Influenza and other Respiratory Viruses Update--2017

Pete Shult, PhD
CDD Director & Emergency Laboratory Response

and

Erik Reisdorf, MPH, M(ASCP)CM
Surveillance and Virology Lab-Team Lead
Learning Objectives

- Review of influenza basics
- Review of the 2016-2017 influenza season.
- Influenza A H7N9 and “variant” virus update.
- RIDT update.
- Discuss surveillance strategy for 2017-2018
Influenza

The latest information

www.cdc.gov/flu/index.htm
Antigenic Drift
Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes

1. Each year’s flu vaccine contains three flu strains — two A strains and one B strain — that can change from year to year.
2. After vaccination, your body produces infection-fighting antibodies against the three flu strains in the vaccine.
3. If you are exposed to any of the three flu strains during the flu season, the antibodies will latch onto the virus’s HA antigens, preventing the flu virus from attaching to healthy cells and infecting them.
4. Influenza virus genes, made of RNA, are more prone to mutations than genes made of DNA.
5. If the HA gene changes, so can the antigen that it encodes, causing it to change shape.
6. If the HA antigen changes shape, antibodies that normally would match up to it no longer can, allowing the newly mutated virus to infect the body’s cells.

This type of genetic mutation is called “ANTIGENIC DRIFT.”

www.flu.gov
Seasonal Influenza-Related Morbidity and Mortality

P-I Mortality

ARD Hospitalizations

Medically Attended Illness

Estimated Annual Burden of Seasonal Influenza in the United States

- Deaths: 12,000 – 56,000 since 2010
- Hospitalizations: 140,000 – 710,000
- Cases: 15 – 60 M

Direct medical costs: $10.4 billion
Influenza in the US: 2016-17

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, 2016-2017 Season

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, 2016–2017 Season
Influenza in WI, 2016-2017

Influenza Type (%) Wisconsin, 2016-2017 Season

- 35% Influenza A
- 65% Influenza B

Influenza Subtype (%) Wisconsin, 2016-2017 Season

- 94% Influenza A H3
- 6% Influenza A H1
- 1% Influenza A H2

% Positive for Influenza by PCR (Wisconsin), Week 2015-2016 & 2016-2017 Seasons

- Blue: No. Positive for Influenza A
- Green: No. Positive for Influenza B
- Black: % Positive for Influenza by PCR
Influenza in the U.S. 2016-17
Number of Influenza-Associated Pediatric Deaths by Week of Death: 2013-2014 season to present

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of Deaths Reported</th>
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<tbody>
<tr>
<td>2013-2014</td>
<td>111</td>
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<tr>
<td>2014-2015</td>
<td>148</td>
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<tr>
<td>2015-2016</td>
<td>92</td>
</tr>
<tr>
<td>2016-2017</td>
<td>105</td>
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</table>

Week of Death

- Green: Deaths Reported Previous Week
- Blue: Deaths Reported Current Week
Influenza Hospitalizations

The Influenza Hospitalization Surveillance Network (FluSurv-NET) conducts population-based surveillance for laboratory-confirmed influenza-associated hospitalizations in children (persons younger than 19 years) and adults. The current network covers 70 counties in the 10 Emerging Infections Program (EIP) states (CA, CO, CT, GA, MD, MN, NY, OR, and TN) and three additional states (MI, UT). The network represents approximately 9% of US population (~21 million people). Cases are identified by reviewing hospital, laboratory, and admission databases and infection control logs for hospitalization during the influenza season with a documented positive influenza test (i.e., viral culture, direct/indirect fluorescent antibody assay (DFA/FIA), rapid influenza diagnostic test (RIDT), or molecular assays including reverse transcription-polymerase-chain reaction (RT-PCR)). Data gathered are used to estimate age-specific hospitalization rates on a weekly basis, and describe characteristics of hospitalizations with associated influenza illness. Laboratory-confirmation is dependent on clinician-ordered influenza testing. Therefore, the unadjusted rates provided are likely to be underestimated as influenza-associated hospitalizations can be missed if influenza is not suspected and tested for. FluSurv-NET hospitalization data are preliminary and subject to change as more data become available. Incidence rates are unadjusted. Please use the following citation when referencing these data: “FluView: Influenza hospitalization Surveillance Network, Centers for Disease Control and Prevention.” Accessed on DATE.
Influenza 2016-17

What was expected...
- A/Hong Kong/4801/2014(H3N2)
- A/California/7/2009
- B/Phuket/3073/2013 (B/Yamagata-lineage)
- B/Brisbane/60/2008 (B/Victoria-lineage)

... and that’s what we got😊
Antigenic Shift
When a new subtype (a novel HA and/or NA) of influenza A emerges in the host (humans)
Infectious Diseases at the Human-Animal Interface

Influenza as an Example
Influenza at the Human-Animal Interface

Influenza A
- H1 - H18
- N1 – N11

Aquatic birds

Poultry
Humans
Pigs
Horses
Aquatic mammals
Cats
Dogs

WISCONSIN STATE LABORATORY OF HYGIENE - UNIVERSITY OF WISCONSIN
Timeline of Pandemic Influenza A Viruses in Humans

Type A


- H1
- H2
- H3

2009 H1pdm A

Timeline includes outbreaks of different subtypes of influenza A viruses, with a significant focus on the 2009 H1pdm A pandemic.
Timeline of Other Emergent Influenza A Viruses in Humans

Type A

- Swine H3
- Swine H1
- Avian H9
- Avian H7
- Avian H5

2009 H1pdm A

This suggests that the virus has spread, and emphasizes that further intensive surveillance and control measures in both the human and animal health sector remain crucial (WHO Risk Assessment, 2017)
FIGURE A: 2016-2017

FIGURE B: 2013-2016

MMWR
Why Avian Influenza A (H7N9)?

- 5th epidemic mutations detected
  - **Highly Pathogenic Avian Influenza (HPAI);** Refers to avian species pathogenicity.
  - Reduced susceptibility to antivirals

- Antigenic drift ---new CVV required

- CDC IRAT Evaluation Tool
  - Highest pandemic risk amongst novel influenza viruses detected.
# Domestic Novel Influenza A

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<td>2</td>
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<td>20</td>
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<td></td>
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<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>309</strong></td>
<td><strong>19</strong></td>
<td><strong>3</strong></td>
<td><strong>3</strong></td>
<td><strong>18</strong></td>
<td><strong>50</strong></td>
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</table>

Source: [https://www.cdc.gov/flu/swineflu/h3n2v-case-count.htm](https://www.cdc.gov/flu/swineflu/h3n2v-case-count.htm)
The Recipe for a Human Influenza Pandemic

- Emergence of a **novel subtype** of influenza
  - An immunologically naïve population
- Replication in humans → disease
  - **Efficient** human-to-human transmission
Influenza surveillance are strengthening (US and globally)

- Enhances our ability to monitor for novel viruses with pandemic potential.
- In Wisconsin, the number of PCR tests performed surpasses RIDT.
- In the US, the number of PCR tests reported (CDC) exceeded 40,000 per week.
- The number of global NIC’s increased.
Rapid Influenza Diagnostic Tests (RIDTs)
A perennial discussion

www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm

www.jointcommission.org/siras.aspx
Improving RIDT Performance


At last, the Final Rule has arrived!
If you are an RIDT user...

What do the new regulations entail?

• Reclassifying RIDTs from Class I to Class II
• Premarket notification to assure safety and effectiveness – 510(k) clearance
• Add “special controls”
  ▪ Set minimum clinical performance criteria for sensitivity and specificity
    ▪ Appropriate comparator tests for new assays
  ▪ Accuracy assessed by manufacturers each year and when novel strain emerges (within 30 days)
  ▪ By July 31, results of past 3 years analytical reactivity testing must be included in labeling
If you are an RIDT user...

When will this happen?

• For existing tests enforcement as of 1/12/2018

What about your particular test?

• Contact the manufacturer; there will not be a central resource of information at this point
• If special controls not met, manufacturers expected to stop sales/distribution. However...
  • You may be able to get test yet – Don’t!
  • Do not use up existing inventory
• Keep an eye on kit labeling and company website

Likely Impact: Better tests? Fewer tests?
Influenza and non-influenza virus respiratory surveillance
Influenza season, 2017-2018

Early season

% Positive for Influenza by PCR (Wisconsin), Week Ending September 9, 2017

Date | Flu A | H1 | H3 | Flu B
--- | --- | --- | --- | ---
7/29/17 | 2 | 0 | 2 | 0
8/5/17 | 5 | 0 | 4 | 1
8/12/17 | 6 | 0 | 4 | 0
8/19/17 | 4 | 0 | 3 | 0
8/26/17 | 3 | 0 | 3 | 0
9/2/17 | 3 | 0 | 1 | 0
9/9/17 | 7 | 1 | 3 | 0
Tasmania (Australia) is in the "peak phase" of the most devastating flu season in recent memory, Health Minister Michael Ferguson warned.

As of [12 Sep 2017], there were 2337 confirmed cases of influenza and 21 deaths since [1 Jan 2017]. Last year [2016], 14 people died, and only 969 influenza cases were reported.

Date: Sun 17 Sep 2017 3:00 pm AEST
Source: The Advocate [edited]
Influenza Vaccine composition

2017-2018 Northern Hemisphere
A/Michigan/45/2015 (H1N1)pdm09-like virus;
A/Hong Kong/4801/2014 (H3N2)-like virus;
B/Brisbane/60/2008-like virus;
B/Phuket/3073/2013-like virus

2018 Southern Hemisphere
A/Michigan/45/2015 (H1N1)pdm09-like virus;
A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;
B/Brisbane/60/2008-like virus
B/Phuket/3073/2013-like virus.
What do we do with the specimens submitted?

• Subtype characterization
• Antiviral resistance monitoring
• Whole genome sequencing
  • 3c.2a and 3c.2a1
• Provide specimen/isolates to CDC
• Provide weekly summary of testing data
## Antiviral Resistance Monitoring - Wisconsin, 2017

**WI neuraminidase inhibition testing 2017**

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<tr>
<th>YR</th>
<th>Month</th>
<th># Reduced inhibition</th>
<th># Tested</th>
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<tr>
<td>2017</td>
<td>January</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>February</td>
<td>0</td>
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<tr>
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<td>March</td>
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<td>April</td>
<td>0</td>
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<td>May</td>
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<td>June</td>
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<td>July</td>
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<td>August</td>
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<tr>
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<td>September</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>0</td>
<td>71</td>
</tr>
</tbody>
</table>

- Oseltamivir
- Zanamivir
- Peramivir
# Flu PCR Labs Reporting Data, WI

![Graph showing the number of Flu PCR Labs reporting data in Wisconsin from 2011 to 2016. The graph includes a linear trend line indicating the increase in the number of labs reporting over time.](image-url)
Wisconsin Labs with Flu PCR & Virus Culture Capacity, September 2016

Influenza PCR Labs (n=49)
Rapid Influenza Reporting Sites, 2014-2017, WI

Number of Wisconsin Rapid Sites Reporting Influenza to WSLH

![Graph showing the number of Wisconsin rapid sites reporting influenza to WSLH from 2014 to 2017. The graph displays a trend line indicating a decrease in the number of sites reporting flu over time.](image-url)
Influenza Surveillance in Wisconsin

Multi-element approach

1. Rapid Influenza Diagnostic Testing (RIDT) Sites

   - Now <50% of influenza testing in WI!
   - Confirmatory testing during periods of low prevalence (June to October).
   - Please notify WSLH of suspected performance issues (e.g. False positives/negatives)

WSLH can provide confirmatory testing for the first positive influenza specimens.
Multi-element approach

2. Enrolled Surveillance Sites
   - 17 labs in 5 public health regions.
   - Provide randomized specimens weekly.

Request to continue to submit the **first 1-2 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.
   - Do NOT need to send positive specimens.

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
• One influenza-related hospitalization per week
• Unusual presentations/results
• Contact with swine/ sick or dead poultry
• Antiviral treatment failure
It is no longer necessary for labs to report testing data to the National Respiratory and Enteric Virus Surveillance System (NRVESS).

The WSLH is now reporting this data electronically to NREVSS for all labs in Wisconsin that report to WSLH.
Summary of Surveillance Changes

RIDT Sites

• Confirm the first influenza positive specimen if needed.

Hospitalized Patients

• Limit to one specimen per week

Enrolled Regional Surveillance Sites

• Send the first 1 to 2 specimens/week

Student Health

• Limit to one specimen/week

All labs: Please continue to send all out-of-season positive influenza A specimens (e.g. June-October 1).
Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing

**All Labs:**
- Send those with international travel histories
- *One* influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure
THANK YOU