Update on pandemic influenza A(H1N1) activity, United States

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

On April 21, this report was posted as an MMWR Early Release on the MMWR website (http://www.cdc.gov/mmwr).

- March 2009
  - 2 cases of febrile respiratory illness in children in late March
  - No common exposures, no pig contact
  - Uneventful recovery
  - Residents of adjacent counties in southern California
  - Tested because part of enhanced influenza surveillance
  - Reported to CDC as possible Novel influenza A virus infections
  - Swine influenza A (H1N1) virus detected on April 15th, 17th at CDC
  - Both viruses genetically identical
  - Contain a unique combination of gene segments previously not recognized among swine or human influenza viruses in the US
Timeline (22 July 2009 onwards)
Pandemic (H1N1) 2009 laboratory confirmed cases
And number of deaths as reported to WHO

Status as of: 06 September 2009

Chinese Taipei has reported five deaths associated with pandemic (H1N1) 2009.

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Epidemiology/Surveillance

Percentage of Visits for Influenza-like Illness (ILI) Reported by the US Outpatient Influenza-like Illness Surveillance Network (ILINet), National Summary 2008-09 and Previous Two Seasons

novel 2009-H1N1 – 11 SEPT 2009

Data are provisional and will not be officially released by the CDC until 1100 EDT

Internal Use Only (FIUO) --- For Official Use Only (FOUO) - Sensitive But Unclassified (SBU)

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Epidemiology/Surveillance

Current Influenza Surveillance – ILINet Regions 1-3

novel 2009-H1N1 – 11 SEPT 2009

Region 1 - CT, ME, MA, NH, RI, VT

Region 2 - NJ, NY

Region 3 - DE, DC, MD, PA, VA, WV

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Epidemiology/Surveillance
Current Influenza Surveillance – ILINet Regions 4-6
novel 2009-H1N1 – 11 SEPT 2009

Region 4 - AL, FL, GA, KY, MS, NC, SC, TN

Region 5 - IL, IN, MI, MN, OH, WI

Region 6 - AR, LA, NM, OK, TX

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Influenza Associated Pediatric Mortality

Number of Influenza-Associated Pediatric Deaths by Week of Death

novel 2009-H1N1 – 11 SEPT 2009

2005-06 season to September 5, 2009

Data are provisional and will not be officially released by the CDC until 1100 EDT

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Weekly Influenza Activity Estimates Reported by State & Territorial Epidemiologists*
Week ending September 5, 2009 - Week 35

* This map indicates geographic spread & does not measure the severity of influenza activity

Data are provisional and will not be officially released by the CDC until 1100 EDT
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Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2008-09

Data are provisional and will not be officially released by the CDC until 1100 EDT
Internal Use Only (FIUO)---For Official Use Only (FOUO) NOT FOR FURTHER DISTRIBUTION -Sensitive But Unclassified (SBU)
Rate per 100,000 Population by Age Group

novel 2009-H1N1 – 24 JUL 2009 (n=37,030*)

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Rate / 100,000 Pop by Age Group</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 Yrs</td>
<td>22.9</td>
<td>4,816</td>
</tr>
<tr>
<td>5-24 Yrs</td>
<td>26.7</td>
<td>22,080</td>
</tr>
<tr>
<td>25-49 Yrs</td>
<td>6.97</td>
<td>7,434</td>
</tr>
<tr>
<td>50-64 Yrs</td>
<td>3.92</td>
<td>2,187</td>
</tr>
<tr>
<td>≥65 Yrs</td>
<td>1.3</td>
<td>513</td>
</tr>
</tbody>
</table>

*Excludes 6,741 cases with missing ages.

Rate / 100,000 by Single Year Age Groups: Denominator source: 2008 Census Estimates, U.S. Census Bureau at:
Epidemiology/Surveillance
Pandemic H1N1 Hospitalizations Reported to CDC
Clinical Characteristics as of 19 JUN 2009 (n=268)

- Fever*: 93%
- Cough: 83%
- SOB: 54%
- Fatigue/weakness: 40%
- Chills: 37%
- Myalgias: 36%
- Rhinorrhea: 36%
- Sore throat: 31%
- Headache: 31%
- Vomiting: 29%
- Wheezing: 24%
- Diarrhea: 24%
Hospitalization Rate per 100,000 Population by Age Group (n=4,738*)

Hospitalizations with unknown ages are not included (n=273)

*Rate / 100,000 by Single Year Age Groups: Denominator source: 2008 Census Estimates, U.S. Census Bureau at:
Influenza-Associated Hospitalizations Deaths By Age Group

*Thompson WW, JAMA, 2004
Distribution by Age Group of Influenza Hospitalized Cases
Emerging Infections Program - Pandemic H1N1 -14 JUL 2009

Seasonal 2007-08
Pandemic 2009*

*April 12 – June 30
Epidemiology/Surveillance
Pandemic H1N1 Hospitalizations Reported to CDC
Underlying Conditions as of 19 JUN 2009 (n=268)

*Excludes hypertension

Prevalence, Hospitalized H1H1 Patients
Prevalence, General US Pop

*Excludes hypertension
Summary of key points

- Once emerged, pandemic H1N1 virus spread to all 50 states and globally quickly
- Some areas more affected than others
- Elderly seemingly relatively spared
- Capable of causing severe disease and death
  - Most severe outcomes among people with underlying health problems that are associated with high risk of influenza complications
- Virus remains sensitive to oseltamivir and zanamivir
- Increases in influenza activity in some parts of the country might be sign of early activity this season
Interim Recommendations for the Use of Antiviral Medications for the 2009 – 2010 Influenza Season

Clinician Outreach and Communication Activity

Sept 16, 2009
Influenza Virus Replication and Targets for Antiviral Inhibition

Neuraminidase Inhibitors

Adamantanes

Endocytosis and fusion

Uncoating

GTP supply

RNA (+/-)

RNA polymerase inhibitors

IMP dehydrogenase inhibitors

siRNAs

mRNA
Neuraminidase Inhibitors

- Oseltamivir (Tamiflu) and Zanamivir (Relenza)

- Randomized clinical trials (RCT): Reduced duration of influenza by 1-1.5 days when administered in 48 hours

- Pooled RCT analysis: Reduced lower respiratory tract complications, pneumonia, and hospitalization

- Observational studies*: Oseltamivir reduced mortality among hospitalized adults with lab-confirmed seasonal influenza A virus infections

Oseltamivir (Tamiflu)

• Oral medication: capsule or suspension
  • Capsule may also be compounded into an oral suspension

• Pediatric dosage depends on age and weight

• FDA approved in persons aged ≥1 year
• Emergency Use Authorization (EUA) approved for use in persons <1 year

• Side effects include nausea, vomiting
  – Reports of neuropsychiatric events (Japan)

• Precautions
  – People with kidney disease (reduce dose)
  – Pregnant or nursing women (safety not well studied)
Zanamivir (Relenza)

- Orally inhaled powder – via special device
- FDA approved for:
  - treatment of seasonal influenza (> 7 years)
  - prevention of seasonal influenza (> 5 years)
- EUA expands treatment indication to hospitalized patients and patients symptomatic for more than 2 days
  - Treatment after 48 hours of symptom onset is still useful in hospitalized patients
- Side effects: wheezing, breathing problems
- Precautions
  - Chronic respiratory disease (bronchospasm)
  - Pregnant or nursing women (safety not well studied)
### Summary of antiviral resistance 2008 - 09

<table>
<thead>
<tr>
<th>Antiviral</th>
<th>2009 H1N1</th>
<th>Seasonal H1N1</th>
<th>Seasonal H3N2</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adamantanes</td>
<td>Resistant</td>
<td>Susceptible</td>
<td>Resistant</td>
<td>N/A</td>
</tr>
<tr>
<td>Oseltamivir</td>
<td>Susceptible*</td>
<td>Resistant</td>
<td>Susceptible</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Zanamivir</td>
<td>Susceptible</td>
<td>Susceptible</td>
<td>Susceptible</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

* 8 of 1372 (0.6%) 2009 H1N1 viruses have been oseltamivir-resistant
Treatment Recommendation

• Clinical judgment is important for treatment decisions

• Predictors of hospitalization* in children have included:
  – young age
  – high risk medical conditions
    • cardiac disease
    • neurologic/neuromuscular disease
  – Evidence of lower respiratory tract disease

* Ref: Bender et al., Pediatr Emer Care 2009;25: 369-375
Coffin et al. Pediatrics 2007;119;740-748
Treatment Recommendation

• Treatment with oseltamivir or zanamivir is recommended for:
  – persons with suspected or confirmed influenza with severe illness (e.g. hospitalized patients)
  – persons with suspected or confirmed influenza who have risk factors for severe illness
Risk Factors for Severe Illness

• Children younger than 5 years old, and especially children younger than 2 years old

• Persons aged 65 years or older

• Pregnant women

• Persons with certain chronic medical or immunosuppressive conditions

• Persons younger than 19 years of age who are receiving long-term aspirin therapy

*Evidence of a positive influenza test result by viral culture, DFA/IFA, RT-PCR, rapid test, serology, or written note in the medical chart.
EIP Influenza Laboratory-Confirmed Cumulative Hospitalization Rates, Spring/Summer 2009

Rate per 10,000 Population**

Week

Oct-Apr Seasonal Average
All Flu Rate (Flu A, Flu B, 2009 Flu A (H1N1) combined)

0-23 mo

2-4 yr

5-17 yr

18-49 yr

50-64 yr

65+ yr
Medical Risk Factors

• Chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological, or metabolic disorders (including diabetes mellitus)

• Disorders that compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) [proposed language]

• Immunosuppression, including that caused by medications or by HIV
• Approximately 70% of persons hospitalized from 2009 H1N1 influenza have had a recognized high risk condition (~60% of children and ~ 80% adults)

• Influenza-Related Pediatric Deaths MMWR – Sept. 3, 2009:
  – 67% percent of children who died with 2009 H1N1 influenza had a high-risk medical condition
  – 4 of 7 children <5 years old who died with 2009 H1N1 influenza did not have a high-risk medical condition

• Among children with high-risk medical conditions, >90% had neurodevelopmental conditions
  – 59% had > 1 neurodevelopmental diagnoses
  – 41% had a pulmonary problem
Underlying conditions among those hospitalized and those who have died from H1N1 compared to general population
Death and Hospitalization Case Series Spring/Summer 2009

- Asthma: 28%
- COPD: 17%
- Diabetes: 22%
- Chronic CVD*: 19%
- Morbid Obesity**: 14%
- Neurocognitive Dis: 21%
- Neuromuscular Dis: 16%
- Pregnant: 11%
- Prevalence, Hospitalized H1N1 Patients
- Prevalence, Novel H1N1 Deaths
- Prevalence, General US Pop

Death and Hospitalization Case Series Spring/Summer 2009

- Prevalence, Hospitalized H1N1 Patients
- Prevalence, Novel H1N1 Deaths
- Prevalence, General US Pop

* Chronic CVD = Chronic Cardiovascular Disease
** Morbid Obesity = Severe Obesity
Clinical Considerations

- Healthy persons who develop an illness consistent with influenza and persons who appear to be recovering from influenza generally do not need antiviral treatment.

- Patients presenting with suspected influenza and warning symptoms (e.g., dyspnea) or signs (e.g., tachypnea, unexplained oxygen desaturation) of lower respiratory tract illness should receive empiric antiviral therapy and evaluation for pneumonia.
Clinical Warning Signs

In young children, warning signs indicating the need for urgent medical attention include:

- Fast breathing or trouble breathing
- Bluish or gray skin color
- Not drinking enough fluids
- Severe or persistent vomiting
- Not waking up or not interacting
- Being so irritable that the child does not want to be held
- Flu-like symptoms improve but then return with fever and worse cough
Influenza Diagnosis

• Treatment, when indicated, should be initiated as early as possible

• Treatment should not wait for laboratory confirmation of influenza

• A negative rapid influenza diagnostic tests (RIDTs) does not rule out influenza

• The sensitivity of RIDTs in detecting 2009 H1N1 has ranged from 10% to 70%
Actions to Improve Early Treatment

• Informing patients at higher risk for influenza complications of the signs and symptoms of influenza and the need for early treatment

• Ensuring rapid access to telephone consultation and clinical evaluation for these patients

• Considering empiric treatment of patients at higher risk for influenza complications based on telephone contact if hospitalization is not indicated
Antiviral Chemoprophylaxis

- Antiviral chemoprophylaxis should be reserved for persons at higher risk for severe illness.

- Early treatment is an emphasized alternative to chemoprophylaxis for persons at higher risk for severe illness who have had contact with someone likely to have been infected with influenza.

- Can counsel about the early signs and symptoms of influenza, and advise to immediately contact health care provider if these signs or symptoms develop.
Outbreaks and Antiviral Chemoprophylaxis

- Outbreaks of influenza in schools, camps, and other group settings of healthy persons without risk factors for severe illness should not be managed with chemoprophylaxis.

- Persons in these settings should be educated about the signs and symptoms of influenza, and urged to consult their health care provider if signs of severe illness develop.
Summary of Interim Recommendations for the Use of Antiviral Medications

- Focus on treating severely ill patients (e.g. hospitalized) and patients with risk factors for severe illness

- Most treatment is empiric, should be started early, and should not wait for an influenza test result

- Healthy patients with mild illness don’t usually require treatment

- Limit use of chemoprophylaxis
  - early treatment of high as an alternative
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