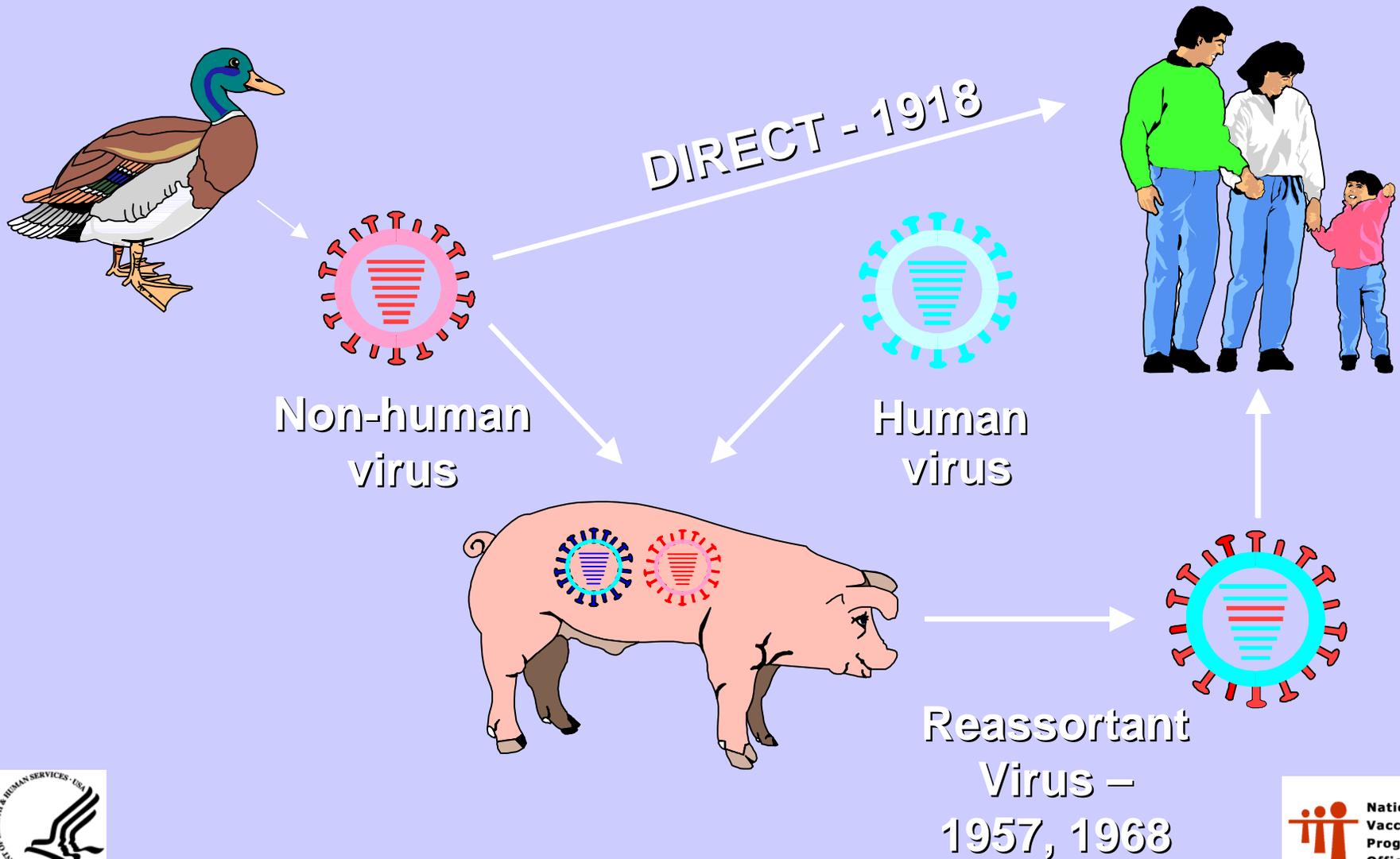
The Pandemic Influenza Cycle

- 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



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)

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

*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

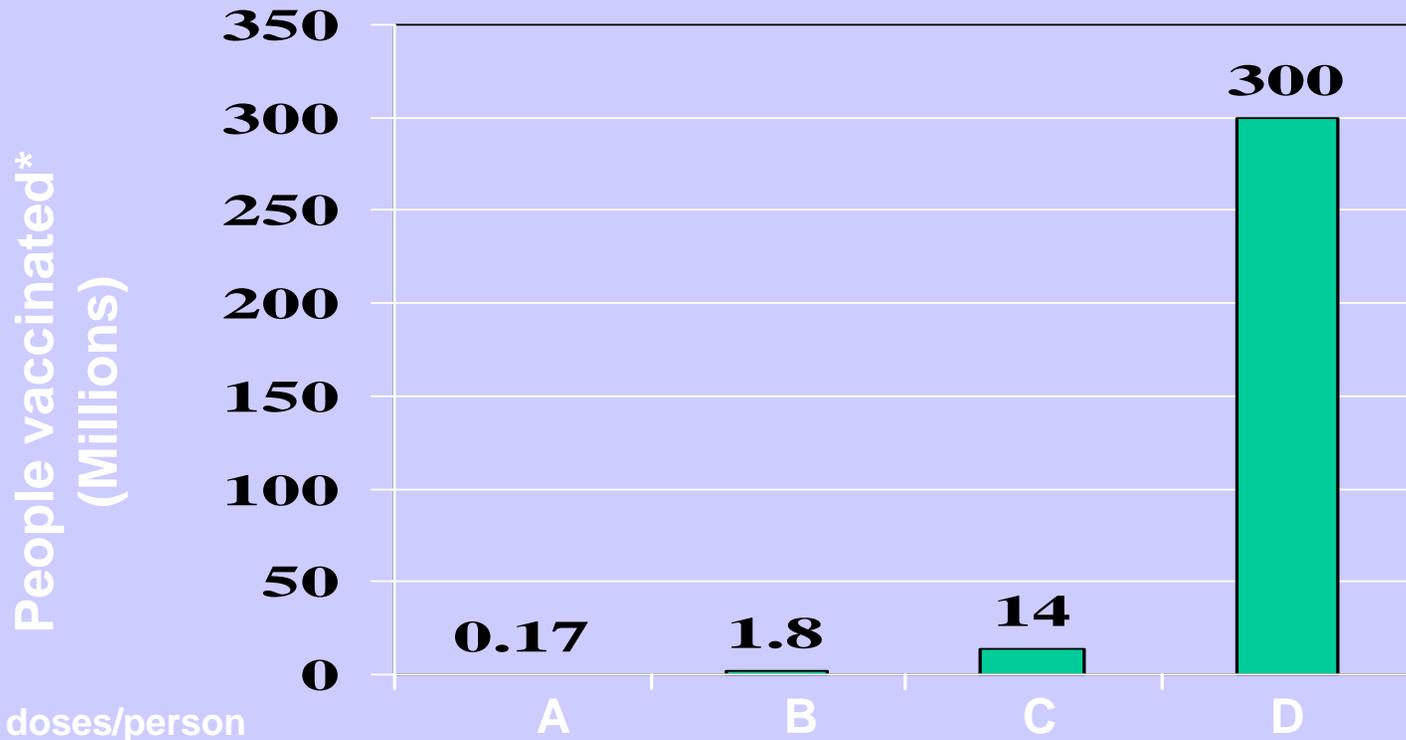


- Antiviral drugs

- 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

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 at 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.