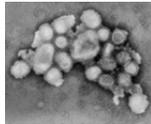


# INFLUENZA (H1N1) UPDATE



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## Roadmap

- ▶ **Background of Influenza**
- ▶ Molecular characteristics H1N1
- ▶ Transmission
- ▶ H1N1 epidemiology in Southern California
- ▶ Diagnosis and Reporting
- ▶ Treatment and prophylaxis
- ▶ Public Health Control Measures

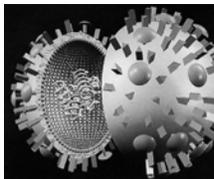


## BACKGROUND: HUMAN INFLUENZA

- ▶ 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 factors
- ▶ 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



## INFLUENZA A VIRUSES: ANTIGENIC "SHIFT"

- ▶ 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 20<sup>TH</sup> CENTURY



Credit: US National Museum of Health and Medicine

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

**1957: "Asian Flu"**  
A(H2N2)  
1-4 million deaths worldwide  
70,000 US deaths

**1968: "Hong Kong Flu"**  
A(H3N2)  
1-4 m deaths worldwide  
34,000 US deaths



## Pandemic (H1N1) 2009

- ▶ Novel Influenza A (H1N1) Declarations
  - ✓ USG: Public Health Emergency (4/26/2009)
  - ✓ WHO: Jump from Pandemic Phase 3 to phase 5 by 4/29/2009
  - ✓ WHO: Pandemic Phase 6 (6/11/2009)



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- ▶ Public Health Control Measures

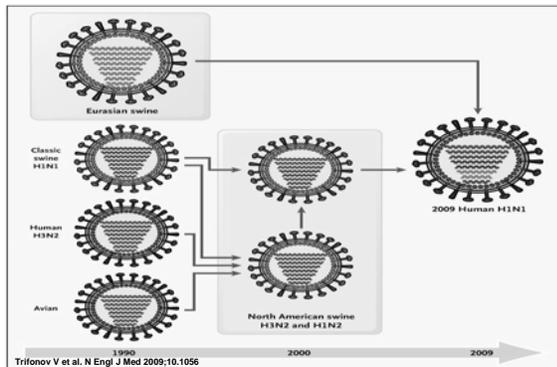


## New Subtype

- ▶ **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



## IMMUNITY

- ▶ 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



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## Influenza Virus Transmission

**Aerosol/Droplet**



GETTY IMAGES

**Fomites**



GETTY IMAGES



## 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])

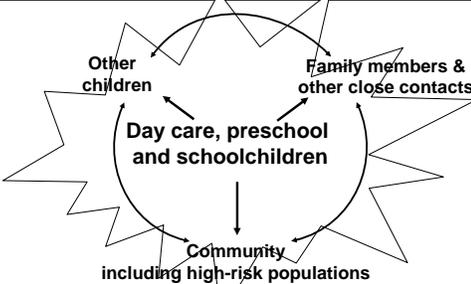


## Transmission

- ▶ 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  $\geq 10$  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



Adapted from: Elveback LR, et al. *Am J Epidemiol.* 1976;103:152-165.







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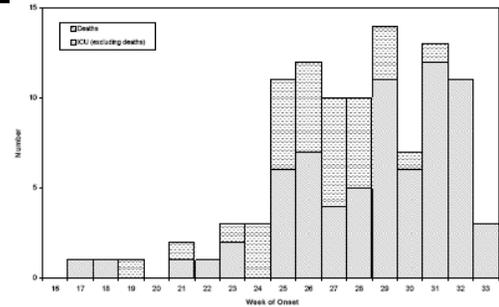
### Swine Influenza A (H1N1) Infection in Two Children – Southern California, March–April 2009

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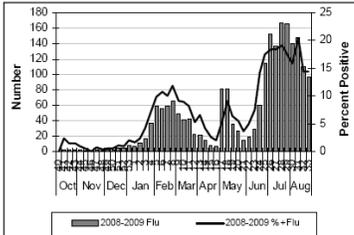


### Epi Curve of Severe Influenza in LAC as of 8/26/2009



### Not Just a Testing Artifact

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



### 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

Age category, in years	HOSPITALIZED AND/OR FATAL CASES <sup>1</sup>		
	Number of cases	Cumulative number of cases	Incidence per 100,000 population
<1	92	92	16.15
1-4	118	210	5.34
5-18	283	493	3.74
19-24	183	676	5.28
25-35	260	936	4.42
36-49	237	1173	2.96
50-64	269	1442	4.02
65+	86	1528	1.97
<b>ALL AGES</b>	<b>1528</b>		<b>3.94</b>

<sup>1</sup>Includes the following individuals: (1) non-fatal hospitalized cases, (2) fatal hospitalized cases, (3) fatal non-hospitalized cases

Rate per 100,000

Age (years)



### Risk Factors for Severe Illness with H1N1

	Age Group	Cardiac	Pulmonary	Metabolic Disorder	Developmental	Immuno-suppression
Deaths	<18	20%	0%	0%	80%	40%
	18+	31%	24%	31%	10%	10%
	All Ages	29%	24%	26%	21%	15%
ICU	<18	21%	47%	5%	37%	5%
	18+	8%	18%	22%	3%	11%
	All Ages	13%	29%	16%	15%	11%
Hospitalized	<18	3%	29%	8%	12%	8%
	18+	14%	16%	16%	4%	11%
	All Ages	9%	22%	12%	8%	8%



### 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

### BMI (ICU/Deaths >= 2years)

Mean	36
Median	33
Range	19-77

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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## Diagnostic Specimens (1)

- ▶ 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

CID 2009;48



## 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

CID 2009;48



## SENSITIVITY\* OF RAPID ANTIGEN DETECTION TESTS

2008-9 Seasonal Influenza type	BinaxNOW A&B	Quidel Quickvue	Directigen EZ Flu
A H3N2	60-80	60-80	60-80
A H1N1	80-83	80-83	80-83
Novel H1N1 High titer	89-100	89-100	89-100
Novel H1N1 Low Titer	40	69	49

\*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



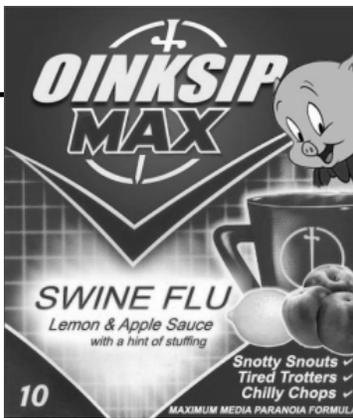
## Current Priorities for Testing for Novel H1N1

- ▶ Influenza-like illness (fever  $\geq 100$  °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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- ▶ **Public Health Control Measures**



## IMPACT 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](http://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, fuel supply, food production, distribution and transport, prisons, education and business

[www.dh.gov.uk/pandemicflu](http://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)



From the Stone Negative Collection, Rochester Museum & Science Center, Rochester, N.Y.  
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?

