Highlighted Topics

- Influenza
- Vaccine Errors
- 2 Dose HPV
- Community protection
  - Tdap in pregnancy
- Future Recs
  - Zoster Candidate
- Provider Information Documents
- Questions
Which vaccine preventable disease causes the most deaths annually in U.S. children?

1. Polio
2. Measles
3. Pertussis
4. Meningococcal Meningitis
5. Influenza
Which vaccine preventable disease causes the most deaths annually in U.S. children?

1. Polio
2. Measles
3. Pertussis
4. Meningococcal Meningitis
5. Influenza
Influenza is a Leading Cause of Vaccine-Preventable Deaths in US Children

Deaths in Children ≤14 Years of Age
From Selected Vaccine-Preventable Diseases (2004-2013)

Data From the CDC Show That Influenza Deaths Affect All Pediatric Age Groups

INFLUENZA
Influenza

2016-2017 Season

2015-2016 Season
• Mild with peak in Feb/March
• 75% of cases were A
• 75% of those were H1N1

2016-2017 Season - Trivalent
• A/California/7/2009 (H1N1) pdm09-like
• A/Hong Kong/4801/2014 (H3N2)-like – NEW
• B/Brisbane/60/2008-like (B/Victoria lineage)

2016-2017 Season – Quadrivalent
• B/Phuket/3073/2013
  (B/Yamagata lineage)

Watch Southern Hemisphere H1N1
How about Egg Allergy?

ACIP 2016-2017 Recs

- Remove egg allergy chart
- 30 minute wait down to 15 minute
- All products can be used including LAIV**
- Be able to recognize and treat severe allergic reactions (all allergy symptoms except hives)
- Do not split dose/give SQ as a test

**CDC has recommended against providing LAIV (FluMist*) for the 2016-2017 season
2 Dose Recommendation for 2016-17 Season

Same as 2015-2016

Ages 6 months through 8 years:
• Give 2 doses one month apart unless child meets criteria for 1 dose

• Criteria for 1 dose:
  • Previously received 2 doses of seasonal vaccine
    • Doses do not need to have been received in the same season
    • Doses do not need to have been received in consecutive seasons
# Influenza Vaccines

## Available Products

<table>
<thead>
<tr>
<th>Age</th>
<th>Type</th>
<th>Trade Name</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 mo +</td>
<td>IIV4</td>
<td>Fluzone®</td>
<td>Sanofi</td>
</tr>
<tr>
<td>6 mo +</td>
<td>IIV</td>
<td>FluLaval®</td>
<td>GSK/ID Biologics</td>
</tr>
<tr>
<td>2-49 years</td>
<td>LAIV</td>
<td>FluMist***</td>
<td>AstraZeneca</td>
</tr>
<tr>
<td>3 years +</td>
<td>IIV4</td>
<td>Fluarix®</td>
<td>GSK</td>
</tr>
<tr>
<td>4 years +</td>
<td>ccIIV4</td>
<td>Flucelvax®</td>
<td>Seqirus</td>
</tr>
<tr>
<td>18 years +</td>
<td>RIV4</td>
<td>FluBlok®</td>
<td>Protein Science</td>
</tr>
<tr>
<td>18-64 years</td>
<td>IIV4</td>
<td>Fluzone® Intradermal</td>
<td>Sanofi</td>
</tr>
<tr>
<td>65 years +</td>
<td>IIV3</td>
<td>Fluzone® High-dose</td>
<td>Sanofi</td>
</tr>
</tbody>
</table>

**CDC has recommended against providing LAIV (FluMist®) for the 2016-2017 season**
FluMist (LAIV)

Concerns of Efficacy
FluMist

2.63 times more likely to get infection

---

### Adjusted odds of influenza for LAIV vs IIV (relative effectiveness) ages 2–17 years

<table>
<thead>
<tr>
<th>Any influenza A or B virus</th>
<th>Vaccine type</th>
<th>Influenza positive</th>
<th>Influenza negative</th>
<th>Adjusted* Influenza Odds Ratio LAIV vs IIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–17 y</td>
<td>IIV</td>
<td>81</td>
<td>672</td>
<td>REF 2.63 (1.59, 4.37)</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>38</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>H1N1pdm09</td>
<td>IIV</td>
<td>41</td>
<td>672</td>
<td>REF 3.67 (1.86, 7.31)</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>23</td>
<td>110</td>
<td></td>
</tr>
<tr>
<td>Influenza B</td>
<td>IIV</td>
<td>40</td>
<td>672</td>
<td>REF 1.62 (0.78, 3.33)</td>
</tr>
<tr>
<td></td>
<td>LAIV</td>
<td>15</td>
<td>110</td>
<td></td>
</tr>
</tbody>
</table>

*Odds Ratios > 1.0 favor IIV. Adjusted for site, age (2–4 y, 5–8 y, 9–17 y), race/Hispanic ethnicity, sex, interval from onset to enrollment, general self/parent-rated health status, and calendar time (biweekly intervals)
FluLaval for Infants

Approved by FDA

FluLaval Quadrivalent™ (IIV4)

New age indication, 6 through 35 months

Different dose than pediatric Fluzone

• FluLaval = 0.5 mL
• Fluzone = 0.25 mL

2017 CPT code determined by dose, not age

• 90686 0.5mL syringe (all ages)
• 90688 0.5mL MVD (all ages)

• 90685 0.25 mL syringe (6-35 mo)
• 90687 0.25 mL MVD (6-35 mo)
Vaccine Errors

Wrong dose for age
- Influenza (0.25mL/0.5mL)
- DTaP/Tdap
- Hep A – adult and ped
- Kinrix/ProQuad

Wrong interval between doses
Wrong diluent

Staff: 10-15 new MA’s every 2 weeks in IMG
Guidelines: New ACIP recommendations 3X per year
Storage: Multiple products, diluent not with vaccine, labels, similar names and colors
2016 Nurse Turnover

<table>
<thead>
<tr>
<th>Region</th>
<th>Turnover Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>System</td>
<td>11.9%</td>
</tr>
<tr>
<td>Central Office Region</td>
<td>9.7%</td>
</tr>
<tr>
<td>Central Region</td>
<td>12.4%</td>
</tr>
<tr>
<td>Homecare Region</td>
<td>19.2%</td>
</tr>
<tr>
<td>Medical Group Region</td>
<td>13.5%</td>
</tr>
<tr>
<td>North Region</td>
<td>11.4%</td>
</tr>
<tr>
<td>Primary Childrens Region</td>
<td>11.3%</td>
</tr>
<tr>
<td>SelectHealth Region</td>
<td>6.7%</td>
</tr>
<tr>
<td>South Region</td>
<td>10.3%</td>
</tr>
<tr>
<td>Southwest Region</td>
<td>12.7%</td>
</tr>
</tbody>
</table>
HPV 2-Dose

Evidence

1 trial of 9vHPV (girls and boys 9-14 v. females 16-26 yo)

• >97.9% seroconverted to all 9 serotypes
• Non-inferiority criteria met for seroconversion and GMTs
• GMTs significantly higher for all 9 serotypes in 2-dose 9-14 yo than 3 dose 16-26 yo

6 additional trials of 4vHPV, 2vHPV – immunogenicity non-inferior in 9-14 yo
HPV 2-Dose

New Recommendation

A 2-dose series of HPV vaccine will be appropriate if:

• Initiate first dose before age 15 years
• If patient is healthy (not immunocompromised)
• If separation of doses is 6 months (5 months minimum interval)

Series can include doses of 2vHPV, 4vHPV or 9vHPV

HPV recommended for females 9 to 26 years, males 9-21 years, high risk males 22-26
Community Protection
Community Immunity

Not “Herd Immunity”

Vaccines reduce the number of vectors/exposures

• Pneumococcal
• Rotavirus
• HPV

Some vaccines less effective because vaccination prevents disease in vaccinated but doesn’t reduce carriage

• Pertussis
• Meningococcal B
Community Immunity

Successes

Pneumococcal
  • Overall 168,000 fewer hospitalizations all ages
  • 555/100,000 less for children
  • 360/100,000 less for ages 75-84
  • 1300/100,000 less for ages 85+

Rotavirus
• Risk of hospital discharges dropped after introduction of the vaccine reduced by
  • 80% in ages 0-4 years
  • 70% in ages 5-14 years
  • 53% in ages 15-24 years
Prevalence of HPV after Introduction of the Vaccination Program in the United States

L E Markowitz, G Liu, S Hariri, M Steinau, E Dunne, E Unger
Pediatrics 2016 Mar

NHANES: Comparing 2003-2006 to 2009-2012 (cervicovaginal swabs)
4v HPV Types (Females)
- 14-19y/o – 64% decrease (11.5% to 4.3%)
- 20-24 y/o – 34% decrease (18.5% to 12.1%)
- >25 y/o – no decrease

HPV 16/18 – 7.1% to 2.8%

2009-2012, 14-24 y/o female, sexually active
Unvaccinated (16.9%) v. Vaccinated with >1 dose (2.1%)
Sexually active – VE >1 dose: 89%
Community Immunity

Vaccines reduce the number of vectors/exposures
- Pneumococcal
- Rotavirus
- HPV

Some vaccines less effective because vaccination prevents disease in vaccinated but doesn’t reduce carriage
- Pertussis – (prenatal vaccination of mother 85% more effective than postnatal vaccination)
- Meningococcal B
Tdap

Duration of Protection

Tdap Vaccine Effectiveness

**TABLE 3 Tdap VE by Year After Tdap Vaccination**

<table>
<thead>
<tr>
<th>Year After Tdap (Time Since Tdap)</th>
<th>HR (95% CI)</th>
<th>Tdap VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1 (8 d to &lt;1 y)</td>
<td>0.31 (0.24 to 0.40)</td>
<td>68.8 (59.7 to 75.9)</td>
</tr>
<tr>
<td>Year 2 (1 to &lt;2 y)</td>
<td>0.43 (0.32 to 0.59)</td>
<td>56.9 (41.3 to 68.4)</td>
</tr>
<tr>
<td>Year 3 (2 to &lt;3 y)</td>
<td>0.75 (0.54 to 1.04)</td>
<td>25.2 (−4.3 to 46.4)</td>
</tr>
<tr>
<td>Year 4+ (≥3 y)</td>
<td>0.91 (0.64 to 1.31)</td>
<td>8.9 (−30.6 to 38.4)</td>
</tr>
</tbody>
</table>

Klein NP et al. Pediatrics, 2016;137(3):e20153326
Pertussis

Morbidity/Mortality
Tdap in Pregnancy

Conferring Passive Immunity

## Tdap Vaccination Leads to Higher Antibody Levels in Infants

<table>
<thead>
<tr>
<th>Outcome Antibodies</th>
<th>Mother did not receive Tdap, mean (SEM) n=52</th>
<th>Mother received Tdap, mean (SEM) n=52</th>
<th>P value*</th>
<th>Pearson correlation coefficient (P value*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT</td>
<td>11.010 (1.796)</td>
<td>28.220 (2.768)</td>
<td>&lt; .001</td>
<td>0.158 (.055)</td>
</tr>
<tr>
<td>FHA</td>
<td>26.830 (4.022)</td>
<td>104.15 (21.664)</td>
<td>.002</td>
<td>0.165 (.045)</td>
</tr>
<tr>
<td>PRN</td>
<td>24.700 (5.765)</td>
<td>333.01 (56.435)</td>
<td>&lt; .001</td>
<td>0.965 (&lt; .001)</td>
</tr>
<tr>
<td>FIM 2/3</td>
<td>82.83 (14.585)</td>
<td>1198.99 (189.937)</td>
<td>&lt; .001</td>
<td>0.293 (&lt; .001)</td>
</tr>
</tbody>
</table>

FHA, filamentous hemagglutinin; FIM, fimbriae; PRN, pertactin; PT, pertussis toxin.

* Significant at .05 level.

Gall SA, Myers J, Picchiiero M. Maternal immunization with tetanus-diphtheria-pertussis vaccine: effect on maternal and neonatal serum antibody levels. Am J Obstet Gynecol 2012;204:e.e.e-e.e.e.

Presented to ACIP on February 2011
Tdap in Pregnancy

Timing during vaccination window

Timing of Tdap vaccination and cord blood antibody levels

<table>
<thead>
<tr>
<th></th>
<th>Cord blood antibody levels (standard deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>InPT</td>
</tr>
<tr>
<td>No Tdap</td>
<td>2.80 (1.20)</td>
</tr>
<tr>
<td>(n=27)</td>
<td></td>
</tr>
<tr>
<td>Tdap at 28-32 wks</td>
<td>4.18 (1.01)</td>
</tr>
<tr>
<td>(n=38)</td>
<td></td>
</tr>
<tr>
<td>Tdap at 33-36 wks</td>
<td>3.50 (1.25)</td>
</tr>
<tr>
<td>(n=44)</td>
<td></td>
</tr>
</tbody>
</table>

ACIP Guidance:
27—36 wks

p-value*<0.001<0.0010.001

InPT = log transformed pertussis toxin; InFHA = log transformed filamentous hemagglutinin; InPRN = log transformed pertactin; SD = standard deviation.

*Analysis of variance for differences across 3 groups

Table 2 from Naidu et al. Pertussis vaccination during pregnancy. Am J Obstet Gynecol. 2016. (Australia)
**Tdap in Pregnancy**

**Summary**

Provide Tdap and Influenza to pregnant mothers at gestational weeks 27-36

- High levels of vaccine effectiveness (71-93% depending on study)

New evidence that earlier in that period may confer higher level of protection (antibodies in cord blood)

Do not have evidence whether the duration of that protection will be impacted by earlier administration
Mening B 2-Dose

Approved, BUT----

Efficacy????

2 doses for both products
• Bexero – (0, 1 month)
• Trumenba (0, 6 month)

Category B - Individual shared clinical decision, allows for insurance coverage (ACA)

Series may be administered to age 16 through 23 years for short-term protection against most strains of serogroup B meningococcal disease

Not Category A because of low incidence of disease, lack of efficacy and safety data

No herd protection----

High risk and outbreak – need 3 doses of Trumenba (0, 1-2 mo, 6 mo)
Zoster Candidate

GSK

2 Components
• Glycoprotein E [gE2] (portion of the VZV coat)
• Strong adjuvant (AS01B)

2 doses separated by 2 months
Improved efficacy and persistence of protection (4 years so far)
Somewhat more reactogenic (but acceptable)
Submitted to FDA for approval
### Zostavax Efficacy

**Merck**

<table>
<thead>
<tr>
<th>Clinical Endpoint</th>
<th>60-80+</th>
<th>60-69</th>
<th>70-79</th>
<th>≥80</th>
<th>50-59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herpes Zoster</td>
<td>51</td>
<td>64</td>
<td>41</td>
<td>18</td>
<td>70</td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>67</td>
<td>66</td>
<td>74</td>
<td>42</td>
<td>--</td>
</tr>
</tbody>
</table>

A New Paradigm

<table>
<thead>
<tr>
<th></th>
<th>HZ/su</th>
<th></th>
<th>Placebo</th>
<th></th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>HZ</td>
<td>Per 10^3-patient-yr</td>
<td>N</td>
<td>HZ</td>
</tr>
<tr>
<td>Subjects (yr)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>3492</td>
<td>3</td>
<td>0.3</td>
<td>3525</td>
<td>87</td>
</tr>
<tr>
<td>60-69</td>
<td>2141</td>
<td>2</td>
<td>0.3</td>
<td>2166</td>
<td>75</td>
</tr>
<tr>
<td>≥70</td>
<td>1711</td>
<td>1</td>
<td>0.2</td>
<td>1724</td>
<td>48</td>
</tr>
<tr>
<td>All</td>
<td>7344</td>
<td>6</td>
<td>0.3</td>
<td>7415</td>
<td>210</td>
</tr>
</tbody>
</table>

ZOE-70 Trial

NEJM Sept 15 2016

13,900 participants, mean age 75.6 years

Efficacy

• Age 70-79 (90.0%)
• Age 80+ (89.1%)
• All (89.8%)

Pooled ZOE-50 and ZOE-70 (91.3% efficacy)

• Postherpetic neuralgia (88.8%)
Provider Information Documents

- Provider Information documents contain additional information to help answer questions that parents or patients may have after reading the VIS.

www.cdc.gov/vaccines/hcp/vis/index.html
Provider Information
Documents

So far, available for:

• 9vHPV
• Influenza
• PCV13
• Rotavirus
• Tdap

Go to each individual VIS form found at:

http://www.cdc.gov/vaccines/hcp/vis/index.html
Questions?

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