Vaccines for Primary Care

Pneumococcal, Shingles, Pertussis

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Pneumococcal Vaccine
Pneumococcal Disease

• 2\textsuperscript{nd} most common cause of vaccine preventable death in the US

• Major Syndromes
  – Pneumonia
  – Bacteremia
  – Meningitis
### Active Bacterial Core Surveillance (ABCs)
Report Emerging Infections Program Network
Streptococcus pneumoniae, 2010 (ORIG)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cases</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1</td>
<td>142</td>
<td>(34.2)</td>
</tr>
<tr>
<td>1</td>
<td>112</td>
<td>(26.6)</td>
</tr>
<tr>
<td>2-4</td>
<td>171</td>
<td>(13.1)</td>
</tr>
<tr>
<td>5-17</td>
<td>111</td>
<td>(2.2)</td>
</tr>
<tr>
<td>18-34</td>
<td>260</td>
<td>(3.8)</td>
</tr>
<tr>
<td>35-49</td>
<td>670</td>
<td>(10.5)</td>
</tr>
<tr>
<td>50-64</td>
<td>1,064</td>
<td>(18.8)</td>
</tr>
<tr>
<td>≥ 65</td>
<td>1,292</td>
<td>(36.4)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3,822</td>
<td>(12.8)</td>
</tr>
</tbody>
</table>

* Cases or deaths per 100,000 population for ABCs areas
Vaccine Target

- Polysaccharide capsule allows bacteria to resist phagocytosis
- Antibodies to capsule facilitate phagocytosis
- >90 different pneumococcal capsular serotypes
- Vaccines contain most common serotypes causing disease
Pneumococcal Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Serotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumovax</td>
<td>1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F</td>
</tr>
<tr>
<td>Prevnar-13</td>
<td>1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F</td>
</tr>
</tbody>
</table>
Pneumococcal Vaccines

• Pneumococcal polysaccharide vaccine (PPSV23; Pneumovax)
  – Contains capsular polysaccharides
  – 23 most commonly infecting serotypes
    • Cause 60% of all pneumococcal infections in adults
  – Not recommended for children <2 due to poor immunogenicity of polysaccharides
Pneumococcal Vaccines

• Pneumococcal conjugate vaccine (PCV13, Prevnar)
  – Polysaccharides linked to nontoxic protein
    • higher antigenicity
  – Stimulates mucosal antibody
    • Eliminates nasal carriage in young children
    • Herd effect in adults
      – Reduction in PCV7 serotype disease >90%
Prevnar 13

• 2000 - PCV7 approved for infants toddlers
• 2010 - PCV13 recommended for infants and toddlers
• 2012 – ACIP recommended PCV13 for high-risk adults
• 2014 – recommended for adults >65
• 2018 – ACIP will revisit PCV13 use in adults
  – Childhood vaccines may eliminate these vaccine strains from population
Adult 65 and Older

• CDC recommends all adult ≥ 65 receive 2 types of pneumococcal vaccines
  – One dose of PCV13 (first)
  – One dose of PPSV23 (6 to 12 months after PCV vaccine)
  – This age group requires both vaccines for the best protection against pneumococcal disease
Adult 19 to 64 Years Who Only Need PPSV23

- Those with chronic conditions
  - Asthma
  - Diabetes
  - Heart disease
  - Alcoholism
  - Liver disease
- Cigarette smokers
- Residents of nursing homes or other long-term care facilities
- When they turn 65 this group should receive a dose of PCV13
Adults 19 to 64 Who Should Receive both PCV13 and PPSV23*

- Functional or anatomic asplenia†
- Cochlear implants
- Cerebrospinal fluid leaks†
- Lymphoma, leukemia, Hodgkin disease,†
- Solid organ transplants†

* PCV13 and PPSV23 cannot be given at the same visit
† A second PPSV23 vaccine is recommended for these individuals five years after the first PPSV23 dose
Age 65 Years or Older

- If PCV13 was given before age 65 years, no additional PCV13 is needed.

**No history of pneumococcal vaccine**

- PCV 13 (Prevnar 13®)
- 6-12 month interval
- PPSV 23 (Pneumovax® 23)

**Received PPSV23 before age 65**

- 1 year interval
- PCV 13
- 6–12 month interval (and at least 5 years after prior dose of PPSV23)
- PPSV 23

**Received PPSV23 at age 65 or older**

- 1 year interval
- PCV 13
Age 19-64 Years with Underlying Conditions

- Smoker,
- Long-term facility resident, or
- Chronic conditions:
  - heart disease (excluding hypertension)
  - lung disease (including asthma)
  - liver disease (including cirrhosis)
  - diabetes
  - alcoholism

- Immunocompromised (including HIV infection),
- Chronic renal failure,
- Nephrotic syndrome, or
- Asplenia

- CSF leaks or
- Cochlear implants

*DO NOT administer PCV13 and PPSV23 at the same visit.*

California Department of Public Health, Immunization Branch [www.EZIZ.org](http://www.EZIZ.org)

This publication was supported by Grant Number H23/CCH922507 from the Centers for Disease Control and Prevention (CDC)
Zoster
VZV

• Shingles recognized in ancient times
• 1875, Steiner inoculated “volunteers” with chicken pox from infected individual
• Only enveloped virions are infectious
  – Sensitive to detergents, air drying
• Spreads from cell to cell by direct contact
• Smallest of the herpesviridae
VZV Epidemiology

**Chicken Pox**
- Childhood
  - 90% < 13yo
- Incubates 14 to 15 days
- More frequent in adults in tropics
- Infectious 48 hrs prior to lesions
- Infectious until lesions crusted over (4-5 days)

**Shingles**
- Reactivation
- All ages affected
- 5-10 cases/1000 age > 60
- 4% experience 2\textsuperscript{nd} episode
- Higher for immune compromised
- Lifetime risk of developing zoster is about 30%
Reactivation

• Decline in cell-mediated immunity with age
• 30-40% over age 55 do not have detectable VZV-specific T cell responses
• Response improves with periodic subclinical VZV reactivation
  – Exposure to children with chickenpox
Herpes Zoster Vaccine - Zostavax

• Licensed by FDA in 2006
  – >38,500 non immunocompromised adults ≥60 years old
  – Median follow-up 3.1 years
  – Live-attenuated Oka-strain VZV (≥14X titer in Varivax)
  – Safety
    • Serious adverse events not more common in vaccinated group
    • Local reactions more common in vaccine group
Efficacy of Zoster Vaccine in the Shingles Prevention Study.

Efficacy (95% Confidence Interval)

Herpes Zoster, Incidence per 1000 person-yr

- All Subjects: 51.3% (44.2-57.6) P < .001
- 60-69: 63.9% (NA)
- ≥70: 37.6% (NA)

Vaccine
Placebo

Age, y

Oxman M N Clin Infect Dis. 2010;51:197-213
Zostavax – Advisory Committee on Immunization Practices

• 2008: Zostavax recommended by ACIP
  – 1 dose for adults ≥60 years
  – Contraindicated in immunocompromised
  – Vaccine efficacy: 51% vs. Herpes Zoster
  – Vaccine efficacy: 67% vs. Post Herpetic Neuralgia
Zostavax ACIP

• 2011: FDA age expansion to 50-59 yr olds
  – ZEST study shows 70% reduction in of HZ in age 50-59
  – No change to ACIP recommendation
    • Vaccine shortages (now resolved)
    • Higher herpes zoster disease burden in people ≥60 years

• 2013: ACIP affirmed recommendation for adults 60 years and older
  – Waning of immunity
Zostavax: Duration of Protection against HZ

Effectiveness of HZ Vaccine by Years After Vaccination
Kaiser Permanente Southern California, 2007-2015

Tseng, et al., JID, 2016
Why has uptake been sluggish?

- Price
- Storage & handling (frozen vaccine)
- Supply shortages (resolved)
- Medicare Part D reimbursement
- Lower prioritization of adult vaccines
- General fragmentation of preventive care for seniors
Contraindications/Precautions

• Immunocompromised – should avoid
  – Primary or acquired immunodeficiency
  – HIV with CD<200
  – Stem cell or organ transplant
  – Biologics or prednisone >20 mg/day

• Lower efficacy with pneumococcal vaccine coadministration
Investigational Vaccine (HZ/su)

- Inactivated zoster vaccine
- Not yet approved
- May be beneficial in those >70 years
- 90%+ efficacy
- Requires 2 doses
Pertussis Vaccine
Almost all deaths among infants < 6 months old

http://www.pkids.org/diseases/pertussis.html
Reported NNDSS pertussis cases: 1922-2015

Number of cases

Year

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service
Reported pertussis incidence by age group: 1990-2015

SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System
Whole cell pertussis vaccine (wP)

- 1st generation vaccine (1940s)
  - heat/formalin killed whole bacterial cells
  - Effective
  - Reactogenic (side-effects)
  - Still used in much of developing world
**Pertussis Vaccines**

- **2nd generation acellular vaccines (1990s):**
  - Approved for use in children in US in 1991 (DTaP)
  - Approved for adults and adolescents in 2005 (Tdap)

**But**
- Immunity wanes rapidly (3-5 yrs)
- Pertactin (PRN)-deficient mutant strains now prevalent (vaccine escape mutants)
Possible reasons for increase in pertussis

Increased awareness and detection – PCR and serology diagnosis

Decrease in vaccination rate / increase in number of vaccine refusers

Ineffectiveness of acellular vaccines

Evolution of *B. pertussis* strains to evade vaccine-elicited immunity
Recommendations

• Single booster with Tdap
  – Adults age 19-64
  – Age >65 who have not previously received Tdap

• Higher importance
  – Adults who have close contacts with infants
    • Grandparents, childcare providers, HCWs
  – Obesity
  – Asthma

• All pregnant women (27-36 weeks gestation)
  – Re-immunization with subsequent pregnancies
Questions?