2009 H1N1 Influenza: What You Need to Know
Jan E. Patterson, MD, FACP, FIDSA

Case Study
- April 19, 2009
  - 33 yo pregnant female presented with 3 days of URI symptoms and mild SOB.
  - Treated by obstetrician with azithromycin
  - Admitted to hospital
    - BP stable, T 100.2°F, P 110, RR 32.
    - O₂ sat on RA - 80's.
  - CXR - mild bilateral pulmonary infiltrates
  - WBC 11,000, 11% Bands

Case Study
- Rx Ceftriaxone.
- PMH - No tobacco or drug use.
  - h/o seasonal flu vaccination
- Within hours, required intubation for respiratory distress
- Stat C-section was performed.
- Antibiotics broadened to vancomycin, levofloxacin, and doxycycline

Case Study
- Fevers continued.
- HD 7 tested for influenza by nasal swab
  - Influenza A antigen was positive
- Patient was started on oseltamivir therapy
- Continued to require maximal ventilatory support for severe ARDS
- Died after 3 weeks in hospital
- Child did well and was discharged to home with father

Case Study
- How are seasonal, pandemic and avian flu different?
  - Seasonal flu –
    - influenza viruses that occur during the typical influenza season.
  - Pandemic flu –
    - causes a global outbreak that spreads easily from person to person and involves multiple countries. Currently, 2009 H1N1 A fits this description
  - Avian flu –
    - caused by avian influenza viruses, which occur naturally among birds, but have not yet become adapted to humans.

Objectives
- Describe the epidemiology to date of pandemic H1N1 A influenza
- Know the differences in risk groups from seasonal influenza
- Describe treatment and prophylaxis guidelines
- Know the vaccine priority issues
- Describe infection control practices to prevent influenza
Influenza

- Acute respiratory illness with fever affecting nose, throat, bronchial tubes, lungs
- Seasonal epidemics caused by influenza viruses A and B
- Occurs worldwide
- Symptoms: fever, myalgias, malaise, dry cough, coryza, sore throat, +/- vomiting and diarrhea

Transmissibility

- Incubation period: 2 days (1-4 days)
- Viral shedding: 1 day before symptoms
  - Peaks first 3 days of illness
  - Correlates with fever
  - Subsides by 5-7th day in adults
  - Can be 10+ days in children

Transmission

- Contact and Droplet
- Hand to hand
  - Antisepsis important in control
- Droplet nuclei (within 3 feet)
  - Droplets generated by coughing, talking, sneezing, close contact

Influenza Annual Morbidity in U.S.

- 5% to 20% of the population gets the flu
- 200,000 people are hospitalized from flu
- ~36,000 people die from influenza/pneumonia

Influenza A viruses

- Subtyped based on glycoproteins
  - 16 hemagglutinins (HA)
  - 9 neuraminidases (NA)
  - Current human subtypes:
    - H1N1, H3N2, H2N2

![Image of droplets generated by sneezing]
Genealogy of Pandemic Influenza Strains


Genetic Reassortment of the 2009 Influenza A (H1N1) Virus


Influenza Positive Tests Reported to CDC by U.S. WHO/NERVSS Collaborating Laboratories. National Summary, 2008-09

Roger Sanchez, SAMHO

Statistics 2009 H1N1

U.S. April – July 2009
- ~44,000 reported cases
- 5,000 hospitalized (11%)
- ~300 deaths; < 1% mortality rate
CDC modeling est. ~1 million actual cases

August – September 2009
- 12,000 hospitalized
- 1200 deaths

Deaths in Children

- September 2009 – 36 deaths
  - 19% < 5 years
  - 67% ≥ 1 underlying conditions
  - 43% bacterial co-infection
- October 2009
  - 200 deaths in children
Pandemic 2009

Reported:
340,000+ cases
4,100+ deaths

Timeline

- April 17 – CDC confirmed 1st novel H1N1 virus in California
- April 23 – Cases confirmed in Texas
- April 24 – Confirmation of flu-like illness in Mexico reported
- Late April - Schertz-Cibolo Universal City schools closed

Timeline

- April 29 – Confirmation of first death in Texas/US
- May 5 – New guidelines for school closure
- May/June – end of school year
- June 11 – WHO declares Pandemic

World Health Organization Pandemic Phases

<table>
<thead>
<tr>
<th>Inter-pandemic phase</th>
<th>Pandemic alert</th>
<th>Pandemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk of human cases</td>
<td>No or very limited human-to-human transmission</td>
<td>Efficient and sustained human-to-human transmission</td>
</tr>
<tr>
<td>Higher risk of human cases</td>
<td>Evidence of increased human-to-human transmission</td>
<td></td>
</tr>
<tr>
<td>New virus in animals, no human cases</td>
<td>Evidence of significant human-to-human transmission</td>
<td></td>
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<tr>
<td>New virus causes human cases</td>
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</table>

Pandemic Mortality

<table>
<thead>
<tr>
<th>Pandemic</th>
<th>US deaths</th>
<th>Global deaths</th>
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<tbody>
<tr>
<td>1918-19 (2% mortality)</td>
<td>500,000+</td>
<td>40,000,000+</td>
</tr>
<tr>
<td>1957-58</td>
<td>70,000+</td>
<td>1 to 2,000,000+</td>
</tr>
<tr>
<td>1968-69</td>
<td>50,000</td>
<td>700,000</td>
</tr>
<tr>
<td>2009 to date (Novel H1N1 only) (&lt; 1% mortality)</td>
<td>300+</td>
<td>2,000+</td>
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http://www.who.int/csr/disease/swineflu/en/; http://cdc.gov/h1n1
Clinical Characteristics in Texas

Symptoms reported in confirmed cases

- Fever (>100°F) (median temp: 102.0°F) 94%
- Cough 87%
- Sore throat 61%
- Diarrhea and/or vomiting 47%

88% of the confirmed H1N1 cases met Influenza Like Illness (ILI) case definition (fever > 100°F and sore throat or cough)

A. Valadez MD, DSHS

Regional Demographics

<table>
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<tr>
<th>Texas (community surveillance)</th>
<th>Mexico (hospitalized)</th>
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</thead>
<tbody>
<tr>
<td>Age median 10 years, range 1 month – 84 yrs</td>
<td>Age median 38 years, range 9 month – 61 yrs</td>
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<tr>
<td>&lt; 5 yrs</td>
<td>16%</td>
</tr>
<tr>
<td>5 – 18 yrs</td>
<td>65%</td>
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<tr>
<td>19 - 45 yrs</td>
<td>15%</td>
</tr>
<tr>
<td>&gt; 45 yrs</td>
<td>4%</td>
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</tbody>
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A. Valadez MD, DSHS; Perez-Padilla. NEJM 2009.

At High Risk for Disease

- Ages 6 months to 45 years old
- High risk for complications
  - Pregnant women
  - Infants
  - Ages 25 – 64 years old with chronic illness
    - Obesity
    - Pulmonary disease

www.cdc.gov/h1n1

Hospitalized Patients in Mexico

Admitted to Natl Institute Resp Diseases
March 24 – April 24, 2009

- 18 cases of confirmed novel H1N1
  - Among 98 cases ARI admitted
- All had: fever, cough, dyspnea,
  - inc. LDH, bilateral patchy pneumonia
  - 60% - inc. CK and lymphopenia
- 12 required mechanical ventilation; 7 died

Perez-Padilla. NEJM August 2009

ICU patients in Michigan

- Limited series of 10 pts from Michigan
- Respiratory failure due to primary pneumonia
- Only 3 had traditional risk factors for influenza complications
  - All mechanical ventilation - 2 ECMO
  - 9/10 patients obese
  - 5/10 had pulmonary emboli
  - 9/10 multi-organ dysfunction
  - 3 died

MMWR, July 10, 2009
ICU Patients in Canada

- 168 pts in 38 adult and pediatric ICUs
- Mean age – 32 yo; 30% children
- Overall MR – 17%
- Median LOS ICU – 12 days
- Lung rescue therapies:
  - NM blockade
  - Nitric oxide
  - HFOV, ECMO

Kumar, JAMA 2009

Collection of Specimen

http://content.nejm.org/cgi/content/full/NEJM0903992/DC1

Photo courtesy of Kathy Lawless

Diagnosis

- Rapid diagnostic test
  - Low sensitivity (40-70%)
  - Specificity varies by season
- RT-PCR, rRT-PCR
- Recommended method for timely confirmation
- Has not been routinely available
- Immunofluorescence (DFA, IFA)
- Viral Culture – gold standard
- Not timely
- Serology – requires paired sera

Rapid Influenza Tests

Algorithm to assist in the interpretation of RIDT results during periods when influenza viruses are circulating in the community

http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm

Priority Testing for PCR Confirmation at UHS

- Priority 1
  - UHS patients hospitalized with influenza
  - Symptomatic UHS health care providers
  - UHS infection control/public health interest
- Priority 2
  - Symptomatic high risk UHS outpatients
- Priority 3
  - Other symptomatic UHS outpatients
  - Select client patients of high infection control/public health interest – VA, UTHSCSA

K. Fiebelkorn, MD

Who to Treat?

- Uncomplicated febrile illness, mild symptoms
  - Therapy may not required – Use clinical judgment
- Treat
  - Hospitalized patients or those with severe illness
  - Clinical deterioriation
  - Those at high risk for complications
    » Pregnant women
    » < 5 years old
    » Chronic underlying illnesses
    » Immunocompromised

http://www.cdc.gov/h1n1flu/recommendations.htm
Antiviral Therapy for Influenza

- Neuraminidase inhibitors
  - Oseltamivir (Tamiflu®)
    - tablet, suspension – EUA < 1 yo
  - Zanamivir (Relenza®)
    - orally inhaled powder
    - Peramivir IV - EUA
- Adamantines
  - Rimantidine, Amantidine

Antiviral Resistance, 2008-9

<table>
<thead>
<tr>
<th>Strain</th>
<th>Oseltamivir</th>
<th>Zanamivir</th>
<th>Rimantidine</th>
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<tbody>
<tr>
<td>Influenza A</td>
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<td></td>
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<tr>
<td>Novel H1N1</td>
<td>S</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>Seasonal H1N1</td>
<td>R</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>H3N2</td>
<td>S</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>Influenza B</td>
<td>S</td>
<td>S</td>
<td>R</td>
</tr>
</tbody>
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- During winter season, may need combination therapy for those severely ill
- Seasonal vaccination important

IV Peramivir

- Pediatric patients for whom an IV agent is clinically appropriate because:
  - patient not responding to either oral or inhaled antiviral therapy, or
  - drug delivery by a route other than IV (e.g. enteral oseltamivir or inhaled zanamivir) is not expected to be dependable or is not feasible

Post-exposure Chemoprophylaxis

- For close contact with
  - Confirmed, suspected or probable case of novel H1N1
  - Contacts at high risk of complications or health care workers
- Duration – 10 days after last exposure
  - Once daily
What can the community do?

Effect of Public Health Measures on the 1918 Epidemic

Influenza Pandemic, 1918

“Obey the law and wear the gauze
Protect your jaws from septic paws.”

Social Distancing as a Control Measure

Randolph, Miller & Patterson, 2007

Public Health Measures for Novel H1N1

- School closures not recommended
- Emphasize hand hygiene and respiratory etiquette
- Work and school exclusion while sick

What can our institutions do?
HIGH AWARENESS OF INFLUENZA OUTBREAK
Veterans, if you are feeling any of these symptoms:

- Fever over 100.4 degrees
- Fatigue and body aches
- Weakness
- Cough/Concentration
- Nausea/Vomiting

Do the following:
- Use a mask
- Use hand sanitizers located on the walls
- and go to the Emergency Room

VISITORS: For your protection and that of our patients, DO NOT enter this facility if you have any of the symptoms listed above. Contact your health care provider.

For questions or concerns, call the CDC National Hotline 1-800-232-4636.

Recommendations for Seasonal Influenza Vaccination

- All persons > 50 years old
- All children 6 months – 18 years of age
- Persons 19-49 years of age
  - Pregnant
  - Chronic illnesses
  - Household contacts of high-risk groups
- Health care workers

ACIP. MMWR 2008

CDC Recommendations for Novel H1N1 Vaccine Priority

- Pregnant women
- Caregivers for children <6 months
- Healthcare workers
- All people from 6 months through 24 years of age
- Persons aged 25 to 64 years with chronic illness

http://www.cdc.gov/h1n1flu/vaccination/acip

Respiratory Etiquette

http://www.youtube.com/watch?v=YgnNRmx7L7U

Infection Control
Hospitalized Patient

- Droplet & Contact Precautions
- Surgical mask or N95 respirator
  - surgical mask likely adequate
- Airborne isolation room with negative pressure air handling, if available
  - Or single patient room with door closed
- For aerosolizing procedures (suctioning, bronchoscopy, intubation)
  - Use N95 mask and room with negative pressure air handling

http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm

Pandemic Preparedness Ethics

- Priority for treatment
- Priority for chemoprophylaxis
  - WHO guideline
  - High, moderate, low risk
- Triage for mechanical ventilation
  - Guideline Development Group
    - DSHS, ID, Critical Care, Emergency Med MDs
  - 3 tiers for triage
SARS 2003

Employee and Visitor Screening

Station #1: Completion of Quick Flu Screening Cards

What can you do?

Health Care Worker Preparedness

- Get vaccinated
  - Seasonal in September
  - Novel H1N1 in October (November)
- Hand hygiene
- Know the treatment and prophylaxis guidelines
- Vaccinate your patients
- Stay home if ill
- Educate pts about staying home if ill

Infection Control
Non-Hospitalized Patient

- Self-isolate until afebrile X 24 hours
- If health care worker
  - 7 days or until afebrile X 24 hours – whichever longer
- Frequent hand hygiene
  - Pt and household contacts
- Respiratory hygiene

http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm
Additional and Updated Information

- [www.cdc.gov/h1n1](http://www.cdc.gov/h1n1)
- [www.texasflu.org](http://www.texasflu.org)
- [www.who.int/pandemic](http://www.who.int/pandemic)
- [www.flu.gov](http://www.flu.gov)
- [http://fluinfo@uthscsa.edu](http://fluinfo@uthscsa.edu)