Evolving Vaccine Guidance: Influenza, Meningococcal & HPV Vaccines

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Disclaimers/Disclosure

• I have no financial relationship with the manufacturer(s) of any commercial product(s) discussed in this presentation

• I may discuss the use of vaccines in a manner not consistent with the Package Insert, but all recommendations are in accordance with recommendations from the ACIP & AAP

Influenza Virus

AAP Influenza Vaccine Recommendations for 2016-17

• Changes to the strains contained in vaccines
• LAIV should not be used in any setting
• Recommendations for persons with egg allergy have been modified
• New vaccine licensures
  – Fluad (aIIV3) Seqirus
  – Flucelvax (ccIV4) Seqirus
Will New Influenza Viruses Circulate In 2016-2017?

2015-16
- A/California/7/2009 (H1N1)pdm
- A/Switzerland/9715293/2013 (H3N2)
- B/Phuket/3073/2013 - Yamagata lineage
- B/Brisbane/60/2008 - Victoria lineage

2016-17
- A/California/7/2009 (H1N1)pdm
- A/Hong Kong/4801/2014 (H3N2)
- B/Brisbane/60/2008 - Victoria lineage
- B/Phuket/3073/2013 - Yamagata lineage
- B/Brisbane/60/2008 - For quadrivalent vaccines

ACIP Voted Down Use of LAIV for 2016-17 Influenza Season

- LAIV VE against any influenza was 3% (-49% to 37%) among children 2 to 17 years
- IIV VE against any influenza was 63% (52% to 72%)
- Other non-CDC studies confirmed LAIV worked less well than IIV
- Data from previous two seasons (2013-14 and 2014-15) showed poor and lower than expected VE for LAIV
- AAP concurred LAIV should not be used
**Inactivated Influenza Vaccines for 2016-17**

- **Trivalent (IIV3)**
  - Fluzone 18-64 yrs (Seqirus)
  - Afluria 60 yrs (Seqirus)
- **Quadrivalent (IIV4)**
  - Fluzone quad. (SP)
  - Fluzone 18-64 yrs (Seqirus)
  - Fluzone 43 yrs (ID Biomedical Corp, GSK)
- **High dose (IIV3)**
  - Fluzone (SP) 65 yrs
- **Intradermal (IIV4)**
  - Fluzone (SP) 18-64 yrs
- **Cell culture derived (cIIV3)**
  - Fluzone (Seqirus) 65 yrs
- **Stratis Jet Injector (IIV3)**
  - Afluria (Seqirus) 18-64 yrs
- **Recombinant purified protein (RIV3)**
  - Fluviral (Protein Sciences Corp) 18 yrs
- **Adjuvanted MF59 (aIIV3)**
  - Fluzone (Seqirus) 65 yrs

**Influenza Vaccine Dosing Algorithm for Children 6 mon Through 8 yr, 2016-17**

1. Has the child received ≥2 total doses of trivalent or quadrivalent influenza vaccines before July 1, 2016? (Does not need to have been received during the same season or successive seasons)
   - Yes
   - No or don’t know

   **Children 6 mos through 8 yrs:**
   - 1 dose of IIV3 or IIV4 influenza vaccine
   - ≥1 doses of ≥4yrs influenza vaccine (administered ≥4 weeks apart)

**Influenza Vaccine Contraindications & Precautions**

- **Precautions**
  - History of Guillain-Barré syndrome within 6 weeks of previous influenza vaccine
  - Acute illness, moderate to severe
- **Contraindications**
  - Severe allergy (anaphylaxis) to vaccine component
  - Age less than 6 months

**Influenza Vaccine Other Considerations**

- Febrile seizures
- Deltoid bursitis
- Guillain-Barré syndrome
- Thimerosal
- No risk of getting influenza from IIV
- Vaccination of Health Care Workers
Egg Allergy is Not a Contraindication for Influenza Vaccine

Warning Signals from the Volatile World of Influenza Viruses

N. meningitidis

N. meningitidis Serogroups

<table>
<thead>
<tr>
<th>Serogroup</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>leading cause of meningitis worldwide, most prevalent serogroup in Africa &amp; China</td>
</tr>
<tr>
<td></td>
<td>rare in Europe and the Americas</td>
</tr>
<tr>
<td>B</td>
<td>major cause of endemic disease in Europe, the Americas</td>
</tr>
<tr>
<td>C</td>
<td>major cause of endemic disease in Europe, the Americas</td>
</tr>
<tr>
<td>Y</td>
<td>associated with pneumonia; increasing problem in U.S.</td>
</tr>
<tr>
<td>W-135</td>
<td>small percentage of infections worldwide, outbreaks associated with Haj pilgrims</td>
</tr>
<tr>
<td>X</td>
<td>rarely encountered</td>
</tr>
</tbody>
</table>
**Meningococcal Incidence in All Ages by Serogroup and Adolescent MenACWY Vaccine Coverage, 1993–2013**

- **Serogroup B**: 2013: 564 cases (0.18/100,000)
  - 2014: 426 cases (0.13/100,000)
  - 2015: 376 cases (0.12/100,000)
- **Serogroup C**: 2013: 564 cases (0.18/100,000)
- **Serogroup Y**: 2013: 165 cases (0.05/100,000)

**% Coverage with ≥1 MenACWY among 13–17 year olds**
- 2013: 564 cases (0.18/100,000)
- 2014: 426 cases (0.13/100,000)
- 2015: 375 cases (0.12/100,000)

**Six Meningococcal Vaccines**

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Vaccine Type</th>
<th>Serogroups</th>
<th>Yr Licensed</th>
<th>Approved Ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menomune</td>
<td>polysaccharide</td>
<td>A,C,W,Y</td>
<td>1981</td>
<td>≥2 yrs</td>
</tr>
<tr>
<td>Menactra</td>
<td>conjugate</td>
<td>A,C,W,Y</td>
<td>2005</td>
<td>9 mon-55 yrs 1,2</td>
</tr>
<tr>
<td>Menveo</td>
<td>conjugate</td>
<td>A,C,W,Y</td>
<td>2010</td>
<td>2 mon-55 yrs 1,2</td>
</tr>
<tr>
<td>MenHibrix</td>
<td>conjugate</td>
<td>C,Y &amp; Hib</td>
<td>2012</td>
<td>6 wk-18 mon</td>
</tr>
<tr>
<td>Trumenba</td>
<td>protein</td>
<td>B</td>
<td>2014</td>
<td>10-25 yrs 3</td>
</tr>
<tr>
<td>Bexsero</td>
<td>protein</td>
<td>B</td>
<td>2015</td>
<td>10-25 yrs 3</td>
</tr>
</tbody>
</table>

1. Administer at least 4 wks after all PCV doses
2. May be given to people 56 years or older
3. May be given to people 26 years or older

**Surface Antigens, N. meningitidis**

- fHbp: Factor H binding protein
- NHBa: Neisserial heparin binding antigen
- NadA: Neisserial adhesin A

**Average Annual U.S. Cases By Age Group & Serogroup, 2009-2013**

<table>
<thead>
<tr>
<th>Serogroup B</th>
<th>Age Group</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;5 years</td>
<td>74-94</td>
</tr>
<tr>
<td></td>
<td>11-24 years</td>
<td>54-67</td>
</tr>
<tr>
<td></td>
<td>All ages</td>
<td>203-260</td>
</tr>
<tr>
<td>Serogroup C &amp; Y</td>
<td>Age Group</td>
<td>Cases</td>
</tr>
<tr>
<td></td>
<td>&lt;5 years</td>
<td>34-43</td>
</tr>
<tr>
<td></td>
<td>11-24 years</td>
<td>562-77</td>
</tr>
<tr>
<td></td>
<td>All ages</td>
<td>207-393</td>
</tr>
</tbody>
</table>
**MCV4 Routinely Recommended**

- All children and teens, ages 11 through 18 years
- People <22 years if a first year college student living in residential dorm

**Two Meningococcal Serogroup B Vaccines for Persons 10 through 25 Years**

- **Trumenba (MenB-fHbp, Pfizer)**
  - Licensed Oct 2014
  - Schedule: 3 dose (0, 1-2, 6m) or 2 dose (0, 6 mon)
  - Components: 2 highly conserved variants of fHbp
  - Strain coverage estimated >90%
- **Bexsero (MenB-4C, Novartis/GSK)**
  - Licensed Jan 2015
  - Schedule: 2 dose series (0, 1-6 m)
  - Components: fHbp subfamily B/v1, Nhba, NadA, PorA1.4
  - Strain coverage estimated >90%
  - Licensed in >35 countries starting at 2 months of age

**ACIP & AAP Recommendations: Use of Serogroup B Vaccines in Adolescents & Young Adults**

May be administered to adolescents and young adults 16 through 23 years of age to provide short term protection against most group B strains (category B)

The preferred age for MenB vaccination is 16 through 18 years of age

Recommended for people ≥10 years at increased risk of MenB (category A)

**Groups at Increased Risk for *N. meningitidis***

<table>
<thead>
<tr>
<th>MenACWY</th>
<th>MenB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complement deficiency</td>
<td>Complement deficiency</td>
</tr>
<tr>
<td>Anatomic/Functional asplenia</td>
<td>Anatomic/Functional asplenia</td>
</tr>
<tr>
<td>Outbreak setting</td>
<td>Outbreak setting</td>
</tr>
<tr>
<td>Microbiologist</td>
<td>Microbiologist</td>
</tr>
<tr>
<td>Traveler to or reside in</td>
<td>Traveler to or reside in</td>
</tr>
<tr>
<td>First year college student</td>
<td>First year college student</td>
</tr>
<tr>
<td>Military Recruit</td>
<td>Military Recruit</td>
</tr>
</tbody>
</table>
People at Increased Risk for Meningococcal Disease

- People >1 month of age
  - functional or anatomic asplenia
    - 100,000 (11 cases since 1995, 2 serogroup B)
  - persistent complement component deficiency
    - 80,000 (8 cases since 2005, none B)
  - during an outbreak of caused by vaccine serotype
    - 80,000 in 5 University outbreaks (all group B)
  - Reside in or travel to country for which meningococcal vaccine is recommended
- Microbiologists who work with meningococcus in a laboratory
  - 100,000 (22 cases 1985-2014, 10 group B)

College Students Have Lower/Equal Risk Of MenB Than Non-College Students

<table>
<thead>
<tr>
<th></th>
<th>College Students</th>
<th>18 through 23 Years Old Non-College Students</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.09/100,000</td>
<td>0.14/100,000</td>
</tr>
</tbody>
</table>

Immunogenicity of a Meningococcal B Vaccine During Princeton Outbreak

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Two Doses (N = 499)</th>
<th>One Dose (N = 17)</th>
<th>No Vaccination (N = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HiSBA ≥ 4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of participants</td>
<td>330</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>% (95% CI)</td>
<td>(61.8–70.3)</td>
<td>(32.9–41.6)</td>
<td>(6.1–45.6)</td>
</tr>
<tr>
<td>GMT (95% CI)</td>
<td>7.6 (6.7–8.5)</td>
<td>5.4 (2.5–11.7)</td>
<td>2.8 (2.3–3.5)</td>
</tr>
</tbody>
</table>

Seroconversion is defined as a human serum bactericidal antibody (HiSBA) titer of 4 or more. CI denotes confidence interval, and GMT geometric mean titer.

Summary of Different MenB Series Cost-Effectiveness Strategies

<table>
<thead>
<tr>
<th></th>
<th>Cases Prevented</th>
<th>Deaths Prevented</th>
<th>NNV to Prevent 1 Case</th>
<th>NNV to Prevent 1 Death</th>
<th>Cost QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 11 yr</td>
<td>15</td>
<td>2</td>
<td>203,000</td>
<td>1,512,000</td>
<td>$8,700,000</td>
</tr>
<tr>
<td>At 16 yr</td>
<td>28</td>
<td>5</td>
<td>107,000</td>
<td>788,000</td>
<td>$4,100,000</td>
</tr>
<tr>
<td>At 18 yr</td>
<td>29</td>
<td>5</td>
<td>102,000</td>
<td>638,000</td>
<td>$3,700,000</td>
</tr>
<tr>
<td>All college students</td>
<td>9</td>
<td>1</td>
<td>368,000</td>
<td>2,297,000</td>
<td>$9,400,000</td>
</tr>
</tbody>
</table>
Unresolved Issues Regarding MenB Vaccines

- Duration of antibody persistence unknown
- Number of vaccine-preventable cases not known
- Impact on carriage not known
- Vaccine pressure on circulating strains not known
- Safety uncertain
  - Theoretical concerns about safety from animal models regarding autoimmune disease
  - FDA aware of concerns at time of licensure
- QALY saved is >20 times higher than any other vaccine

Age at Peak Prevalence for Each Stage in Cervical Carcinogenesis

![Diagram showing age at peak prevalence for each stage in cervical carcinogenesis.]

Average Annual HPV Associated Cancers, United States 2008-2012

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Carcinoma</td>
<td>11,771</td>
<td>802</td>
</tr>
<tr>
<td>Vaginal SCC</td>
<td>237</td>
<td>513</td>
</tr>
<tr>
<td>Vulvar SCC</td>
<td>3,554</td>
<td></td>
</tr>
<tr>
<td>Penile SCC</td>
<td>1,168</td>
<td></td>
</tr>
<tr>
<td>Rectal SCC</td>
<td>12,638</td>
<td>3,100</td>
</tr>
<tr>
<td>Oropharyngeal SCC</td>
<td>1,750</td>
<td>3,260</td>
</tr>
<tr>
<td>Anal SCC</td>
<td>15,793</td>
<td>23,000 (59%)</td>
</tr>
</tbody>
</table>

Updated 9vHPV Recommendations

- Vaccinate females and males 9 through 26 years
- If series begun before 15 years of age:
  - 2 dose schedule at 0, 6-12 months
  - If 2 doses 2vHPV, 4vHPV, 9vHPV ≥6 mon apart then adequately vaccinated
  - Begin series at 9-11 years
- If begun at 15 years or later:
  - 3 doses recommended at 0, 1-2, 6 months
- For immunocompromised host of any age, 3 doses recommended
Recommendation for HPV Series if 1 or 2 Doses Administered Before 15th Birthday

- For persons initiating series before 15th birthday with 9vHPV, 4vHPV or 2vHPV and
  - Received 2 doses ≥6 months apart, are considered adequately vaccinated
  - Received 2 doses <6 months apart, should receive a 3rd dose ≥6 months after 1st dose
  - Received 1 dose, should receive a 2nd ≥6 months after 1st dose

Thank You