Pneumococcal Disease and Pneumococcal Vaccines

Andrew Kroger, M.D., M.P.H.
Medical Educator

Pink Book Webinar Series
October 4, 2017
Streptococcus pneumoniae

- Gram-positive bacteria
- 92 known serotypes
- Polysaccharide capsule important virulence factor
- Type-specific antibody is protective
- Limited cross-reactivity
Pneumococcal Disease

- Second most common cause of vaccine-preventable death in the U.S.

- Major clinical syndromes
  - Pneumonia
  - Bacteremia
  - Meningitis
Invasive Pneumococcal Disease Incidence by Age Group – 2013*

Risk Factors for Invasive Pneumococcal Disease

- Functional or anatomic asplenia, including sickle-cell disease
- Altered immunocompetence
- Underlying medical conditions, including chronic renal disease, nephrotic syndrome, and CSF leak
- Cigarette smoking (adults 19 years and older)
- Cochlear implant
Pneumococcal Disease Epidemiology

- **Reservoir**: Human carriers
- **Transmission**: Respiratory and autoinoculation
- **Temporal pattern**: Winter and early spring
- **Communicability**: Unknown; probably as long as organism in respiratory secretions
Pneumococcal Vaccines

- **1977**: 14-valent polysaccharide vaccine licensed
- **1983**: 23-valent polysaccharide vaccine licensed (PPSV23)
- **2000**: 7-valent polysaccharide conjugate vaccine licensed (PCV7)
- **2010**: 13-valent polysaccharide conjugate vaccine licensed (PCV13)
Pneumococcal Polysaccharide Vaccine (PPSV23) Characteristics

- Purified capsular polysaccharide antigen from 23 types of pneumococcus

- Not effective in children younger than 2 years
Pneumococcal Conjugate Vaccine (PCV13) Characteristics

- Contains 13 serotypes of *S. pneumoniae* conjugated to nontoxic diphtheria CRM$_{197}$ carrier protein

- Approval based on demonstration of immunologic noninferiority to PCV7 rather than clinical efficacy

*MMWR* 2010;59(No. 9):258-61
PCV7 Introduction Among U.S. Children and its Impact on Invasive Pneumococcal Disease

- PCV7 introduced into routine schedule 2000

Moore, IDSA, 2009 and CDC, unpublished data
In 2008, 61% of invasive pneumococcal disease cases among children younger than 5 years were attributable to the serotypes included in PCV13.
Pneumococcal Conjugate Vaccine (PCV13) in Adults

- In 2013, 20%-25% of invasive pneumococcal disease cases among adults 65 years old and older were attributable to PCV13 serotypes

- 10 percent of community-acquired pneumonia in adults due to PCV13 serotypes (Pfizer urine studies)
Pneumococcal Polysaccharide Vaccine (PPSV23) Immunogenicity/Effectiveness

- Most estimates range between 60%-70% effective against invasive disease among immunocompetent older persons and adults with underlying illnesses.
- Effectiveness among immunocompromised or very old persons not demonstrated.
Pneumococcal Conjugate Vaccine (PCV13) Immunogenicity/Efficacy

- Highly immunogenic in infants and young children, including those with high-risk medical conditions

- PCV7 was 97% effective against invasive disease caused by vaccine serotypes (presumably PCV13 as well)
# New Evidence Supporting PCV13 use among Adults, CAPiTA Results

<table>
<thead>
<tr>
<th>Study/Population</th>
<th>Endpoint</th>
<th>Vaccine Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPiTA</td>
<td>PCV13-serotype IPD</td>
<td>75% (41%, 91%)</td>
</tr>
<tr>
<td>~85,000 Adults 65+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netherlands</td>
<td>PCV13-serotype nonbacteremic pneumonia</td>
<td>45% (14%, 65%)</td>
</tr>
</tbody>
</table>

CAPiTA, ACIP, June 2014
Prevention of Pneumococcal Disease Among Infants and Children — Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine

Recommendations of the Advisory Committee on Immunization Practices (ACIP)
PCV13 Licensure

- PCV13 is approved by the Food and Drug Administration for:
  - Children 6 weeks through 17 years of age
  - Adults 50 years of age and older

- ACIP recommended use of PCV13 for immunocompromised persons 6 years and older (2012, 2013)

- ACIP recommended use of PCV13 for all adults 65 years or older in 2014
PCV13 IN CHILDREN
ACIP Recommendations for PCV13

- Routine vaccination recommendation the same as for PCV7 (children 2-59 months)
  - 4 doses at 2, 4, 6, and 12 to 15 months
  - Fewer doses if series started at 7 months of age or older

- Children who have received 1 or more doses of PCV7 should complete the immunization series with PCV13

*MMWR* 2010;59(No. 9):258-61
# Pneumococcal Conjugate Vaccine Schedule for Unvaccinated Older Children - Primary Series

<table>
<thead>
<tr>
<th>Age at First Dose</th>
<th># of Doses</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-11 months</td>
<td>2 doses</td>
<td>Yes</td>
</tr>
<tr>
<td>12-23 months</td>
<td>2 doses*</td>
<td>No</td>
</tr>
<tr>
<td>24-59 months</td>
<td>1 dose</td>
<td>No</td>
</tr>
<tr>
<td>24-71 months, medical conditions**</td>
<td>2 doses*</td>
<td>No</td>
</tr>
</tbody>
</table>

*Separated by at least 8 weeks; see *MMWR* 2010;59(RR-11):1–19

**Chronic heart, lung disease, diabetes, CSF leak, cochlear implant, sickle cell disease, other hemoglobinopathies, functional or anatomic asplenia, HIV infection, immunocompromising conditions
ACIP Recommendations for PCV13 Supplemental Dose

- A single supplemental dose of PCV13 is recommended for children who have received a complete age-appropriate series of PCV7:
  - Healthy children 14 through 59 months
  - Children 14 through 71 months with an underlying medical condition (including those who have already received a dose of PPSV)

*MMWR 2010;59(No. 9):258-61*
ACIP Recommendations for PCV13 Children

- Children aged 24–71 months with underlying medical conditions who received an incomplete schedule of PCV7 should receive 2 doses of PCV13 (8 weeks apart)
ACIP Recommendations for PCV13 Dose

- A dose of PCV13 should be administered to children 6 through 18 years of age who are at increased risk for invasive pneumococcal disease* (and no prior PCV13 doses)
  - Functional or anatomic asplenia, including sickle cell disease
  - HIV infection and other immunocompromising conditions
  - Cochlear implant
  - CSF leak

- Regardless of previous history of PCV7 or PPSV vaccine

*Off-label recommendation, ACIP vote, February 20, 2013
PCV13 USE IN ADULTS
PCV13 for Adults

- Licensed for use among adults >50 years old on 12/30/11
- FDA approved under the Accelerated Approval Pathway
- Based on noninferior immunogenicity compared to PPSV23
- Postapproval condition of licensure:
  - Randomized controlled trial of PCV13 against pneumococcal pneumonia among adults ≥65 years old in the Netherlands
PCV13 for Adults (2014)

- ACIP now recommends PCV13 for adults 65 years old and older
- Some adults have received PCV13 already
Incidence of IPD in Adults Aged 18-64 Years with Selected Underlying Conditions, United States, 2009

Unpublished data, Active Bacterial Core surveillance, 2009
PCV13 for Immunocompromised Adults*

- Adults 19 years of age or older with:
  - Immunocompromising conditions
  - Functional or anatomic asplenia
  - CSF leaks
  - Cochlear implants

- Those who have not previously received PCV13 or PPSV23 should receive a single dose of PCV13 followed by a dose of PPSV23 at least 8 weeks later, with a booster dose of PPSV23 5 or more years later

*MMWR. October 12, 2012; 61(40):816-819
PPSV23 USE IN CHILDREN AND ADULTS
Pneumococcal Polysaccharide Vaccine Recommendations

- Persons 2 years and older with normal immune systems who have chronic illness

<table>
<thead>
<tr>
<th>Cardiovascular of pulmonary disease (asthma if 19 years old or older)</th>
<th>Smoking (19 years old or older)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>CSF leak</td>
</tr>
<tr>
<td>Liver disease</td>
<td>Cochlear implant</td>
</tr>
<tr>
<td>Alcoholism</td>
<td></td>
</tr>
</tbody>
</table>

- Persons in environments or settings with increased risk
Pneumococcal Polysaccharide Vaccine Recommendations

- Persons 2 years and older who are immunocompromised (due to disease or treatment)
  - Asplenia (functional or anatomic)
  - Chronic renal failure
  - Nephrotic syndrome
  - Hodgkin disease
  - Lymphoma and leukemia
  - Multiple myeloma
  - Organ transplant
  - HIV infection
Pneumococcal Polysaccharide Vaccine
Revaccination

- Routine revaccination of immunocompetent persons is not recommended
- Revaccination recommended for persons 2-64 years of age who are at highest risk of serious pneumococcal infection

*MMWR* 2010;59(No.34):1102-5
Pneumococcal Polysaccharide Vaccine Candidates for Revaccination

- 5-year interval (2-64 years) with additional dose after 65th birthday, 5 years after previous dose:
  - Functional or anatomic asplenia (including sickle cell disease)
  - Immunosuppression (including HIV infection)
  - Transplant
  - Chronic renal failure
  - Nephrotic syndrome

- 1 dose is recommended after the 65th birthday, but only 1 dose recommended after 65th birthday

MMWR 2010;59(No.34):1102-5 and 2010;59(RR-11)
Administering PCV13 and PPSV23 Vaccines
General Rules

- PCV13 and PPSV23 should not be administered during the same clinic visit
  - Either vaccine may be administered simultaneously with influenza vaccine

- Administer PCV13 before PPSV23 whenever possible
<table>
<thead>
<tr>
<th>Medical indication</th>
<th>Underlying medical condition</th>
<th>PCV13 for ≥18 years</th>
<th>PPSV23* for 19 through 64 years</th>
<th>PCV13 at ≥65 years</th>
<th>PPSV23 at ≥65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>None of the below</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunocompetent</td>
<td>Alcoholism</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>persons</td>
<td>Chronic heart disease*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic liver disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cigarette smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cochlear implants</td>
<td>✓</td>
<td>≥8 weeks after PCV13</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>CSF leaks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons with</td>
<td>Congenital or acquired</td>
<td>✓</td>
<td>≥8 weeks after PCV13</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>functional or</td>
<td>asplenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>anatomic asplenia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sickle cell disease/other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>hematologicopathies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>Chronic renal failure</td>
<td>✓</td>
<td>≥8 weeks after PCV13</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>persons</td>
<td>Congenital or acquired</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>immunodeficiencies*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Generalized malignancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>HIV infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hodgkin disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Idiopathic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immunosuppression*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Leukemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple myeloma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neoplastic syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Solid organ transplant</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*This PPSV23 column only refers to adults 19 through 64 years of age. All adults 65 years of age or older should receive one dose of PPSV23 or more doses after any prior dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine. No additional doses of PPSV23 should be administered following the dose administered at 65 years of age or older.

*Including chronic obstructive pulmonary disease, emphysema, and asthma

*Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease)

*Includes treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy

PCV13 and PPSV23 for Adults 19 – 64 Years

Immunocompromised, asplenic (sickle cell, hemoglobinopathy), CSF leaks, cochlear implants who are pneumococcal-naïve

PCV13 + PPSV23 + PPSV23* + PPSV23 (@ ≥65 years)

>8 weeks  >5 years  >5 years

*Second PPSV23 dose before age 65 years NOT recommended for adults with CSF leaks or those with cochlear implants

*ACIP off-label recommendation for PCV13 for adults 19 through 49 years of age
PCV13 and PPSV23 for Adults 19 – 64 Years

Immunocompromised, asplenic (sickle cell, hemoglobinopathy), CSF leaks, cochlear implants
who have previously received PPSV23

PPSV23 + PCV13 + PPSV23* + PPSV23 (@ >65 years)

>1 year >8 weeks >5 years

>5 years

*Second PPSV23 dose before age 65 years NOT recommended for adults with CSF leaks or those with cochlear implants
*ACIP off-label recommendation for PCV13 for adults 19 through 49 years of age
PCV13 and PPSV23 for Adults 65 Years and Older

- Pneumococcal-naïve or unknown vaccination history
- Healthy adult

PCV13 (@ >65 years) + PPSV23

12 months

- If PPSV23 cannot be given at 12 months later, it should be given during the next visit
PCV13 and PPSV23 for Adults 65 Years and Older

- Pneumococcal-naïve or unknown vaccination history
- High-risk immunocompromised adult

PCV13 (@ ≥65 years) + PPSV23

8 weeks
PCV13 and PPSV23 for Adults 65 Years and Older

- Previously received 1 or more doses of PPSV23
- High-risk immunocompromised adult

1. **PPSV23** *(@ > 65 years)*
   - + **PCV13**
   - > 1 year

2. **PPSV23** *(@ < 65 years)*
   - + **PCV13** *(@ > 65 years)*
   - > 1 year
   - + **PPSV23** *(@ > 65 years)*
   - > 8 weeks

*Doses already administered* > 5 years
Pneumococcal Vaccines
Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose of vaccine
- Moderate or severe acute illness
## Pneumococcal Vaccines
### Adverse Reactions

<table>
<thead>
<tr>
<th>adverse reaction</th>
<th>PPSV23</th>
<th>PCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions</td>
<td>30%-50%</td>
<td>5%-49%</td>
</tr>
<tr>
<td>Fever, myalgia</td>
<td>&lt;1%</td>
<td>24-35%</td>
</tr>
<tr>
<td>Febrile seizures</td>
<td>---</td>
<td>Rare:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1-14/100,000; with IIV 4 -45/100,000</td>
</tr>
<tr>
<td>Severe adverse reactions</td>
<td>rare</td>
<td>8% (local)</td>
</tr>
</tbody>
</table>