

Clinical Aspects of Pandemic H1N1 Influenza

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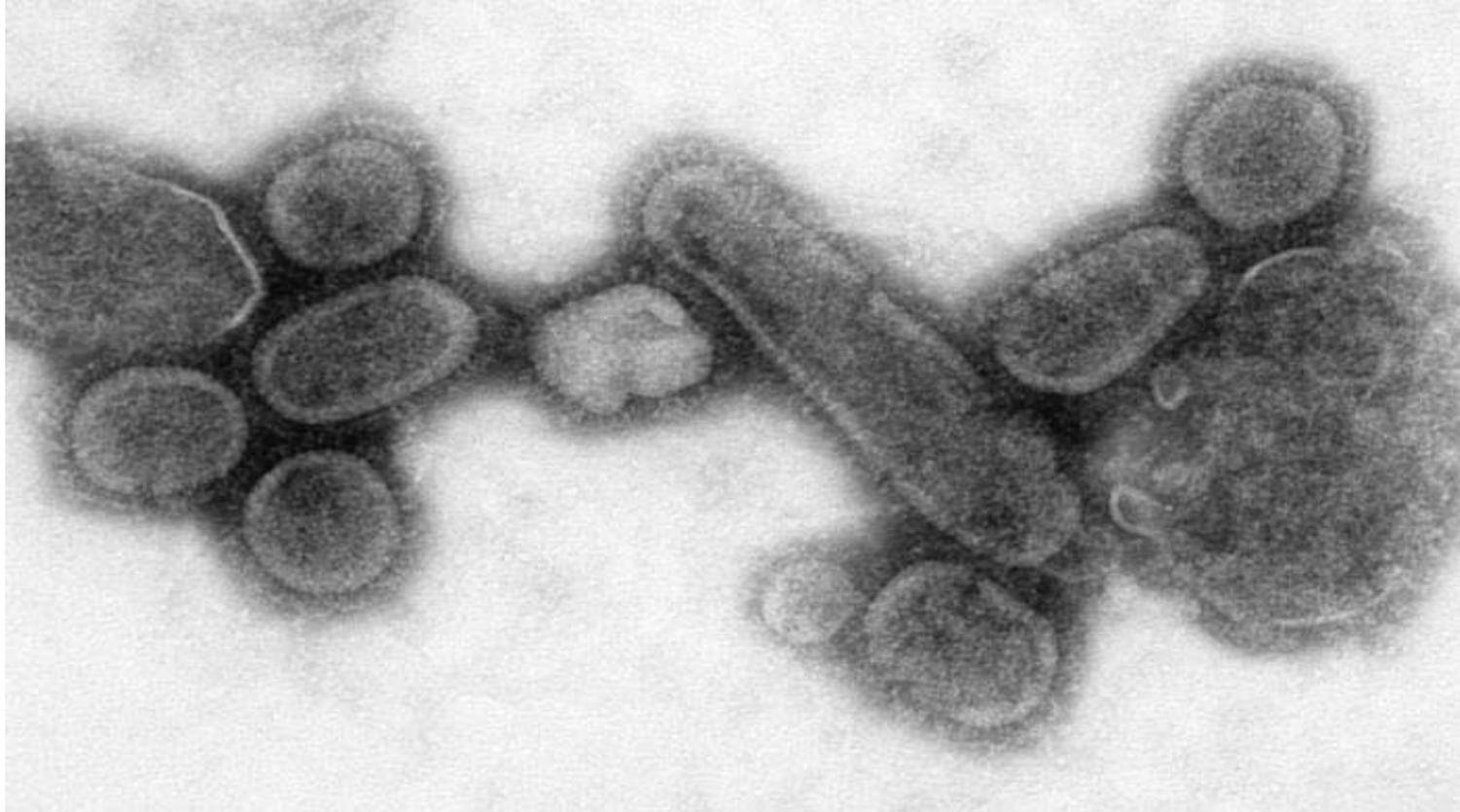
Finally a new flu pandemic !

- 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

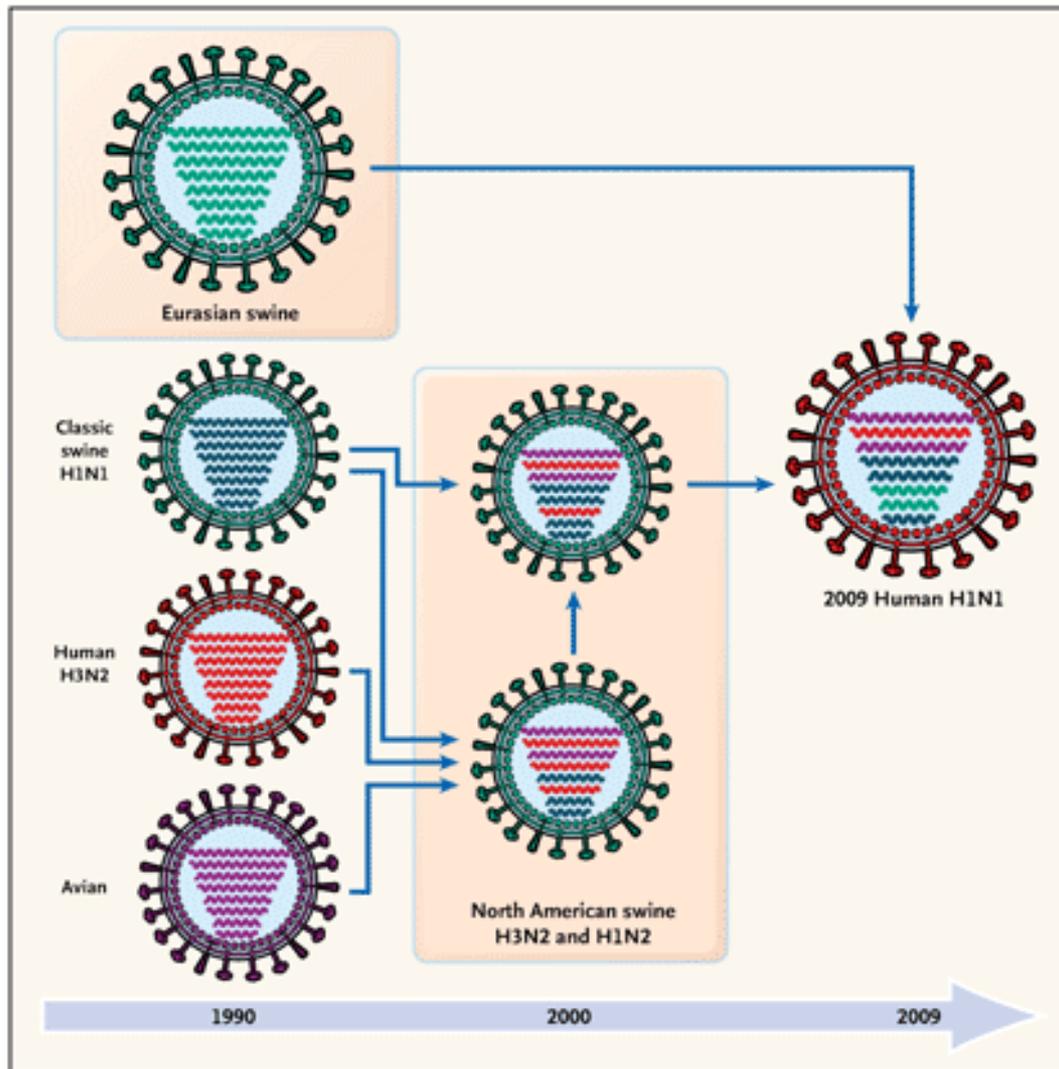


Pandemic Influenza Virus H1N1

- 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 | Gene |
|----------------------|-------------|
| • Classic swine | HA, NP, NS |
| • Eurasian swine | NA, M |
| • Seasonal H3N2 | PB1 |
| • Avian, No. America | PB2, PA |



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

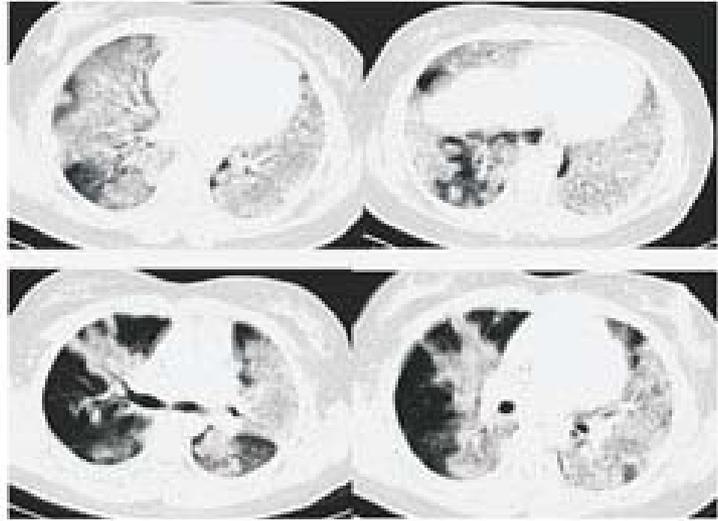
- Median duration of illness 6d (4-9)
- Hospitalized 1.1%
- Missed work/class 60.6%
- Median days missed 2 (1-3)
- Visited HCP 59.4%
- Received OST 33.2%
- Ref. CID 2009:49, 1811-19.

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



A



B



C



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 2nd and 3rd
- 50% underlying disease
 - Asthma 23%, obesity 13%, diabetes 3.9%

Pandemic Flu in Pregnancy, US cont.

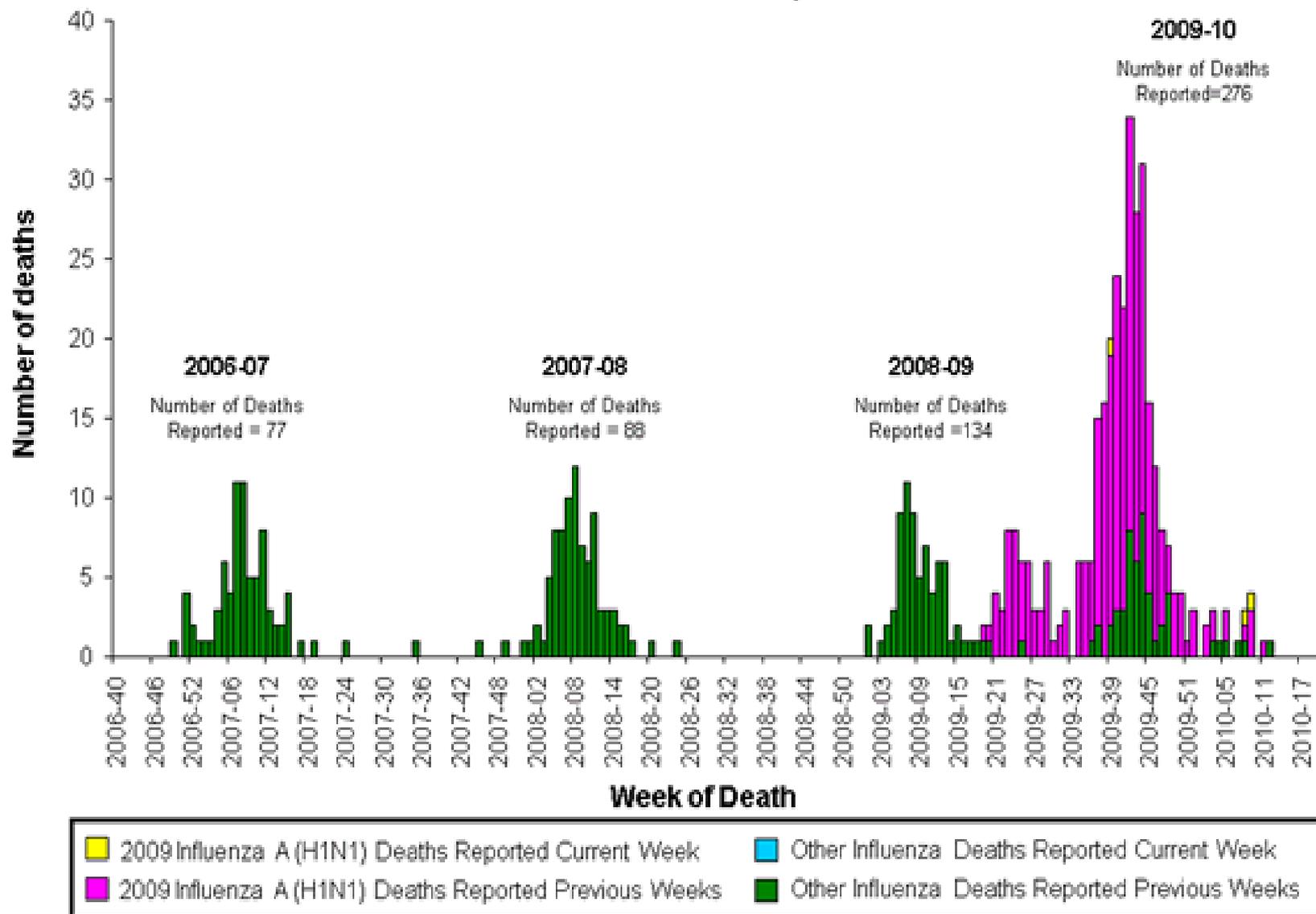
- 10 of the 30 fatal cases had asthma
- Trimester matters. 60% of deaths in 3rd
30% in 2nd, 10% in 1st.
- Oseltamivir matters if given early
 - <2days after onset only 1 of 219 died
 - >4days after onset 20 of 81 died (25%)

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



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: \Rightarrow 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
 - >40 kg: 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