

Pneumococcal Disease: Treatment and Prevention

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Donald Bennett has no relevant financial relationships to disclose.

Goal. The goals of this lesson are to give an overview of the treatment of pneumococcal disease and the vaccines to prevent it.

Objectives. At the completion of this activity, the participant will be able to:

1. recognize the types and prevalence of pneumococcal disease in the United States;
2. list the available pneumococcal vaccines and their indications;
3. recognize the preferred timing of vaccine administration in adult and pediatric populations;
4. identify contraindications, precautions, and potential adverse reactions associated with pneumococcal vaccines; and
5. demonstrate an understanding of high-risk populations which need to be targeted for vaccination.

Streptococcus pneumoniae, also known as pneumococcus, is a Gram-positive bacterium that is capable of causing pneumonia, and invasive bacteremia and meningitis. Pneumococcal disease is one of the most prevalent vaccine-preventable infections in the United States. It is a common secondary infection to influenza. Several decades ago, *S. pneumoniae* was extremely susceptible to parenteral penicillin G and even oral penicillin V potassium. Unfortunately, like many other bacteria, antibiotic

resistance has developed over the years which makes the prevention of this disease even more important.

According to the Centers for Disease Control and Prevention (CDC), pneumococcal disease causes four million disease episodes and 22,000 deaths annually. Pneumococcal ear infections (otitis media) are the most common type of pneumococcal disease among children, causing 1.5 million infections that often result in antibiotic use. Each year, nearly 160,000 children younger than five years of age see a doctor or are admitted to the hospital with pneumococcal pneumonia. Pneumococcal pneumonia accounts for 72 percent of all direct medical costs for treatment of pneumococcal disease. In 30 percent of severe *S. pneumoniae* cases, the bacteria are fully resistant to one or more of the clinically relevant antibiotics. Resistant infections complicate treatment and can result in almost 1,200,000 illnesses and 7,000 deaths per year. The excess costs associated with these cases are approximately \$96,000,000 annually.

Most of the more than 90 known serotypes of pneumococci are encapsulated, with their surfaces composed of complex polysaccharides. Capsular polysaccharides inhibit phagocytosis and are one determinant of the pathogenicity of the organism. They are antigenic, and provide the foundation for classifying pneumococci by serotypes.

Type-specific antibodies facilitate phagocytosis and clearance of the organism. Antibodies to some pneumococcal capsular polysaccharides may cross-react with related types providing protection against additional serotypes.

Most *S. pneumoniae* serotypes have been shown to cause serious disease, but only a few serotypes produce the majority of pneumococcal infections. The 10 most common serotypes are estimated to account for about 62 percent of invasive disease worldwide.

Efforts to develop effective pneumococcal vaccines began as early as 1911. However, with the advent of penicillin in the 1940s, interest in pneumococcal vaccination declined, until it was observed that many patients still died despite antibiotic treatment. By the late 1960s, efforts were again being made to develop a polyvalent pneumococcal vaccine. The first pneumococcal vaccine was licensed in the United States in 1977. The first conjugate pneumococcal vaccine was licensed in 2000.

The prevalence of serotypes causing disease differs by patient age group and geographic area. In the United States, prior to widespread use of 7-valent pneumococcal conjugate vaccine (PCV7), the seven most common serotypes isolated from blood or cerebrospinal fluid (CSF) of children younger than five years of age accounted for 80 percent of infections. These seven serotypes accounted for only

about 50 percent of isolates from older children and adults.

Pneumococci are common inhabitants of the respiratory tract, and may be isolated from the nasopharynx in up to 90 percent of healthy persons. Rates of asymptomatic carriage vary with age, environment, and the presence of upper respiratory infections. Among school-aged children, 20 to 60 percent may be colonized. The duration of carriage varies and is generally longer in children than adults. In addition, the relationship of carriage to the development of natural immunity is poorly understood.

Clinical Features

The major clinical syndromes of pneumococcal disease are pneumonia, bacteremia, and meningitis.

Pneumonia. Pneumonia is a disease of the lung that is caused by a variety of bacteria including *Streptococcus*, *Staphylococcus*, *Pseudomonas*, *Haemophilus*, *Chlamydia* and *Mycoplasma*, in addition to several viruses and, less frequently, fungi. Pneumonia can be divided into two forms: bronchial pneumonia and lobar pneumonia. Bronchial pneumonia is frequently found in infants, young children, and older adults. It is caused by a variety of bacteria including *S. pneumoniae*. Bronchial pneumonia involves the alveoli in the larger bronchioles. Lobar pneumonia involves an entire single lobe of the lungs or sometimes more than one lobe. Lobar pneumonia is more prone to occur in younger adults. *S. pneumoniae* causes more than 80 percent of the cases of lobar pneumonia. The incubation period of pneumococcal pneumonia is short, about one to three days. Symptoms generally include an abrupt onset of fever and chills or rigors. Classically there is a single rigor, and repeated shaking chills are uncommon. Other common symptoms include pleuritic chest pain, cough productive of mucopurulent sputum, dyspnea, tachypnea, hypoxia, tachycardia, malaise, and weakness. Nausea,

vomiting, and headaches occur less frequently.

Approximately 400,000 hospitalizations from pneumococcal pneumonia are estimated to occur annually in the United States. Pneumococci account for up to 36 percent of adult community-acquired pneumonia. Pneumococcal pneumonia has been demonstrated to complicate influenza infection. About 25 to 30 percent of patients with pneumococcal pneumonia also experience pneumococcal bacteremia. The case-fatality rate of pneumococcal pneumonia is 5 to 7 percent, and may be much higher among the elderly. Other complications of pneumococcal pneumonia include empyema (pus in the pleural space), pericarditis (inflammation of the sac surrounding the heart), and endobronchial obstruction with atelectasis (complete or partial collapse of the lung) and lung abscess formation.

Bacteremia. More than 12,000 cases of pneumococcal bacteremia without pneumonia occur each year. The overall case-fatality rate for bacteremia is about 20 percent, but may be as high as 60 percent among elderly patients. Patients with asplenia who develop bacteremia may experience a very rapid and severe clinical course.

Meningitis. Pneumococci cause over 50 percent of all cases of bacterial meningitis in the United States. An estimated 3,000 to 6,000 cases of pneumococcal meningitis occur each year. Some patients with pneumococcal meningitis also have pneumonia. The clinical symptoms, CSF profile, and neurologic complications are similar to other forms of purulent bacterial meningitis. Symptoms may include headache, lethargy, vomiting, irritability, fever, nuchal rigidity, cranial nerve signs, seizures, and coma. The case-fatality rate of pneumococcal meningitis is about 8 percent among children and 22 percent among adults. Neurologic sequelae are common among survivors.

Adults with certain medical conditions are at highest risk for

invasive pneumococcal disease (bacteremia and/or meningitis). For adults aged 18 to 64 years with hematologic cancer, the rate of invasive pneumococcal disease in 2010 was 186 per 100,000; and for persons with human immunodeficiency virus (HIV), the rate was 173 per 100,000. Other conditions that place adults at highest risk for invasive pneumococcal disease include other immunocompromising conditions (either from disease or medications), functional or anatomic asplenia, and renal disease. Additional conditions that increase the risk of invasive pneumococcal disease include chronic heart disease, pulmonary disease (including asthma in adults), liver disease, cigarette smoking, CSF leak, and cochlear implant.

Pneumococcal Disease in Children

Bacteremia, without a known site of infection, is the most common invasive clinical presentation of pneumococcal infection among children two years of age and younger, accounting for approximately 70 percent of invasive disease in this age group. With the decline of invasive *Haemophilus influenzae* Type B (Hib) disease, *S. pneumoniae* has become the leading cause of bacterial meningitis among children younger than five years of age in the U.S. Before routine use of pneumococcal conjugate vaccine, children younger than one year had the highest rates of pneumococcal meningitis with approximately 10 cases per 100,000 population.

Pneumococci are a common cause of acute otitis media and are detected in 28 to 55 percent of middle ear aspirates. By age 12 months, more than 60 percent of children have had at least one episode of acute otitis media. Middle ear infections are the most frequent reasons for unscheduled pediatric office visits in the United States, resulting in more than 20 million visits annually. Complications of pneumococcal otitis media may include mastoiditis and meningitis.

Before routine use of pneumococcal conjugate vaccine, the burden of pneumococcal disease among children younger than five years of age was significant. An estimated 17,000 cases of invasive disease occurred each year, of which 13,000 were bacteremia without a known site of infection, and about 700 were meningitis. An estimated 200 children died every year as a result of invasive pneumococcal disease. Although not considered invasive disease, an estimated five million cases of acute otitis media occurred each year among children younger than five years of age.

Children with functional or anatomic asplenia, particularly those with sickle cell disease, and children with immune compromise, including HIV infection, are at very high risk for invasive disease. Rates in some studies are more than 50 times higher than those among children of the same age without these conditions. Rates are also increased among children of certain racial and ethnic groups, including Alaska Natives, African Americans, and certain American Indian groups (Navajo and Apache). The reason for this increased risk by race and ethnicity is not known with certainty, but was also noted for invasive *H. influenzae* infection (also an encapsulated bacterium). Children in childcare centers have been shown to have increased risk of invasive pneumococcal disease, and acute otitis media two- to three-fold among children younger than 59 months of age. Children with cochlear implants are at increased risk for pneumococcal meningitis.

Laboratory Diagnosis

A definitive diagnosis of infection with *S. pneumoniae* generally relies on isolation of the organism from blood or other normally sterile body sites. Tests are also available to detect capsular polysaccharide antigen in body fluids. The appearance of lancet-shaped diplococci on Gram stain is suggestive of pneumococcal infection, but interpretation of stained sputum specimens

may be difficult because of the presence of normal nasopharyngeal bacteria.

A urinary antigen test based on an immunochromatographic membrane technique has been approved by FDA and is commercially available. The test is rapid and simple to use, has a reasonable specificity in adults, and has the ability to detect pneumococcal pneumonia after antibiotic therapy has been started.

Medical Management

Resistance of *S. pneumoniae* to multiple antibiotics is an increasingly important clinical problem. For previously healthy individuals with no significant risk factors for drug resistance to *S. pneumoniae*, community-acquired pneumonia (CAP) may be treated empirically with an oral macrolide antibiotic (azithromycin, clarithromycin, or erythromycin). According to the Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults, 2007, in the presence of comorbidities (e.g., chronic heart, lung, liver or renal disease, diabetes mellitus, alcoholism, malignancy, asplenia, immunosuppressive conditions including medications, use of antimicrobials within the previous three months, or other risk factors for drug-resistant *S. pneumoniae*), the choices include 1) a respiratory fluoroquinolone (moxifloxacin, gemifloxacin, or levofloxacin 750 mg); 2) a combination of a beta-lactam with a macrolide antibiotic; or 3) high dose amoxicillin or amoxicillin-clavulanate.

Although a number of studies cite bacteremia as a predictor for a poor outcome or complications in the absence of critical illness, recommendations for choice of therapy for bacteremic versus non-bacteremic pneumococcal pneumonia do not differ. Therapy is generally continued for five to seven days for uncomplicated disease or until the patient is afebrile for three to five days. In more severe cases, patients with bacteremic pneumo-

coccal disease should receive a total of 10 to 14 days of antimicrobial therapy.

Meningitis is a neurological emergency. Treatment should be initiated at the first suspicion of the diagnosis. Recommendations for antimicrobial therapy in adults with *S. pneumoniae* meningitis include starting empiric therapy while waiting for culture and susceptibility testing results. Antibiotic therapy should be administered for 10 to 14 days at a minimum. It is safe to begin outpatient therapy when the patient has received inpatient therapy for at least seven days, has been afebrile for 24 to 48 hours, demonstrates no neurologic dysfunction, is clinically stable, and shows overall improvement. Intravenous penicillin G is the preferred antibiotic for meningitis caused by susceptible *S. pneumoniae* because it readily crosses the blood-brain barrier. Other recommended empiric therapy includes vancomycin plus a third-generation cephalosporin (ceftriaxone or cefotaxime). Alternative therapy may include meropenem or a fluoroquinolone (gatifloxacin or moxifloxacin).

Pneumococcal Vaccines

Pneumococcal Polysaccharide Vaccine. Pneumococcal polysaccharide vaccine is composed of purified preparations of pneumococcal capsular polysaccharide. The first polysaccharide pneumococcal vaccine was licensed in the United States in 1977. It contained purified capsular polysaccharide antigens from 14 different types of pneumococcal bacteria. In 1983, a 23-valent polysaccharide vaccine (PPSV23) was licensed and replaced the 14-valent vaccine, which is no longer produced. PPSV23 contains polysaccharide antigen from 23 types of pneumococcal bacteria that cause 60 to 76 percent of invasive disease.

The polysaccharide vaccine currently available in the United States (Pneumovax® 23, Merck) contains 25 mcg of each antigen per dose and contains 0.25 percent phe-

nol as a preservative. The vaccine is available in a single-dose vial or syringe, and in a five-dose vial. PPSV23 may be administered as a 0.5 mL dose either intramuscularly or subcutaneously.

Pneumococcal Conjugate Vaccine. The first pneumococcal conjugate vaccine (PCV7) was licensed in the United States in 2000. It included purified capsular polysaccharides of seven serotypes of *S. pneumoniae* conjugated to a nontoxic variant of diphtheria toxin to improve efficacy in children. In 2010, a 13-valent pneumococcal conjugate vaccine (PCV13) was licensed in the U.S. for children. It contains the seven serotypes of *S. pneumoniae* as PCV7 plus five additional serotypes, which are also conjugated to the same non-toxic diphtheria toxin.

In December 2011, FDA approved PCV13 (Prevnar 13[®], Pfizer) as a single 0.5 mL intramuscular dose for the prevention of pneumonia and invasive disease in persons 50 years of age and older, in addition to children. In two randomized, multicenter studies conducted in the United States and Europe, immunocompetent adults aged 50 years and older received a single dose of PCV13 or PPSV23. In adults age 60 through 64 years and age 70 years and older, PCV13 elicited opsonophagocytic (pathogen-specific antibody) activity that was comparable with, or higher than, responses elicited by PPSV23. Persons who received PPSV23 as the initial study dose had lower opsonophagocytic antibody responses after subsequent administration of a PCV13 dose one year later than those who had received PCV13 as the initial dose. Approximately 20 to 25 percent of invasive pneumococcal disease cases and 10 percent of community-acquired pneumonia cases in adults aged ≥ 65 years are caused by PCV13 serotypes, and are potentially preventable with the use of PCV13 in this population. More than 80 percent of healthy adults who receive PPSV23 develop antibodies against the serotypes contained in the vaccine,

usually within two to three weeks after vaccination. Older adults and persons with some chronic illnesses or immunodeficiency may not respond as well, if at all. Elevated antibody levels persist for at least five years in healthy adults, but decline more quickly in persons with certain underlying illnesses. In children younger than two years of age, antibody response to PPSV23 is generally poor.

PPSV23 vaccine efficacy studies have resulted in various estimates of clinical effectiveness. Overall, the vaccine is 60 to 70 percent effective in preventing invasive disease caused by serotypes included in the vaccine. Despite the vaccine's reduced effectiveness among immunocompromised persons, PPSV23 is still recommended for such persons because they are at high risk of developing severe disease. There is no consensus regarding the ability of PPSV23 to prevent non-bacteremic pneumococcal pneumonia. For this reason, CDC recommends that providers should avoid referring to PPSV23 as the "pneumonia vaccine."

In a large clinical trial, PCV7 was shown to reduce invasive disease caused by vaccine serotypes by 97 percent. Children who received PCV7 had 20 percent fewer episodes of chest X-ray-confirmed pneumonia, 7 percent fewer episodes of acute otitis media and underwent 20 percent fewer tympanostomy tube placements than did unvaccinated children. There is evidence that among children PCV7 reduces nasopharyngeal carriage of pneumococcal serotypes included in the vaccine.

PCV13 was licensed in the United States based upon studies that compared the serologic response of children who received PCV13 to those who received PCV7. These studies showed that PCV13 induced levels of antibodies that were comparable to those induced by PCV7 and shown to be protective against invasive disease.

A randomized placebo-controlled trial (CAPIITA trial) was conducted in the Netherlands

among approximately 85,000 adults 65-years-old or older during 2008-2013 to evaluate the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia. The results of the CAPIITA trial demonstrated 45.6 percent efficacy of PCV13 against vaccine-type pneumococcal pneumonia, and 75 percent efficacy of PCV13 against vaccine-type invasive pneumococcal disease.

Vaccination Schedule and Use

Pneumococcal Conjugate Vaccine. All children two through 59 months of age should be routinely vaccinated with PCV13. The primary series beginning in infancy consists of three doses routinely given at two, four, and six months of age. The first dose can be administered as early as six weeks of age. A fourth (booster) dose is recommended at 12 to 15 months of age. PCV13 should be administered at the same time as other routine childhood immunizations, using a separate syringe and injection site. For children vaccinated at younger than 12 months of age, the minimum interval between doses is four weeks. Doses given at 12 months of age and older should be separated by at least eight weeks.

Unvaccinated children seven months of age and older do not require a full series of four doses. The number of doses a child needs to complete the series depends on the child's current age and the age at which the first dose of PCV13 was received. Unvaccinated children aged seven through 11 months should receive two doses of vaccine at least four weeks apart, followed by a booster dose at age 12 through 15 months. Unvaccinated children aged 12 through 23 months should receive two doses of vaccine, at least eight weeks apart. Previously unvaccinated healthy children 24 through 59 months of age should receive a single dose of PCV13.

Unvaccinated children 24 through 71 months of age with certain chronic medical conditions should receive two doses of PCV13

separated by at least eight weeks. These conditions include chronic heart and lung disease, diabetes, CSF leak, cochlear implant, sickle cell disease and other hemoglobinopathies, functional or anatomic asplenia, HIV infection, or immunocompromising conditions resulting from disease or treatment of a disease. A single supplemental dose of PCV13 is recommended for all children 14 through 59 months of age who have received four doses of PCV7 or completed another age-appropriate PCV7 schedule. For children who have an underlying medical condition, a single supplemental PCV13 dose is recommended through 71 months. This includes children who have received PPSV23 previously. PCV13 should be administered at least eight weeks after the most recent dose of PCV7 or PPSV23. This will constitute the final dose of PCV for these children.

A single dose of PCV13 should be administered to children six through 18 years of age who have not received PCV13 previously, and 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. Routine use of PCV13 is not recommended for healthy children five years of age or older.

When elective splenectomy, immunocompromising therapy, or cochlear implant placement is being planned, PCV13 and/or PPSV23 vaccination should be completed at least two weeks before surgery or initiation of therapy.

Adults 65 years old or older who have not previously received pneumococcal vaccine or whose previous vaccination history is unknown, should receive a dose of PCV13. A dose of PPSV23 should be given at least 12 months after the dose of PCV13. The two vaccines should not be administered simultaneously.

Adults 65 years old or older who have previously received one or more doses of PPSV23 should receive a dose of PCV13 if they have not received it. A dose of PCV13 should be given one or more years after receipt of the most recent PPSV23 dose. For those for whom an additional dose of PPSV23 is indicated, this subsequent PPSV23 dose should be given one or more years after PCV13, and five or more years after the most recent dose of PPSV23. Only one dose of PPSV23 is recommended on or after the 65th birthday.

In June 2012, the CDC Advisory Committee on Immunization Practices (ACIP) recommended vaccination of adults with specific risk factors. All PCV13-naïve adults 19 years and older with functional or anatomic asplenia (e.g., from sickle cell disease or splenectomy), HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, or other conditions associated with immunosuppression (e.g., organ or bone marrow transplantation) and those receiving immunosuppressive chemotherapy, including long-term systemic corticosteroids (14 days or longer of prednisone 20 mg or equivalent per day), or those with CSF leak or cochlear implants, should receive a dose of PCV13 vaccine. PCV13 should be administered to eligible adults with one of these risk factors prior to PPSV23, the vaccine recommended for these groups of adults since 1997. Eligible adults with one of these risk factors who have not previously received PPSV23 should receive a dose of PCV13 first, followed by a dose of PPSV23 at least eight weeks later. Subsequent doses of PPSV23 should follow PPSV23 recommendations for these adults. Adults 19 years of age or older with the aforementioned conditions who have previously received one or more doses of PPSV23 should be given a dose of PCV13 at least eight weeks after the last PPSV23 dose. For those who require ad-

ditional doses of PPSV23, the first such dose should be given no sooner than eight weeks after PCV13, and at least five years since the most recent dose of PPSV23 (see Table 1).

Providers should not withhold vaccination in the absence of a complete immunization record. The patient's verbal history may be used to determine vaccination status. Persons with uncertain or unknown vaccination status should be vaccinated.

The target groups for pneumococcal vaccines (polysaccharide or conjugate) and influenza vaccine overlap. Either pneumococcal vaccine can be given at the same time as influenza vaccine, but at different sites. Pneumococcal polysaccharide vaccine should never be given during the same visit as pneumococcal conjugate vaccine. Most adults need only a single lifetime dose of each PCV13 and PPSV23 (see *Revaccination with PPSV23* below).

Pneumococcal Polysaccharide Vaccine. Pneumococcal polysaccharide vaccine should be administered routinely to all adults 65 years of age and older, regardless of previous PCV receipt. A single dose of PPSV23 is also indicated for immunocompetent persons, two years of age and older, with normal immune systems who have a chronic illness, including cardiovascular disease, pulmonary disease, diabetes, alcoholism, chronic liver disease, cirrhosis, CSF leak, or a cochlear implant.

Immunocompromised persons two years of age and older who are at highest risk of pneumococcal disease or its complications should also be vaccinated. This group includes persons with splenic dysfunction or absence (either from disease or surgical removal), Hodgkin's disease, lymphoma, multiple myeloma, chronic renal failure, nephrotic syndrome, asymptomatic or symptomatic HIV infection, or conditions such as organ transplantation associated with immunosuppression. Individuals immunosuppressed from chemotherapy

Table 1
Summary of recommended intervals between the two pneumococcal vaccines by age and risk groups

Risk	Age	PCV13-PPSV23 Sequence				PPSV23-PCV13 Sequence			
		24-71 mo	6-18 yr	19-64 yr	≥65 yr	24-71 mo	6-18 yr	19-64 yr	≥65 yr
No underlying conditions		NA	NA	NA	≥1 yr	NA	NA	NA	≥1 yr
Immunocompetent with chronic conditions		≥8 wk	NA	NA	≥1 yr	≥8 wk	NA	NA	≥1 yr
Immunocompetent, but with CSF leak, cochlear implant		≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥1 yr	≥1 yr
Functional or anatomic asplenia		≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥1 yr	≥1 yr
Immunocompromised		≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥8 wk	≥1 yr	≥1 yr

Adapted from *Intervals Between PCV13 and PPSV23 Vaccines: Recommendations of ACIP, Morbidity and Mortality Weekly Report*, September 4, 2015, Vol. 64, No. 34.

or high-dose corticosteroid therapy should be vaccinated. PPSV23 should be considered for persons living in special environments or social settings with a person identified at increased risk of pneumococcal disease or its complications, such as certain Native American (i.e., Alaska Native, Navajo, and Apache) populations.

In 2010, ACIP added asthma and cigarette smoking to the list of indications for receipt of PPSV23 due to increased risk of invasive pneumococcal disease among these groups. Available data do not support asthma or cigarette smoking as indications for PPSV23 among persons younger than 19 years.

If elective splenectomy or cochlear implant is being considered, PPSV23 should be given at least two weeks prior to the procedure. If vaccination before the procedure is not feasible, the vaccine should be given as soon as possible after surgery. Similarly, there should also be a two-week interval between vaccination and initiation of cancer chemotherapy or other immunosuppressive therapy, if possible.

Revaccination with PPSV23.

Following vaccination with PPSV23, antibody levels decline after five to 10 years, and decrease more rapidly in some groups than others. However, the relationship

between antibody titer and protection from invasive disease is not certain for adults, so the ability to define the need for revaccination based only on serology is limited. In addition, currently available pneumococcal polysaccharide vaccines elicit a T-cell-independent response, and do not produce a sustained boost in antibody titers. Available data do not indicate a substantial increase in antibody levels in the majority of revaccinated persons.

For immunocompetent adults 19 through 64 years of age with chronic heart disease, pulmonary disease (including asthma), liver disease, alcoholism, CSF leaks, cochlear implants, or those who smoke cigarettes, only one dose of PPSV23 is recommended before the 65th birthday. Those who received a dose of PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later, if at least five years have elapsed since their previous PPSV23 dose.

A second PPSV23 dose is recommended five years after the first PPSV23 dose for persons aged 19 to 64 years with functional or anatomic asplenia or other conditions associated with immunosuppression, and those receiving immunosuppressive chemotherapy

or long-term corticosteroids. The above group includes the same conditions as adult indications for PCV13, with the exception of CSF leak and cochlear implants. Persons with CSF leaks or cochlear implants should receive no additional doses of PPSV23 until age 65 years. Those who received one or two doses of PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later, if at least five years have elapsed since their previous PPSV23 dose.

Summary of Recommendations for PCV13 and PPSV23 Use in Series

Both PCV13 and PPSV23 are recommended for

- Adults 65 and older (*ACIP August 2014*)
- Individuals two to 64 years of age (*ACIP: Feb 2010, June 2012, June 2013*)
 - Immunocompromising conditions
 - Functional or anatomic asplenia
 - CSF leaks or cochlear implants

Recommended sequence PCV13 → PPSV23 (slightly higher effectiveness than reverse sequence)

- PCV13 recommended even if previously received PPSV23
- Recommended intervals between doses vary by age and risk group, and vaccine sequence (see Table 1)

Effective September 19, 2014, CMS specified payments under Medicare Part B whereby vaccination for PCV13 and PPSV23 were in alignment with ACIP recommendations. They also specified that at least 11 full months had to pass between vaccinations for payment to occur. Pneumococcal vaccines were not covered under Medicare Part D at time of publication.

Contraindications and Precautions to Vaccination

For both pneumococcal polysaccharide and conjugate vaccines, a severe allergic reaction (anaphylaxis)

to a vaccine component or following a prior dose is a contraindication to further doses of vaccine. Such allergic reactions are rare. Persons with moderate or severe acute illness should not be vaccinated until their condition improves. However, minor illnesses, such as upper respiratory infections, are not contraindications to vaccination.

The safety of PPSV23 vaccine for pregnant women has not been studied, although no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated during pregnancy. Women who are at high risk of pneumococcal disease and who are candidates for pneumococcal vaccine should be vaccinated before pregnancy, if possible.

Adverse Reactions Following Vaccination

Pneumococcal

Polysaccharide Vaccine. The most common adverse events following either pneumococcal polysaccharide or conjugate vaccine are local reactions. For PPSV23, 30 to 50 percent of vaccinees report pain, swelling, or erythema at the site of injection. These reactions usually persist for less than 48 hours.

Local reactions are reported more frequently following a second dose of PPSV23 vaccine than following the first dose. Moderate systemic reactions (such as fever and myalgia) are not common (fewer than 1 percent of vaccinees), and more severe systemic adverse reactions are rare.

Pneumococcal Conjugate Vaccine. Local reactions (such as pain, swelling or redness) following PCV13 occur in up to half of recipients. Approximately 8 percent of local reactions are considered to be severe, such as tenderness that interferes with limb movement. This pain and tenderness may be related to the vaccine or it may be related to the intramuscular injection technique, e.g., injecting the vaccine too high in the deltoid muscle. In children, local reactions are generally more common with the fourth dose than with the first

three doses. In clinical trials of pneumococcal conjugate vaccine, fever (higher than 100.4°F [38°C]) within seven days of any dose of the primary series was reported for 24 to 35 percent of children. High fever was reported in fewer than 1 percent of vaccine recipients. Nonspecific symptoms such as decreased appetite or irritability were reported in up to 80 percent of recipients.

Vaccine Storage and Handling

PCV13 and PPSV23 should be maintained at refrigerator temperature between 35°F and 46°F (2°C and 8°C). Manufacturer package inserts contain additional information and can be found at <http://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093830.htm>. For complete information on best practices and recommendations, please refer to CDC's Vaccine Storage and Handling Toolkit, www.cdc.gov/vaccines/recs/storage/toolkit/storage-handling-toolkit.pdf.

Goals and Coverage Levels

The Healthy People 2020 goal is to achieve at least 90 percent coverage for pneumococcal polysaccharide vaccine among persons 65 years of age and older. Data from the 2005 Behavioral Risk Factor Surveillance System (BRFSS, a population-based, random-digit-dialed telephone survey of the non-institutionalized U.S. population 18 years of age and older) estimate that 64 percent of persons 65 years of age or older had ever received pneumococcal polysaccharide vaccine. Vaccination coverage levels were lower among persons 18 to 64 years of age with a chronic illness.

Opportunities to vaccinate high-risk persons are missed both at the time of hospital discharge, during visits to clinicians' offices, and routine visits to pharmacies. More effective programs for vaccine delivery are needed including a focus on long-term care facilities.

More than 65 percent of persons who have been hospitalized

with severe pneumococcal disease had been admitted to a hospital in the preceding three to five years, yet few had received pneumococcal vaccine. In addition, persons who frequently visit physicians and who have chronic conditions are more likely to be at high risk of pneumococcal infection than those who require infrequent visits. Screening and subsequent immunization of hospitalized persons found to be at high risk could have a significant impact on reducing complications and death associated with pneumococcal disease.

Conclusion

Pharmacists completing medication histories and current medication reviews, or performing medication therapy management should assess vaccination status and reinforce the need for specific vaccines including pneumococcal.

This lesson represents the most current recommendations at the time of publication. Immunization schedules change frequently. For the most current information, go to www.cdc.gov/vaccines.

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Pneumococcal Disease: Treatment and Prevention

1. What type of bacterium is *Streptococcus pneumoniae*?
a. Gram-negative b. Gram-positive
2. All of the following are major clinical syndromes caused by *S. pneumoniae* EXCEPT:
a. bacteremia. c. meningitis.
b. cellulitis. d. pneumonia.
3. All of the following are clinical symptoms of meningitis EXCEPT:
a. dyspnea. c. nuchal rigidity.
b. headache. d. seizure.
4. The decreased prevalence of what organism led to *S. pneumoniae* being the leading cause of bacterial meningitis in children ages five years and younger in the U.S.?
a. *Haemophilus influenzae* c. *Neisseria meningitidis*
b. *Listeria monocytogenes* d. *Streptococcus agalactiae*
5. All of the following put children at very high risk for developing invasive pneumococcal disease EXCEPT:
a. functional or anatomic asplenia.
b. HIV infection.
c. infectious mononucleosis.
d. sickle cell disease.
6. For severe bacteremic pneumococcal disease, antimicrobial therapy should be continued:
a. 3 to 5 days. c. 10 to 14 days.
b. 5 to 7 days. d. 14 to 21 days.
7. The antibiotic of choice for treating meningitis caused by susceptible *S. pneumoniae* is intravenous:
a. azithromycin. c. clarithromycin.
b. penicillin G. d. trimethoprim/sulfamethoxazole.

8. What is the current pneumococcal polysaccharide vaccine in the U.S.?
a. PCV7 c. PPSV14
b. PCV13 d. PPSV23
9. Routine use of PCV13 is not recommended for otherwise healthy children five years of age or older unless they have which of the following conditions?
a. Asthma c. HIV infection
b. Diabetes
10. Persons with uncertain or unknown vaccination status should be vaccinated with PVC13 and/or PPSV23, if indicated.
a. True b. False
11. Which vaccines may be administered simultaneously, but at different sites?
a. PCV13 and PPSV23 c. None of the above
b. PPSV23 and influenza
12. All of the following chronic conditions are an indication for PPSV23 vaccination in immunocompetent adults 19 to 64 years of age EXCEPT:
a. asthma. c. alcoholism.
b. gastritis. d. cochlear implant.
13. Following vaccination with PPSV23, antibody levels decline after:
a. 2 to 5 years. c. 10 to 12 years.
b. 5 to 10 years. d. 12 to 15 years.
14. CMS will cover PCV13 and PPSV23 vaccines under:
a. Medicare Part A. c. Medicare Part C.
b. Medicare Part B. d. Medicare Part D.
15. What is the most common adverse event with administration of PCV13 and PPSV23?
a. Headache c. Myalgia
b. Flu-like symptoms d. Local reactions

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Completely fill in the lettered box corresponding to your answer.

- | | | |
|--------------------|--------------------|---------------------|
| 1. [a] [b] | 6. [a] [b] [c] [d] | 11. [a] [b] [c] |
| 2. [a] [b] [c] [d] | 7. [a] [b] [c] [d] | 12. [a] [b] [c] [d] |
| 3. [a] [b] [c] [d] | 8. [a] [b] [c] [d] | 13. [a] [b] [c] [d] |
| 4. [a] [b] [c] [d] | 9. [a] [b] [c] | 14. [a] [b] [c] [d] |
| 5. [a] [b] [c] [d] | 10. [a] [b] | 15. [a] [b] [c] [d] |

I am enclosing \$5 for this month's quiz made payable to: Ohio Pharmacists Association.

1. Rate this lesson: (Excellent) 5 4 3 2 1 (Poor)
2. Did it meet each of its objectives? yes no
If no, list any unmet _____
3. Was the content balanced and without commercial bias?
 yes no If no, why? _____
4. Did the program meet your educational/practice needs?
 yes no
5. How long did it take you to read this lesson and complete the quiz? _____
6. Comments/future topics welcome.

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