An update on pneumococcal vaccination in children and adults

Jacqui Souter, BPharm

Amayeza Info Centre

Correspondence to: Jacqui Souter, e-mail: jsouter@amayeza-info.co.za

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Abstract

Streptococcus pneumoniae can cause acute, invasive bacterial infections, such as meningitis, bacteraemia and pneumonia, as well as less invasive diseases, such as sinusitis and otitis media. Infants and young children, adults over 65 years of age, and individuals with underlying medical conditions are at greatest risk of infection. Invasive pneumococcal disease can be prevented by vaccination. Infants routinely receive pneumococcal conjugate vaccines as part of the Expanded Programme on Immunisation. It is recommended that adults who are older than 65 years receive a single dose of the pneumococcal polysaccharide vaccine (PPSV23). For individuals between the ages of two and 64 years with underlying medical conditions, both pneumococcal conjugate vaccine 13 (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) may be recommended. In this article, we discuss the pneumococcal conjugate vaccines and pneumococcal polysaccharide vaccine, and when to use them in healthy individuals and in those at increased risk of invasive pneumococcal disease.

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Introduction

Meningitis, bacteraemia and pneumonia are serious diseases that may be caused by pneumococcal infections.[1] Individuals at highest risk of invasive pneumococcal disease are infants and young children, adults over the age of 65 years, and those with certain underlying medical conditions.[2]

Pneumococcal disease

Streptococcus pneumoniae colonises the nasopharynx and is mainly transmitted through respiratory droplets. Infants and young children are thought to be the main reservoirs of *S. pneumoniae*.[1] Many healthy adults are asymptomatic carriers thereof. Rates of asymptomatic carriage vary with age, the environment and the presence of upper respiratory infections. It is not yet fully understood how *S. pneumoniae* causes invasive disease in a patient who was previously an asymptomatic carrier.[3] However, invasive disease may occur when a predisposing condition exists, particularly pulmonary disease.[3]

More than 90 distinct pneumococcal serotypes are defined by differences in the composition of the bacterial polysaccharide capsule. Immunity following infection is serotype specific, but cross-protection between related serotypes may occur. Serotypes 1, 5, 6A, 14, 19F and 23F are common causes of invasive pneumococcal disease in children younger than five years worldwide.[1]

Pneumococcal vaccines

Two types of pneumococcal vaccines are available:

- Pneumococcal polysaccharide vaccine (PPSV23)
- Pneumococcal conjugate vaccine.

Both vaccines are used to stimulate an immune response to the serotypes of *S. pneumoniae* contained in the vaccine. However, the vaccines contain a different number and form of these serotypes, and are used in different situations.[3]

Pneumococcal polysaccharide vaccine (PPSV23)

PPSV23 has been available for many years. It has broader coverage than PCV, providing protection against 23 serotypes. However, it is not effective in children who are younger than two years.[3] PPSV23 is indicated for individuals over the age of two years and who are at an increased risk of invasive pneumococcal disease and its complications.[4,5]

Pneumococcal conjugate vaccines

Young children are at increased risk of invasive pneumococcal disease. Therefore, a vaccine was needed to protect this population. PCV was developed, and is highly immunogenic in young children.[3] Unlike the PPSV23 vaccine, PCV also stimulates mucosal immunity, resulting in the prevention of nasopharyngeal colonisation.[6] This effect on colonisation results in a reduction of pneumococcal disease in the unvaccinated community, i.e. the so-called "herd effect".[6] PCV is given routinely to infants, and forms part of the Expanded Programme on Immunisation (EPI) in South Africa.[7]

Two PCV vaccines are available in South Africa; Synflorix® and Prevenar 13®.

Synflorix® (PCV10) is indicated for active immunisation of infants and children up to two years of age against disease caused by *S. pneumoniae* serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F, and against acute otitis media caused by Non-Typeable *Haemophilus influenzae*. The primary series can be started from six weeks of age and consists of three doses, with an interval of at least four weeks between doses. A booster dose is recommended at least six months after the final dose of the primary series.[8]

Prevenar 13® (PCV13) is indicated for the prevention of invasive disease, pneumonia and otitis media caused by *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F, in children up to their sixth birthday. The primary series can be started from six weeks of age, and consists of three doses, with an interval of at least four weeks between doses. A fourth dose is recommended between 12 and 15 months of age.[9] The EPI follows a slightly different schedule in respect of Prevenar 13®. Vaccine doses are given at six weeks, 14 weeks and nine months of age.[7] Prevenar 13® is also registered for use in adults who are older than 50 years to prevent pneumonia and invasive disease caused by the *S. pneumoniae* vaccine serotypes.

Immunisation schedules

Prevenar13® and Synflorix® are registered for use in infants as three primary series, plus one booster dose. However, alternative schedules have been investigated and appear to be immunogenic in preventing invasive pneumococcal disease.[10] The optimal immunisation schedule protects the infant at the time of the greatest risk of infection.[10]

The World Health Organization recommends either of the following schedules for the PCV vaccination of infants:[1]

- *Three primary doses and no booster:* This is given from six weeks of age, with a minimum interval of four weeks between doses
- *Two primary doses, plus one booster dose:* The primary doses are given from six weeks of age, with a minimum interval of eight weeks between them. The booster dose can be given between nine and 15 months of age.

The three primary doses and no booster may offer better individual protection against certain serotypes, such as 6B and 23F, particularly in the absence of herd immunity. However, the higher antibody response to the third dose in the two primary plus one booster dose option, than that to the third dose in the three primary doses, may be important for the duration of immunity against some serotypes.[1]

However, abbreviated schedules may not provide optimal protection particularly in infants with underlying medical conditions placing them at a higher risk of invasive pneumococcal disease.[11] Further information is needed with regard to the need for a booster dose of PCV to be given to children over 12 months of age to ensure long-term immunity.[10]

Vaccination against *Streptococcus pneumoniae* in different scenarios

Healthy individuals

It is recommended that all children up to five years of age are vaccinated with PCV.[3] Routine vaccination is usually started within the first few months of life. Children who were not vaccinated at this time may still receive PCV13 up to five years of age.[3] The number of doses needed will depend on the age of the child and whether or not any doses were previously given. The relevant package insert for specific details on catch-up doses should be consulted.

PPSV23 is not recommended in healthy children over two years of age. PCV is more immunogenic than PPSV23 in children,[3] protects against the serotypes that are most likely to cause invasive disease in children,[1] and has the benefit of creating "herd immunity".[2]

It is recommended that adults who are older than 65 years receive a single dose of PPSV23.[12]

Individuals at increased risk of invasive pneumococcal disease

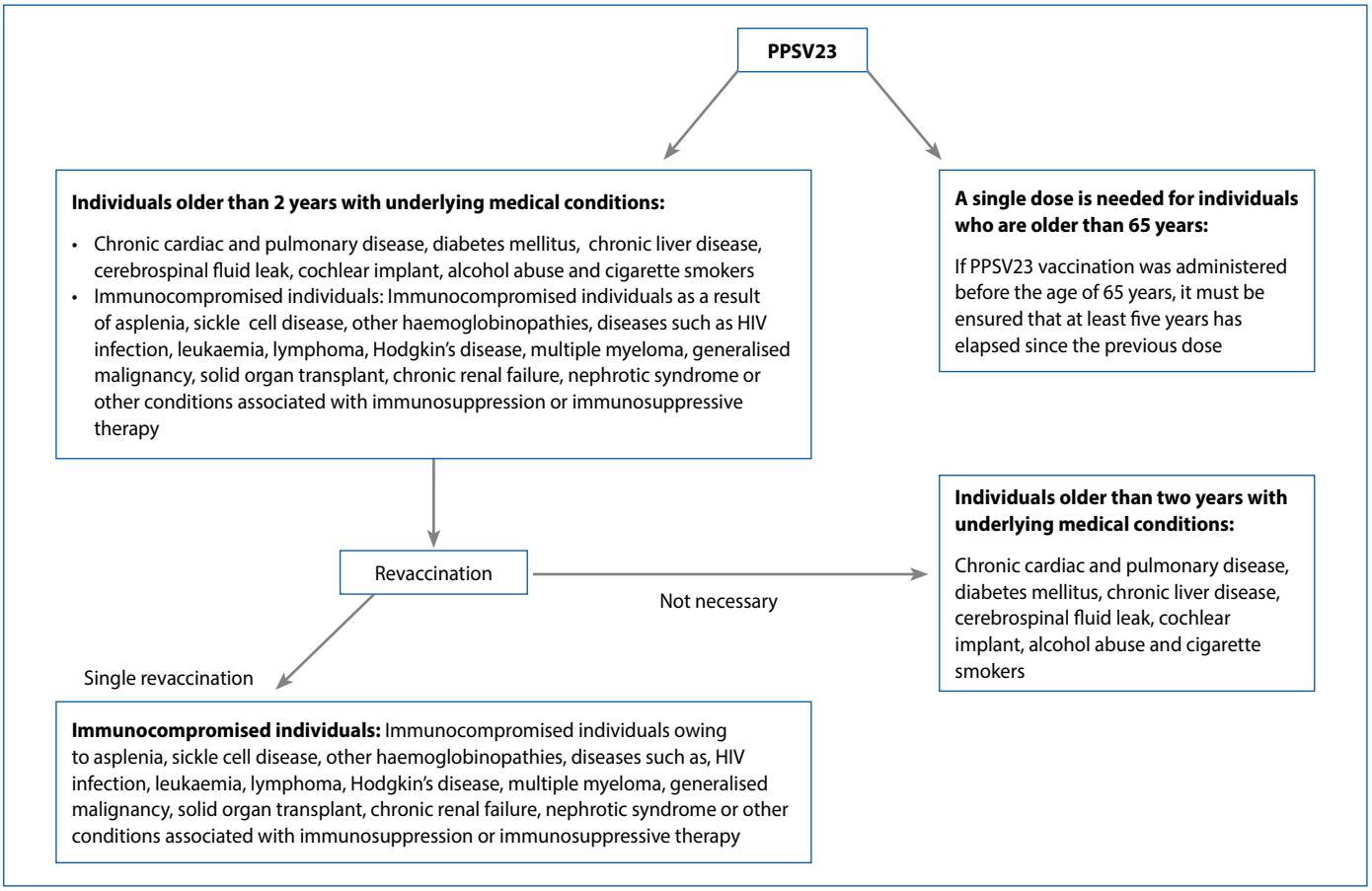
Besides young infants and adults who are older than 65 years, individuals with the following underlying medical conditions are considered to be an increased risk of invasive pneumococcal disease:[12-14]

- Chronic cardiac and pulmonary disease, including asthma in adults and asthma that is treated with high-dose oral corticosteroids in children
- Diabetes mellitus
- Chronic liver disease
- Cerebrospinal fluid leak
- Cochlear implant
- Functional or anatomical asplenia, including sickle cell disease or other haemoglobinopathies
- Immunocompromising conditions that result from diseases such as human immunodeficiency virus (HIV) infection, leukaemia, lymphoma, Hodgkin's disease, multiple myeloma, generalised malignancy, solid organ transplants, chronic renal failure, nephrotic syndrome or other conditions associated with immunosuppression or immunosuppressive therapy
- Alcohol abuse
- Cigarette smokers who are older than 19 years.

It is recommended that individuals with any of these conditions over the age of two years should be vaccinated with PPSV23.[3]

Is there a need for revaccination with pneumococcal polysaccharide vaccine?

Antibody levels decline 5-10 years after receiving PPSV23. However, the relationship between antibody titre and protection from invasive pneumococcal disease is uncertain.[3] In addition, revaccination with PPSV23 does not produce a sustained increase



HIV: human immunodeficiency virus, PPSV23: pneumococcal polysaccharide vaccine

Figure 1: When to vaccinate with pneumococcal polysaccharide vaccine

in antibody titre. There does not appear to be a substantial increase in protection in the majority of revaccinated individuals.[3] Therefore, revaccination of immunocompetent individuals with any listed underlying medical condition is not usually recommended.[3]

However, revaccination is recommended in individuals who are at highest risk of invasive pneumococcal disease, and in those who are likely to have a rapid decline in antibody titres.[3,4]

The highest risk group includes individuals with splenic dysfunction and immunocompromising conditions, or those receiving immunosuppressive therapy.[12,13] A second dose is recommended in these individuals at least five years after the previous dose of PPSV23 was administered. No further doses are recommended.

It is also recommended that individuals who are older than 65 years, and who previously received a PPSV23, receive another dose of PPSV23, provided at least five years have elapsed since the first dose[12] (Figure 1).

Additional recommendations for pneumococcal conjugate vaccination in individuals at increased risk owing to underlying medical conditions

Young children

Children with any of the previously mentioned underlying medical conditions should receive PCV according to the schedule for healthy children.[13] Once these children are older than two years, PPSV23 is recommended at least eight weeks after completion of the PCV immunisation.[13]

Children with any of the previously mentioned underlying medical conditions who have not previously received PCV, and who are now aged 2-6 years, should receive two PCV13 vaccines, separated by eight weeks.[3] PPSV23 is also recommended at least eight weeks after completion of the PCV13 immunisation.

The Advisory Committee on Immunization Practices, which is part of the Centers for Disease Control and Prevention in the USA, has added to its pneumococcal vaccination recommendations for children aged 6-18 years, and for adults, as follows.

Children aged 6-18 years who have not previously received the pneumococcal conjugate vaccine

Children from 6-18 years who are at increased risk of invasive pneumococcal disease owing to anatomical or functional

asplenia, HIV, cochlear implants, cerebrospinal fluid leaks or other immunocompromising conditions, should receive a single dose of PCV13, followed eight weeks later by a single dose of PPSV23. If these children had received a previous dose of PPSV23, PCV13 can be given after an interval of at least eight weeks.[14]

Adults

Adults with splenic dysfunction, cerebrospinal fluid leaks, cochlear implants, immunocompromising conditions or those receiving immunosuppressive therapy, who have not previously received PPSV23, should receive a PCV13 dose, followed by a PPSV23 dose at least eight weeks later. If these adults have previously received a PPSV23 vaccine, an interval of one year should elapse before the PCV13 vaccine is administered.[12]

It should be noted that although PCV13 is registered for use in adults who are older than 50 years, it is not recommended in healthy adults.[2]

Conclusion

Invasive pneumococcal disease can be prevented by vaccination. PCV is highly immunogenic in infants and young children, and its use may result in "herd protection" of the unvaccinated community. PPSV23 offers broader protection against additional pneumococcal serotypes. Therefore, the choice of which vaccine to use depends on the age of the individual, and whether or not he or she has any underlying medical conditions that may increase the risk of invasive pneumococcal disease. The manufacturer's literature should be consulted before the vaccination is administered.

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