SWINE FLU AND THE THREAT OF PANDEMIC DISEASE

Update on the Current Outbreak, Management Prevention, and Pandemic Preparedness

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INVALUABLE RESOURCES ON THE CURRENT OUTBREAK AND INFLUENZA PREPAREDNESS

- http://www.cdc.gov/swineflu/
- www.hhs.gov/nvpo/pandemics/dhhs.html
- http://www.cidrap.umn.edu/index.html
Preparation for Pandemic Swine Flu 2009

1. The pathophysiology of influenza. Why does it kill? Why was the 1918 H1N1 strain so virulent?

2. Status of the current A / H1N1 swine flu outbreak.

3. Management of suspected swine flu, precautions to protect oneself and minimize spread.

4. Pandemic preparedness -- at UWHC-UWMF, regionally and nationally.
Preparation for Pandemic Swine Flu 2009
Pathophysiology of Influenza. Why does it kill?
Pathophysiology of Influenza
INFLUENZA - THE DISEASE-I

- A **RESPIRATORY TRACT INFECTION**
  caused by Influenza A or B virus

- Ubiquitous human pathogen producing much *morbidity* and excess *mortality*:

  **Endemically:**
  
  10-30% attack rates / yr
  
  300,000 hospitalizations / yr U.S.
  
  20-40,000 deaths / yr (90% > 65 yo)

  **Next Pandemic:**
  
  50-75% Attack Rate
  
  300,000 - 750,000 deaths
  
  $160 billion in costs
Clinically Relevant Influenza Viruses

**Type A**
Potentially severe illness
*Rapidly changing*
**Epidemics and pandemics**

**Type B**
Usually less severe illness
Epidemics
More uniform

**Type C**
Usually mild or asymptomatic illness
Minimal public health impact

Centers for Disease Control and Prevention. Influenza Prevention and Control. Influenza.
Available at: http://www.cdc.gov/ncidod/diseases/flu/fluinfo.htm.
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  - **Next Pandemic:**
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    - 300,000 - 750,000 deaths
    - $160 billion in costs

- **DEATHS due to decompensation underlying disease and pneumonia**
Risk Factors for Influenza Complications

- Age ≥50 yrs
- Residence in nursing home/chronic care facilities
- Chronic pulmonary disease (eg, asthma, COPD)
- Chronic cardiovascular disease
- Chronic metabolic diseases, renal dysfunction, hemoglobinopathy
- Immunosuppression
- Long-term aspirin therapy (ages 6 mos-18 yrs)
- Second or third trimester pregnancy
Influenza Complications

- Pneumonia
  - secondary bacterial
  - primary influenza viral
- Reye syndrome
- Myocarditis
- Death 0.1 to 2.5 per 1,000 cases
Pneumonia and Influenza Mortality Rates by Age

Glezen WP. Epidemiol Rev. 1996;18:73, with permission.
Endotoxin activates macrophages, leading to the release of proteins, oxygen free radicals, and lipids.

- **Proteins:** Tumor necrosis factor, interleukin-1, interleukin-6, interleukin-8.
- **Oxygen Free Radicals:** Oxygen (O$_2^-$), hydrogen peroxide (H$_2$O$_2$), nitric oxide (NO).
- **Lipids:** Prostaglandin E$_2$, thromboxane A$_2$, platelet-activating factor.

When mediator levels are low, beneficial effects include moderate fever, generalized stimulation of the immune system, and microbial killing.

When mediators are overproduced, harmful effects include high fever, hypotension (low blood pressure), disseminated blood clotting, and lethal shock.
CYTOKINE RESPONSE

- Influenza infection is localized within the respiratory tract but the release of cytokines produces a systemic response\(^\text{10}\).
- Systemic symptoms induced by this cytokine response include myalgia, malaise, and fever\(^\text{10}\).

COMMUNITY-ACQUIRED PNEUMONIA
THE PROBLEM

- ~6 million cases/yr in the U.S.
- ~1 million hospitalized
- Mortality:
  - Outpatient-managed: 1-5%
  - Hospital-managed: 15-25%
  - ICU care needed: 35%
- Pneumonia 6th leading cause of death, #1 cause of death due to infection, $23 billion annual cost
- Of all common infections, pneumonia the most challenging to manage well
## LEADING CAUSES OF MORTALITY CAUSED BY INFECTIOUS DISEASES IN THE U.S. -- 1980 AND 1992

<table>
<thead>
<tr>
<th>Rank</th>
<th>Infectious Disease Group</th>
<th>1980</th>
<th>1992</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. of Deaths</td>
<td>Mortality per 100,000</td>
</tr>
<tr>
<td>1</td>
<td>Respiratory tract infections</td>
<td>56,966</td>
<td>25.1</td>
</tr>
<tr>
<td>2</td>
<td>Septicemia</td>
<td>9,438</td>
<td>4.2</td>
</tr>
<tr>
<td>3</td>
<td>Infections of kidney/urinary tract</td>
<td>8,006</td>
<td>3.5</td>
</tr>
<tr>
<td>4</td>
<td>Infections of the heart</td>
<td>2,486</td>
<td>1.1</td>
</tr>
<tr>
<td>5</td>
<td>Tuberculosis</td>
<td>2,333</td>
<td>1.0</td>
</tr>
<tr>
<td>6</td>
<td>Bacterial meningitis</td>
<td>1,402</td>
<td>0.6</td>
</tr>
<tr>
<td>7</td>
<td>Gastrointestinal tract infections</td>
<td>1,377</td>
<td>0.6</td>
</tr>
<tr>
<td>8</td>
<td>Hepatobiliary disease</td>
<td>1,227</td>
<td>0.5</td>
</tr>
<tr>
<td>9</td>
<td>Perinatal infections</td>
<td>1,035</td>
<td>0.5</td>
</tr>
<tr>
<td>10</td>
<td>Mycoses</td>
<td>680</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>Total infectious diseases</td>
<td>93,407</td>
<td>41.1</td>
</tr>
<tr>
<td></td>
<td>All deaths</td>
<td>1,989,841</td>
<td>878.0</td>
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## PNEUMONIA IN INFLUENZA: 1° INFLUENZA vs 2° BACTERIAL

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<td>CV Disease</td>
<td>Usual for bacterial pneumonia</td>
</tr>
<tr>
<td></td>
<td>Renal Disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic Pulmonary Disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pregnancy</td>
<td></td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Early (often &lt; 48 hrs)</td>
<td>Later (&gt;3-5 days)</td>
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<tr>
<td><strong>White blood count</strong></td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Chest x-ray</strong></td>
<td><em>Diffuse, interstitial-alveolar</em></td>
<td><em>Focal alveolar</em></td>
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<tr>
<td><strong>Sputum</strong></td>
<td></td>
<td></td>
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<tr>
<td>quantity</td>
<td>scant, pulmonary edema</td>
<td>thick, purulent</td>
</tr>
<tr>
<td>Gram-stain</td>
<td>few PMNs</td>
<td>many PMNs</td>
</tr>
<tr>
<td></td>
<td>no bacteria</td>
<td>many bacteria</td>
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Grady Memorial Hospital medical emergency clinic visits and pneumonia admissions related to pneumonia and influenza deaths in Atlanta during 1968-69 influenza epidemic.

# Pneumonia in Influenza: 1° Influenza vs 2° Bacterial

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Preparation for Pandemic Swine Flu 2009

General measures to control spread of influenza virus
PERSONAL MEASURES TO CONTROL SPREAD OF INFLUENZA

• Cover your nose and mouth with a tissue when you cough or sneeze—throw the tissue away after you use it.

• Try not to touch your eyes, nose, or mouth.

• Wash your hands often, especially after you cough or sneeze. If you are not near water, use an alcohol-based hand cleaner.

• If you get the flu, stay home from work or school.
Droplet Nuclei Transmission...
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INFLUENZA VACCINE

INDICATIONS:

1. **Age > 65 (AAFP > 50 yo) and children 2-9 years**
2. **Compromised of any age:**
   - Heart disease
   - Pulmonary disease (COPD, Asthma...)
   - Renal insufficiency
   - Diabetes
   - Chronic anemia
   - Immunocompromised, HIV infection
   - Cancer
3. Members of household with compromised
4. Pregnant women
5. All HCWs, employees institutions for DD
6. All adults encouraged to take vaccine

CONTRAINDICATION: Anaphylactic allergy to eggs
INFLUENZA VACCINE

DISEASE: Influenza A & B
Excessive mortality in aged, medically compromised, due to influenza or bacterial pneumonia other cardiorespiratory complications

VACCINE: Killed whole virus; purified subunit; "split" subvirion
Each contain 3 strains (2A, 1B), updated annually

EFFICACY: Approximately 60-80 % for homologous strains

SCHEDULE: Children: 0.5 mL IM x 2 doses, 1 mo apart
Adults: 0.5 mL (any) IM x 1 dose
Both: Annual boosters (Oct-Nov)

SIDE EFFECTS & COMPLICATIONS:
Local
SYSTEMIC
Common (20-30%)
Fever, myalgias (common)
Guillain-Barre syndrome (1:100,000), only with 1976 (Swine Flu) vaccine

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   - Renal insufficiency
   - Diabetes
   - Chronic anemia
   - Immunocompromised, HIV infection
   - Cancer
3. Members of household with compromised
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Influenza Immunization of Children

- Children 6-59 months at increased risk of hospitalization and physician visits
- Inactivated influenza immunization of healthy children 6-59 months is recommended
- Immunization of household contacts and other caregivers of children younger than 59 months is encouraged
Inactivated Influenza Vaccine Efficacy

- 70%-90% effective among healthy persons <65 years of age
- 30%-40% effective among frail elderly persons
- 50%-60% effective in preventing hospitalization
- 80% effective in preventing death
Hospitalizations for

Pneumonia and Influenza

<table>
<thead>
<tr>
<th>Year</th>
<th>Hospitalizations per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990-1991</td>
<td>2.5</td>
</tr>
<tr>
<td>1991-1992</td>
<td>5.8</td>
</tr>
<tr>
<td>1992-1993</td>
<td>11.2</td>
</tr>
</tbody>
</table>

P: 0.002, P < 0.001, P: 0.001

Hospitalizations for

All Respiratory Conditions

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>1990-1991</td>
<td>15.5</td>
</tr>
<tr>
<td>1992-1993</td>
<td>39.0</td>
</tr>
</tbody>
</table>

P: 0.002, P < 0.001, P: 0.01

### Influenza and Pneumococcal Vaccination Levels

Persons aged ≥65 years in U.S. who reported receiving influenza or pneumococcal vaccine, 2005

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Influenza</th>
<th></th>
<th></th>
<th>Pneumococcal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (95% CI*)</td>
<td>% point difference from 2000 objective</td>
<td>% (95% CI)</td>
<td>% point difference from 2000 objective</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>65.5 (64.6-66.4)</td>
<td>5.5</td>
<td>45.4 (44.4-46.3)</td>
<td>-14.6</td>
<td></td>
</tr>
<tr>
<td>Age group (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>63.2 (62.0-64.3)</td>
<td>3.2</td>
<td>41.7 (40.4-42.9)</td>
<td>-18.3</td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>69.1 (67.8-70.5)</td>
<td>9.1</td>
<td>51.3 (49.8-52.8)</td>
<td>-8.7</td>
<td></td>
</tr>
</tbody>
</table>
PRE-MODERN: Most flu vaccines today are cultured in chicken eggs.
THE GREAT INFLUENZA VACCINE SHORTAGE OF 2004-5

- We had planned to give ~110 million doses this year
- ~50 million doses made by Chiron Corp in UK was found to be contaminated
- We have ~56 million doses from Aventis-Pasteur, 1.1 million IAIV/FluMist, 5 million from foreign manufacturers
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• We have ~56 million doses from Aventis-Pasteur, 1.1 million IAIIV/FluMist, 5 million from foreign manufacturers
• Priority System for allocation of remaining vaccine

• WE NEED A BETTER SYSTEM
Preparation for Pandemic Swine Flu 2009

Treatment of influenza
DRUGS FOR PROPHYLAXIS AND TREATMENT OF INFLUENZA A

M2 Channel Inhibitors:

*Amantadine* (Symmetrel®)
*Rimantadine* (Flumadine®)

- Effective *only* against Influenza A, not B
- Treatment: 100 mg po bid x 5-7 d
  >65 yo, 100 mg qd; CRF, adjust dose
- Prophylaxis: 100 mg d x 2-6 wks
- CNS side effects:
  - confusion, agitation, falls, seizures
- Efficacy for culture + influenza A:
  - Treatment: Shorten illness 1-2 d
    High risk, 50% ↓ hospitalization
    >50% resistant mutants...
  - Prophylaxis: 70-80% protective
  - Cost (x 7 d):
    - Amantadine, $10
    - Rimantadine, $25
Influenza Surface Proteins

- Neuraminidase
- Hemagglutinin
- RNA
- M₂ protein (only on type A)
DRUGS FOR PROPHYLAXIS AND TREATMENT OF INFLUENZA A

Neuraminidase Inhibitors:

**Zanamavir (Relenza®)**

**Oseltamavir (Tamiflu®)**

- Effective against *both* Influenza A *and* B
- Treatment: Zanamavir, 10 mg inhaled bid x 5 d  
  Oseltamavir, 75 mg po bid x 5 d
- Prophylaxis: each qd x 2-6 wks
- Side effects:
  Zanamavir: bronchospasm if COPD or Asthma (*caution*)
  Oseltamavir: nausea/vomiting 5-10% (give with food)
- Efficacy for culture + influenza:
  Treatment: Both shorten illness 1-2.5 d
  Reduce complications 25%
  Prophylaxis: 80-85% protective
- Cost: $40 - $50
PARTS OF THE DISKHALER

- COVER
- WHITE MOUTHPIECE
- DARK BROWN WHEEL
- NEEDLE
- DISKHALER BODY
- HALF-CIRCLE FLAP
- SILVER MEDICINE DISK
LOGICAL TREATMENT MODALITY
diskhaler delivery system

Patients should be instructed in the use of the diskhaler, including a demonstration whenever possible.
DRUGS FOR PROPHYLAXIS AND TREATMENT OF INFLUENZA A

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- **Oseltamivir (Tamiflu®)**

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Preparation for Pandemic Swine Flu 2009
Lessons from history:
The Asian H5N1 outbreak and the Great Influenza Pandemic of 1918
INFLUENZA
FREQUENTLY COMPLICATED WITH
PNEUMONIA
IS PREVALENT AT THIS TIME THROUGHOUT AMERICA.
THIS THEATRE IS CO-OPERATING WITH THE DEPARTMENT OF HEALTH.
YOU MUST DO THE SAME
IF YOU HAVE A COLD AND ARE COUGHING AND
SNEEZING DO NOT ENTER THIS THEATRE.
GO HOME AND GO TO BED UNTIL YOU ARE WELL.

Coughing, Sneezing or Spitting Will Not Be
Permitted In This Theatre. In case you
come rough of nerves, go with your own hand
kerchief, and if the Coughing or Sneezing
Permits Leave The Theatre At Once.

This Theatre has agreed to cooperate with
the Department Of Health in disseminating
the truth about Influenza, and thus serve
a great educational purpose.

HELP US TO KEEP CHICAGO THE
HEALTHIEST CITY IN THE WORLD

JOHN DILL ROBERTSON
COMMISSIONER OF HEALTH
FLU

The Story of the Great Influenza Pandemic of 1918 and the Search for the Virus That Caused It

GINA KOLATA

“A chilling read...packed with new information and astonishments.” —R. Z. Sheppard, Time magazine
Free Press newboys don protective masks during the 1918 influenza epidemic, which killed 824 people in Winnipeg.
What can we learn from the Great 1918 Pandemic?
INFLUENZA MORTALITY BY AGE IN CERTAIN EPIDEMIC YEARS

THE THREAT OF GLOBAL PANDEMIC INFLUENZA A H5N1
Bird flu strikes Asia

China to probe massive duck cull, Tuesday

Countries with virus
- Red: infecting people and chickens
- Green: infecting chickens

Human cases, including deaths

* Suspected
FEATURES OF ASIAN H5N1 INFLUENZA

Children and young adults >> older adults
Risk factors: close contact with birds or infected humans

Fever, cough, sore throat 100%
Diarrhea >50%
Encephalopathy 10-20%
Shock

Hypoxemia
Pancytopenia
DIC
MODS

Mortality 58%
http://who.int
AVIAN H5N1 FLU OUTBREAK 2003-09

Countries reporting human H5N1 infection:
Cambodia, China, Laos, South Korea, Thailand, Vietnam, China, Azerbaijan, Turkey, Egypt, Indonesia, Iraq, Nigeria, Djibouti, Bangladesh, Pakistan....

Human H5N1 infections (as of April 23, 2009):
Laboratory-confirmed cases 427
Deaths 257 (58%)
Median age of victims 13 years (range 4-58 years)

Probable Person-to-Person Transmission of Avian Influenza A (H5N1)


ABSTRACT

BACKGROUND
During 2004, a highly pathogenic avian influenza A (H5N1) virus caused poultry disease in eight Asian countries and infected at least 44 persons, killing 32; most of these persons had had close contact with poultry. No evidence of efficient person-to-person transmission has yet been reported. We investigated possible person-to-person transmission in a family cluster of the disease in Thailand.

METHODS
For each of the three involved patients, we reviewed the circumstances and timing of exposure to poultry and evidence of illness. We also conducted interviews to determine any potential transmission between individuals.
Preparation for Pandemic Swine Flu 2009

Why was the 1918 H1N1 strain so virulent?
Why was the 1918 H1N1 strain and why is the current Avian H5N1 strain so virulent?

Approximate overall mortalities:

1968 Hong Kong H3N2  ~ 0.1%
1957 Asian H2N2      ~ 0.3%
1918 Spanish H1N1    ~ 2.5%
2003-7 Asian H5N1    ~ 59%
Yoshihiro Kawaoka
UW Professor of Virology
RECONSTRUCTION OF THE 1918 H1N1 STRAIN IN VITRO AND ITS GENOMIC AND BIOLOGIC CHARACTERIZATION

WHY WAS 1918 H1N1 AND WHY IS 2003-5 H5N1 SO VIRULENT?

Molecular Mechanisms of Virulence

Infect lung cells efficiently

WHY WAS 1918 H1N1 AND WHY IS 2003-5 H5N1 SO VIRULENT?

Molecular Mechanisms of Virulence

Infect lung cells efficiently

Infect efficiently in absence of trypsin (an endogenous protease)

- Brown et al. PNAS (2005)
WHY WAS 1918 H1N1 AND WHY IS 2003-5 H5N1 SO VIRULENT?

**Molecular Mechanisms of Virulence**

- Infect lung cells efficiently
- Infect efficiently in absence of trypsin (an endogenous protease)

**Incite extraordinary cytokine response**

WHY WAS 1918 H1N1 AND WHY IS 2003-5 H5N1 SO VIRULENT?

Molecular Mechanisms of Virulence

- Infect lung cells efficiently
- Infect efficiently in absence of trypsin (an endogenous protease)
- Incite extraordinary cytokine response

Virulence factors appear linked to H1 or H5 hemagglutinin genes

- Brown et al. PNAS (2005)
Preparation for
Pandemic Swine Flu
2009

Pandemic preparedness --
regionally and nationally
[It is] an ill wind that bloweth no man to good.

John Haywood (1546)
A "FEW" LETTERS

- Someone sent approximately 6-10 letters laced with weaponized anthrax spores through the U.S. mails from NJ to Florida, NYC and Washington DC.
- **22 cases of anthrax, 11 cutaneous and 11 inhalation disseminated, 5 deaths**
- >10,000 exposed given 60+ days ciprofloxacin prophylaxis, none developed infection
- U.S. government spent >$1-2 billion in reactive response
CDC’s Emerging Infectious Disease Threats Plan and Its Terrorism Preparedness and Response Strategy

- Addressing New Emerging Infectious Disease Threats
  - Surveillance and response--detect, promptly investigate, and monitor emerging pathogens, the diseases they cause, and the factors influencing their emergence
  - Applied research--integrate laboratory science and epidemiology to optimize public health practice
  - Prevention and control--enhance communication of public health information about emerging diseases and ensure prompt implementation of prevention strategies
  - Infrastructure--strengthen local, state, and federal public health infrastructures to support surveillance and implement prevention and control programs

- Terrorism Preparedness and Response Strategy
  - Timely, effective and integrated detection and investigation
  - Sustained prevention and consequence management programs
  - Coordinated public health emergency preparedness and response
  - Qualified, equipped and integrated laboratories
  - Competent and sustainable workforce
  - Protected workers and workplaces
  - Innovative, relevant and applied research and evaluation
  - Timely, accurate and coordinated communications
  - Achieving Shared Goals Through Partnerships
  - Integrated and secure information systems
  - Creative and effective management services
Stages of Federal Government Response

**STAGE 0**
- New Domestic Animal Outbreak in At-Risk Country

**GOALS**
- Provide coordination, support, technical guidance
- Track outbreaks to resolution
- Monitor for recurrence of disease

**ACTIONS**
- Support coordinated international response
- Prepare to deploy rapid response team and materiel
- Offer technical assistance, encourage information sharing

**POLICY DECISIONS**
- Deployment of countermeasures

**WHO Phase 1 or 2**
- Inter-Pandemic Period

**STAGE 1**
- Suspected Human Outbreak Overseas

**GOALS**
- Rapidly investigate and confirm or refute
- Coordination and logistical support

**ACTIONS**
- Initiate dialogue with WHO
- Deploy rapid response team
- Amplify lab-based and clinical surveillance to region
- Prepare to implement screening and/or travel restrictions from affected area

**POLICY DECISIONS**
- Pre-positioning of U.S. contribution to international stockpile assets
- Use of pre-pandemic vaccine

**STAGE 2**
- Confirmed Human Outbreak Overseas

**GOALS**
- Contain outbreak and limit potential for spread
- Activate domestic medical response

**ACTIONS**
- Declare Incident of National Significance
- Support international deployment of countermeasures
- Implement layered screening measures; activate domestic quarantine stations
- Prepare to limit domestic ports of entry
- Prepare to produce monovalent vaccine

**POLICY DECISIONS**
- Contribution to countermeasures for affected region
- Entry/exit screening criteria; isolation/quarantine protocols
- Diversion of trivalent vaccine production to monovalent
- Revise prioritization and allocation of pandemic vaccine and antiviral medications

**WHO Phase 3**
- Pandemic Alert Period

**WHO Phase 4 or 5**
- Pandemic Alert Period
STAGE 3
Widespread Outbreaks Overseas

GOALS
Delay emergence in North America
Ensure earliest warning of first case(s)
Prepare domestic containment and response mechanisms

ACTIONS
Activate domestic emergency medical personnel plans
Maintain layered screening measures at borders
Deploy pre-pandemic vaccine and antiviral stockpiles; divert to monovalent vaccine production
Real-time modeling; heighten hospital-based surveillance
Prepare to implement surge plans at Federal medical facilities

POLICY DECISIONS
Prioritize efforts for domestic preparedness and response

STAGE 4
First Human Case in North America

GOALS
Contain first cases in North America
Antiviral treatment and prophylaxis
Implement national response

ACTIONS
Ensure pandemic plans activated across all levels
Limit non-essential domestic travel
Deploy diagnostic reagents for pandemic virus to all laboratories
Continue development of pandemic vaccine
Antiviral treatment and targeted antiviral prophylaxis

POLICY DECISIONS
Revision of prioritization and allocation scheme for pandemic vaccine

STAGE 5
Spread throughout United States

GOALS
Support community response
Preserve critical infrastructure
Mitigate illness, suffering, and death
Mitigate impact to economy and society

ACTIONS
Maintain overall situational awareness
Evaluate epidemiology; provide guidance on community measures
Deploy vaccine if available; prioritization guidance
Sustain critical infrastructure, support health and medical systems, maintain civil order
Provide guidance on use of key commodities

POLICY DECISIONS
Federal support of critical infrastructure and availability of key goods and services
Lifting of travel restrictions

WHO Phase 6
Pandemic Period
# PANDEMIC INFLUENZA

## WHO Global Pandemic Phases and the Stages for Federal Government Response

<table>
<thead>
<tr>
<th>WHO Phases</th>
<th>Federal Government Response Stages</th>
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</thead>
<tbody>
<tr>
<td><strong>INTER-PANDEMIC PERIOD</strong></td>
<td></td>
</tr>
<tr>
<td>1. No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human disease is considered to be low.</td>
<td>0. New domestic animal outbreak in at-risk country</td>
</tr>
<tr>
<td>2. No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.</td>
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<tr>
<td><strong>PANDEMIC ALERT PERIOD</strong></td>
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<tr>
<td>3. Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.</td>
<td>0. New domestic animal outbreak in at-risk country</td>
</tr>
<tr>
<td>4. Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.</td>
<td>1. Suspected human outbreak overseas</td>
</tr>
<tr>
<td>5. Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).</td>
<td>2. Confirmed human outbreak overseas</td>
</tr>
<tr>
<td><strong>PANDEMIC PERIOD</strong></td>
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<tr>
<td>6. Pandemic phase: increased and sustained transmission in general population.</td>
<td>3. Widespread human outbreaks in multiple locations overseas</td>
</tr>
<tr>
<td></td>
<td>4. First human case in North America</td>
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<tr>
<td></td>
<td>5. Spread throughout United States</td>
</tr>
<tr>
<td></td>
<td>6. Recovery and preparation for subsequent waves</td>
</tr>
</tbody>
</table>
U.S. GOVERNMENT (DHHS) PREPARATIONS FOR PANDEMIC INFLUENZA

- Surveillance
- Vaccine Development
- Antivirals
- Research
- Preparedness Activities

www.hhs.gov/nvpo/pandemics/dhhs.html
Preparation for Pandemic Swine Flu 2009

The current A/H1N1 Swine Flu Outbreak
EVOLUTION OF A PANDEMIC?

<table>
<thead>
<tr>
<th>April</th>
<th>Rest of World</th>
<th>U.S.A</th>
<th>Mexico</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>&gt;1000</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>22</td>
<td>&gt;1000</td>
<td>2</td>
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<td>23</td>
<td>&gt;1000</td>
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<td>15</td>
<td>64</td>
<td>28</td>
</tr>
<tr>
<td>29</td>
<td>xx</td>
<td>91</td>
<td>xx</td>
</tr>
</tbody>
</table>
What is known to the present?

- As of April 29, there have been \( \sim 2100 \) cases of influenza-like illness in Mexico, with \( >150 \) putatively related deaths, 22 confirmed as swine influenza. Disease has been reported from 19 states throughout Mexico.

- These figures suggest a mortality much higher than the 1918 H1N1 strain (\( \sim 2.5\% \)). The influenza A strains of the past 50 years have had a case-fatality \( \sim 0.1\% \).
What is known to the present?

- There have been **91 confirmed U.S. cases**, 51 in New York, 16 in Texas, 14 in California, 2 each in Kansas, Massachusetts and Michigan, and 1 each in Indiana, Nevada and Ohio.

- **Thus far, disease in U.S. patients has been inexplicably mild**, with only 1 death to date. Most of these individuals had recently been in Mexico or had contact with an individual recently in Mexico.
What is known to the present?

- There have been 6 cases in Canada, 3 in New Zealand, and 2 each in the UK, Spain, and Israel.
- All of these individuals had recently been in Mexico.
What is known to the present?

- The strain is resistant to amantadine and rimantadine but susceptible to oseltamivir (Tamiflu) and zanamavir (Relenza).

- It is not yet known whether individuals who had the current 2008-9 U.S. H3N2-H1N1 influenza vaccine have any immunity against this strain, however, limited testing at CDC has reportedly shown very little cross-reactive activity of vaccine antibody against the new swine flu strain.
What is known to the present?

- The U.S. government has not yet decided whether to undertake to manufacture a vaccine against this strain in time for the Fall 2009-10 influenza season.
Management of suspected swine flu, precautions to protect oneself and minimize spread.
Precautions to Prevent Spread of Swine Influenza A (H1N1)

- Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it.
- Wash your hands with soap and water, especially after you cough or sneeze. Alcohol-based hands cleaners are also effective.
- Try to avoid close contact with sick people.
- If you get sick, stay home from work or school and limit contact with others to keep from infecting them.
- Avoid touching your eyes, nose or mouth.
CDC Definitions of Respiratory Illness

- **Acute respiratory illness:**
  - Recent onset of at least two of the following:
    - rhinorrhea or nasal congestion
    - sore throat
    - cough
    - fever or feverishness

- **Influenza-like illness:**
  - Fever >37.8°C (100°F) + cough or sore throat
Infectious Period of Swine Influenza A (H1N1)

= 1 day before to 7 days after onset of illness

Day before onset = Day -1
Onset day = Day 0
Days after onset = Days 1-7
Case Definitions for Infection with Swine Influenza A (H1N1) Virus

- A **Confirmed case** of swine influenza A (H1N1) virus infection is defined as a person with an acute respiratory illness with laboratory-confirmed swine influenza A (H1N1) virus infection at CDC by one or more of the following tests:
  - Real-time RT-PCR
  - Viral culture
Case Definitions for Infection with Swine Influenza A (H1N1) Virus

- A **Probable case** of swine influenza A (H1N1) virus infection is defined as a person with an acute respiratory illness with:
  - An influenza test that is positive for influenza A, but H1 and H3 negative, by RT-PCR.
  - Positive for influenza A by an influenza rapid DFA plus meets criteria for a suspected case.
Case Definitions for Infection with Swine Influenza A (H1N1) Virus

- A **Suspected case** of swine influenza A (H1N1) is defined as a person with an acute respiratory illness with onset:
  - Within 7 days of a close contact to a confirmed case of symptomatic swine influenza A (H1N1)
  - OR
  - Within 7 days of travel to a community either within the United States or internationally where there are one or more confirmed swine influenza A(H1N1) cases,
  - OR
  - Resides in a community where there are one or more confirmed swine influenza cases.
Clinicians evaluating patients with respiratory illness-1:

- Should consider the possibility of swine influenza in patients presenting with febrile respiratory illness who:
  - Live in an area where human cases of swine influenza A (H1N1) have been identified.
  - Have traveled to an area where human cases of swine influenza A (H1N1) have been identified within 7 days of the onset of their illness.
  - Have been in contact with ill persons from these areas in the 7 days prior to their illness onset.
Clinicians evaluating patients with respiratory illness-2:

- If swine flu is suspected, clinicians should obtain a nasopharyngeal swab for swine influenza testing to be sent to the UWHC microbiology laboratory.

- The specimen will undergo rapid DFA testing and viral culture at the UWHC Lab and will be immediately forwarded to the Wisconsin State Laboratory of Hygiene and CDC for PCR.
Treatment of Suspected, Probable or Confirmed Swine Flu

- Empiric antiviral treatment is recommended for any ill person suspected to have swine influenza A (H1N1) virus infection: either zanamivir alone or a combination of oseltamivir and amantadine or rimantadine should be initiated ASAP and continued for 5 days.

- For confirmed swine influenza A (H1N1), oseltamivir or zanamivir for 5 days.
Prophylaxis for Swine Flu

- Antiviral chemoprophylaxis (pre-exposure or post-exposure) with either oseltamivir or zanamivir is recommended for the following individuals:
  - Household contacts of a confirmed or suspected case, who are at high-risk for complications of influenza.
  - School children at high-risk for complications who had close contact (face-to-face) with a confirmed or suspected case.
  - Travelers to Mexico at high-risk for complications of influenza.
  - Border workers (Mexico) at high-risk for complications of influenza.
  - Health care workers or public health workers who had unprotected close contact with an ill confirmed active case of swine influenza A (H1N1)

Antiviral chemoprophylaxis can be considered for:
- Any health care worker at high-risk for complications of influenza working in an area with confirmed swine influenza A (H1N1) cases.
- Non-high risk persons who are travelers to Mexico, first responders, or border workers working in areas with confirmed cases of swine influenza A (H1N1).

- Duration of antiviral chemoprophylaxis is 7 days after the last known exposure to an ill confirmed case of swine influenza A (H1N1).
Infection Control for Inpatient Settings-1

• All confirmed, probable and suspected cases should be managed with standard, contact, and droplet precautions.

• Precautions should be observed until 7 days after illness onset or until symptoms resolve, whichever is longer.
Infection Control for Inpatient Settings-2

- No modification of standard precautions are necessary when caring for patients with confirmed or suspected swine influenza.
- Practice routine infectious waste management, environmental cleaning/disinfection, and handling of laundry and linens.
- Alcohol-based hand sanitizers may be used to decontaminate hands.
- Used dietary items such as cups, utensils and dishes may be routinely sanitized.
- Environmental cleaning/disinfection may be done using any of the current EPA-registered hospital-approved disinfectants.
Infection Control for Inpatient Settings-3

- Hand hygiene and cough etiquette should be emphasized and enforced among healthcare workers, patients and their family members and all visitors to UWHC.

- Persons with signs and symptoms of acute respiratory illnesses should be asked to wear surgical masks upon entry to UWHC and taken to private rooms or areas ASAP after arrival.
Infection Control for Inpatient Settings-4

- Place infected patients in private rooms and allow them to leave room only when medically necessary. If available, a negative-pressure room is preferred.

- All healthcare personnel should wear gloves and gowns each time they enter the room. Remove gloves and gowns prior to leaving the isolation room and decontaminate hands immediately afterwards.

- Medical equipment and patient care items must be disposed of or disinfected before removing.
Infection Control for Inpatient Settings-5

- Personnel providing direct patient care for suspected or confirmed swine influenza A cases should wear a **fit-tested disposable N95 respirator** when entering the room.

- An N95 respirator **may be reused** by the same person as long as it is intact and dry. If there is moisture or breakage it should be discarded.

- **Goggles or face shields** should be worn during all patient care activities and collection of clinical specimens.
Infection Control for Inpatient Settings-5

- Personnel providing direct patient care for suspected or confirmed swine influenza A cases should wear a fit-tested disposable N95 respirator when entering the room.

- An N95 respirator may be reused by the same person as long as it is intact and dry. If there is moisture or breakage it should be discarded.

- Goggles or face shields should be worn during all patient care activities and collection of clinical specimens.
Tecnol face shield
Infection Control for Inpatient Settings-6

- Visitors of patients with confirmed, probable or suspected swine influenza A infection should be limited to one or two designated family members or contacts. Visitors should be instructed on good hand hygiene and should wear gowns, gloves, eye protection and either surgical masks or N-95 masks when entering isolation rooms. Fit testing for visitors is not necessary.
Strongly Recommend Home Isolation of Active Swine Influenza-1

- Persons who develop influenza-like-illness should self-isolate in their home for 7 days after the onset of illness or until 24 hours after symptoms have resolved, whichever is longer.
- Persons with influenza-like-illness seeking medical care should contact their HCP by telephone before coming to a clinic, office or hospital.
- Persons who have difficulty breathing or shortness of breath or appear to be severely ill should seek immediate medical attention.
Strongly Recommend Home Isolation of Active Swine Influenza-2

- If ill persons must go into the community they should wear a face mask or, if unavailable, they should use a handkerchief or tissues to cover any coughing.

- Persons in home isolation and their household members should be given infection control instructions, including hand washing with soap and water or alcohol-based hand gels.

- When the ill person is within 6 feet of others at home, the ill person should wear a face mask if one is available.
Strongly Recommend Home Isolation of Active Swine Influenza-3

- Avoid close contact (< 6 feet away) with the sick person AMAP.
- If you must have close contact with the sick person, minimize the contact AMAP and wear a facemask (surgical mask or N95 respirator).
- Wear an N95 respirator if you help a sick person with respiratory treatments.
- Used facemasks and N95 respirators should be placed in the trash.
- Avoid re-using disposable facemasks and N95 respirators, if possible. After you take off a facemask or respirator, clean your hands.
Preparation for Pandemic Swine Flu 2009

Pandemic preparedness -- at UWHC-UWMF
UWHC PREPARATIONS-1

• All ED personnel, primary care providers and infectious disease consultants will be in-serviced and fully apprised of CDC recommendations for the management of patients with possible swine influenza or who have been potentially exposed to infection.

• The UWHC Biologic Event Plan (12.20, September 15, 2006) should be reviewed by all hospital and clinic personnel.
UWHC PREPARATIONS-2

- We are reviewing our current inventory of masks, particularly N95 respirators, and other protective apparel and will procure additional stocks.

- We have preexistent plans in place to secure additional ventilators if necessary.

- Restrictions on oseltamivir (Tamiflu) prescribing by UWMF healthcare providers.

- All hospital departments will have plans in place to be able to deal with the large numbers of ill staff to assure adequate numbers of well-trained staff are available to care for critically ill patients with swine flu.
UWHC PREPARATIONS-3

- Patients who are not critically ill and are not at high risk of complications will not be hospitalized but will be treated and followed in the outpatient setting.

- Frail elderly or compromised patients and critically ill patients will be admitted to the dedicated F6/5 Emerging Infections Unit.
UWHC PREPARATIONS-4

• The Hospital will shortly undertake a 4th tabletop practice exercise.

• An ongoing liaison with the Madison/Dane County Department of Health, Wisconsin Division of Health and the other State agencies responsible for emergency preparedness is in place.

• The hospital will be prepared to provide a hotline for staff and the lay public.
Are we adequately prepared?

- UWHC-UWMF have had comprehensive plans in place to deal with biologic disaster, either bioterrorism or pandemic emerging infectious disease, for a number of years.

- We have had hospital-wide practice exercises to try to improve our efficiency with emergency implementation of the plan, if needed.
Are we adequately prepared?

- Institutional preparations have included retrofitting a 36-room patient care unit to be convertible within hours into a dedicated negative-pressure, self-contained Emerging ID Isolation Unit for the care of exposed or critically ill infected and highly contagious patients, a unit which has built-in capacity for full critical care support, including up to eight mechanically ventilated patients.
Are we adequately prepared?

- We have more than 20 board-certified critical care staff physicians and 12 infectious disease staff consultants available to provide 24/7 patient care and leadership of the institutional efforts to deal with a global pandemic.

- We have the most qualified and most experienced Infection Control Department we have ever had – it is world-class.
Are we adequately prepared?

- No healthcare system can prepare in isolation for biologic disaster or, especially, pandemic disease that might last for many months or even years. **Our planning has been carried out in conjunction with the preparations of the other Madison hospitals, the Madison/Dane County Department of Public Health, and the Wisconsin Division of Health**, and throughout its implementation, **the Centers for Disease Control and the Department of Health and Human Services.**
Are we adequately prepared?

Finally, the Asian and Canadian SARS epidemic of 2006 showed that while preexistent planning is extremely important, implementation of such plans is always a work in progress, and it is essential to have the capacity to quickly adapt, to revise and change, as the circumstances dictate.
Are we adequately prepared nationally?

- The U.S. government has *not* yet decided whether to undertake to manufacture a vaccine against this strain in time for the Fall 2009-10 influenza season.
The 1976 Swine Flu Vaccine “Debacle”

- In early 1976 an H1N1 swine-like Influenza A virus strain was implicated in an outbreak on a military base in NJ, causing illness in 13 young soldiers, 2 died; 217 also become infected but had no illness.
- The linkage of this new 1918-like strain in fatal disease in young adults prompted the U.S. government to rush to produce a new vaccine against the strain, “the swine flu vaccine,” which was given to more than 40 million Americans that fall, in anticipation of a global 1918-like pandemic.
- However, no further infections with that strain were identified during the 1976-77 influenza season.
- But the vaccine was linked to a ~1:100,000 risk of Guillain-Barre syndrome.
- The Director of the CDC lost his job.
What can we learn from the Great 1918 Pandemic?
If massive pandemic swine flu occurs, the world and our country will be sorely tested, and we will be greatly tested as healthcare professionals... ...but I believe we are up to the challenge