Novel Influenza A H1N1 Update

Dan Jernigan, MD MPH
Deputy Director
Influenza Division
National Center for Immunization and Respiratory Diseases

www.cdc.gov/H1N1flu
Objectives

- Describe the initial detection of the novel H1N1
- Give an update of current status
- Discuss issues around test development and use

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Increasing Detection of Swine Flu

- Increasing numbers of swine influenza cases being detected over past five years from improved surveillance – Shinde, NEJM 2009
- Increasing efforts at states, CDC, and USDA to investigate human cases of swine influenza
- Limited secondary transmission

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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).

- Southern California, 2009 - *MMWR 58(15);400-02*
  - April 13 – 10 yo boy, recovered
  - April 17 – 9 yo girl, recovered
- Exposure to swine unknown
- Surveillance showed no other unsubtypeable influenza A PCR results
Detection of First Case

- Mesoscale device used to diagnose influenza in 10 year old boy during clinical trial run by Naval Health Research Center (NHRC) in San Diego on April 1, 2009
- Result is influenza A positive, however, H1, H3, H5 negative
Detection of First Case

- San Diego public health notified
- Recommends sending specimen on to designated reference laboratory in Wisconsin as part of the clinical trial
“Unsubtypable” confirmed by reference laboratory and by designated State Public Health Laboratory using FDA-cleared 5 Target PCR.
Specimen tested at CDC
Identified as a novel H1N1 Swine, triple reassortant, where are the infected swine?
Novel case reported to WHO…end of story?
1. Patient 1  
2. Patient 2  
3. Recognition of potential match between Mexico and US viruses  
4. US declares a public health emergency  
5. WHO raises to Pandemic Phase 4  
6. WHO raises to Pandemic Phase 5

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Origin of “Swine-Origin” H1N1
Garten et al
Science, 2009
Response to H1N1

- Strategic National Stockpile
  - Distributed 25% pro rata supply
- Enhanced Surveillance Initiated
- PCR panH1N1 kits for testing
  - Development at CDC, EUA at FDA, manufacture at ATCC, and ready to ship in ~ 2.5 weeks
- Distributed Kits, so far:
  - Domestic: 95 labs
  - DOD: 15 labs
  - International: >250 labs in 140 countries
- Virus Characterization
  - >1000 genes sequenced from >260 viruses
  - Submitted to GenBank

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H1N1 Current Status

- Lab-Confirmed Cases
  - 44,317 total cases when reporting stopped in July
  - As of August 28, 2009
    - 8,842 hospitalized
    - 555 deaths
- Represents approximately 3 M cases
- Overall activity has declined since schools closed, but focal areas of activity have increased
- Viruses in US and Internationally show no evidence of significant genetic/antigenic change
Percentage of Visits for Influenza-like Illness (ILI) Reported by the US Outpatient Influenza-like Illness Surveillance Network (ILINet), novel 2009-H1N1 – 01 SEP 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)

NOT FOR FURTHER DISTRIBUTION
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 – 01 SEP 2009

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Teens and young adults disproportionately affected
Few cases among elderly

Seasonal 2007-08

- 0-4 yrs
- 5-9 yrs
- 10-17 yrs
- 18-49 yrs
- 50-64 yrs
- 65+ yrs

N=3,930

2009 H1N1 (April - Jun)

- 0-4 yrs
- 5-9 yrs
- 10-17 yrs
- 18-49 yrs
- 50-64 yrs
- 65+ yrs

N=312

*April 12-June 30

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Testing for 2009 H1N1

- Pandemic preparedness included diagnostic development
  - PCR for influenza at CDC
  - Point of Care devices through HHS-CDC contracts
- Pandemic preparedness included support
  - Public Health Laboratory staff
  - Equipment
  - Reagents
- New tests developed
  - EUA for Focus Diagnostics
  - LDTs for H1N1
PCR Assay
Lindstrom et al

- FDA cleared in September 2008 with special controls
- Five targets (A, B, H1, H3, H5)
  - All targets maintaining high sensitivity, specificity
- Reagents distributed from CDC to qualified laboratories

Sept 2008

AB 7500 Fast DX RT-PCR
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Lindstrom et al

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Sept 2008

- FDA grants Emergency Use Authorization
- New targets: Influenza A (swine) and H1 (swine)
  - All targets maintaining high sensitivity, specificity
- Reagents distributed from CDC to qualified laboratories
- Qualified laboratories asked to verify accurate testing with 5 known positive specimens
- Protocol published at WHO website

May 2009
PCR Assay
Lindstrom et al

CDC 5 Target PCR

AB 7500 Fast DX RT-PCR

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2009/2010 Potential
- ? Submission of additional targets for 510K
- ? Submission of EUA/510K for additional platforms
Reagents distributed by CDC’s Influenza Reagent Resource under contract with ATCC, www.influenzareagentresource.org

Orders available through fluorder@cdc.gov

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Point of Care: Mesoscale Diagnostics

- Detects A, B, H1, H3, H5 antigens
- Hands-off 15 min test
- Reader controls reagents, fluidics, detection, results
- Clinical trials underway
- Seeking EUA for use this fall
- CLIA complexity determination?

Monoclonal antibodies detect antigen with electrochemiluminescence
Rapid Influenza Diagnostic Tests

- Nine FDA-Approved Rapid Influenza Diagnostic Tests
- Evaluated seven RIDTs compared to PCR
  - Sensitivity ranged 18-69%
- Interpretation
  - Positive results = flu likely in specimen
  - Negative results = cannot rule out flu
    - Caution with cohorting or return to settings where transmission is a concern
Antiviral Resistance

- Oseltamivir Resistance in US
  - H1N1 seasonal – 99.6% (1123/1128)
  - H3N2 – 0% (0/222)
  - B – 0% (0/635)
  - H1N1 novel – 0.6% (7/1117)

- Zanamivir Resistance
  - None reported for all subtypes/types

- Capacity for antiviral resistance testing is limited
  - Pyrosequencing: plan to expand at PHLs
  - Functional testing: difficult/costly to perform
Observations

- FDA Approval of CDC 5 Target Test
  - Costly to develop, to clear, and to maintain
  - Allowed for standard quality, rapid distribution
- EUA for swine primers
  - Easier to implement because of 5 target clearance
  - Allowed distribution to qualified laboratories
  - Ends when emergency ends
- WHO web posting of swine PCR protocol
  - Allowed for rapid increase in detection of 2009 H1N1
  - Led to laboratory developed tests
  - Distributed testing helps with surge, hard to verify accuracy
- Antiviral testing needs greater availability
- Rapid test performance is variable, clear need for POC detection

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Questions?

Dan Jernigan, MD MPH
dbj0@cdc.gov