Clinical Aspects of Pandemic H1N1 Influenza

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Finally a new flu pandemic!

- Spring of 2009, Mexico and SW USA
- Unique virus (with a history in pigs)
- Two waves - spring and fall
- Rapid spread. March to June for pandemic declaration
- Moderate virulence
Unusual Features

• Age distribution
  – Children and young adults
  – Age>50 yrs fewer cases than expected

• Severe disease in morbidly obese
It’s all about the virus
Pandemic Influenza Virus H1N1

• Isolated from humans with influenza in March, April 2009.
• All 8 RNA segments sequenced
• H1N1 sequences compared to sequences of other Influenza A isolates stored in the National Center for Biotechnology Information
History of Reassortment Events H1N1
(NEJM 2009;361:115-19.)
Pandemic H1N1 Scorecard

- **Source**
  - Classic swine
  - Eurasian swine
  - Seasonal H3N2
  - Avian, No. America

- **Gene**
  - HA, NP, NS
  - NA, M
  - PB1
  - PB2, PA
YOU GOT IT?

YEAH, TIME TO PAY 'EM BACK FOR "BACON"

IT'S CLEAR

THE TRUE ORIGIN OF THE SWINE FLU
Big Picture in USA
April 2009 - Mar 13, 2010
(CDC, 4/19/10)

- Estimate cases ~ 60 million
- Estimate hospitalizations ~ 270,000
- Estimate deaths ~ 12,270
- Case Fatality Rate 0.048 %
Clinical Features

• Incubation Period: 1.5 to 3 days
• Mild illness (no fever) 8 to 32 % of cases
• Typical: fever, cough, myalgia, headache
  – US and Mexico; diarrhea in 11 to 25%
• Diagnosis: early in season, use epi reports and specific pH1N1 nucleic acid tests
  – later in season, clinical and epi
Course of Typical Cases
University of Delaware

• Median duration of illness 6d (4-9)
• Hospitalized 1.1%
• Missed work/class 60.6%
• Median days missed 2 (1-3)
• Visited HCP 59.4%
• Received OST 33.2%
• Ref. CID 2009:49, 1811-19.
The other end of the spectrum

- pH1 N1 has an affinity for pulmonary tissue
- Principal illness is diffuse viral pneumonia with severe hypoxia and ARDS
  - accounts for 49 to 72% of ICU admissions
- Rapid progression. 4-5 d after onset
- Bacterial infection ~20%. *S.pneumoniae*, *S.aureus* (MRSA), *S. pyogenes*
Radiographs and Laboratory

- **CXR**: mixed interstitial and alveolar infiltrates
- **CT of chest**: Areas of “ground glass” opacities, air bronchograms
- **WBC**: normal or low with lymphopenia.
- **Chem**: increased ALT/AST, LDH, CK
Hospitalized Cases, USA

NEJM 2009: 361,1935-44

- 272 cases,
- 25% admitted to ICU, 7% died
- 45% children (< 18yrs), 5% 65 yrs or older
- 73% at least 1 underlying condition
  - Asthma, diabetes, lung condition, neurologic disease, pregnancy
- 26% were morbidly obese (5% in gen pop)
- 7% pregnant (1% in gen pop)
Hospitalized Cases, USA cont.

- Onset to hospitalization median 3 days
- 19 deaths. All in ICU and on vents
- Median age 26 yrs, range 1.3 to 57
- Median time onset to death 15 days
- Treatment: 75% antiviral but only 39% within 48hrs of onset. 79% antibiotic.
Fatal pH1N1 Influenza, NYC
(CID 2009:50, 1498-1504.)

• 47 fatalities, NYC, spring 2009
• Age: 60% 18-49 yrs, 30% 50-64 yrs
• Median time onset to death: 9 days (1-44)
• Pulmonary infection leading cause of death. 50% ARDS, 45% renal failure
• 79% underlying diseases, 57% >1 underlying disease
• 58% obese or morbidly obese
Pandemic Flu in Pregnancy, USA
JAMA 2010;303:1517-24

- 788 proven cases in pregnant women, April to August, 2009
- 509 (65%) hospitalized
- 30 deaths, CFR 3.8%
- Flu occurs in all trimesters but 90% in 2\textsuperscript{nd} and 3\textsuperscript{rd}
- 50% underlying disease
  - Asthma 23%, obesity 13%, diabetes 3.9%
Pandemic Flu in Pregnancy, US cont.

- 10 of the 30 fatal cases had asthma
- Trimester matters. 60% of deaths in 3rd trimester, 30% in 2nd, 10% in 1st.
- Oseltamivir matters if given early
  - <2 days after onset only 1 of 219 died
  - >4 days after onset 20 of 81 died (25%)
Pediatric Hospitalizations, Argentina
NEJM 2010:362;45-55

• 251 cases, 6 public hosp in Buenos Aires
• Hosp rate 20.9 per 100,000. Twice rate for seasonal flu.
• 75% < 2yrs and 60%<1 yr.
• 32% had pre existing illness
• 82% were hypoxic on admission and 20%admitted to ICU for mech vent
• 13 (5%) deaths. 62% from refractory hypoxia
Number of Influenza-Associated Pediatric Deaths by Week of Death:
2006-07 season to present

- 2006-07: Number of Deaths Reported = 77
- 2007-08: Number of Deaths Reported = 88
- 2008-09: Number of Deaths Reported = 134
- 2009-10: Number of Deaths Reported = 276

Legend:
- Yellow: 2009 Influenza A (H1N1) Deaths Reported Current Week
- Light Blue: Other Influenza Deaths Reported Current Week
- Purple: 2009 Influenza A (H1N1) Deaths Reported Previous Weeks
- Green: Other Influenza Deaths Reported Previous Weeks
Antiviral Treatment

• Two drugs; oseltamivir and zanamivir
• Resistance not a problem…. yet!
• Oseltamivir efficacious if given early
  – Early is <48 hrs of symptom onset
  – Sooner is better
• Adult dose: 75 mg po, BID for 5 days
  – Can increase (150mg) dose or duration as needed
Antiviral Treatment, cont.

• Children: => 1 year
  – 15 kg or less: 30mg BID for 5 days
  – 16-23 kg: 45mg BID for 5 days
  – 24-40kg: 60mg BID for 5 days
  – >40kg: 75 mg BID for 5 days

• Children < 1 year
  – <3 mo: 12mg BID, 5 days
  – 3-5 months: 20 mg BID, 5 days
  – 6-12 months: 25 mg BID, 5 days
Zanamivir

- Inhaled route of administration
- Adult dose: Two 5mg inhalations BID, 5d
- Children: Age 7yrs or > same as adults
- Intra venous preparation in development
  - Case reports of success with oseltamivir failure.
When to treat, who to treat

• Treat early in the infection
  – Rely on clinical and epidemiologic data
  – Do not wait for laboratory confirmation

• Treat patients with known risk factors
  – Asthma, obesity, pregnant, pulmonary, cardiac, diabetes, neurologic, diabetes
  – Patients who are sicker than you expect
Oseltamivir Resistance

- Infrequent but increased as pandemic progressed. 3 isolates in July ’09, 299 isolates in June ‘10
- Due to a single mutation, H275Y
- Not due to drug use
- Clusters among immunosuppressed
- Good news: ost resistant are susceptible to zanamivir
Action!

• Vaccinate
  – Especially kids, pregnant women, asthmatics, obese, COPD, neurologic, seniors

• Treat early. Do not wait for lab confirmation.

• Refer quickly if sicker than expected
One paper to read.

• Clinical Aspects of Pandemic 2009 Influenza A (H1 N1) Virus Infection
  – Writing Committee of WHO
• NEJM 2010:362; 1707-19
• Available free on line at www.nejm.org
  – Past issues>may 2010>issue 18
Epidemiologic Information

• cdc.gov click on diseases>seasonal>flu weekly

• azdhs.gov click on public health services>flu information