INFLUENZA (H1N1) UPDATE

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August 28 and September 4, 2009
Roadmap

- Background of Influenza
- Molecular characteristics H1N1
- Transmission
- H1N1 epidemiology in Southern California
- Diagnosis and Reporting
- Treatment and prophylaxis
- Public Health Control Measures
BACKGROUND: HUMAN INFLUENZA

- Acute febrile respiratory illness (AFRI)
  - Symptoms, signs may differ by age
- Annual epidemics occur in fall and winter
- Rates of serious illness and death due to influenza: increased for \( \geq 65 \) yrs, children <2 yrs, and persons w/ underlying risk facts
- Annually estimated 36,000 deaths and 226,000 hospitalizations
- Types A and B cause most disease
KEY INFLUENZA VIRAL FEATURES

Surface proteins (major antigens)

- **Hemagglutinin (HA)**
  - Site of attachment to host cells
  - Antibody to HA is protective

- **Neuraminidase (NA)**
  - Helps to release virions from cells
  - Antibody to NA can help modify disease severity
INFLUENZA A VIRUSES

- Infect multiple species
  - Humans
  - Birds (wild birds, domestic poultry)
  - Pigs (wild, domesticated)
  - Other animals: horses, dogs, marine mammals (seals, whales)

- Subtypes based on surface glycoproteins (HA and NA)
  - 16 HA, 9 NA
  - Currently 3 human influenza A virus subtypes:
    - H1 (H1N1, H1N2)
    - H3 (H3N2)

- Genetic Variation in HA and NA
  - Cause epidemics and pandemics
INFLUENZA A VIRUSES: ANTIGENIC “DRIFT”

- Antigenic “drift”: Point mutations in the hemagglutinin gene cause minor antigenic changes to HA
  - Continuous process
- Antigenic “drift” causes seasonal epidemics
  - May be limited cross immunity
  - Need new vaccine every year
Antigenic “shift”: Emergence of a novel human influenza A virus subtype (new HA subtype +/- NA) through:

✓ Genetic reassortment (human and animal viruses) (Novel H1N1)

✓ Direct animal (poultry) to human transmission (H5N1)
DEFINITION OF PANDEMIC

- Isolation from humans of a novel influenza A virus
- Little or no immunity in the population
- Demonstrated ability of the virus to replicate and cause disease
- Efficient person to person transmission
- Found around the world
INFLUENZA PANDEMICS
20th Century

1918: “Spanish Flu”
A(H1N1)
20-40 million deaths worldwide
675,000 US deaths

1957: “Asian Flu”
A(H2N2)
1-4 million deaths
70,000 US deaths

1968: “Hong Kong Flu”
A(H3N2)
1-4 million deaths
34,000 US deaths
Pandemic (H1N1) 2009

- Novel Influenza A (H1N1) Declarations
  - WHO: Jump from Pandemic Phase 3 to phase 5 by 4/29/2009
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New Subtype

- Novel H1N1 Influenza A Virus is a new subtype not previously found in humans/swine.
- Genomic analysis of A (H1N1) segments from re-assortment of 4 different Influenza A:
  - North American human H3N2
  - North American avian
  - North American swine and Eurasian swine
History of Reassortment Events in the Evolution of the 2009 Influenza A (H1N1) Virus

Appears that people born before 1957 have some protection (MMWR, May 22, 2009)

- 1/3 adults >60 years have cross reactive antibody
  - Possibly due to exposure to H1N1 that was circulating before H3 took over
- No immunity for younger individuals

Reflected in rare occurrence of illness in those over 65 years
Roadmap

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- **Clinical/ Transmission**
  - H1N1 epidemiology in Southern California
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Influenza Virus Transmission

Aerosol/Droplet

Fomites
TRANSMISSION

- Spread by respiratory droplets: person-to-person, direct contact
  - Requires close contact btw source and recipient, travel < 1 meter
  - Rarely respiratory
- Ferret study showed Novel H1N1 more direct contact, less droplet than seasonal flu (Science June 09 [Maines])
Transmission

- Short incubation period, usually 1-4 days
- Highly contagious; infectious period:
  - Adults: 1 day prior to symptoms thru 5 - 10 days post illness
  - Children: several days before onset to ≥10 days
    - Generally shed virus longer than adults due to lack of immunity
  - Immune compromised: can shed virus for weeks to months
- Transmission similar for novel H1N1
  - 90% of household transmission within 5 days
Children Play an Important Role in the Transmission of Influenza

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Swine Influenza A (H1N1) Infection in Two Children — Southern California, March–April 2009

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Epi Curve of Severe Influenza in LAC as of 8/26/2009
Not Just a Testing Artifact

Figure 1: Total Positive Flu and % Positive Flu by Week

- Number
- Percent Positive

- 2008-2009 Flu
- 2008-2009 % + Flu

Oct, Nov, Dec, Jan, Feb, Mar, Apr, May, Jun, Jul, Aug
Incidence of Hosp/ Deaths by Age in California due to H1N1

Table 2. Total number of hospitalized and/or fatal cases reported and incidence rate, by age group, of pandemic (H1N1) 2009 in California, April 3–August 25, 2009

<table>
<thead>
<tr>
<th>Age category, in years</th>
<th>Number of cases</th>
<th>Cumulative number of cases</th>
<th>Incidence per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>92</td>
<td>92</td>
<td>16.15</td>
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<tr>
<td>1-4</td>
<td>118</td>
<td>210</td>
<td>5.34</td>
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<tr>
<td>5-18</td>
<td>283</td>
<td>493</td>
<td>3.74</td>
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<tr>
<td>19-24</td>
<td>183</td>
<td>676</td>
<td>5.28</td>
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<tr>
<td>25-35</td>
<td>260</td>
<td>936</td>
<td>4.42</td>
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<tr>
<td>36-49</td>
<td>237</td>
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<tr>
<td>50-64</td>
<td>269</td>
<td>1442</td>
<td>4.02</td>
</tr>
<tr>
<td>65+</td>
<td>86</td>
<td>1528</td>
<td>1.97</td>
</tr>
<tr>
<td>ALL AGES</td>
<td>1528</td>
<td></td>
<td>3.94</td>
</tr>
</tbody>
</table>

Includes the following individuals: (1) non-fatal hospitalized cases, (2) fatal hospitalized cases, (3) fatal non-hospitalized cases.
## Risk Factors for Severe Illness with H1N1

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Cardiac</th>
<th>Pulmonary</th>
<th>Metabolic Disorder</th>
<th>Developmental Delay</th>
<th>Immunosupression</th>
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<tr>
<td><strong>Deaths</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;18</td>
<td>20%</td>
<td>0%</td>
<td>0%</td>
<td>80%</td>
<td>40%</td>
</tr>
<tr>
<td>18+</td>
<td>31%</td>
<td>24%</td>
<td>31%</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>All Ages</td>
<td>29%</td>
<td>21%</td>
<td>26%</td>
<td>21%</td>
<td>15%</td>
</tr>
<tr>
<td><strong>ICU</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>21%</td>
<td>47%</td>
<td>5%</td>
<td>37%</td>
<td>0%</td>
</tr>
<tr>
<td>18+</td>
<td>8%</td>
<td>19%</td>
<td>22%</td>
<td>3%</td>
<td>11%</td>
</tr>
<tr>
<td>All Ages</td>
<td>13%</td>
<td>29%</td>
<td>16%</td>
<td>15%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Hospitalized</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18</td>
<td>3%</td>
<td>29%</td>
<td>8%</td>
<td>12%</td>
<td>8%</td>
</tr>
<tr>
<td>18+</td>
<td>14%</td>
<td>16%</td>
<td>16%</td>
<td>4%</td>
<td>11%</td>
</tr>
<tr>
<td>All Ages</td>
<td>9%</td>
<td>22%</td>
<td>12%</td>
<td>8%</td>
<td>9%</td>
</tr>
</tbody>
</table>
Other Clinical Observations

- 14 pregnant women: 4 in ICU and 2 died
- Kids:
  - Asthma
  - Developmental conditions
- Adults
  - Diabetes, BMI, lung disease
- Many seen and treated with antibiotics days before admission to hospital
- Very little secondary bacterial infections
- Some nosocomial outbreaks
## ICU/Deaths by BMI

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>36</td>
</tr>
<tr>
<td>Median</td>
<td>33</td>
</tr>
<tr>
<td>Range</td>
<td>19-77</td>
</tr>
</tbody>
</table>

14% of adult deaths with obesity as only risk factor
Epidemiologic Characteristics of Novel H1N1

- Mortality rates consistent with seasonal influenza
- Majority of cases <18 years
- Late season peak in cases
  - 99% or more of current isolates novel H1N1
- Not much hospitalization in >60 yrs
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Nasopharyngeal aspirates or swab is the diagnostic specimen of choice.

Serologic testing not recommended to detect evidence of human influenza or management of acute illness.

Specimen collection:
- Obtain specimen within 5 days of symptom onset.
- Refrigerate specimen and test for flu ASAP.
- Note: immunocompromised may shed virus for weeks to months.
Diagnostic Specimens (2)

- RT-PCR testing—most sensitive and specific of testing modalities, results within 4-6 hrs
  - Public Health Laboratory

- Viral Isolation—standard culture and shell vial culture—at least a few days

- Commercial Rapid flu tests—ready in 10-30 minutes, variable sensitivity and specificity depending on test kit and lab experience
SENSITIVITY* OF RAPID ANTIGEN DETECTION TESTS

<table>
<thead>
<tr>
<th>2008-9 Seasonal Influenza type</th>
<th>BinaxNOW A&amp;B</th>
<th>Quidel Quickvue</th>
<th>Directigen EZ Flu</th>
</tr>
</thead>
<tbody>
<tr>
<td>A H3N2</td>
<td>60-80</td>
<td>60-80</td>
<td>60-80</td>
</tr>
<tr>
<td>A H1N1</td>
<td>80-83</td>
<td>80-83</td>
<td>80-83</td>
</tr>
<tr>
<td>Novel H1N1 High titer</td>
<td>89-100</td>
<td>89-100</td>
<td>89-100</td>
</tr>
<tr>
<td>Novel H1N1 Low Titer</td>
<td>40</td>
<td>69</td>
<td>49</td>
</tr>
</tbody>
</table>

*Using RT-PCR as the gold standard MMWR 2009 58(30)
Original Priorities for Laboratory testing of Novel H1N1

- Early in outbreak - wider testing of ILI illness - late April through mid-May
  - Hospitalized cases
  - Non-hospitalized cases
  - School Outbreaks
  - Recent travel to Mexico
  - Elderly
  - Immunocompromised
  - Pregnant women
  - Healthcare workers
  - Recent contact with suspect/known Novel H1N1
Current Priorities for Testing for Novel H1N1

- Influenza-like illness (fever $\geq 100^\circ$F and cough/or sore throat)
- One of the following:
  - ICU admission
  - Death
  - Outbreak
- For individual cases: must get pre-approval from ACDC prior to submission
Reporting Requirements

- All outbreaks are reportable
- All hospitalizations in the ICU or deaths due to ANY influenza are reportable as individual cases
- Aggregate reporting, by age group, for all hospitalizations, ICU admissions, and deaths
  - Include total count of pregnant women and healthcare workers
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ANTI VI RALS: ADAMANTANES AND NEURAMINIDASE INHIBITORS
Treatment of Influenza

- Treatment Recommended
  - All hospitalized patients with confirmed, probable or suspect Influenza
  - Patients at high risk for influenza complications
  - Consider doubling dose for obese patients

- Antivirals should be started w/in 48 hrs
  - Hospitalized patients may still benefit even > 48 hrs
High Risk Groups for Treatment of Influenza

- High-risk groups for influenza complications:
  - Children <5 years
    - Children <2 years highest risk for hospitalization, death, complications
  - Adults ≥ 65 years
  - Immunosuppressed persons - medications, HIV
  - Pregnant women
  - Persons <19 yrs on long-term ASA Rx
  - Resident in nursing home/chronic care facilities
Treatment of Influenza

- Pregnant women
  - No clinical studies have been conducted to assess safely safety of neuraminidase inhibitors
  - Pregnancy should not be considered a contraindication to oseltamivir or zanamivir

- Children under 1 year of age
  - Oseltamivir is not licensed for children <1 year
  - Limited safety data on treatment for <1 year suggest severe adverse events are rare
  - Emergency use authorization for Tamiflu was granted due to high rates of morbidity and mortality
## Treatment of Influenza

<table>
<thead>
<tr>
<th></th>
<th>Adamantanes</th>
<th>Tamiflu®</th>
<th>Relenza ®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonal H1N1</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>Seasonal H3N2</td>
<td>R</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Influenza B</td>
<td>R</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Novel H1N1</td>
<td>R</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
PROPHYLAXIS GUIDANCE

- Healthcare workers who provided care to a confirmed influenza patient AND did not use proper PPE
  - Relenza for pregnant contacts
- Asymptomatic household and other close contacts of a confirmed influenza patient who are at high risk for complications
- In an outbreak setting in a closed facility (SNF, LTC)
Swine Flu!
Bacon's Revenge
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Impacts on Influenza Pandemic on Health Services

- Likely to place great pressure on health and social services
- Increased numbers of patients requiring treatment
- Depletion of the workforce due to illness and other disruption

[www.dh.gov.uk/pandemicflu]
CHALLENGES TO MAINTAINING QUALITY MEDICAL CARE

- Ability to effectively triage patients
- Ability to care for ill outpatients
  - Delivery of medical care, medications, and food
- High demand for inpatient services
  - Estimated >25% increase in demand for inpatient beds, ICU beds, & ventilators for a mild pandemic
  - Staff absenteeism
  - Limited availability of critical resources
- Surge capacity for inpatient care
IMPACT ON SCHOOLS AND SERVICES

- Likely to spread rapidly in schools and other closed communities
- Impact on all services including police, fire, the military, duel supply, food production, distribution and transport, prisons, education and business

www.dh.gov.uk/pandemicflu
Control Activities

- Prevention
- Surveillance
- Improve medical response
- Outbreak control
Prevention

- Vaccines!
  - Seasonal influenza
  - H1N1 monovalent
  - Pneumococcal

- Community Mitigation Messaging
  - Hands
  - Noses/mouths
  - When to see the doctor/when to stay home
Community Mitigation

- Self-isolation encouraged
  - Masks for HH contacts
  - Quarantine for contacts not practical
- Business preparedness
  - Discourage “presenteeism”
  - Develop contingency plans/telecommute
- Community education
Self-Isolation

- People with novel H1N1 flu who are cared for at home should:
  - Wear a facemask - if available and tolerable - when sharing common spaces with other household members. This is especially important if other household members are at high risk for complications from influenza.
  - Stay at home for at least 24 hours after resolution of fever off anti-pyretics

[http://www.cdc.gov/h1n1flu/guidance_homecare.htm](http://www.cdc.gov/h1n1flu/guidance_homecare.htm)
WARNING
MUMPS
NOTICE

WARNING
MEASLES
NOTICE

WARNING
CHICKEN POX
NOTICE
A newspaper photograph published Oct. 17, 1918, demonstrated health officials’ suggestion on how to kiss during the epidemic.
Surveillance

Goal: provide accurate, useful, and timely information about the effects of Influenza on residents in Los Angeles County. Results in Influenza Watch.

- Individual cases/reportable diseases
- Syndromic
- Outbreaks
- Relational (IZ versus DZ)
Improve Medical Response

- Identify risk groups
- Treatment recommendations
- Diagnostic recommendations
- Assist with infection control recommendations and requirements
- Provide SNS supplies
Outbreaks!
Conclusions

- We are already in a pandemic
- Severity unknown
  - Absolute # of cases likely to be higher than "regular" season
- Goal: reduce morbidity and mortality, not transmission
- Community mitigation will only go so far
- Prompt Public Health response-vaccines and outbreak control will save lives
Questions?