Reflections on the 2017-2018 Influenza Season and Insights into 2018-2019

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OBJECTIVES
At the end of the presentation, participants will be able to:
- describe the clinical and laboratory features of influenza
- outline the expected morbidity and mortality of seasonal influenza
- plan for diagnosis and treatment of influenza patients
- understand the principles of prevention—influenza vaccine and develop a plan for immunization for the 2018-2019 season

Influenza Season is Unpredictable in 5 Ways

- When the season begins
- How severe the disease is
- How long the season lasts
- Which viruses are spread
- Whether there is a good match between circulating virus and the vaccine
Influenza burden of disease

- Influenza A and B strains often co-circulate during the season
- Drift and shift of strains define impact of the season
- >200,000 influenza associated hospitalizations per year
- ~23-36,000 excess deaths per year
- Older adults, infants, and those in certain high risk groups have greater morbidity and higher mortality rates
- Annual immunization=most effective way to prevent influenza outbreaks

2017-2018 Seasonal Influenza Vaccine Strains

<table>
<thead>
<tr>
<th>Type</th>
<th>Strains</th>
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</thead>
<tbody>
<tr>
<td>Trivalent</td>
<td>A/Michigan/45/2015 (H1N1)pdm09-like virus</td>
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<tr>
<td></td>
<td>A/Hong Kong/4801/2014 (H3N2) like virus</td>
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<td></td>
<td>B/Brisbane/10/2007-like virus (B/Victoria lineage)</td>
</tr>
<tr>
<td>Quadrivalent</td>
<td>Adds B/Phuket/3073/2013-like virus (B/Yamagata lineage)</td>
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</tbody>
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One strain change from prior season
LAIV4 should NOT be used in any setting during the 2017-2018 season

Benefits of Influenza Vaccine

- Lower rates of cardiac events among people with heart disease
- Reduced hospitalizations among people with diabetes (79%) and chronic lung disease (52%).
- In pregnant women found that vaccination reduced the risk of flu-associated acute respiratory infection by about one half
  - Reduced risk of flu illness in her baby by up to half. This protective benefit was observed for several months after birth

Benefits of Influenza Vaccine

- Reduced child deaths (case–cohort analysis comparing vaccination uptake among laboratory-confirmed influenza-associated pediatric deaths with estimated vaccination coverage among pediatric cohorts in the US; Pediatrics April 2017)
**FluVaxView data**

**United States Flu Vaccine Uptake in Pediatric Populations**

**Influenza Epidemiology and Manifestations**

- Incubation period: 1–4 days, (average of 2 days)
- Adults infectious from the day before symptoms to approximately 5 days after illness onset
- Children infectious for > 10 days
  - Shed for several days before their illness onset
  - Immunocompromised persons can shed virus for weeks or months
- Abrupt onset: symptoms last 7-10 days
  - fever, myalgia, headache, malaise, cough, sore throat, and rhinitis
### Influenza Complications
- Otitis media, sinusitis
- Pneumonia
  - Bacterial
    - *S. pneumoniae*, *S. aureus*, GAS, meningococcus, *H. influenzae*
  - Other foci bacterial superinfections/toxic shock syndrome
- Encephalitis, encephalopathy
- Myocarditis
- Myositis

### 2017-2018 influenza season
- High severity H3N2 year
- High levels of outpatient and ED visits
- High influenza hospitalization rates
  - Highest >65 years (58%)
- Extended season-19 weeks

### Vaccine Effectiveness Mid-Season Estimates
- Overall adjusted vaccine effectiveness (VE) against influenza A and influenza B virus infection associated with medically attended ARI was 36% (95% confidence interval [CI] = 27%–44%)
- Most (69%) influenza infections were caused by A(H3N2) viruses; VE was estimated to be 25% (CI = 13% to 36%) against illness caused by influenza A(H3N2) virus
- VE 67% (CI = 54%–76%) against A(H1N1)pdm09 viruses
- VE 42% (CI = 25%–56%) against influenza B viruses
From 10/1/17-5/29/18, 98,446 specimens, 53,796 positive
71% influenza A
29% influenza B

Influenza A subtypes
84.9% H3N2
15% H1N1pdm09
-9% central US
-24% NW and SE US

Influenza B lineage
89%B/Yamagata lineage
11%B/Victoria lineage
-early March to late May
-23% MW; 41% NW US
Above epidemic threshold for 16 wks

Influenza Hospitalizations by Age

• 0-4 years 74/100,000
• 5-17 years 20/100,000
• 18-29 years 32/100,000
• 50-64 years 115/100,000
• ≥65 years 461/100,000

Underlying Conditions Hospitalized with Influenza

• 92% adults
  – Cardiovascular, metabolic, obesity, CLD
  – Among women 15-44 years, 31% pregnant
• 57% children
  – Asthma, neurologic disorders, obesity
Comparing Clinical Characteristics Between Hospitalized Adults With Laboratory-Confirmed Influenza A and B Virus Infection

Su Su, Sandra S. Chaves, Alejandro Perez, Tiffany D’Mello, Pam D. Kiley, Kimberly Yousey-Winder, Monica M. Farley, Meghan Harris, Rupa Sharangadkar, Ruth Lynfield ... Show more

Published: 18 April 2014 Article history »
Top chronic medical conditions in children:
1. Asthma (21.5%)
2. Neurologic/NM Disorder (15.4%)
3. Obesity (9.6%)
51% healthy
Erythematous tonsils in a child with group A streptococcal pharyngitis.

Figure Legend:

Orbital abscess with proptosis of the globe due to Staphylococcus aureus in a 12-year-old boy. Delayed surgical drainage contributed to permanent visual impairment due to central retinal vascular involvement. The patient also had left ethmoid and maxillary sinusitis.

Figure Legend:
Group A streptococcal cellulitis and arthritis of the left ankle in a 4-year-old white female. Copyright Michael Regis, MD, FAAP.

Legend:
Group A streptococcal cellulitis and arthritis of the left ankle in a 4-year-old white female. Copyright Michael Regis, MD, FAAP.

Legend:
Necrotizing fasciitis of the left upper arm and shoulder secondary to group A streptococcus.

Figure Legend:
Necrotizing fasciitis of the left upper arm and shoulder secondary to group A streptococcus.

Figure Legend:
Streptococcus pneumoniae pneumonia with pneumatocele formation in the left lung. Courtesy of Benjamin Estrada, MD.

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Streptococcus pneumoniae pneumonia with pneumatocele formation in the left lung. Courtesy of Benjamin Estrada, MD.
Influenza Neurologic Complications

- Acute presentations
  - Febrile seizures
  - Afebrile seizures
  - Encephalitis/encephalopathy
    - Necrotizing encephalitis with thalamic involvement

- Post viral
  - Transverse myelitis
  - Guillain Barré Syndrome
  - ADEM

Influenza Myositis

- Usually benign associated with influenza B and school age boys
  - Bilateral calf pain develops 3-4 days into influenza illness
  - Pain may be so severe that children refuse to walk
  - Diagnosis is confirmed by measurement of creatinine kinase
  - Disease is self-limited with recovery within a week.
- Influenza associated rhabdomyolysis and myoglobinuria more often follows influenza A
  - More often in girls (80%)
  - Renal failure in 80%

What's New for the 2018-2019 Season?

- New vaccine strains
- LAIV is back

Upcoming Influenza Vaccine

2017-2018
- an A/Michigan/45/2015 (H1N1)pdm09-like virus;
- an A/Hong Kong/4801/2014 (H3N2)-like virus; and
- a B/Brisbane/60/2008-like virus (Victoria lineage).
- Quadrivalent: B/Phuket/3073/2013-like virus (Yamagata

2018-2019
- an A/Michigan/45/2015 (H1N1)pdm09-like virus;
- an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus;
- B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage.
- Quadrivalent: B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage).

LAIV Immunogenicity

Seroconversion Rates in LAIV Recipients (N=79 in Slovenia group)

- 2018-2019:
  - A/Michigan/45/2015 (H1N1)pdm09-like virus
  - A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus
  - B/Colorado/06/2017-like virus of the B/Victoria/2/87-lineage
  - Quadrivalent: B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage)
LAIV-Nasal vaccine is back for the 2018-2019 season though controversy

- 200 U.S. children older than 2 but younger than 4 years of age
  - FluMist Quadrivalent included A/Slovenia H1N1 strain
  - 23% of children vaccinated with the 2017–2018 H1N1 LAIV strain developed a fourfold antibody rise, compared to 5% with the 2015–2016 H1N1 LAIV strain
  - After second dose, increase to 45% vs 12%, respectively
  - Also noted increased vaccine virus replication in vaccinated children
- Overall VE: 45% against influenza A and B, with 25% protection against influenza A (H1N1)pdm09 compared with unvaccinated children

AAP Discussion

- Data from 2010-2017, LAIV as effective as IIV against influenza B and H3N2; poorly effective against H1N1 in 2-17 year olds
- New LAIV4 includes Slovenia/2903/2015 A(H1N1)pdm09-like virus strains has “improved fitness” but no effectiveness estimates
Take Home Points

• The 2017-2018 influenza season most severe on record since pandemic H1N1
• Co-circulation of multiple strains from beginning; H3N2 predominant
• Most IFI visits by % seen by PCPs of any prior season
• Hospitalizations most in >65 yrs but high in 50-64 yrs, 0-4 yrs
• Only 50% of population immunized overall
• Deaths in children increased
• VE overall ~40% but higher for H1N1 and B strains
• LAIV available for 2018-2019 season-AAP prefers inactivated