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Pneumococcal Immunization for Adults in 2022

John H. O'Neill, Jr., DO, MACP

Internal Medicine Physician, Academic Hospitalist, Faculty Member, ChristianaCare; Co-Chair, Immunization Coalition of Delaware

Introduction

Infections caused by *Streptococcus pneumoniae* continue to be a significant cause of morbidity and mortality worldwide. Pneumococcal infections cause an estimated 150,000 hospitalizations per year in the USA, and pneumococcal bacteremia and meningitis (with case fatality rates of 12% and 14%, respectively) caused approximately 3,250 deaths in the USA in 2019.[1,2] The World Health Organization estimates that more than 300,000 deaths occur globally each year in children under the age of 5 as a result of pneumococcal infections.[3] The discovery and subsequent development of penicillin in 1941 has substantially reduced suffering and mortality. Vaccines against pneumococcal infection have a greater proven potential to prevent illness and death, and also to reduce the problem of emergence of antimicrobial resistance.[2] Recently, the recommendations for immunization of adults against pneumococcal infections have been updated by the Advisory Committee on Immunization Practices (ACIP),[4] and are presented here.

The History of the Pneumococcal Vaccines

Vaccines against the pneumococcus have been available for over 40 years, beginning with pneumococcal polysaccharide vaccine, 14 valent (PPSV14), in 1977, which was replaced by PPSV23 in 1983. This vaccine induces an antibody response to its 23 polysaccharide bacterial surface antigens in 80% of adults who receive it, but antibody levels decline more than five years after vaccination, and antibody response is reduced in immunosuppressed persons. PPSV23 has not conclusively been shown to prevent (non-bacteremic) pneumococcal pneumonia, but it has been shown in clinical trials to reduce the incidence of invasive pneumococcal disease (IPD) caused by the strains of pneumococcus included in the vaccine by 60-70%.[5] The range of pneumococcal infections includes acute otitis media, sinusitis, pneumonia, and IPD, which includes bacteremia, pneumococcal pneumonia with bacteremia, meningitis, osteomyelitis and septic arthritis. More than 100 serotypes of pneumococcus are known, most can cause serious illness, but the majority of cases of pneumococcal infections are caused by relatively few serotypes, which vary by patient age and geographic area.[2]

Pneumococcal conjugate vaccine, 7 valent (PCV7), was introduced in 2000 for use in the pediatric population. This vaccine conjugates the surface polysaccharide antigens of the seven serotypes of pneumococcus covalently to a non-toxic diphtheria toxin protein called CRM147. Polysaccharide vaccines such as PPSV23 have been shown to be ineffective in children under the age of 2, and conjugated vaccines such as PCV have been shown to stimulate more effective plasma cell transformation and antibody production, as well as enhanced T cell responses.[6] Large clinical trials have demonstrated a 97% reduction of IPD in children caused by the strains in PCV7, a 7% reduction in acute otitis media, a 20% reduction in the need for tympanostomy tubes, a 20% reduction in the incidence of pneumonia, and decreased nasal carriage of these strains from the vaccine.[7]

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PCV7 was replaced by PCV13 in 2010. PCV13 has 12 antigens in common with the PPSV23 vaccine. PCV10 has also been used in other countries since 2009. For adults with immunosuppression, Cerebrospinal fluid (CSF) leaks, or cochlear implants, PCV13 was recommended by the ACIP starting in 2012, followed by an expanded indication for all adults 65 years of age and older in 2014. PPSV23 was recommended 2-12 months following PCV13 in adults, with up to two additional doses at five year intervals depending on the presence and severity of immunosuppression. In 2015, Bonten and colleagues published their study demonstrating the effectiveness of PCV13 with a 45% reduction in vaccine-type non-bacteremic pneumococcal pneumonia as well as a 75% reduction in IPD in older adults.[8]

In 2019, ACIP recommended shared decision making between the patient and their physician regarding the indication for PCV13, given the observed decline in the incidence of vaccine-type pneumococcal disease to historic lows in the adult population, attributed to more than a decade of use of PCV7 and PCV13 in the pediatric schedule and the ensuing community immunity.[9] The observed decline in antimicrobial resistance of pneumococcus in the United States over the past decade has been attributed to the success of these conjugate vaccines as well.[2] PCV13 was also recommended for patients who lived in long term care institutions, who were living in or travelling to areas where pediatric access to PCV13 was low, or where there was known increased incidence of non-PCV13 vaccine-type pneumococcal infection.

The Updated ACIP recommendations for Pneumococcal Immunization of Adults

For 2022, we now have the availability of PCV15 and PCV20 vaccines for use in adult patients. PCV15 has two additional conjugated polysaccharide antigens compared to PCV13, and PCV20 has seven additional antigens, including the two new antigens found in PCV15. Based on a review of the data on immunogenicity, safety, and cost effectiveness from clinical trials associated with these vaccines, on October 20, 2021, the ACIP recommended that adults 65 years of age and older who have not previously received a pneumococcal conjugate vaccine in adulthood (or if the vaccination history is unknown), be given either PCV20 (but not PPSV23), or PCV15 followed in at least a year by PPSV23. The one year duration between vaccines in immunocompetent patients over 65 years of age results in optimal antibody production, compared to a shorter duration. No booster of any PCV vaccine is recommended subsequently after a person has received PCV13, PCV15, or PCV20 once. If the patient has previously received PCV13, but has not yet received PPSV23, they should receive PPSV23 if it has been a year since getting PCV13. Following receipt of one dose of PPSV23 vaccine, no additional booster doses are recommended going forward. If an adult patient who has an indication for pneumococcal vaccine has previously received PPSV23, but not a PCV, they should receive either PCV15, or PCV20, at least a year after having received PPSV23. No additional doses of PPSV23 are necessary, subsequently.[4]

Figure 1. Serotypes Contained in Current and New Pneumococcal Vaccines

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For adult patients age 19-64 with immunosuppression/special conditions or risk factors listed in Table 1, a dose of PCV20 (but not PPSV23), or a dose of PCV15, followed by a dose of PPSV23 in at least 2-12 months, should be administered. If PCV13 has previously been given, but not PPSV23, then the dose of PPSV23 may be administered at least two months following PCV13, to receive extra protection against the vaccine strains in PPSV23 in the near term. No booster doses of PPSV23 are necessary subsequently, after this first dose. No additional doses of PCV15 or PCV20 are indicated if a patient has previously received PCV13, PCV15 or PCV20 in adulthood.[4]

Safety of PCV Vaccines

Adverse reactions to PCV15 included fatigue, malaise and injection site discomfort. There were no serious adverse reactions (SAE) or deaths attributed to PCV15 compared to PCV13. Similar reactions were noted with PCV20, including myalgia, joint pain, headache, fatigue, and injection site discomfort, and no SAEs or deaths were attributed to PCV20 compared to controls.[4]

Table 1. Indications for Pneumococcal Vaccine, Ages 19-64[4]

Underlying Condition/Risk Factor	
Alcoholism	
Chronic heart disease	(includes CHF, cardiomyopathy)
Chronic liver disease	
Chronic lung disease	(includes COPD and asthma)
Cigarette smoking	
Diabetes Mellitus	
Cochlear implant	
CSF leak	
Congenital or acquired asplenia	
Sickle cell disease/other hemoglobinopathy	
Congenital or acquired immunodeficiency	
HIV infection	
Iatrogenic immunosuppression	
Chronic renal failure	
Nephrotic syndrome	
Generalized malignancy	
Hodgkin Disease	
Lymphomas	
Leukemias	
Multiple myeloma	
Solid organ transplant	

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Conclusion

Vaccination of immunocompetent adult patients 65 years and over, and adults age 19-64 with immunosuppression or other high risk conditions against *Streptococcus pneumoniae* has the potential to dramatically reduce the incidence of IPD, related morbidity and mortality, pneumococcal pneumonia, and hospitalizations. Potential cost savings associated with such a public health intervention could be enormous. ACIP's updated recommendations for 2022 make pneumococcal vaccination simpler for clinicians, and more effective for patients with the additional pneumococcal antigens covered by the regimen options. With disease prevention comes an added benefit of reduced antimicrobial resistance of the pneumococcus to current antibiotics as a result of the effectiveness of the conjugate vaccines. The calling for our health care system and its "immunization neighborhoods" is to maximize adult immunization rates. Currently we fall far short of where we need to be to realize the benefits of our interventions. The most recently published National Health Interview Survey (NHIS) data from 2017 indicate that only 69% (73% White, 57% Black, 51% Hispanic) of persons 65 or older had received a pneumococcal immunization (PI), and only 24.5% of persons in the 19-64 age group with immunosuppression/other high risk conditions had received PI.[10] The low vaccination rates are disturbing, and the racial disparities are alarming. Immunization of our population against vaccine preventable diseases remains one of the huge public health challenges of our present and future. Healthy People 2030 goals for ACIP recommended vaccines are > 90%.[11] We have good work to do!

Dr. O'Neill can be contacted at johnoneill@christianacare.org

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