

Current Recommendations for Pneumococcal Vaccination of Children and Adults

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Streptococcus pneumonia remains one of the most commonly identified pathogen associated with hospitalization and death among children and adults (1).

Despite improvements in diagnostic tests and treatment regimens, mortality remains high ranging from 5 to 35% (1).

Worldwide, an estimated 541,000 deaths were attributed to pneumococcal disease in children <5 years in 2008 and nearly all of them occurred in low-income countries. Among the wealthy population, nearly all deaths due to pneumococcal disease occur in the elderly, as children in these populations are routinely vaccinated against pneumococcal disease using pneumococcal conjugate vaccines (PCVs) (1,2).

Pneumococcus has different serotypes that differ based on their antigenically distinct polysaccharide capsules. These serotypes have variable virulence. Some of them are associated with increased degree of disease severity, increased risk of invasiveness (meningitis and bacteremia), increased fatality rate and exhibit antibiotic resistance (3,4).

Pneumococcal disease is largely preventable. Two main types of vaccines are available, and approved for use in adults:

- 1) Polysaccharide 23-valent pneumococcal vaccine.
- 2) 13-valent PCVs.

The routine use of 13-valent PCV in children has markedly reduced pneumococcal disease not only in children, but also in adults by the way of indirect protection also known as herd effect (2,5).

In adults, the incidence of meningitis and bacteremia caused by the serotypes in the 13-valent pneumococcal vaccine decreased by 50% in those over 65 years of age between 2010-2013. This effect was parallel to the mass vaccination of children less than 5 years in the same population (5-7). But there is still large burden of disease on this population; 10% of cases of community acquired pneumonia (CAP) are still caused by one of the PCV 13 serotypes, and more than 13000 cases of invasive pneumococcal infections occur each year in this group (5-7).

A recent placebo-controlled clinical trial of PCV 13 in 850,000 adults aged 65 years and older conducted in the Netherlands from 2008 to 2013 showed reduction of disease incidence by 45.6% for pneumonia and 75% for invasive pneumococcal disease caused by the vaccine serotypes (8).

Twelve of the 13 serotypes in PCV 13 are in PPSV23. PPSV23 can protect against invasive pneumococcal disease but its effectiveness against CAP has not been well proven. Unlike PCV13, PPSV23 is not approved for children less than 2 years of age (9, 10).

Candidates of vaccine:

While any one can develop pneumococcal disease, it most often affects susceptible individuals such as infants, the elderly and people of any age with underlying medical conditions causing immunodeficiency.

For example, patients with AIDS have disease rates up to 100 times than those seen in healthy persons (11, 12).

Although effective in relatively healthy individuals, many studies have shown that PPV23 is ineffective in reducing invasive pneumococcal disease in the elderly and immunocompromised patients including transplant patients and HIV infected patients with low CD4 count (11,12).

Two randomized multicenter immunogenicity studies conducted in the United States and Europe on older adults showed that PCV13 induces an immune response as good as or better than that induced by PPSV23 (10).

Who should be vaccinated? (10, 12)

- 1- Children <5 years (only PCV for children less than 2 years of age)
- 2- Adults \geq 65 years

- 3- Chronic heart disease (adults and children)
- 4- Diabetes mellitus (adults and children)
- 5- Alcoholism (adults)
- 6- Chronic liver disease, cirrhosis (adults)
- 7- Cigarette smoking (adults)
- 8- Cerebrospinal fluid leak (adults and children)
- 9- Cochlear implant (adults and children)
- 10- Persons with functional or anatomical asplenia (adults and children)
- 11- Congenital or acquired immunodeficiency (adults and children)
- 12- HIV (adults and children)
- 13- Chronic renal failure (adults and children)
- 14- Nephrotic syndrome (adults and children)
- 15- Leukemia (adults and children)
- 16- Lymphoma (adults and children)
- 17- Hodgkin disease (adults and children)
- 18- Generalized malignancy (adults and children)
- 19- Iatrogenic immunosuppression (adults and children)
- 20- Solid organ transplant (adults and children)
- 21- Multiple myeloma (adults and children)

PPSV 23:

PPSV23 contains 12 serotypes in common with PCV13 and 11 additional serotypes. In 2013, 38% of Invasive Pneumococcal Diseases (IPD) among adults aged over 65 years was caused by serotypes unique to PPSV23. Given the high proportion of IPD caused by serotypes unique to PPSV23, broader protection is expected to be provided through the use of both PCV13 and PPSV23 in series (10, 13).

Optimal interval between dose of PCV13 and PPSV23 has been shown in Table 1 (adopted from reference 10).

Table 1. Summary of recommended intervals, by risk and age groups, for persons with indications to receive PCV 13 and PPSV23 sequence- advisory committee on immunization practices, United States, September 2015 (10)

Risk group/Underlying medical condition	Intervals for PCV13- PPSV23 Sequence, by age group				Intervals for PPSV23- PCV13 Sequence, by age group			
	24-71 months	6-18 years	19-64 years	≥65 years	24-71 months	6-18 Years	19-64 years	≥65 years
No underlying conditions	NA	NA	NA	≥1year	NA	NA	NA	≥1year
Immunocompetent persons Chronic heart disease Chronic lung disease Diabetes mellitus Alcoholism * Chronic liver disease, cirrhosis* Cigarette smoking*	≥8weeks	≥8weeks	≥8weeks	≥1year	≥8weeks	≥8weeks	≥1year	≥1year
Immunocompetent persons Cerebrospinal fluid leak Cochlear implant	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥1year	≥1year
Persons with functional or anatomic asplenia Sickle cell disease/ other hemoglobinopathy Congenital or acquired asplenia	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥1year	≥1year
Immunocompetent persons Congenital or acquired immunodeficiency Human immunodeficiency virus infection Chronic renal failure Nephritic syndrome Leukemia Lymphoma Hodgkin disease Generalized malignancy Iatrogenic immunosuppression Solid organ transplant Multiple myeloma*	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥8weeks	≥1year	≥1year

Abbreviation: NA= Not applicable, sequential use of PCV13 and PPSV23 is not recommended for these and risk group.

*Underlying medical conditions that are not included in the recommendations for children aged <2 years.

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