

Influenza and other Respiratory Viruses Update-- 2018

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Learning Objectives

- Review of influenza basics.
- Review of the 2017-2018 influenza season.
- Influenza vaccine updates.
- Emerging viral diseases.
- Seasonal respiratory virus activity review.
- Discuss surveillance strategy for 2018-2019.

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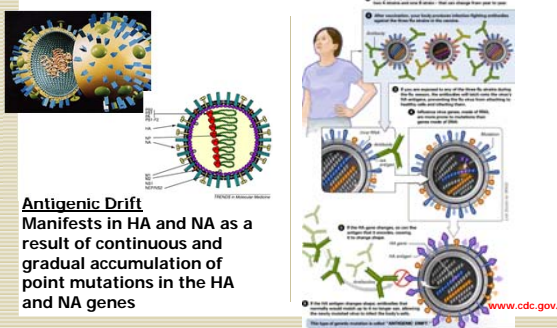
Influenza *The latest information*

www.cdc.gov/flu/



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The Changeability of Influenza *Antigenic Drift → Seasonal Influenza*

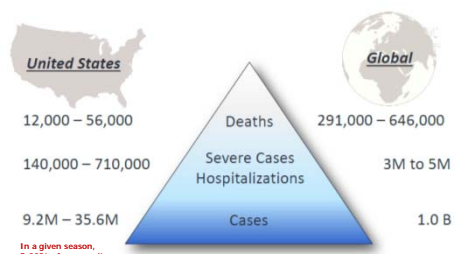


Antigenic Drift
Manifests in HA and NA as a result of continuous and gradual accumulation of point mutations in the HA and NA genes

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Significant Annual Burden of Influenza in Humans

Influenza CDC



Category	United States	Global
Deaths	12,000 – 56,000	291,000 – 646,000
Severe Cases Hospitalizations	140,000 – 710,000	3M to 5M
Cases	9.2M – 35.6M	1.0 B

In a given season, 5-20% of community may experience illness.

https://www.cdc.gov/flu/about/diseases/2013-14.htm; http://www.who.int/communication/topics/influenza/en/; Milano et al Lancet 2017

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Influenza 2017-18 *An historically severe year*

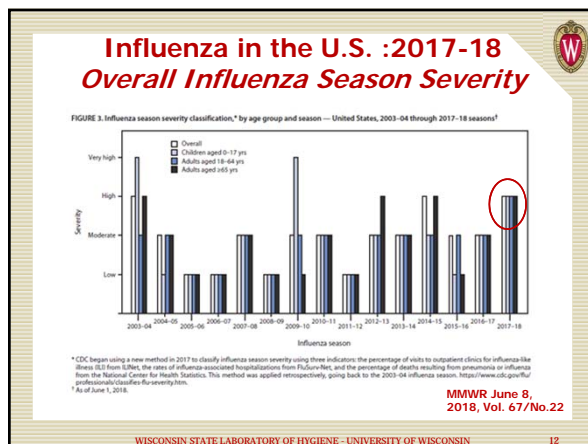
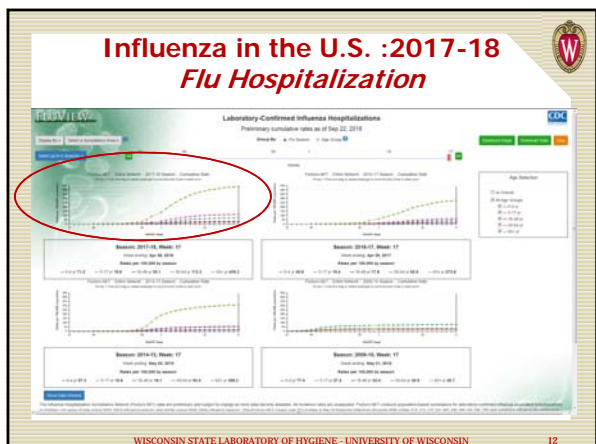
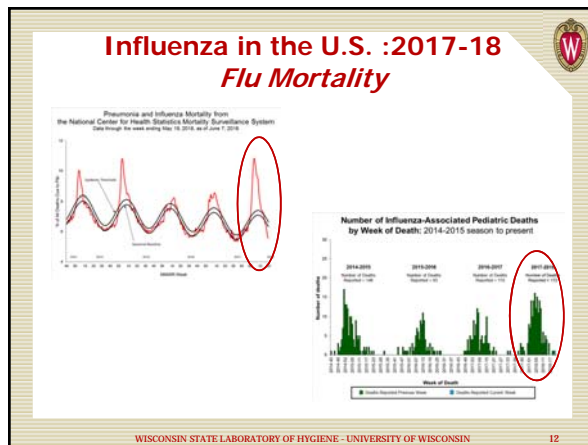
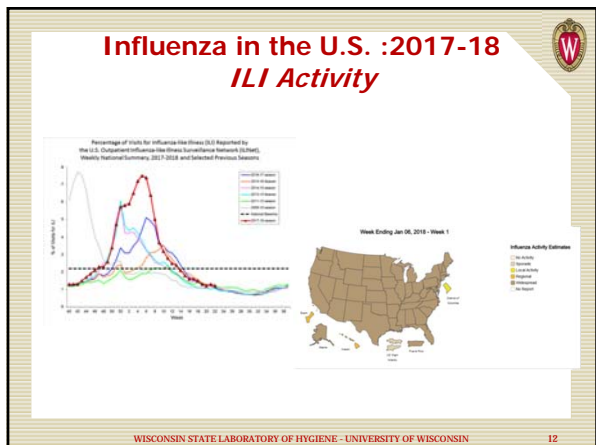
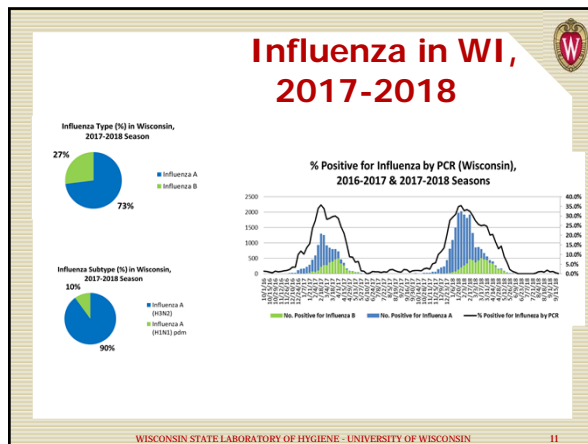
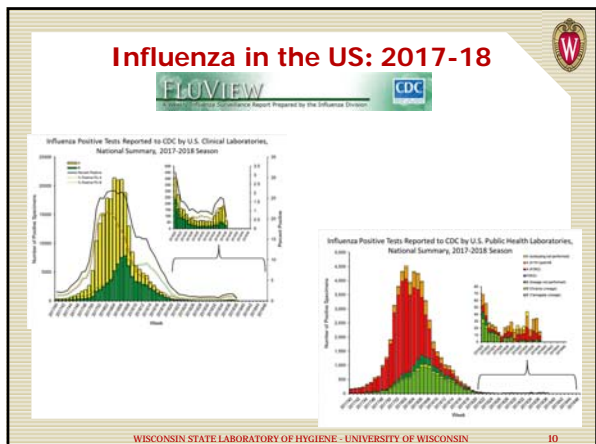
Flu outbreak in Wisconsin severe and expected to be widespread at least another month

“Some hospitals have had to temporarily divert patients from emergency departments because they ran out of hospital beds... Meriter and UW hospitals in Madison were at or approaching capacity at one point last week.”
---M.J.S, Jan 19, 2018---

Severe flu in California brings medicine shortages, kills 27



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Influenza in the U.S. :2017-18

Why was the past season so severe?

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Influenza – Prevention and Treatment

http://www.cdc.gov/flu/professionals/index.htm

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Seasonal Influenza

Antivirals

- Adamantanes (Amantadine & Rimantadine)
 - No longer effective against influenza type A,
- Neuraminidase inhibitors [Tamiflu & Zanamivir; Peramivir(i.v.)]
 - Effective against influenza subtypes A and B
 - Both oral, inhalant and i.v. preparations available
 - Differ in age ranges, routes of administration, costs, and adverse events
 - Development of complete resistance by former seasonal H1N1; pdmH1N1 and H3N2 remains susceptible

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Seasonal Influenza

Vaccine

- Primary strategy to reduce influenza infections and their complications
 - Safe and effective(?)
- 2 options:
 - Inactivated influenza vaccine
 - Trivalent and quadrivalent
 - Egg or cell culture grown
 - For all age groups ≥ 6 months (Universal)
 - Options now include high potency and adjuvanted
 - Live attenuated influenza vaccine
 - Licensed for non-pregnant persons aged 2-49 years
- Vaccine is matched to circulating strains of seasonal types A (2 subtypes) and B (2 lineages) influenza

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Influenza 2017-18

What was expected...

- A/Hong Kong/4801/2014(H3N2)
- A/Michigan/45/2015 (H1N1pdm09)
- B/Phuket/3073/2013 (B/Yamagata-lineage)
- B/Brisbane/60/2008 (B/Victoria-lineage)

... and that's largely what we got, however ...

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Seasonal Influenza Vaccines

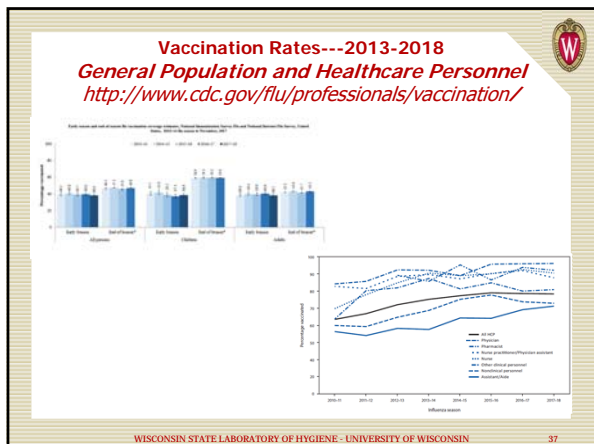
How effective ?

http://www.cdc.gov/flu/professionals/vaccination/effectiveness-studies.htm

Flu Season	Percent Reduction
2004-05	23
2005-06	21
2006-07	53
2007-08	42
2008-09	42
2009-10	58
2010-11	52
2011-12	47
2012-13	48
2013-14	52
2014-15	42
2015-16	48
2016-17	42
2017-18**	38

VE= percent reduction of frequency of flu among vaccinated people compared to unvaccinated people

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Seasonal Influenza Vaccines

Why isn't everyone getting vaccinated?

"Influenza is a trivial disease...why bother?"
 "Influenza is not safe during pregnancy"
 "Flu vaccine gives me the flu"
 "Not another vaccine for my children!"
 "I got the flu shot and still got the flu"
 "Bad things, e.g. GBS, happen after vaccination"
 "The flu vaccine still has thimerosal in it"
 "It costs too much"

"It's not as effective as the Govt. says"

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Seasonal Influenza Vaccines

Could there be other problems with the vaccines?

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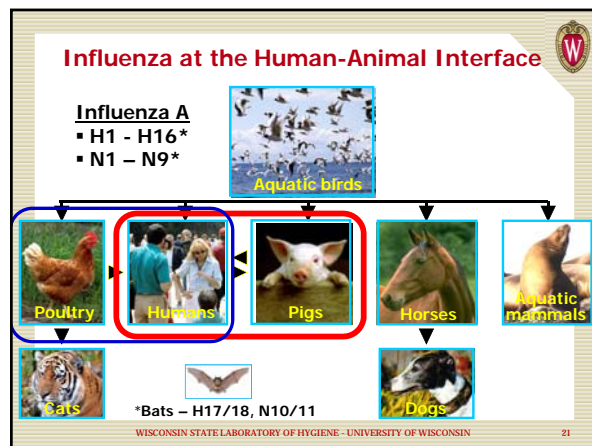
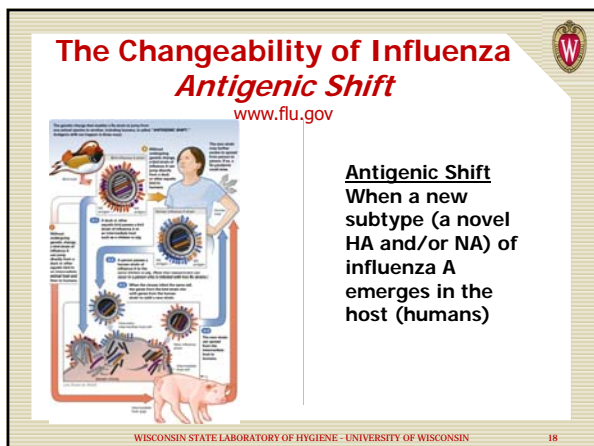
Vaccine Effectiveness : 2014-15

<http://www.cdc.gov/flu/professionals/vaccination/effectivenessqa.htm>

"It may not be perfect, but it protects a substantial number of people and it's the best we have"

-CDC Source-

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Infectious Diseases at the Human-Animal Interface

Influenza as an Example

Circulation of animal influenza viruses within and among animal species

Circulation of seasonal and pandemic influenza viruses in humans

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Timeline of Other Emergent Influenza A Viruses in Humans

Type A

Swine H3
Swine H1
Avian H9
Avian H7
Avian H5

2009 H1pdm A

H1
H2
H3

1918 1940 1957 1968 1977 1999 2003 2009 2013

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H7N9
H3v
H5N1
MERS-CoV

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Influenza A (H7N9)

The latest global concern

Human infections of A(H7N9) - 6 Waves

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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.

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Avian Influenza A (H5N1)

Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2018

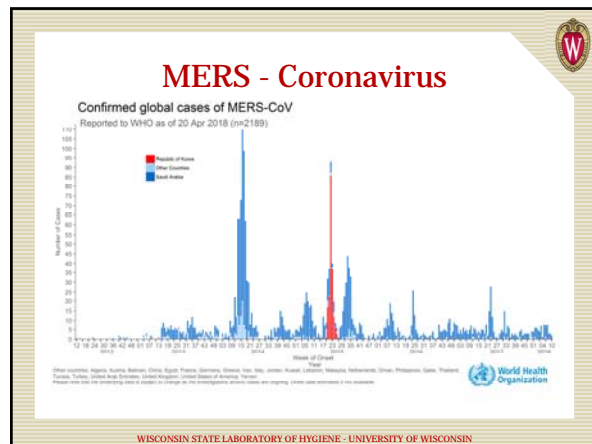
Country	2003-2009	2010-2014*	2015	2016	2017	2018	Total
	cases	deaths	cases	deaths	cases	deaths	cases
Azerbaijan	0	0	0	0	0	0	0
Bangladesh	1	0	0	0	0	0	1
Cameroon	0	0	0	0	0	0	0
Canada	0	0	0	0	0	0	0
China	38	25	0	0	0	0	63
Dominik	1	0	0	0	0	0	1
Egypt	190	27	120	10	130	30	577
Indonesia	152	114	35	3	0	0	304
IRAN	0	0	0	0	0	0	0
Lat. Pacific's	0	0	0	0	0	0	0
Myanmar	1	0	0	0	0	0	1
Nigeria	1	0	0	0	0	0	1
Philippines	0	0	0	0	0	0	0
Thailand	25	17	0	0	0	0	42
Turkey	12	0	0	0	0	0	12
Unk. Men	112	12	15	0	0	0	139
Total	688	266	226	13	130	30	1353

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MERS-CoV What we know!

- Virus is *different* than SARS-Coronavirus and seasonal coronaviruses.
- First cases in 2012.
- All cases linked to the Arabian Peninsula (80% Saudi Arabia).
- 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.
- WSLH performs RT-PCR on PUI's.

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Domestic Novel Influenza A

Table. Case Count: Detected U.S. Infections with Variant Influenza Viruses by State since December 2005-2018

Reporting State	H3N2v	H5Nx	Total Detected Influenza Variant Virus Infections
Alabama	0	0	
Alaska	0	0	
Arizona	0	0	
Arkansas	0	0	
California	0	0	
Colorado	0	0	
Connecticut	0	0	
Delaware	0	0	
District of Columbia	0	0	
Florida	0	0	
Georgia	0	0	
Idaho	0	0	
Illinois	0	0	
Indiana	0	0	
Iowa	0	0	
Kansas	0	0	
Kentucky	0	0	
Louisiana	0	0	
Maine	0	0	
Maryland	0	0	
Massachusetts	0	0	
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Mississippi	0	0	
Montana	0	0	
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Nevada	0	0	
New Hampshire	0	0	
New Jersey	0	0	
New Mexico	0	0	
New York	0	0	
North Carolina	0	0	
North Dakota	0	0	
Ohio	0	0	
Oklahoma	0	0	
Oregon	0	0	
Pennsylvania	0	0	
Rhode Island	0	0	
South Carolina	0	0	
South Dakota	0	0	
Tennessee	0	0	
Texas	0	0	
Utah	0	0	
Vermont	0	0	
Virginia	0	0	
Washington	0	0	
West Virginia	0	0	
Wisconsin	0	0	
Wyoming	0	0	
Total	0	0	0

For more detailed information about previously detected human cases of variant influenza infection, see <https://www.cdc.gov/flu/swineflu/h3n2v-case-count.htm>
Source: <https://www.cdc.gov/flu/swineflu/variant-cases-us.htm>

Source: <https://www.cdc.gov/flu/swineflu/h3n2v-case-count.htm>

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The Recipe for a Human Pandemic

- ✓ Emergence of a novel virus
- ✓ An immunologically naïve population
- ✓ Replication in humans → disease
- ✗ **Efficient human-to-human transmission**

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Virus Activity Resources

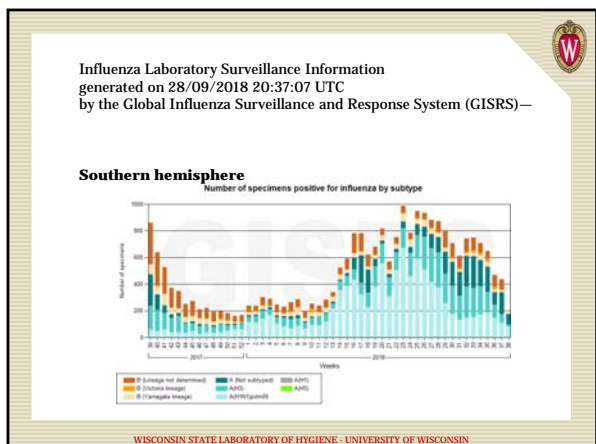
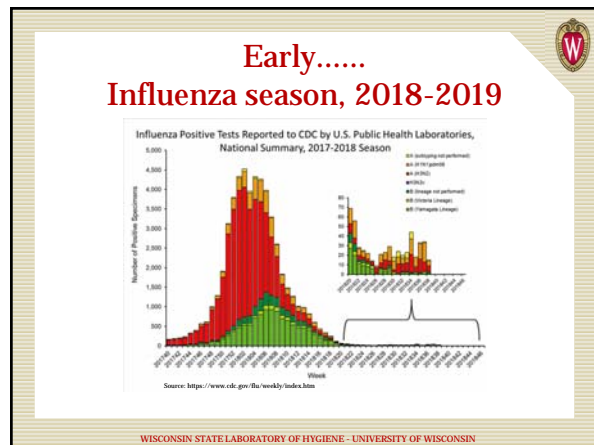
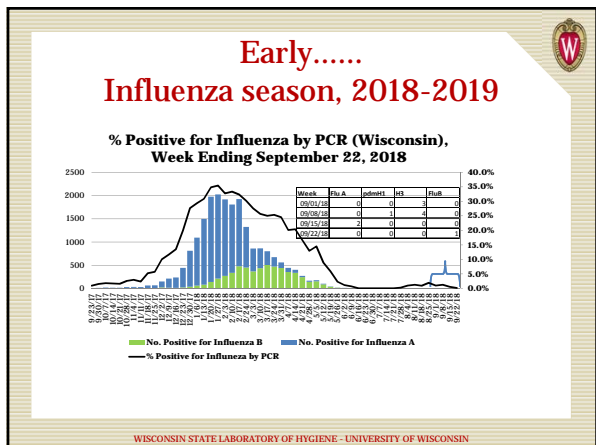
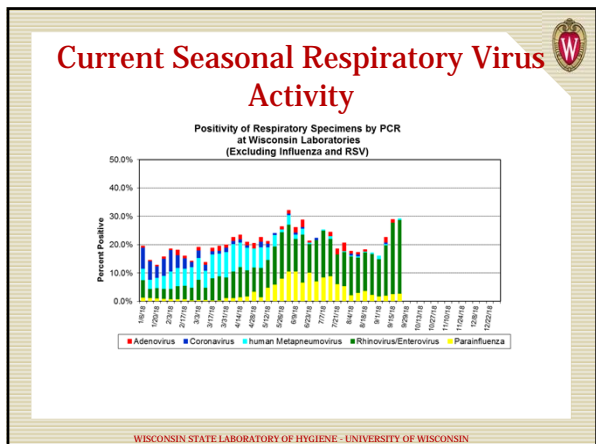
Wisconsin

- Bi-weekly Laboratory Surveillance Report
Subscribe at: wcln@slh.wisc.edu
- Virus Activity Graphs
<http://www.slh.wisc.edu/wcln-surveillance/surveillance/virology-surveillance/>

National

- FluView (CDC)
- NREVSS (CDC)

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What do we do with the specimens submitted?

- Subtype characterization
- Antiviral resistance monitoring
- Whole genome sequencing
 - 3c.2a, 3c.2a1, **3c.3a**
- Provide specimen/isolates to CDC
- Provide weekly summaries

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Antiviral Resistance Monitoring- Wisconsin, 2018

WI neuraminidase inhibition testing			
YR	Month	# Reduced inhibition	# Tested
2018	January	0	18
	February	0	16
	March	0	12
	April	0	10
	May	0	6
	June	0	5
	July	0	3
	August	0	7
	September	0	11
	Total	0	88



- Oseltamivir
- Zanamivir
- Peramivir
- Laninamivir

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Respiratory Pathogen Surveillance 2018-2019 Season



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Influenza Surveillance in Wisconsin

Multi-element approach

- 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 specimen of the season.

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Influenza Surveillance in Wisconsin

Multi-element approach

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



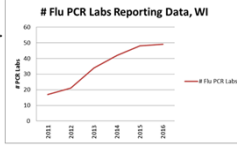
Request to continue to submit the first 1-2 specimens per week with influenza test requests to WSLH.

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Influenza Surveillance in Wisconsin

Multi-element approach

- 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 unsubtypeable specimens when subtyping for both 2009 H1N1 and seasonal H3 were attempted (Ct<35).

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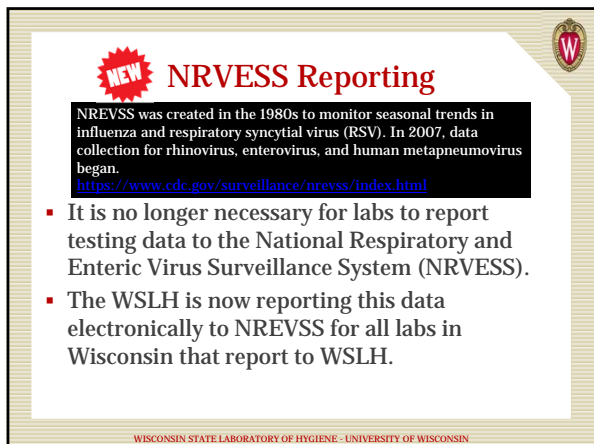
Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing

All Labs:

- Send those with international travel histories
- *Up to one* influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Antiviral treatment failure

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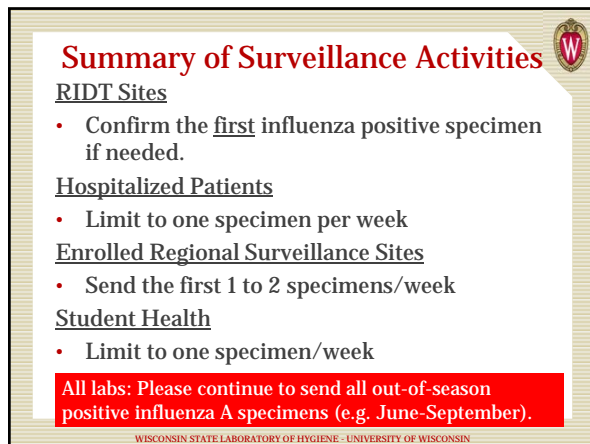


NEW NRVES Reporting

NRVSS was created in the 1980s to monitor seasonal trends in influenza and respiratory syncytial virus (RSV). In 2007, data collection for rhinovirus, enterovirus, and human metapneumovirus began.
<https://www.cdc.gov/surveillance/nrvss/index.html>

- It is no longer necessary for labs to report testing data to the National Respiratory and Enteric Virus Surveillance System (NRVSS).
- The WSLH is now reporting this data electronically to NREVSS for all labs in Wisconsin that report to WSLH.

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Summary of Surveillance Activities

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-September).

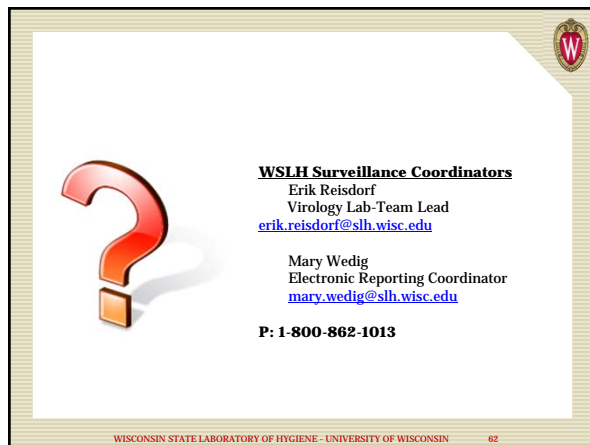
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THANK YOU

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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