Influenza A H1N1: The Forgotten Pandemic

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“Setting the Stage”

Goals:
- A broad appreciation of the medical, biological, epidemiological and public health challenges in managing influenza pandemics
- Setting the stage for a more detailed discussion of the Government (Federal, State and Local) role(s) in pandemic emergency preparedness and response

ROE:
- Collegial exchange, questions anytime

Acknowledgements:
- Rashid A. Chotani, MD, MPH, DTM; USUHS
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- David Siegrist, PhD; Lynn Cooper, PhD; MITRE
Overview

The Agent “Novel H1N1”
- Influenza Virus
- Host Interaction

The Disease ”The Flu”

Pandemics
- Historical Framework
- Situation (Then & Now)
  -- US, Global

Management Guidelines
- Federal, State & Local
- Individual & Community
- Risk Communication

Preparedness & Response
- Conclusion & Recommendations
Background Definitions: Round #1

- **Antigenic drift**
  - Changes in proteins by genetic point mutation & selection
  - Ongoing and basis for change in vaccine each year

- **Antigenic shift**
  - Changes in proteins through genetic reassortment
  - Produces different viruses not covered by annual vaccine

- **Isolation**
  - Separation of ill persons with contagious diseases
  - Often in a hospital setting, could be at home

- **Quarantine**
  - Restriction of persons who are not ill but presumed exposed, usually in the home or a designated facility

- **Social Distancing**
  - “social measures to decrease the frequency of contact among people in order to diminish the risk of spread from communicable diseases”

- **Epidemic** – a located cluster of cases

- **Pandemic** – worldwide epidemic
The Agent: Influenza A
Characteristics

- Obligate intracellular parasite, not “alive” and must “invade” a host
- Details
  - Family: Orthomyxoviridae
  - Type: Enveloped RNA
  - Size: 80-200nm (.08-.12 microns)
  - Class: A
- Surface antigens
  - H (haemaglutinin), Entry “Key”
  - N (neuraminidase), Exit “Key”
- Target: Alpha 2-6 Glycan Receptors

8 RNA Gene Segments
Host Cell Viral Infection and Replication

Vaccines

Medications

Respiratory Epithelium

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Novel H1N1 Genome

HA  Hemagglutinin
NA  Neuraminidase
M   M Protein Gene
NP  Nucleoprotein Gene
NS  Non Structural Protein Gene
PA  Polymerase PA Gene
PB1 Polymerase PB1 Gene
PB2 Polymerase PB2 Gene

NEJM, May 09
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The Agent: The Current H1N1 Swine Flu Reassortment Summary

First swine flu virus isolated in 1930 – H1N1 descendant of the 1918 pandemic strain called classical swine viruses

Classical swine flu viruses (H1N1) circulated widely; common in pigs in US, Mexico, Canada, SA, Europe, Kenya, Mainland China, Taiwan, and Japan

Caused rare human cases ~1 per year; usually associated with underlying chronic condition and/or contact with pigs

Swine are susceptible to human strains, avian strains and swine strains – mixing bowl concept

In late 1990s new triple-reassortant swine strains emerged in US combinations of swine, avian, and human genes: H3N2 with HA, NA, PB1 (human seasonal), PA and PB2 (avian), other 3 genes swine origin; H1N2 triple-reassortants; H1N1 classic swine triple-reassortants

Current H1N1 outbreak strain*:

- HA  H1 swine origin gene of a lineage midway between Eurasian and North American
- NA + M  genes are Eurasian swine new to North America
- PA + PB2  avian from North American from a triple reassortant swine virus
- PB1  human seasonal H3N2 from a North American triple reassortant in swine

* Source: Science Insider, 29 APRIL; interview with Ruben Donis – CDC Atlanta, Dr Dave Siegrist, MITRE

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The Disease: “The Flu”

- **Who? Where?:** Humans, all ages, anterior nares, nasopharynx
- **Modes of Transmission (fomites)**
  - Virus laden droplets in the breathing zone---cough, sneeze
  - Contaminated Surfaces, Viral Survival: 8-12 hrs (paper), 24-48 hrs (glass), may vary with change in temperature or humidity---touch, cough, sneeze
- **Symptoms/case definition:** Rapid onset of high fever, NP Cough, HA (90%); fatigue, myalgias/arthritis (80%), GI complaints (50%)
- **Contagious Period:**
  - Adults—24 hrs prior and up to 7 days post symptoms onset
  - Children—24 hrs prior and up to 14 days post symptoms onset
- **Individual Treatment:**
  - Judicious use of antivirals
  - Vaccination
  - Symptomatic Treatment
- **Complications** can include bacterial pneumonia, dehydration, and worsening of chronic medical conditions.
- **Epidemiology (Seasonal Flu):**
  - Between 5-20% of the U.S. population each year
  - 200,000 hospitalizations
  - 36,000 US deaths and 250,000 Global deaths

Emergency hospital during the 1918 influenza epidemic, Camp Funston, Kansas

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The Immune System Response

Figure 34-2. Time course of the antibody response in the circulating blood to a primary injection of antigen and to a secondary injection several months later.
Background Definitions: Round #2

- **Population Health** = Population Resilience
- **Epidemiology**: “The Study of the distribution and determinants of disease and injuries in human populations”
- **Infectious Disease Epidemiology**: Host-Parasite Interaction, Mechanisms of Transmission, Type of Epidemic, Epidemic Control Mechanisms
- **Agent Assessment**: Pathogenicity—Attack Rate, Virulence, CFR, Reservoirs—human/animal
- **Epidemic Type**: Common Source (John Snow—cholera) vs Propagated (index case, secondary attack rate—“Waves”)
- **Herd Immunity**: > 90% immune (vaccinated or previous infection)
- **High risk cohorts**: elderly, young children, pregnant women, and people with certain health conditions
- **Pandemic**: A Global Epidemic

Influenza germs spread through the air when someone coughs.

Emergency hospital during the 1918 influenza epidemic, Camp Funston, Kansas
Timeline of Influenza A Emergence and Pandemics

1918: “Spanish Flu” 20-40 million deaths
1957: “Asian Flu” 1 million deaths
1968: “Hong Kong Flu” 1 million deaths

- 1918: Spanish Influenza H1N1
- 1957: Asian Influenza H2N2
- 1968: Hong Kong Influenza H3N2
- 1998/9: Swine Flu (Reassorted Influenza virus)
- 2009: Pandemic Influenza A (H1N1)

Reassorted Influenza virus (Swine Flu)
H1
Avian Influenza
H9 → H7
H5 → H5
H1
H3
H2
1918
1957
1968
1977
1997
2003
2009
2010

1918: “Spanish Flu”
1957: “Asian Flu”
1968: “Hong Kong Flu”
The Next Pandemic: Elevated Risk for an “Aggressive Event”

Global Scientific, Technical, Social, Political and Economic Issues that put us at increased risk of a PI event now and in the future:

- New/Novel Strain Appearance (e.g. herd immunity low)
- Difficult Initial Identification (inter mixing of seasonal vs new)
- Increased World Population & Density
- Increased World Travel/Mixing
- Antiviral resistance
- Vaccine Development Technology Limitations (egg vs cell based)
- Traditional Screening Tools (POE’s) Less Valuable
- Significant Chronic Disease Population Vulnerability
Influenza A(H1N1)  
Winter 2009 (US, Globally)

THEN:

- CDC (US)*
  » “Regional or Widespread H1N1 activity,” (A/California/7/2009)
  » 12,384 hospitalizations, 1,544 ILI/pneumonia deaths; CFR-0.1%
- WHO
  » 340,000 Lab Confirmed cases (A/California/7/2009), 4,100 deaths
- Southern Hemisphere Experience (SA, Australia, NZ)
  » 722 ICU admissions, 66% req’d ventilator, 83% BMI > 35, 93% < 65, lower SES
- High Risk Groups
  » Pregnant, household contacts or caregivers of children 6 mos or younger, Healthcare & EMS personnel, 6 mos-18 yrs in school & childcare, 19-24 yrs who travel, 25-64 yrs with RAD, COPD, DM, CVD
- Case Definition
  » Rapid onset of high fever, NP Cough, HA (90%); fatigue, myalgias/arthralgias (80%), GI complaints (50%)
- Communicating Risk
  » Vaccine—Harvard Survey (Spring 2010): 51% of the general population would “absolutely get the vaccine” but many parents are concerned about Thimerisol (autism)

*Source: CDC  http://www.cdc.gov/h1n1flu/updates/us/
Influenza A(H1N1)

Fall/Winter 2010 (US, Globally)

NOW:

- **CDC (US)**
  - “The US Public Health Emergency for 2009 H1N1 Influenza A expired on 23 June 2010.”

- **WHO**
  - “On August 10, 2010, the World Health Organization (WHO) International Health Regulations (IHR) Emergency Committee declared an end to the 2009 H1N1 pandemic globally.”

- **Southern & Northern Hemisphere Experiences**
  - Resurgence of 2009 H1N1 Influenza A & Appearance of Influenza B
  - Oseltamivir (Tamiflu) resistance; histidine to tyrosine substitution at N1 (H275Y)

- **High Risk Groups**
  - Pregnant, household contacts or caregivers of children 6 mos or younger, Healthcare & EMS personnel, 6 mos-18 yrs in school & childcare, 19-24 yrs who travel, 25-64 yrs with RAD, COPD, DM, CVD

- **Case Definition**
  - Rapid onset of high fever, NP Cough, HA (90%); fatigue, myalgias/arthritis (80%), GI complaints (50%)

- **Communicating Risk**
  - Vaccine—Aug 2010, CDC, Advisory Committee on Immunization Practices (ACIP) = “Vaccine is Safe”
  - Reports of GBS (Guillain-Barré syndrome) increase appear not to be significant

*Source: CDC  http://www.cdc.gov/h1n1flu/updates/us/
Influenza A(H1N1)
Summer 2010

Southern Hemisphere Experience

*Source: CDC  http://www.cdc.gov/h1n1flu/updates/us/
Influenza A(H1N1) Summer 2010

Southern Hemisphere Experience
Influenza A(H1N1)  
Winter 2010

Northern Hemisphere Experience

Influenza Laboratory Surveillance Information  
Data source: FluNet (www.who.int/flunet), Global Influenza Surveillance Network (GISN)

Northern hemisphere

Number of specimens positive for influenza by subtypes

Weeks

Number of specimens positive for influenza

2010

B (Lineage not determined)  
A (H5)  
B (Victoria lineage)  
Pandemic A (H1N1) 2009  
A (H1)

1/19/2011
Influenza A(H1N1)  
*Winter 2010*

Global Experience
A “Step-Wise” Approach for Infectious Agent Management (Fed/State & Local—Hospital to the Individual)

- Planning and Preparation: Fed Authorities, S&L Execution
  » (F) CONOPS: Fed to State, Local & Tribal Authorities & Responsibilities
  » (F) DHS, HHS, CDC; HSPD-21

- Disease Surveillance
  » (F, S&L) CDC, Nat’l Respiratory & Enteric Virus Surveillance Syst (NREVSS)
  » DHS/HHS, “Knitting together” data base analysis and reporting tools

- Measures directed against the agent reservoir (H1N1, H5N1…)
  » (S&L) Isolation—imposed on individual for maximum incubation period
  » (F, S&L) Quarantine—imposed on groups for maximum incubation period
  » (F, S&L) Culling

- Measures to reduce host susceptibility, Individual interventions
  » Intact Immune System, Good Hygiene Practices
  » (F—SNS, S&L) Vaccination

- Measures that interrupt transmission, Individual & Community interventions
  » Individual: Medications—Neuraminidase Inhibitors, Tamiflu & Relenza
  » Hospital: Universal Precautions & Ventilation Systems, Infection Control
  » Community Based Interventions: Social Distancing, PPE--N95 Mask

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High-level CONOPS for national disaster response

**Local**
- Mayor or Emergency Manager
- First Responders
- Law Enforcement
- Medical Facilities
- Incident Commander
- ICP
- Incident Occurs

**State**
- Governor
- State/Local Fusion Center
- National Guard
- Public Health
- EOC
- State/Local Liaisons

**Federal**
- President
- Secretary of Health and Human Services (HHS)
- Secretary of Homeland Security (DHS)
- Federal Emergency Management Agency (FEMA)
- HSC
- NCC
- NRCC
- JIC
- JOC
- FBI
- Northcom
- DOD
- Joint Operations Center (JOC)
- Joint Task Force (JTF)
- Operations/Watch Center
- EOCs (10)
- NCTC
- TSC
- SOC
- PFO (5-10)
- FCO (5-10)
- CI Lead Agencies (17)
- EEEFs (15)
- Operations/Watch Center

**Communications and Resource Movement**
- Manual or automated communications
- Movement of resources
ESF COORDINATING, PRIMARY, AND SUPPORT DESIGNATIONS

Table 2. Designation of ESF Coordinator and Primary and Support Agencies

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<th>Emergency Support Functions</th>
<th>#1 - Transportation</th>
<th>#2 - Communications</th>
<th>#3 - Public Works and Engineering</th>
<th>#4 - Firefighting</th>
<th>#5 - Emergency Management</th>
<th>#6 - Mass Care, Emergency Assistance, Housing, and Human Services</th>
<th>#7 - Logistics and Resource Support</th>
<th>#8 - Public Health and Medical Services</th>
<th>#9 - Search and Rescue</th>
<th>#10 - Oil and Hazardous Materials Response</th>
<th>#11 - Agriculture and Natural Resources</th>
<th>#12 - Energy</th>
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TABLE CONTINUED ON THE NEXT PAGE

C = ESF coordinator    P = Primary agency    S = Support agency

Note: Components or offices within a department or agency are not listed on this chart unless they are the ESF coordinator or a primary agency. Refer to the ESF Annexes for details.
WHO: Global Alert and Response (GAR) & CDC: National Respiratory and Enteric Virus Surveillance System

U.S. Virologic Surveillance:

WHO and NREVSS collaborating laboratories located in all 50 states and Washington D.C. report to CDC the number of respiratory specimens tested for influenza and the number positive by influenza type and subtype. The results of tests performed during the current week are summarized in the table below.

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<tr>
<th>Week 30</th>
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<td>No. of specimens tested</td>
<td>10,816</td>
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<tr>
<td>No. of positive specimens (%)</td>
<td>2,968 (27.4%)</td>
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</table>

Positive specimens by type/subtype

| Influenza A | 2,959 (99.7%) |
| A (2009 H1N1) | 1,549 (52.3%) |
| A (subtyping not performed) | 1,368 (46.2%) |
| A (unable to subtype) | 40 (1.4%) |
| A (H3) | 1 (0.1%) |
| A (H1) | 1 (0.1%) |
| Influenza B | 9 (0.3%) |

The Challenge: Integrating multiple data collection engines to give decision makers a coherent picture = Situational Awareness
Individual Interventions: Good Hygiene Practices

- Covering nose and mouth with a tissue when coughing or sneezing
  » Dispose the tissue in the trash after use.
- Hand washing with soap and water
  » Especially after coughing or sneezing.
- Cleaning hands with alcohol-based hand cleaners
- Avoiding close contact with sick people (6 Feet Rule)
- Avoiding touching eyes, nose or mouth with unwashed hands
- If sick with influenza, staying home from work or school and limit contact with others to keep from infecting them

Source: CDC
H1N1 Vaccination

- Why vaccinate?
  » Projected exposed in the next year—2.2 Billion* (*Science, Sep 09)

- [http://www.cdc.gov/h1n1flu/vaccination/general.htm](http://www.cdc.gov/h1n1flu/vaccination/general.htm)

- Production, Delivery & Recommendations (2010):
  » 160-165 Million doses
  » CDC, ACIP: Everyone over 6 months old
Individual: Medication and Vaccines

Vaccines

Tamiflu & Relenza

Medications

Respiratory Epithelium
## Influenza A(H1N1) Medication

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<th>Zanamivir (Relenza)</th>
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<td>Treatment</td>
<td>Prophylaxis</td>
</tr>
<tr>
<td>Adults</td>
<td>75 mg capsule twice per day for 5 days</td>
<td>75 mg capsule once per day</td>
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<tr>
<td>Children</td>
<td>15 kg or less: 60 mg per day divided into 2 doses</td>
<td>30 mg once per day</td>
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<td>15–23 kg: 90 mg per day divided into 2 doses</td>
<td>45 mg once per day</td>
</tr>
<tr>
<td></td>
<td>24–40 kg: 120 mg per day divided into 2 doses</td>
<td>60 mg once per day</td>
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<tr>
<td></td>
<td>&gt;40 kg: 150 mg per day divided into 2 doses</td>
<td>75 mg once per day</td>
</tr>
</tbody>
</table>

Dosing recommendations for antiviral treatment of children younger than 1 year using oseltamivir. Recommended treatment dose for 5 days. <3 months: 12 mg twice daily; 3-5 months: 20 mg twice daily; 6-11 months: 25 mg twice daily

Dosing recommendations for antiviral chemoprophylaxis of children younger than 1 year using oseltamivir. Recommended prophylaxis dose for 10 days. <3 months: Not recommended unless situation judged critical due to limited data on use in this age group; 3-5 months: 20 mg once daily; 6-11 months: 25 mg once daily

Source: CDC
Community-Based Interventions: Non-Pharmaceutical Interventions/Social Distancing

1. Delay disease transmission and outbreak peak
2. Decompress peak burden on healthcare infrastructure
3. Diminish overall cases and health impacts

Pandemic outbreak:
- No intervention
- With intervention
Social Distancing Measures/NPI’s used in the 1918 “Spanish Flu”

- Making influenza a reportable disease
- Isolating sick individuals
- Quarantine of households with sick individuals
- School closure
- Protective sequestration of children or adults
- Cancellation of worship services
- Closure of public gathering places [e.g., saloons, theatres, etc.]
- Staggered business hours to decrease congestion on trams, etc.
- Mandatory or recommended the use of masks in public
- Closing or discouraging the use of public transit systems
- Restrictions on funerals, parties, and weddings
- Restrictions on door-to-door sales
- Community-wide curfew measures and business closures
- Social distancing strategies for those encountering others
- Public health risk communication measures
- Declaration of public health emergency
1918 Death Rates: Philadelphia v St. Louis

Deaths Rates / 100,000 Population (Annual Basis)

<table>
<thead>
<tr>
<th>Date</th>
<th>Philadelphia</th>
<th>St. Louis</th>
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</thead>
<tbody>
<tr>
<td>9/14/1918</td>
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<tr>
<td>9/21/1918</td>
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<tr>
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<tr>
<td>10/5/1918</td>
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<tr>
<td>12/28/1918</td>
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</tbody>
</table>
Who Infects Whom? Value of NPI/Social Distancing
NISAC, SAND Number: 2005-7955J

<table>
<thead>
<tr>
<th>From</th>
<th>To Children</th>
<th>To Teenagers</th>
<th>To Adults</th>
<th>To Seniors</th>
<th>Total From</th>
</tr>
</thead>
<tbody>
<tr>
<td>From Children</td>
<td>21.4</td>
<td>3.0</td>
<td>17.4</td>
<td>1.6</td>
<td>43.4</td>
</tr>
<tr>
<td>From Teenagers</td>
<td>2.4</td>
<td>10.4</td>
<td>8.5</td>
<td>0.7</td>
<td>21.9</td>
</tr>
<tr>
<td>From Adults</td>
<td>4.6</td>
<td>3.1</td>
<td>22.4</td>
<td>1.8</td>
<td>31.8</td>
</tr>
<tr>
<td>From Seniors</td>
<td>0.2</td>
<td>0.1</td>
<td>0.8</td>
<td>1.7</td>
<td>2.8</td>
</tr>
<tr>
<td>Total To</td>
<td>28.6</td>
<td>16.6</td>
<td>49.0</td>
<td>5.7</td>
<td>7.8</td>
</tr>
</tbody>
</table>

Likely sites of transmission
- School
- Household
- Workplace

Demographics
- Children/Teens: 29%
- Adults: 59%
- Seniors: 12%
Individual NPI’s: N95 Masks

- Surgical masks
  » Easily available and commonly used for routine surgical and examination procedures

- High-filtration respiratory mask
  » Special microstructure filter disc to flush out particles bigger than 0.3 micron. These masks are further classified:
    • oil proof
    • oil resistant
    • not resistant to oil
  » The more a mask is resistant to oil, the better it is
  » The masks have numbers beside them that indicate their filtration efficiency. For example, a N95 mask has 95% efficiency in filtering out particles greater than 0.3 micron under normal rate of respiration.

- The next generation of masks use Nano-technology which are capable of blocking particles as small as 0.027 micron.
WEST NILE VIRUS!

SARS!

THE FLU!!

Actually, can we get vaccinated against obsessive media hype?
Communicating Risk: CONOPS!

- **Technical Expert's definition**
  - Hazard + probability = risk assessment
  - Relies upon research and statistics
  - Characterized by health risk assessments

- **Public's definition**
  - Consequences of hazards
  - Individual feelings about likelihood that something bad will happen to them

Risk is about **FEAR**
- Public versus Expert “gap”

Risk is about **DANGER**
- Emotional
- Contentious

Risk is about **SURVIVAL**
- Disagreement can be fierce
Preparedness Recommendations

- Stay or Get Informed
  [http://www.cdc.gov/h1n1flu/#stay_healthy](http://www.cdc.gov/h1n1flu/#stay_healthy)

- Vaccination
  - Flu shot or nasal flu spray (age 2-49)
  - Recommended for “at-risk” groups
  - Given during flu season, starting in October

- Good health habits
  - Have an N95 Mask available
  - Wash hands
  - Avoid touching nose, mouth, and eyes
  - Cover mouth and nose when coughing or sneezing
  - Avoid close contact with infected individuals
  - Avoid public areas when infected

- Develop a family EP&R Plan
  - Communicate about Finances, Legal, Health
  - At the “End of the Day”…………….
Questions