Influenza and other Respiratory Viruses Update--2015

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Learning Objectives

- Review of the 2013-2014 influenza season.
- Avian influenza
- Emerging diseases impacting community health.
- Review of new point-of-care nucleic acid amplification assays.
- Discuss surveillance strategy for 2015-2016

Influenza

The latest information

www.cdc.gov/flu/index.htm

What We’re Dealing with Now

- Ebola virus
- EV-D68
- MERS CoV
- Dengue fever
- Chikungunya
- Anthrax
- Measles/mumps

... So what’s the big deal with influenza?

The Changeability of Influenza

Antigenic Drift → Seasonal Influenza

Antigenic Drift
Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes

Estimated Annual Burden of Seasonal Influenza in the United States

- Deaths: 3,000 – 49,000
- Hospitalizations: 54,000 – 430,000
- Cases: 15 – 80 M

Direct medical costs: $10.4 billion
Influenza in the U.S. 2014-15

Influenza Positive Tests Reported to CDC by U.S. WHO-NREVSS Collaborating Laboratories, National Summary, 2014-15

So what?

Influenza in WI, 2014-2015

Influenza Type B in Wisconsin, 2014-2015 Season

A Peak (%) was 12/20/14
A Peak (# positives) was 1/3/15

So what?

Influenza 2014-15

What was expected...
- A/Texas/50/2012(H3N2), the vaccine strain

What we got instead...
- A/Switzerland/9715293/2013(H3N2)
  ... a significant antigenic drift!

What were the consequences...
- Vaccine ineffectiveness
- Difficult virus to work with and characterize

Seasonal Influenza Vaccines

How effective?
http://www.cdc.gov/flu/professionals/vaccination/efficacyqa.htm
http://www.cdc.gov/flu/professionals/vaccination/efficacy-studies.htm

Vaccination Rates---2013-14 and 2014-15

General Population

http://www.cdc.gov/flu/professionals/vaccination/

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Vaccination Rates---2013-14 and 2014-15

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http://www.cdc.gov/flu/professionals/vaccination/
Influenza in the U.S. 2014-15

Pneumonia and Influenza Mortality for 122 U.S. Cities
Week Ending August 22, 2015

H3N2  pH1N1  H3N2

Influenza Hospitalizations 2014-15

In contrast, 2013-14

Influenza in the U.S.
Early 2015-2016 Season…

Influenza Positive Tests Reported to CDC by U.S. WHONET Pools
Collaborating Laboratories, Nine Regions, 2014-15

Early 2015-2016 Season…

PH Region  Date Received  Influenza type
S  8/7/2015  Flu A (H3)
S  8/18/2015  Flu A (H3)
NE  8/25/2015  Flu A (H3);  Flu B
S  8/28/2015  Flu A (H3)
S  9/2/2015  Flu A (H3)

… plus several other Flu A (H3) reported by clinical labs, not confirmed by WSLH, in S and SE Regions

The Changeability of Influenza
Antigenic Shift

www.flu.gov

Antigenic Shift
When a new subtype (a novel HA and/or NA) of influenza A emerges in the host (humans)

Influenza at the Human-Animal Interface

Influenza A
• H1 - H17
• N1 - N10

Aquatic birds
Dogs
Pigs
Horses
Cats
Aquatic mammals

Influenza A
• H1 - H17
• N1 - N10

Poultry
Hogs
Pigs
Horses
Antigenic shift

Influenza: Emergence of Novel Flu A Subtypes

- Chickens and turkeys take center stage

Influenza A
- H1 - H17
- N1 – N10

Influenza B
- B/Yam
- B/Vic

Avian Influenza Terminology

- Highly Pathogenic Avian Influenza
- Bird flu
- Pathogenicity refers to avian NOT human
- H5N1, H5N2 and H5N8 are collectively referred to as H5Nx
- H5N2 and H5N8 have both been detected in the US in 2015.

Emergence of Avian Flu (H5)

- Avian Influenza (H5) emerged in North America (November 2014).
- Many flocks in the area were infected by December including those in the US.
Since December 2014, the United States Department of Agriculture has confirmed several cases of highly pathogenic avian influenza (HPAI) H5 in the Pacific, Central, and Mississippi flyways (or migratory bird paths). The disease has been found in wild birds, as well as in a few backyard and commercial poultry farms. The Centers for Disease Control and Prevention (CDC) considers the risk to people from these HPAI H5 infections to be low. No human cases of these HPAI H5 viruses have been detected in the United States, Canada, or internationally.

**Wisconsin:**
- 10 flocks infected
- Almost 2 million infected
- Last detection in May 2015

**H5Nx Diagnostic Testing**
- Most commercial assays will NOT be able to differentiate seasonal viruses from novel strains.
- The WSLH and MHDL have PCR tests that can identify H5Nx strains.
- Preferred specimen are combined NP/OP swab in virus transport medium.
- Testing is performed on WDPH approved specimens.

**Key Points**
- There have been NO human cases.
- CDC considers general risk is low.
- Risk for people handling sick/dead poultry.
- No risk for eating cooked poultry products.
- Symptoms may be atypical. **Patients with illness and close contact should contact their LHD or WDPH epidemiologist for follow-up evaluation.**

**Enterovirus D68**
**Current Situation**
- August 2014 to Jan. 2015 >1,100 EV D68 cases.
- Majority of cases in children with asthma or a history of wheezing.
- 33% tested positive for rhinovirus or another enterovirus.
- Many experienced severe disease.
- No cases reported this season
**Enterovirus D68**

**Background**
- Enteroviruses are very common respiratory viruses (10-15M/year).
- Transmission respiratory route (person-to-person)
- Cause a wide variety of illnesses.
- Sometimes disease can be severe.
- There are no vaccines or antiviral therapeutics.
- Children with asthma are more vulnerable.

**Enterovirus D68**

- Large diversity of enteroviruses circulate seasonally.
- EV D68 has been rare.

**Emerging Disease Threats**

**MERS-Coronavirus**

**Diagnostic Testing**
- Genetically very similar to rhinoviruses.
- Most PCR assays cannot accurately discriminate!
- Some commercial PCR assays may have variable sensitivities for EV D68.
- Testing is limited to cases that are WDPH approved.
- Combined NP/OP is the preferred specimen.
- WSLH is performing Enterovirus PCR on approved specimens.
- Specific EV D68 typing at CDC.
- EUA test will be available should the situation warrant.

http://www.slh.wisc.edu/enterovirus-d68-confirmed-in-wisconsin/
MERS-CoV

What we know!

- Virus is different than SARS-CoV and seasonal coronaviruses.
- First cases in 2012.
- All cases linked to the Arabian Peninsula.
- Virus does not easily transmit from person-to-person.
- Requires close personal contact.
- Genetically stable.
- Bats and camels play a role in host transmission; dynamics not well understood.
- Healthcare workers at higher risk.

Influenza Diagnostic Technology Update

Rapid Influenza Diagnostic Tests (RIDTs)

A perennial discussion

If you are an RIDT user...

- What would the new regulations entail?
  - Reclassifying RIDTs from Class I to Class II
  - Add "special controls" to ensure device safety and effectiveness
  - Set minimum clinical performance criteria for sensitivity and specificity
  - Identify appropriate comparator tests for new assays
  - Accuracy assessed by manufacturers each year and when novel strain emerges

- When will this happen?
- Possible impacts:
  Better tests? Fewer tests?
Rapid Influenza Diagnostic Tests

**The Next Generation**

- Incorporates reader instrument
- Reduces subjectivity
- Improved sensitivity
- CLIA-waved
- Data transmission capabilities
- A step in the right direction

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**Quidel Sofia sites within WI Summer 2014-15**

Temte, et al study, 2015
The power of rapid real-time reporting

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**Rapid Influenza Diagnostic Tests**

**Molecular Results in Minutes!**

- [U.S. Influenza Surveillance](http://www.cdc.gov/flu/weekly)
- CDC periodically updates list
- More and more clinical labs using these
- Literature in general indicates high level of performance
- Concerns:
  - **Detection** of novel influenza A's
  - Variable subtyping capabilities
- CDC

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**Influenza Molecular Tests - PCR**

- Commercially Available - FDA Cleared
- CDC periodically updates list
- More and more clinical labs using these
- Literature in general indicates high level of performance
- Concerns:
  - **Detection** of novel influenza A's
  - Variable subtyping capabilities

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**Wisconsin Labs with Flu PCR Capacity, 2015**

- [U.S. Influenza Surveillance](http://www.cdc.gov/flu/weekly)
- [Virologic Surveillance](http://www.cdc.gov/flu/weekly)
- [Morbidity Surveillance](http://www.cdc.gov/flu/weekly)
- [Mortality Surveillance](http://www.cdc.gov/flu/weekly)
“Right-Sizing” Influenza Virologic Surveillance
The Importance of “Alternative Data”

Alternative data is existing virologic data from non-PHL sources that can be used to supplement PHL data for improved situational awareness

Influenza Virologic Surveillance
Increasing Role for the Clinical Lab

- Provide situational awareness
  - Clinical lab testing data → CDC
- Detect novel or reassortant viruses
- Inform vaccine strain selection
- Detect and monitor antiviral resistance
  - Specimens/isolates → WSLH → CDC from clinical labs

Laboratory Surveillance Plan, 2015-2016
What YOU need to know!

Influenza Surveillance in Wisconsin
Multi-element approach
1. Rapid Influenza Diagnostic Testing (RIDT) Sites
   - >50% of Influenza testing in WI.
   - Confirmatory testing during periods of low prevalence!

WSLH can provide confirmatory testing for out-of-season positives and the first two positive influenza A and influenza B specimens.

Influenza Surveillance in Wisconsin
Multi-element approach
2. Enrolled Surveillance Sites
   - 18 labs in 5 public health regions.
   - Provide randomized specimens weekly.

Request to continue to submit the first 3 specimens per week with influenza test requests to WSLH.

Influenza Surveillance in Wisconsin
Multi-element approach
3. PCR Labs
   - “Gold Standard” testing.
   - Provide weekly testing data summary reports.
   - 48 WI PCR labs!

Request to report both the number positive and the number tested weekly.
**Send Flu A unsubtypable specimens when subtyping for both 2009 H1N1 and seasonal H3 were attempted (Ct<35).**
Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing

**All Labs:**
- Send those with international travel histories
- **Sampling** of influenza-related hospitalizations
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure

Other Pathogens of Public Health Importance to Report

- B. pertussis/ parapertussis
- RSV
- Non-influenza respiratory viruses
- Grp A Strep
- VZV
- Rotavirus
- **NEW!** Gastropathogen PCR

Reporting Lab Results

There are two options.....

1. Web-based reporting
   ![Web-based reporting](http://example.com)

2. FAX reporting
   ![FAX reporting](http://example.com)

What is the WSLH able to provide to support participating labs?

- Specimen collection supplies.
- Specimen shippers & packaging supplies.
- NO cost specimen transport.
- Influenza confirmatory testing.
- Influenza PCR validation specimen panel.
- Weekly updated surveillance data (B. pertussis, Influenza, RSV & others).
- Laboratory Surveillance Reports

Educational Opportunities

WCLN Regional Meeting (2015)
- Laboratory preparedness and biosafety
- P.A.C.E® approved.

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<tr>
<td>Kimberly, WI</td>
<td>Oct. 14</td>
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<tr>
<td>Wisconsin Dells, WI</td>
<td>Oct. 16</td>
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Your participation in the Wisconsin surveillance system is **vital** to monitor for emerging novel strains with pandemic potential and other pathogens that impact community health.
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