Influenza and other Respiratory Viruses Update--2020

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and

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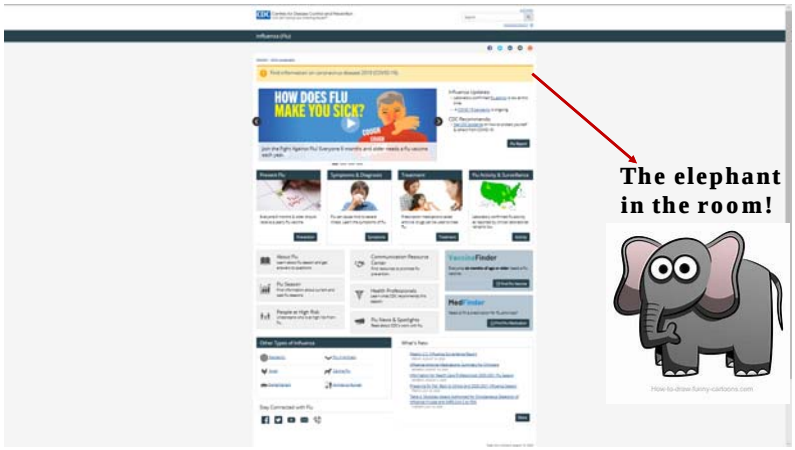
Learning Objectives

- Review of influenza basics.
- Review of the 2019-2020 influenza season.
- Influenza vaccine updates.
- Review laboratory issues related to diagnosis and surveillance.
- Describe why specimens and testing data is vital for public health programs.
- Discuss surveillance strategy for 2020-2021.

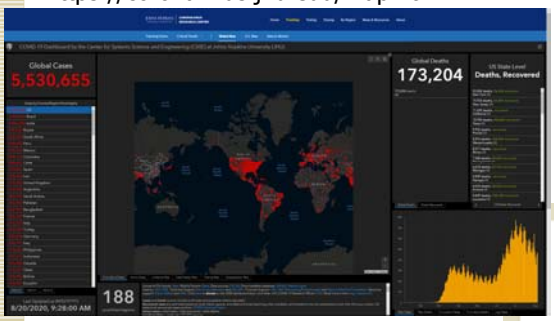
Influenza
The latest information

www.cdc.gov/flu/index.htm

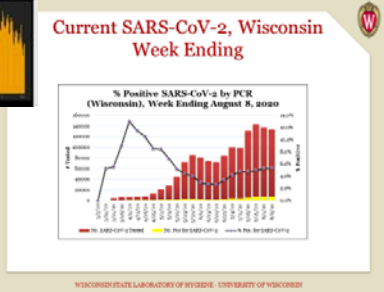


Current SARS-CoV-2 Impact

https://coronavirus.jhu.edu/map.html



http://www.slh.wisc.edu/wcln-surveillance/surveillance/

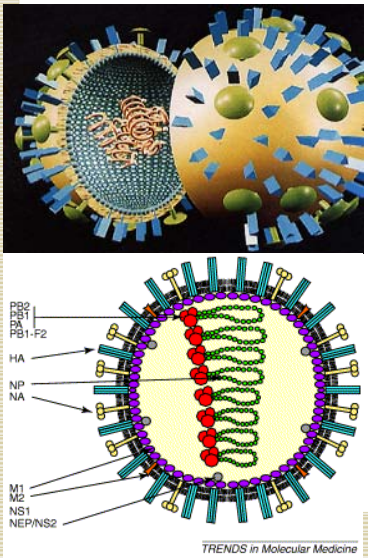


Why should we still worry about flu?

- Significant morbidity and mortality
- Clinical and epidemiological (age, seasonality, risk groups) overlap with COVID-19
- Vaccines and treatments available
- Recent very severe seasonal flu epidemics
- Ongoing threat of novel flu emergence and pandemics.

…and don't forget the impact of a host of other respiratory pathogens

Influenza Virus Basics
"Changeability is its hallmark"



- Influenza **types** A, B, C and D
  - A and B are major human pathogens
- Negative-sense segmented RNA genome
  - 10 major proteins
- Two major surface proteins of A and B viruses: Hemagglutinin (HA) and Neuraminidase (NA)
  - Nomenclature
  - Role in pathogenesis
  - Defines **subtypes**

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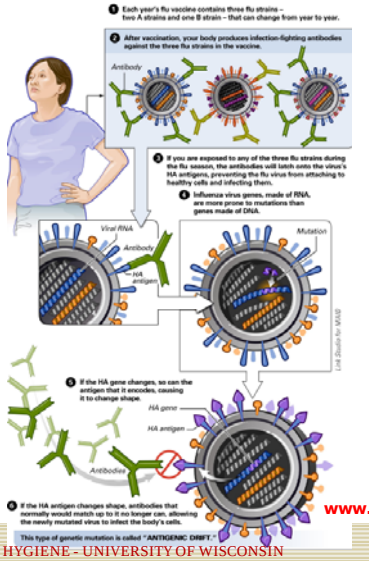
The Changeability of Influenza

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 within a subtype



www.cdc.gov/flu

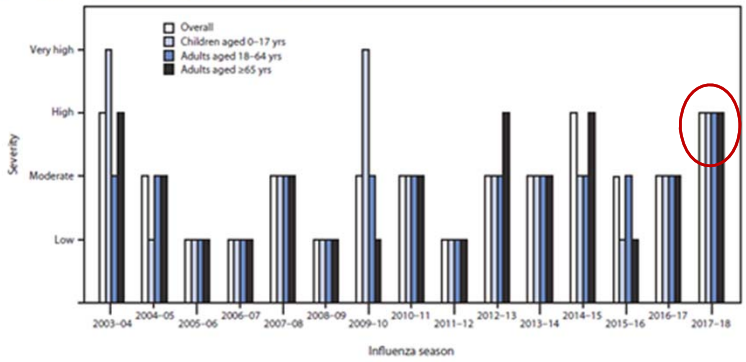
The Annual Impact of Seasonal Influenza

*The top range of these burden estimates are from the 2017-2018 flu season. These are preliminary and may change as data are finalized.

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

Influenza in the U.S. :2003-18
Overall Influenza Season Severity

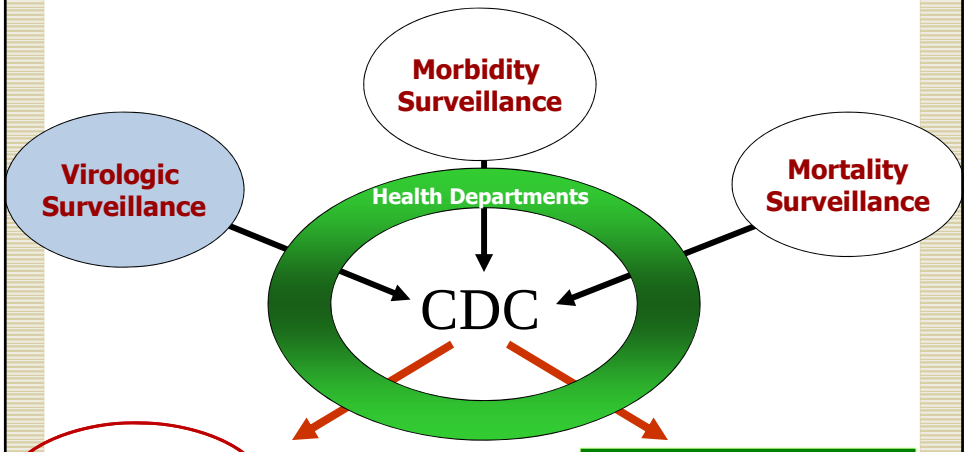
FIGURE 3. Influenza season severity classification,* by age group and season — United States, 2003–04 through 2017–18 seasons†



* CDC began using a new method in 2017 to classify influenza season severity using three indicators: the percentage of visits to outpatient clinics for influenza-like illness (ILI) from ILINet, the rates of influenza-associated hospitalizations from FluSurv-Net, and the percentage of deaths resulting from pneumonia or influenza from the National Center for Health Statistics. This method was applied retrospectively, going back to the 2003–04 influenza season. https://www.cdc.gov/flu/professionals/classifies-flu-severity.htm.
† As of June 1, 2018.

MMWR June 8, 2018, Vol. 67/No.22

U.S. Influenza Surveillance
www.cdc.gov/flu/weekly/overview.htm



Influenza Virologic Surveillance

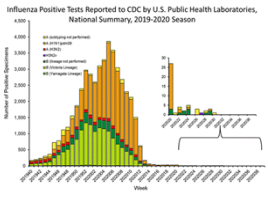
How we monitor the virus

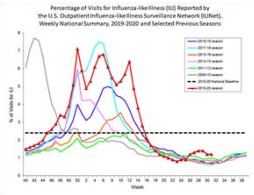
- Provide situational awareness
  - **Clinical lab testing data** → **CDC** (Via PHL or directly)
- **Detect novel or reassortant viruses**
- Inform vaccine strain selection
- Detect and monitor antiviral resistance
  - **Specimens/isolates from clinical labs** → **PHL** → **NIRC** → **CDC**

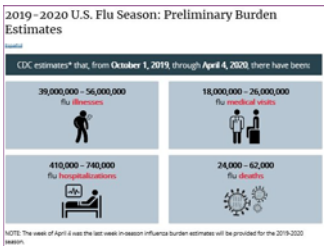
FLUVIEW
A Weekly Influenza Surveillance Report Prepared by the Influenza Division

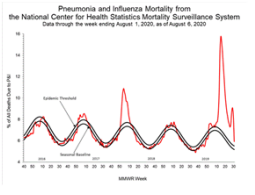
The 2019-20 Influenza Epidemic

Key Virologic and Epidemiologic Indicators

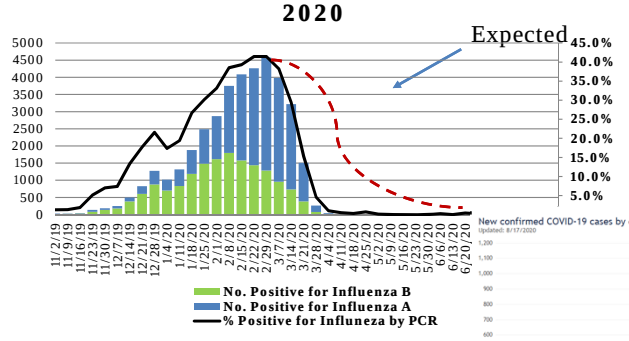


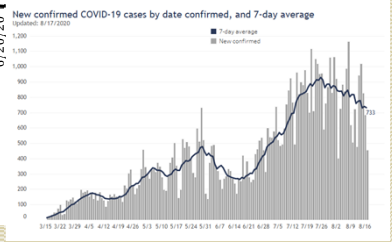






2019-2020 Seasonal Influenza Activity, Wisconsin





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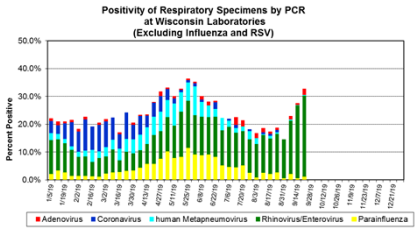
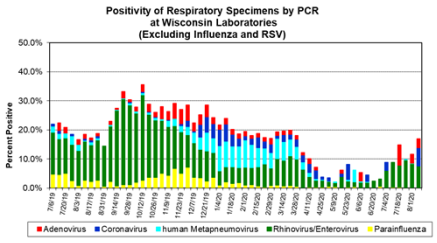
2019-2020 Seasonal Respiratory Virus Activity, Wisconsin

2019



2020



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Influenza – Prevention and Treatment

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

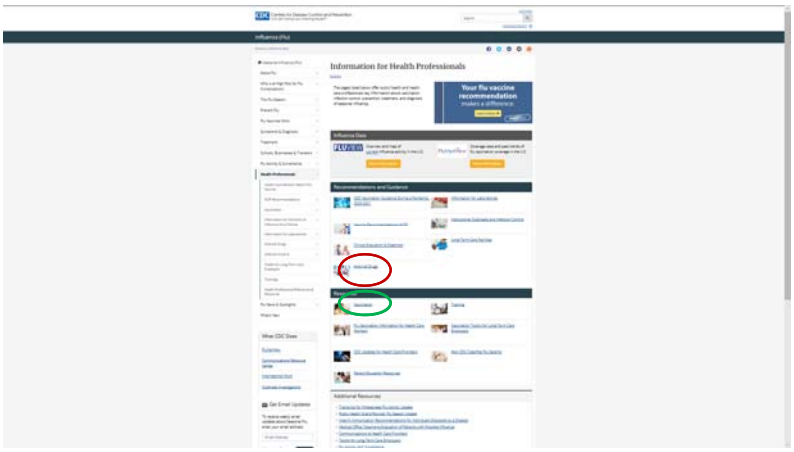

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Table 1. Antiviral Medications Recommended for Treatment and Chemoprophylaxis of Influenza

Antiviral Agent	Activity Against	Use	Recommended For	Not Recommended for Use in	Adverse Events
Oral Oseltamivir	Influenza A and B	Treatment	Any age[1]	N/A	**Adverse events:** nausea, vomiting, headache. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis	3 months and older[1]	N/A	
Inhaled Zanamivir	Influenza A and B	Treatment	7 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	**Adverse events:** risk of bronchospasm, especially in the setting of underlying airways disease; sinusitis, and dizziness. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis	5 yrs and older[3]	people with underlying respiratory disease (e.g., asthma, COPD)[3]	
Intravenous Peramivir	Influenza A and B[4]	Treatment	2 yrs and older[4]	N/A	**Adverse events:** diarrhea. Post marketing reports of serious skin reactions and sporadic, transient neuropsychiatric events[2]
		Chemo-prophylaxis[5]	Not recommended	N/A	
Oral Baloxavir	Influenza A and B[6]	Treatment	12 yrs and older[6]	N/A	**Adverse events:** none more common than placebo in clinical trials
		Chemo-prophylaxis[7]	Not recommended	N/A	

Abbreviations: N/A = not applicable, COPD = chronic obstructive pulmonary disease.

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Seasonal Influenza

Vaccine

- **Primary strategy to reduce influenza infections and their complications**
  - Safe and **effective(?);** usage rates **disappointing**
- 2 options:
  - **Inactivated influenza vaccine**
    - Trivalent and quadrivalent
    - Egg or cell culture grown and recombinant
    - 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 Vaccine 2019-20

What was expected….

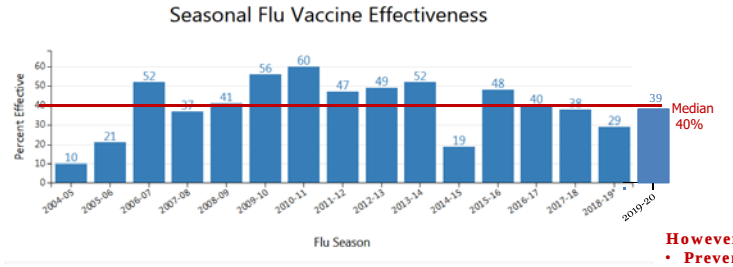
- A/Kansas/14/2017 A(H3N2)-like
- A/Brisbane/02/2018 A(H1N1)pdm09-like
- B/Phuket/3073/2013-like (B/Yamagata-lineage)
- B/Colorado/06/2017-like (B/Victoria-lineage)

…basically what we got

Seasonal Influenza Vaccines

How effective?

https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm



However:

- **Prevents office visits**
- **Prevent hospitalization**
- **Prevents death**

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

Influenza Vaccine 2020-21

https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6908a1-H.pdf

- A/Hong Kong/2671/2019 A(H3N2)-like [egg- based]
- A/Hong Kong/45/2019 A(H3N2) [cell-based and recombinant]
- A/Guangdong-Maonan/SWL1536/2019 A(H1N1)pdm09-like [egg-based]
- A/Hawaii/70/2019 A(H1N1)pdm-09-like [cell-based and recombinant]
- B/Washington/02/2019 (B/Victoria lineage)-like [egg & cell-based]
- B/Phuket/3073/2013 (B/Yamagata-lineage)-like [egg & cell-based]

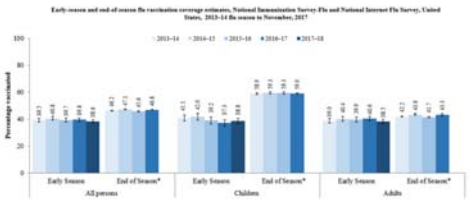
Influenza Vaccine 2020-21

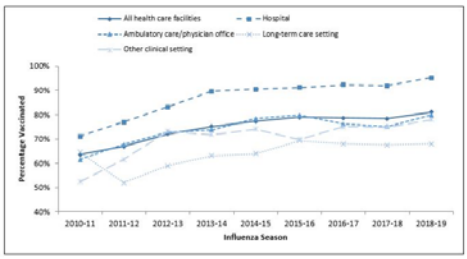
In light of the SARS-CoV-2 pandemic, more important than ever to get your flu vaccine!

Vaccination Rates---2013-2019

General Population and Healthcare Personnel

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





1918 Influenza Pandemic

100 Year Anniversary of the Great Pandemic

https://www.cdc.gov/flu/pandemic-resources/index.htm

Influenza at the Human-Animal Interface

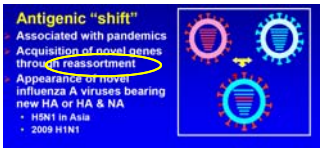
Influenza A
- **H1 - H16***
- **N1 – N9***

*Bats – H17/18, N10/11

The Changeability of Influenza

Antigenic Shift → Pandemic Influenza

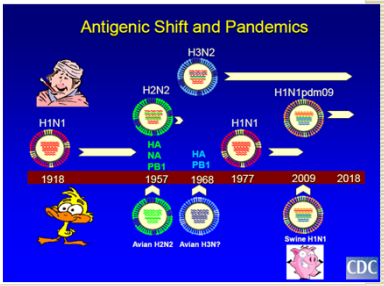
www.cdc.gov/flu



Pandemic Influenza

Replication in Humans

Efficient and sustained human-to-human transmission

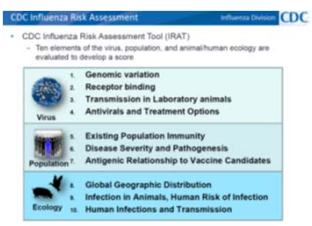


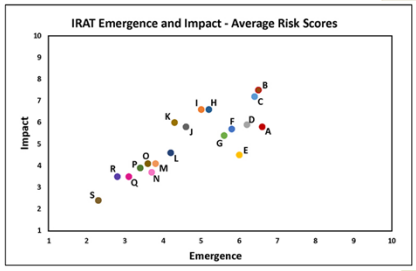
A Global Tool for Pandemic Preparedness

Influenza Risk Assessment Tool - IRAT Influenza CDC

- A global public health tool to prioritize pandemic preparedness activities
  - Evaluates risk from novel viruses currently circulating in animals, i.e. in pre-pandemic period
- Assess potential pandemic risk for:
  - Emergence of a novel influenza virus in humans
    - Human-to-human transmission
  - Public health impact
    - Severity
- The IRAT can prioritize readiness activities
  - Diagnostics, reagents, vaccines and antivirals development
  - Stockpiling and deployment
- The IRAT cannot predict the next pandemic strain

CDC. https://www.cdc.gov/flu/pandemic-resources/monitoring/irat.htm





	Virus	Emergence Score	Impact Score
A	A(H3N2) variant [A/Ohio/13/2017]	6.6	5.8
B	A(H7N9) [A/Hong Kong/125/2017]	6.5	7.5
C	A(H7N9) [A/Shanghai/02/2013]	6.4	7.2
D	A(H9N2) Y280 lineage [A/Anhui-Lujiang/13/2018]	6.2	5.9
E	A(H3N2) variant [A/Indiana/08/2011]	6.0	4.5
F	A(H1N2) variant [A/California/62/2018]	5.8	5.7
G	A(H9N2) G1 lineage [A/Bangladesh/0994/2011]	5.6	5.4
H	A(H5N1) Clade 1 [A/Vietnam/1203/2004]	5.2	6.6
I	A(H5N6) [A/Yunnan/14564/2015] - like	5.0	6.6
J	A(H7N7) [A/Netherlands/219/2003]	4.6	5.8
K	A(H10N8) [A/Jiangxi-Donghu/346/2013]	4.3	6.0
L	A(H5N8) [A/gyrfalcon/Washington/41088/2014]	4.2	4.6
M	A(H5N2) [A/Northern pintail/Washington/40964/2014]	3.8	4.1
N	A(H3N2) [A/canine/Illinois/12191/2015]	3.7	3.7
O	A(H5N1) [A/American green-winged teal/Washington/1957050/2014]	3.6	4.1
P	A(H7N8) [A/turkey/Indiana/1573-2/2016]	3.4	3.9
Q	A(H7N9) [A/chicken/Tennessee/17-007431-3/2017]	3.1	3.5
R	A(H7N9) [A/chicken/Tennessee/17-007147-2/2017]	2.8	3.5
S	A(H1N1) [A/duck/Nev York/1996]	2.3	2.4

Wisconsin Testing and Surveillance 2020-2021

Possible Impacts of COVID on flu testing

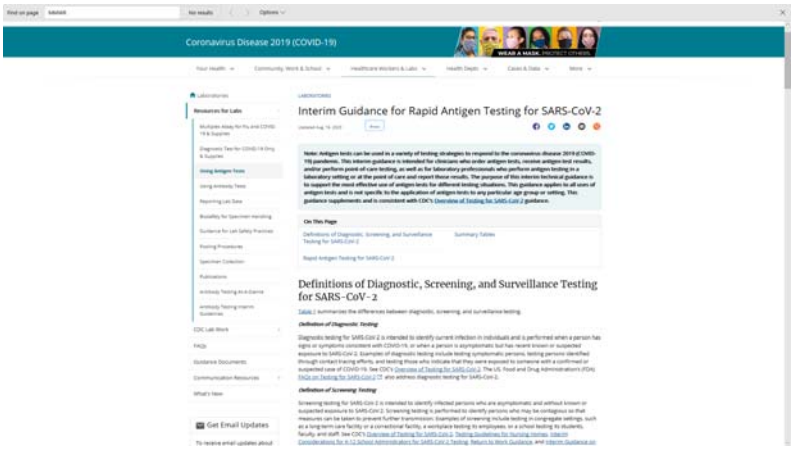
- Lab supply chain shortages and disruptions
- Less staffing resources for flu and other diagnostic testing
- Managing multiple testing platforms
- Coordinating specimen types
- Trend toward testing asymptomatics
- Expanding COVID testing beyond traditional labs
  - "Tack on" flu testing as well

↓

Impacts on surveillance: a PH concern

Excellent Resource

https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html



WSLH Testing Strategy for Influenza and SARS-CoV-2

- Implementing CDC Multiplex PCR assay in September.
- Surveillance testing & outbreak response for suspected influenza or SARS-CoV-2.
- Commercial tests include BioFire, Luminex and Qiagen. Cepheid 4 targets coming soon!
- Many commercial manufacturers developing tests.

CDC Influenza SC2 Multiplex PCR

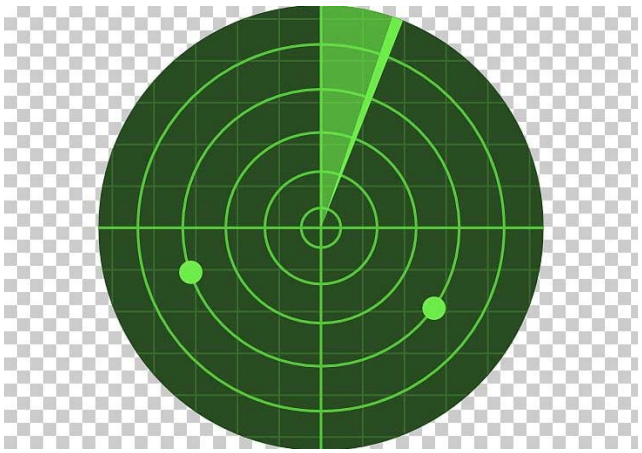
- Targets include InfA, InfB, SC2 and RP
- Equipment needed: real-time PCR instrument (96well) and NA extraction platform.
- Sensitivity for SC2 improved. Similar for influenza viruses.
- PCR sequences available at: https://www.cdc.gov/coronavirus/2019-ncov/lab/multiplex-primer-probes.html

Influenza subtyping changes

2020-2021 Strategy

- Characterize H1 and H3 subtypes.
- Select samples based upon CDC criteria.
- Reduced number.
- Reporting to labs will be RUO.

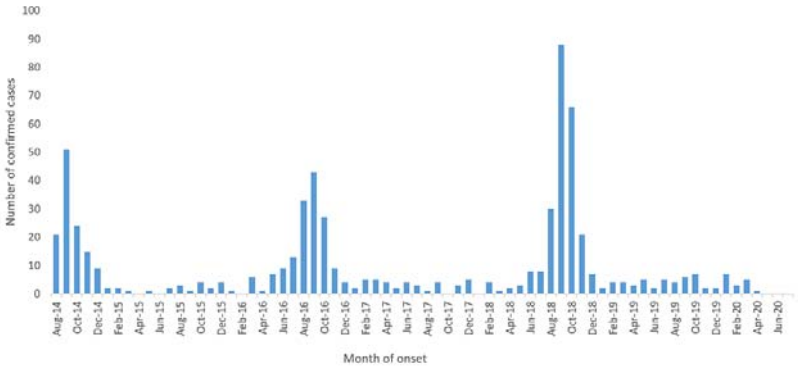
Viral Monitoring Activities (other than Flu)



Severe Adenovirus

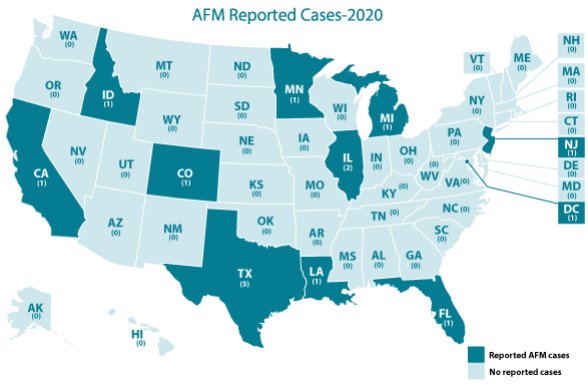
- Adenovirus outbreak occurred in NJ
  - >24 severe illnesses and 11 deaths
  - Children with compromised immune systems
- University of Maryland
  - Freshman death
- University of Wisconsin

Acute Flaccid Myelitis (AFM)



Source: https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

Acute Flacid Myelits (AFM)



Source: https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html

Virus Activity Resources

Wisconsin

- Bi-weekly Laboratory Surveillance Report

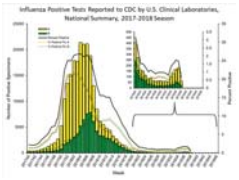
  Subscribe at: wcln@slh.wisc.edu

- Virus Activity Graphs

  http://www.slh.wisc.edu/wcln-surveillance/surveillance/virology-surveillance/

National

- FluView (CDC)
- COVID View (CDC) NEW!
- NREVSS (CDC)



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Influenza and non-influenza virus respiratory surveillance

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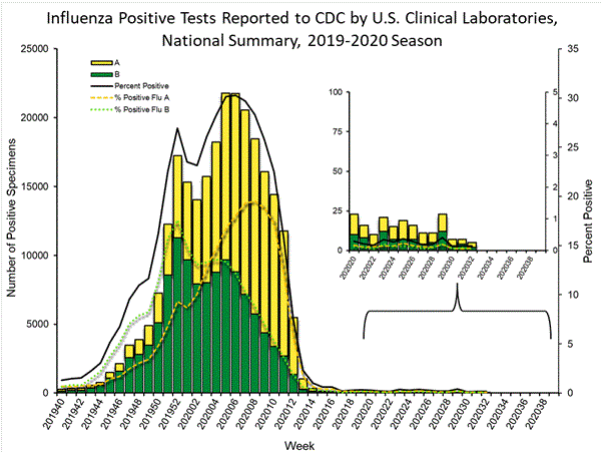
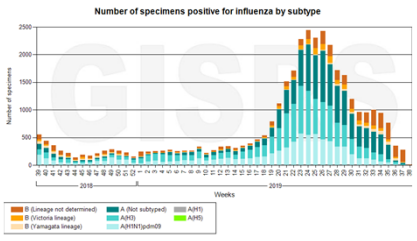
Early.....
Influenza season, 2020-2021

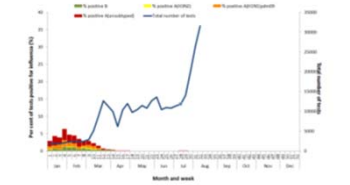


Source: https://www.cdc.gov/flu/weekly/index.htm

WHO Global Influenza Surveillance and Response System (GISRS)—
https://apps.who.int/flumart/Default?ReportNo=5&Hemisphere=Southern

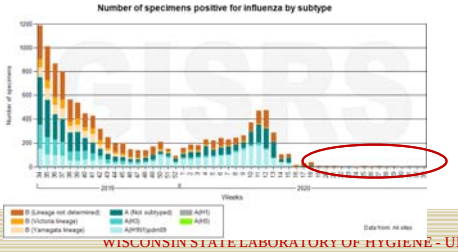
Southern hemisphere, 2019





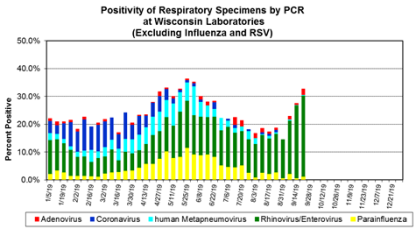
Source: Australian Influenza Surveillance Report No. 9 (2020)

Southern hemisphere, 2020

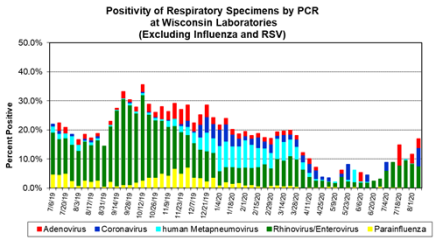


Current Seasonal Respiratory Virus Activity, Wisconsin

2019

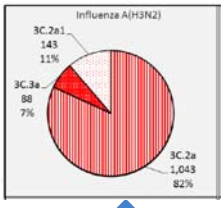


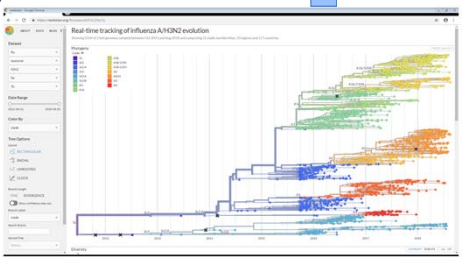
2020



Why is influenza surveillance important?

- Provide specimen/ isolates to characterize and inform vaccine strain selection
- Situational awareness
- Antiviral resistance testing
- Detect novel viruses with pandemic potential





Respiratory Pathogen Surveillance

2020-2021 Season

All Clinical Laboratories Performing Influenza Testing

Please send early season positive influenza specimens to WSLH.

- Early season positives are critical:
  1. Inform vaccine strain selection.
  2. Provide samples to make CVV.

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 may be warranted.
   - Please notify WSLH of suspected performance issues (e.g. False positives/negatives)

Influenza Surveillance in Wisconsin

Multi-element approach

2. Enrolled Surveillance Sites
   - 17 labs in 5 public health regions.
   - Provide randomized specimens weekly.
   - Provided a "blue" specimen submission form.

Request to continue to submit the first 2 or 3 specimens per week from symptomatic patients with influenza test requests to WSLH.

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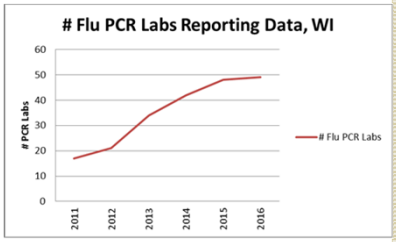
Influenza Surveillance in Wisconsin

Multi-element approach

3. PCR Labs
   - "Gold Standard" testing.
   - Provide weekly testing data summary reports.
   - **Provide early season influenza 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).

Influenza Surveillance in Wisconsin

Multi-element approach

4. University Health Clinics
   - Monitor severe adenovirus infections.
   - Monitor influenza,SCV2 and other respiratory pathogens impacting student health.

Request to up to 3 specimens per week for respiratory pathogen testing and characterization.

Laboratory-based Surveillance

All Clinical Laboratories performing influenza diagnostic testing send positives

After activity increases:
- Send those with international travel histories
- *Up to one* influenza-related hospitalization per week
- Unusual presentations/results
- Contact with swine/ sick or dead poultry
- Pediatric deaths

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Summary of Surveillance Activities

PCR Labs & RIDT Sites

- Early season positive influenza specimens
- Continue to report testing data weekly

Enrolled Regional Surveillance & Student Health Sites

- Send the first 2 to 3 specimens/week

University Health Clinics

- Send up to 3 specimens per week

All labs: Please continue to send all positive influenza specimens.

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WSLH has Influenza Surveillance Supplies!!

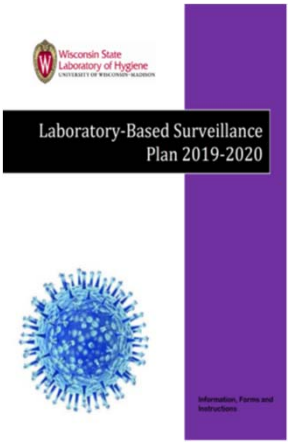
- Specimen collection supplies
  - VTM and swabs
- Shipping supplies
  - Insulated shippers
  - Cold packs
- Specimen submission forms

Contact our Clinical Orders Department at

800-862-1088

Laboratory-based Surveillance Plan

- Detailed instructions
- Description of surveillance requests other than influenza
- Web-based reporting instructions
- SARS-CoV-2 testing criteria



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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