ACIP Recommendation Update

Mark H. Sawyer, MD
UCSD School of Medicine
Rady Children’s Hospital San Diego
What has ACIP been up to lately?

New Recommendations

- Tdap vaccination for each pregnancy
- Meningococcal conjugate vaccine use in infants and young children
- Meningococcal conjugate vaccine booster for adolescents
- Influenza vaccine-new products
- Conjugated pneumococcal vaccine for high risk older children and adults
Objectives

- Discuss the rationale for repeat Tdap immunization during each pregnancy
- Describe why conjugated meningococcal vaccine is not recommended routinely for young children
- Explain why adolescents need a booster dose of conjugated meningococcal vaccine
- Discuss the probable ACIP recommendations for the various new influenza products
- Describe the new uses for conjugated pneumococcal vaccine in high risk individuals
Tdap vaccination during pregnancy
New Tdap Pregnancy Recommendation

ACIP recommends that providers of prenatal care implement a Tdap immunization program for all pregnant women. Healthcare providers should administer a dose of Tdap during each pregnancy irrespective of the patient’s prior history of receiving Tdap. If not administered during pregnancy, Tdap should be administered immediately postpartum.

MMWR 2013; 62(07):131-135
Cocooning Recommendation

- Adolescents and adults who have or who anticipate having close contact with an infant aged less than 12 months (e.g., parents, siblings, grandparents, child-care providers and healthcare providers) and who previously have not received Tdap should receive a single dose of Tdap.
Annual Incidence by State, 2012*

2012 incidence = 13.4
(n=41,880)

*2012 data are provisional.

Source: CDC National Notifiable Disease Surveillance System, 2012

2011 Census data used for population estimates; Incidence is per 100,000 population
## Reported pertussis-related deaths by age-groups, U.S., 1980-2009

<table>
<thead>
<tr>
<th>Age-group</th>
<th>1980-1989¹</th>
<th>1990-1999¹</th>
<th>2000-2009²</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 month</td>
<td>38</td>
<td>68</td>
<td>152</td>
</tr>
<tr>
<td>2-3 month</td>
<td>11</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>4-5 month</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6-11 month</td>
<td>7</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>1-4 years</td>
<td>13</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5-10 years</td>
<td>1</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>11-18 years</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>1</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>*<em>77</em></td>
<td>**103</td>
<td>**194</td>
</tr>
</tbody>
</table>

* Includes one case with unknown age


² National Notifiable Diseases Surveillance System, CDC, 2009
DTaP Vaccine Efficacy

<table>
<thead>
<tr>
<th>Estimated VE Model</th>
<th>Cases, No. (n=682)</th>
<th>Controls, No. (n=2016)</th>
<th>OR (95% CI)</th>
<th>Estimated VE, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall No. of doses</td>
<td>53</td>
<td>19</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>0</td>
<td>53</td>
<td>19</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>5</td>
<td>629</td>
<td>1997</td>
<td>0.11 (0.06-0.21)</td>
<td>88.7 (79.4-93.8)</td>
</tr>
<tr>
<td>Time since fifth dose, mo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 doses</td>
<td>53</td>
<td>19</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>&lt;12</td>
<td>19</td>
<td>354</td>
<td>0.02 (0.01-0.04)</td>
<td>98.1 (96.1-99.1)</td>
</tr>
<tr>
<td>12-23</td>
<td>51</td>
<td>391</td>
<td>0.05 (0.02-0.09)</td>
<td>95.3 (91.2-97.5)</td>
</tr>
<tr>
<td>24-35</td>
<td>79</td>
<td>366</td>
<td>0.08 (0.04-0.13)</td>
<td>92.3 (86.6-95.5)</td>
</tr>
<tr>
<td>36-47</td>
<td>108</td>
<td>304</td>
<td>0.13 (0.07-0.24)</td>
<td>87.3 (76.2-93.2)</td>
</tr>
<tr>
<td>48-59</td>
<td>141</td>
<td>294</td>
<td>0.17 (0.09-0.31)</td>
<td>82.8 (68.7-90.6)</td>
</tr>
<tr>
<td>≥60</td>
<td>231</td>
<td>288</td>
<td>0.29 (0.15-0.54)</td>
<td>71.2 (45.8-84.8)</td>
</tr>
</tbody>
</table>

Misegades L et al, JAMA. 2012;308(20):2126-2132
# Tdap Vaccine Effectiveness Studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Age Range</th>
<th>Study Design</th>
<th>VE (Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pichichero</td>
<td>2005</td>
<td>US</td>
<td>11-64</td>
<td>Immunogenicity</td>
<td>85-89*</td>
</tr>
<tr>
<td>Ward</td>
<td>2005</td>
<td>US</td>
<td>15-65</td>
<td>Randomized Clinical Trial</td>
<td>92 (32-99)</td>
</tr>
<tr>
<td>Rank</td>
<td>2009</td>
<td>Australia</td>
<td>12-19</td>
<td>Screening</td>
<td>78 (61-88)</td>
</tr>
<tr>
<td>Wei</td>
<td>2010</td>
<td>St. Croix</td>
<td>11-18</td>
<td>Cohort</td>
<td>66 (-36-91)</td>
</tr>
<tr>
<td>CDC</td>
<td>2011</td>
<td>US</td>
<td>11-17</td>
<td>Case-Control</td>
<td>72 (38-87)</td>
</tr>
<tr>
<td>CDC</td>
<td>2012</td>
<td>US</td>
<td>11-19</td>
<td>Cohort</td>
<td>69 (38-86)</td>
</tr>
<tr>
<td>CDC</td>
<td>2012</td>
<td>US</td>
<td>11-14</td>
<td>Case-control</td>
<td>66 (52-76)</td>
</tr>
</tbody>
</table>

CDC unpublished data.

Skoff et al. NIC 2011, Washington, DC.
Terranella et al. EIS Conference 2012, Atlanta.
Two goals for maternal Tdap immunization

- Protect the mother from getting pertussis and transmitting it to her baby
  - Prenatal, intrapartum, post-natal maternal immunization
  - Re-immunization not recommended

- Generating maternal antibody so that she transfers it to her baby in utero thus protecting the baby beginning at day one of life
  - Immunization during pregnancy
  - Re-immunization with each pregnancy
Rationale for Tdap during pregnancy
Pertussis antigens GMC up to 10 years after Tdap (Adacel)

Adults (n=644)
Evidence used to support Tdap revaccination during pregnancy

- General lack of problem with inactivated vaccines during pregnancy
- VAERS-no pattern of severe adverse events seen with Tdap during pregnancy
- Decades of experience with Td vaccine in pregnancy
- Lack of adverse reactions with Tdap revaccinations in non-pregnant adults
- Manufacturer registries and ongoing clinical trials using Tdap during pregnancy
### Tdap revaccination - Published clinical trials

#### 5 years after previous Tdap

<table>
<thead>
<tr>
<th>Country</th>
<th>Product</th>
<th>Previously received (n)</th>
<th>N</th>
<th>Mean age (yrs)</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany</td>
<td>Boostrix</td>
<td>Tdap-IPV</td>
<td>415</td>
<td>11.4 ± 0.94* (range: 9 to 13)</td>
<td>Knuf et al (2010)</td>
</tr>
<tr>
<td></td>
<td>(Tdap-IPV)</td>
<td>Tdap + IPV</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Received first Tdap at age 4-8 years (replaced 5\textsuperscript{th} DTaP dose)

#### 10 years after previous Tdap

<table>
<thead>
<tr>
<th>Country</th>
<th>Product</th>
<th>Previously received (n)</th>
<th>N</th>
<th>Mean age (yrs)</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finland</td>
<td>Boostrix</td>
<td>Tdap (75) DT + ap (7)</td>
<td>82</td>
<td>21.1 ± 0.31</td>
<td>Mertsola et al (2010)</td>
</tr>
<tr>
<td>Australia</td>
<td>Boostrix</td>
<td>Tdap (153) DT + ap (35)</td>
<td>164</td>
<td>50.3 ± 9.74</td>
<td>Booy et al (2010)</td>
</tr>
</tbody>
</table>
## Summary of adverse events: 2\textsuperscript{nd} Tdap 5 years after previous dose

<table>
<thead>
<tr>
<th></th>
<th>Injection site (%)</th>
<th>Systemic (%)</th>
<th>Serious AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pain</td>
<td>Erythema</td>
<td>Swelling</td>
</tr>
<tr>
<td>Adacel - 1 to 14 days post-vaccination (Halperin 2011)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1\textsuperscript{st} Tdap (n=532)</td>
<td>73.8</td>
<td>19.2</td>
<td>16.2</td>
</tr>
<tr>
<td>2\textsuperscript{nd} Tdap (n=539)</td>
<td>87.6</td>
<td>28.6</td>
<td>25.6</td>
</tr>
<tr>
<td>Boostrix-IPV - 1 to 4 days post-vaccination (Knuf 2010)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Tdap-IPV# (n=351)</td>
<td>54.4</td>
<td>52.1</td>
<td>46.4</td>
</tr>
<tr>
<td>2\textsuperscript{nd} Tdap-IPV (n=351)</td>
<td>73.2</td>
<td>48.1</td>
<td>40.2$</td>
</tr>
</tbody>
</table>

* Deemed to be unrelated to vaccination

\# 1\textsuperscript{st} Tdap at age 4-8 years (replaced 5\textsuperscript{th} DTaP dose)

\$ 2 large injection site swellings reported (0.6%)
Tdap immunization related to pregnancy

- Do re-immunize pregnant women at every pregnancy to protect their infants
- Do not re-immunize women prenatally or post-partum
- Do not re-immunize the cocoon
- Do immunize the cocoon and everyone else 11 years of age and older one time with Tdap
Objectives

- Discuss the rationale for repeat Tdap immunization at each pregnancy
- Describe why conjugated meningococcal vaccine is not recommended routinely for young children
- Explain why adolescents need a booster dose of conjugated meningococcal vaccine
- Discuss the ACIP recommendations for the various new influenza products
- Describe the new uses for conjugated pneumococcal vaccine in high risk individuals
Meningococcemia
Caused by Neisseria meningitidis
## Licensed Meningococcal Conjugate Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Licensed Age Group</th>
<th>Serogroups</th>
<th>Dose(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Menactra® (MenACWY-D)</strong></td>
<td>9 months - 55 years</td>
<td>A, C, W-135 and Y</td>
<td>Single dose (2-55 years) 2 doses (9-23 months)</td>
</tr>
<tr>
<td>Sanofi Pasteur</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Menveo® (Men ACWY-CRM)</strong></td>
<td>2 - 55 years</td>
<td>A, C, W-135, and Y</td>
<td>Single dose</td>
</tr>
<tr>
<td>Novartis*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MenHibrix® (Hib-MenCY-TT)</strong></td>
<td>6 weeks – 18 months</td>
<td>C and Y</td>
<td>4-dose series</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Menveo®: FDA review pending (2, 4, 6, 12 through 16 months)

From: [http://aapredbook.aappublications.org/site/news/vaccstatus.xhtml](http://aapredbook.aappublications.org/site/news/vaccstatus.xhtml)
Meningococcal Disease Incidence, United States, 1970-2011


*In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative.
Incidence Declines in All Age Groups

ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
*In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative
50-60% of Disease in Children <5 Years is Due to Serogroup B

- **Serogroup B**
- **Serogroup C**
- **Serogroup Y**
- **Other**

*Other includes: serogroup W-135, nongroupables, and other serogroups
ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative
## Annual Serogroup C and Y Meningococcal Cases, Deaths, and Serious Sequelae in Children <5 Years

<table>
<thead>
<tr>
<th></th>
<th>1997-1999 &quot;High Incidence Years&quot;</th>
<th>1993-2011</th>
<th>2007-2009 &quot;Low Incidence Years&quot;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>475</td>
<td>206</td>
<td>77</td>
</tr>
<tr>
<td>Incidence</td>
<td>2.50</td>
<td>1.04</td>
<td>0.37</td>
</tr>
<tr>
<td>Deaths *</td>
<td>24-48</td>
<td>10-21</td>
<td>4-8</td>
</tr>
<tr>
<td>Sequelae**</td>
<td>48-71</td>
<td>21-30</td>
<td>8-12</td>
</tr>
</tbody>
</table>

Average annual cases, incidence, deaths, and serious sequelae
*5-10% case-fatality ratio, **10-15% of survivors with serious sequelae
ABCs cases from 1993-2011 estimated to the U.S. population with 18% correction for under reporting
In 2010, estimated case counts from ABCs were lower than cases reported to NNDSS and may not be representative.
Disease in 2011 and 2012, NNDSS*

- **139 cases reported in children <5 years in 2011**
  - 92/139 (66%) cases with serogroup available
    - 60 (65%) serogroup B
    - 10 (11%) serogroup C – 8 in children >6 months
    - 14 (15%) serogroup Y – 9 in children >6 months

- **72/139 (52%) cases with outcome available**
  - All deaths in serogroup B (n=7) or unknown serogroup (n=1)
  - Among children >6 months, all deaths from serogroup B (n=4)

- **Disease is tracking lower in 2012**
  - 407 (week 41, 2012) vs. 541 (week 41, 2011) total cases reported
  - 7 cases and 2 deaths from serogroup C & Y in children 6-59 months

*National Notifiable Diseases Surveillance System, suspect case status are excluded (n=2)
Proportions are out of cases with known serogroup result
Cost per QALY saved with HibMenCY depends on incidence during period of time evaluated. Vaccine price = $30 a dose.
Short Period of Risk for Infants Not at Increased Risk for Meningococcal Disease

Dose 2

Dose 1

Dose 3

Dose 4

Cases per 100,000

Age (months)

0-1 2-3 4-5 6-7 8-9 10-11 12-17 18-23 24-35 36-47 48-59

*ABCs, 1998-2007 average annual estimated rates to the U.S. population
No current recommendation for routine use of conjugated meningococcal vaccines in children <11 years of age
Community or organizational outbreak

- Vaccination may be recommended for target groups during outbreaks of meningococcal disease in communities and organizations

- Need for multiple doses limits benefit of HibMenCY in this setting

- However, availability of vaccine for infants useful if infants are targeted for vaccination in response to an outbreak
What about the 2nd dose of conjugated meningococcal vaccine in adolescents?
The problem

- Meningococcal infection is the most rapidly fatal infection known
- There is no time for your immune system to react
- There is no time for your memory T cells to remember
- You have to have circulating levels of antibody all the time to be protected
## Summary: Serogroup C Antibody Persistence Studies

<table>
<thead>
<tr>
<th>Age at vaccination</th>
<th>Vaccine</th>
<th>N</th>
<th>Years post-vaccine</th>
<th>Serogroup C SBA</th>
</tr>
</thead>
<tbody>
<tr>
<td>11-18 years*</td>
<td>Mencevo, Menactra</td>
<td>273, 185</td>
<td>2</td>
<td>% hSBA ≥ 1:8; 62% Mencevo, 58% Menactra</td>
</tr>
<tr>
<td>11-18 years**</td>
<td>Menactra, MPSV4</td>
<td>52, 48</td>
<td>3</td>
<td>% hSBA ≥ 1:4; 35% Menactra, 35% MPSV4</td>
</tr>
<tr>
<td>11-18 years***</td>
<td>Menactra, MPSV4</td>
<td>71, 72</td>
<td>3</td>
<td>% brSBA ≥ 1:128 75% Menactra, 60% MPSV4</td>
</tr>
<tr>
<td>2-10 years***</td>
<td>Menactra, MPSV4</td>
<td>108, 207</td>
<td>5</td>
<td>% brSBA ≥ 1:128 55% Menactra, 42% MPSV4</td>
</tr>
<tr>
<td>11-18 years***</td>
<td>Menactra, MPSV4</td>
<td>16, 10</td>
<td>5</td>
<td>% brSBA ≥ 1:128 56% Menactra, 60% MPSV4</td>
</tr>
</tbody>
</table>

New 2\textsuperscript{nd} dose of conjugated meningococcal vaccine

- Routine booster dose at age 16 for those immunized at 11-12 years of age
- For those immunized at age 13-15, booster at 16-18 (particularly before college)
- No booster for those first immunized at age 16 or above
- No vaccine at age 22 or above
Current Recommendations for use of Conjugate Meningococcal Vaccines

- Routine immunization at age 11-12 with a second booster dose beginning at age 16
- No routine immunization recommendation for those less than 11 years of age or for those 21 years or older
- High risk individuals (asplenia, compliment deficiency) should be immunized beginning at 2 months of age
- Vaccine may be used in outbreak situations for all ages 2 months-55 years
- Number of doses needed depends on age at vaccination
- Booster doses for high risk needed every 5 years
Objectives

- Discuss the rationale for repeat Tdap immunization at each pregnancy
- Describe why conjugated meningococcal vaccine is not recommended routinely for young children
- Explain why adolescents need a booster dose of conjugated meningococcal vaccine
- Discuss the ACIP recommendations for the various new influenza products
- Describe the new uses for conjugated pneumococcal vaccine in high risk individuals
Expected ACIP Influenza Recommendations 2013-2014

- Continue to support annual immunization for everyone 6 months of age and older
- All available vaccine products are acceptable for indicated age groups
- No preference for any one vaccine product
- Ample supply of vaccine
Objectives

- Discuss the rationale for repeat Tdap immunization at each pregnancy
- Describe why conjugated meningococcal vaccine is not recommended routinely for young children
- Explain why adolescents need a booster dose of conjugated meningococcal vaccine
- Discuss the ACIP recommendations for the various new influenza products
- Describe the new uses for conjugated pneumococcal vaccine in high risk individuals
Incidence of IPD in adults aged 18-64 years with selected underlying conditions, United States, 2009

- 20 fold increased risk
- 3-7 fold increased risk

CDC, ABCs, unpublished, 2011; based on Kyaw, JID 2005;192:377-86
ACIP Recommendations for PCV13 use in High Risk Adults

- Routinely recommended for PCV13-naïve adults 19 years of age or older
  - Anatomic or functional asplenia, (sickle cell)
  - Cochlear implant, CSF leaks
  - Immunocompromised (e.g. HIV, nephrotic syndrome)
- PPSV23-naïve adults
  - 1 dose of PCV13
  - PPV23 at least 8 weeks after PCV13
- Adults who have received PPV23 previously
  - 1 dose of PCV13 at least one year after PPSV23
  - If additional PPSV23 doses needed, at least 8 weeks after PCV13 dose and at least 5 years after previous PPSV23 dose

Category A

- MMWR Oct 2012
Prevention of pneumococcal disease among children 6 through 18 years old with immunocompromising conditions

- A single dose of PCV13 is recommended for children aged 6–18 years who have not received PCV13 previously and who are at increased risk for invasive pneumococcal disease because of anatomic or functional asplenia, including sickle cell disease, immunocompromising conditions such as HIV-infection, cochlear implant, or cerebrospinal fluid leaks, regardless of whether they have previously received PCV7 or PPSV23.
- Recommendations for PPSV23 use for children in this age group remain unchanged.
What will ACIP be up to next?

- Conjugated pneumococcal vaccine for adults in general
- Tdap revaccination for the general population
- Product preference for some influenza vaccines
- Zoster vaccine at age 50