Adult Pneumococcal Vaccination Guideline

SAMA-SA Pulmonology Society Working Group

Objective. To outline a rational cost-effective protocol for pneumococcal vaccination of adults in South Africa.

Vaccine description. A highly purified vaccine containing 25 μg of each of 23 capsular polysaccharides representing ≥ 85% of the serotypes causing pneumonia and invasive pneumococcal disease in the community. Polysaccharide antigens induce type-specific antibodies that enhance opsonisation, phagocytosis and killing of pneumococci by phagocytic cells. Factors influencing the efficacy of the vaccine include the age of the individual, the state of their immune response, the presence/absence of underlying medical disorders, and the level of pneumococcal antibodies attained. Protection is only against infection caused by pneumococci of a serotype included in the vaccine.

Recommendations. Vaccination is

- potentially beneficial to any individual
- very effective in young otherwise healthy individuals
- targeted at high-risk groups when there are cost considerations.

Evidence. Detailed literature review with emphasis on local South African studies.

Benefits, harms, costs.

- Vaccine is very effective in preventing pneumonia and invasive disease in young otherwise healthy individuals .
- Efficacy is greater against bacteraemic pneumonia than against non-bacteraemic pneumonia. Efficacy may be less in the elderly aged > 65 years and in some of the high-risk categories of individuals targeted for vaccination.
- Vaccine is safe with only occasional reports of anaphylaxis, although local reactions to the vaccine are quite common.
- Contraindications: Exercise care when administering the vaccine to allergic individuals. Delay immunisation if possible in the case of fever, acute disease, and relapse of chronic disease until recovery.
- Relatively few data are available on cost-effectiveness of the vaccine. However, recent studies suggest that the vaccine is cost saving in developed countries in terms of prevention of bacteraemia alone.

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Validation. Endorsement by the SA Pulmonology Society, SAMA and all who attended a multidisciplinary consensus meeting to consider the draft guideline.

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General introduction

Infections with *Streptococcus pneumoniae* and the influenza virus are associated with considerable morbidity and mortality, both in developed and developing countries. Although vaccines are available for the prevention of both these infections, concerns about their safety, efficacy and cost-effectiveness have resulted in limited use in the community. While both vaccines have been shown to be highly effective in preventing these infections in young healthy individuals, because of availability and cost considerations most international recommendations for vaccine use target the elderly and certain other groups of patients who are at increased risk of acquiring these infections and their associated complications. The purpose of this guideline is to provide rational and cost-effective recommendations for pneumococcal vaccination in adults in South Africa.

Abbreviations

AIDS = acquired immune deficiency syndrome; CDC = Centers for Disease Control and Prevention, Atlanta, Georgia; CNS = central nervous system; COPD = chronic obstructive pulmonary disease; CSF = cerebrospinal fluid; H = haemagglutinin; HIV = human immunodeficiency virus; ICU = intensive care unit; MIC = minimum inhibitory concentration; N = neuraminidase; RNA = ribonucleic acid; SA = South Africa; SAMA = South African Medical Association; SAPS = South African Pulmonology Society; USA = United States of America.

Levels of evidence

In this guideline the following levels of evidence have been used to indicate the strength of the supporting research.

Evidence level	*Description*
A	Very good evidence of efficacy of the vaccine including data from studies at least one of which is a prospective, randomised, double-blind, placebo-controlled trial.
B	Good evidence of efficacy of the vaccine including data from prospective cohort studies and retrospective case-control trials.
C	Efficacy of the vaccine is not consistently demonstrated, but the high risk for disease as well as the potential benefit and the safety of the vaccine justify its use in the circumstances.

Methodology

This project was initiated by C Feldman of the SAPS and a collaborative venture with the SAMA Centre for Quality Care was established. Funding was obtained from Pasteur Mérieux Connaught (Rhône-Poulenc Rorer) in terms of an unrestricted educational grant. A draft guideline was developed in conjunction with the authors.

On 20 February 1999 a nationally representative adult respiratory vaccinations consensus meeting was held in Gauteng (see below). Participants were invited as representatives of professional, government and consumer groups with an interest in the adult respiratory vaccination field. Each organisation so invited nominated its own representatives. All participants received a copy of the draft guideline developed previously together with the relevant references before the meeting. The meeting was chaired by a neutral chairperson. The purpose of the meeting was to consider the content of the draft guideline and either endorse or amend the document. The proceedings were audio recorded and transcribed for future reference.

The endorsement document was revised according to the proceedings of the national consensus meeting. The endorsement draft document was circulated to all participants and many other interested persons. The endorsement draft was also available on the Centre for Quality Care's Internet site, via SAMA-online for further comment. (**www.samedical.org/cqc**)

Amendments to this endorsement draft were made where there was sufficient need as indicated by the comments received. All major debates and areas where it was not possible to come to agreement were highlighted. The document as revised was submitted to SAMA's Guideline Committee for endorsement according to the set criteria. Once endorsed the guideline was sent for publication to the *South African Medical Journal*. The guideline will also be available in the compendium and on the SAMA Centre for Quality Care's Internet site.

The grants were made in accordance with the SAMA code of sponsorship which precludes attempts by sponsors to unethically influence the content of the guideline. All funds were paid directly into SAMA's accounts and all disbursements were made from that fund.

SAMA-SAPS Adult Respiratory Vaccinations Working Group

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1. Introduction[1-15]

Streptococcus pneumoniae (the pneumococcus) remains an important cause of significant morbidity and mortality in both the First World and developing countries. This organism is one of the most common causes of pneumonia, meningitis, and otitis media. Since pneumococcal infections are not notifiable in South Africa, the true incidence of these infections is uncertain. Nevertheless, based on estimated disease rates in the USA, it has been suggested that >150 million cases occur annually worldwide. While the pneumococcus can produce infections in otherwise healthy individuals, pneumococcal infections are particularly common at the extremes of age and in patients with underlying immunocompromising disorders. In this regard pneumococcal infections are extremely important in countries such as South Africa owing to their significant association with the HIV epidemic. It is an interesting paradox that while several important studies showing considerable benefit of the vaccine were undertaken on the goldmines in South Africa, and current research on the pneumococcus and pneumococcal diseases emanating from South Africa is considered to be of world class, use of the pneumococcal vaccine in this country is considerably less than in many other countries in the world. The focus of this part of the report is the prevention of pneumococcal disease through the use of the pneumococcal polyvalent vaccine.

2. The micro-organism[3,5,9,16]

S. pneumoniae is a Gram-positive diplococcus that usually grows in pairs or in short chains. The organisms are surrounded by capsules consisting of complex polysaccharides that are the basis for dividing pneumococci into serotypes. Organisms exposed to type-specific antiserum show a positive capsular precipitin reaction, the quellung reaction. By this means, 90 serotypes have been identified. While a number of these serotypes are pathogenic in man, types 1, 3, 4, 7, 8 and 12 are encountered most frequently in clinical practice. In general the types causing infection in adults and children are similar, although types 6, 14, 19 and 23 are more common in children and less common in adults. It is important to have knowledge of the commonly encountered serotypes in one's patient population to ensure that the current vaccine formulations remain appropriate. Several studies of pneumococcal bacteraemia in both HIV-seropositive and HIV-seronegative individuals have been undertaken in South Africa. These studies describe the pneumococcal serotype distribution and confirm that the commonly encountered serotypes are similar to those in developed countries and the vast majority are represented in the 23-valent polysaccharide vaccine.

3. Antimicrobial resistance[2,3,5,9,10,12,13,16-28]

While for many years the pneumococcus was considered to be fully sensitive to penicillin, in 1967 the first clinical isolate demonstrating penicillin resistance was documented. Initial reports of penicillin resistance were from Australia, New Guinea and South Africa. More recent reports have shown a dramatic increase in pneumococcal resistance to penicillin even in countries such as the USA. Some penicillin-resistant isolates are also resistant to other antimicrobial agents. Penicillin-resistant pneumococcal infections are significantly associated with HIV-seropositivity. The clinical outcome of patients infected with penicillin-resistant pneumococcal organisms depends on the degree of resistance and the concentration of penicillin that is able to be achieved at the site of infection. Whereas recent studies have failed to find a difference in outcome of penicillin therapy when comparing penicillin-resistant pneumococcal pneumonia with pneumonia caused by penicillin-sensitive strains, this is not the case with otitis media and meningitis, which require alternative antibiotic therapy for successful outcome. High-level penicillin resistance and multidrug resistance may well complicate the management of pneumococcal infections in the future. Emerging resistance emphasises the potential benefit of prevention of pneumococcal infections by vaccination.

*A number of working group members have been nominated by more than one professional group.

4. RISK FACTORS FOR INFECTION[2,9,11,13,15,16,23,25,29,34]

A number of factors have been shown to increase the susceptibility of individuals to pneumococcal infections, and some of these are also associated with a higher case fatality rate when infection occurs. These high-risk conditions have been ranked 1 - 4, with 1 and 2 representing most risk, 3 representing intermediate risk and 4 representing mild risk. High-risk conditions include:

- **Age > 65 years.** Although the healthy elderly > 65 years are believed to be at increased risk of pneumococcal infection, there is somewhat limited evidence for this assumption. A recent hospital-based study from South Africa noted an increased incidence of pneumococcal bacteraemia in individuals > 65 years (risk 4).
- **Chronic bronchopulmonary disorders.** Chronic obstructive airways disease is a risk factor for pneumococcal infections, at least partly due to impaired pulmonary clearance mechanisms (risk 3).
- **Chronic cardiovascular disease.** Chronic cardiac conditions, especially cardiomyopathy and other disorders associated with congestive heart failure, are a risk factor for pneumococcal infections (risk 3).
- **Other chronic diseases.** Chronic liver disease, cirrhosis, alcoholism, chronic renal failure requiring dialysis and diabetes mellitus are also predisposing factors (risk 3).
- **Conditions associated with immune deficiency.** These patients are at particular increased risk for pneumococcal infections and include cases with Hodgkin's disease, multiple myeloma, immunoglobulin deficiency, systemic lupus erythematosus, drug-induced immunodeficiency, renal transplantation, malignancies (including haematological malignancies), HIV infection, and AIDS (risk 1).
- **Splenectomy or splenic dysfunction.** Patients who have undergone splenectomy or those with splenic dysfunction due to diseases such as sickle cell anaemia are at higher risk for pneumococcal infection because the major organ for clearance of encapsulated bacteria from the blood is lost. Also in this risk category are patients with nephrotic syndrome (risk 2).
- **Patients with chronic cerebrospinal fluid (CSF) leaks.** Patients with CSF leaks due to congenital abnormalities, surgical procedures or trauma are at considerable increased risk for meningitis (risk 1).
- **Other conditions.** A number of other conditions including cigarette smoking, malnutrition, and recent hospitalisation or institutionalisation are risk factors for pneumococcal infections.

5. MORTALITY[1-3,9,11,35,36]

Despite the availability of appropriate antimicrobial chemotherapy and even the establishment of intensive care unit facilities, there is still a significant mortality in patients with pneumococcal infections. Pneumococcal infections cause approximately 40 000 deaths per year in the USA, and are said to account for more deaths than any other vaccine-preventable bacterial disease. Case-fatality rates are higher for meningitis and bacteraemia than for non-bacteraemic pneumonia, and the highest mortality occurs among the elderly and in patients with underlying medical disorders. The overall case fatality rate for pneumococcal bacteraemia is said to be 15 - 20%, and was 13.5% overall in a study from Hillbrow Hospital, being 60% in cases admitted to an ICU and 9.2% in cases not admitted to the unit.

6. CLINICAL SYNDROMES

6.1 Pneumococcal bacteraemia[3,9,11,12,16,24,35,37]

A number of studies have been undertaken in South Africa investigating pneumococcal bacteraemia in both HIV-seropositive and HIV-seronegative individuals. An increasing rate has been noted at Chris Hani Baragwanath Hospital in association with HIV; a recent study showed that the estimated annual incidence of pneumococcal bacteraemia was 50 per 100 000 in paediatric patients (0 - 2 years), 24 per 100 000 in adults aged 18 - 40 years and 64.2 per 100 000 in adults aged > 65 years. There was a significant increase in pneumococcal bacteraemia in HIV-seropositive adults (8.2-fold) and children (36.9-fold). In a study from Hillbrow Hospital in Johannesburg there was a 6.2-fold increased risk of invasive pneumococcal disease in HIV-seropositive adults. Most episodes of bacteraemia are associated with pneumonia. The attack rate is higher in certain population groups, such as among black mine workers, who have a particularly high attack rate even in comparison to other high-risk groups. The overall annual incidence in the USA has been estimated at 15 - 30 cases per 100 000.

6.2 Lower respiratory tract infections[1,9,16,38-42]

S. pneumoniae is the commonest bacterial cause of community-acquired pneumonia, and this has been confirmed in several studies from South Africa, which have included both critically ill and less severe cases of infection. The incidence of pneumonia is difficult to ascertain, at least partly owing to the insensitivity of the diagnostic tests used, but it has been said to occur in 1 - 2 per 1 000 population. Approximately 500 000 cases are estimated to occur annually in the USA. Concomitant bacteraemia occurs in approximately 25% of cases with pneumonia.

6.3 Otitis media[9,16]

S. pneumoniae is also an important cause of acute otitis media, as well as other upper respiratory tract infections, such as sinusitis. Otitis media is most commonly an infection of childhood and although it does not usually progress to invasive disease, it can be a cause of considerable morbidity, as well as of medical costs. Unfortunately, the burden of this disease occurs in children less than 2 years of age, at which age the 23-valent vaccine is not effective.

6.4 Meningitis[9,10]

While CNS infections with *S. pneumoniae* occur most commonly in children, they also occur in adults, particularly the elderly and in patients with underlying predisposing factors. Pneumococcal meningitis is the most serious of the common bacterial causes of meningitis, and is the commonest form of meningitis in children at Chris Hani Baragwanath Hospital. The case fatality rate often exceeds 20% in most of the developing world. Even with appropriate antimicrobial chemotherapy the prognosis is guarded. The question of therapy is further complicated by the very high prevalence of penicillin-resistant isolates (almost 50% in Soweto children). An even more alarming trend has been the development of cephalosporin-resistant strains and the increasing MICs for the cephalosporins that have been developing over the years.

7. PNEUMOCOCCAL POLYSACCHARIDE VACCINE

7.1 The vaccine[2,3,5,9,35,37,43,44]

The currently available pneumococcal vaccines in South Africa are Imovax Pneumo 23 (Pasteur Mérieux Connaught) and Pneumovax 23 (MSD), both containing 25 μg of each of 23 purified capsular polysaccharide antigens, namely 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. The 23 capsular types present in these vaccines represent ≥ 85% of the serotypes causing invasive disease in South Africa.

The pneumococcal polysaccharide antigens induce type-specific antibodies that enhance opsonisation, phagocytosis and killing of pneumococci by leucocytes and other phagocytic cells. After vaccination, an antibody response occurs, indicated by a twofold or greater rise in serotype-specific antibody which develops in > 80% of healthy young adults. The antibody levels that correlate with protection against pneumococcal disease have not been clearly defined.

The vaccine should be stored at 2 - 8°C. It should be kept in the fridge and not the freezer and should be kept out of the reach of children.

7.2 Antibody responses[2,15,31,45-54]

Antibody responses in the elderly and in patients with alcoholic cirrhosis, chronic obstructive pulmonary disease (COPD) and insulin-dependent diabetes mellitus may be lower than in young healthy adults. Although effective antibody responses have been noted in patients aged ≥ 2 years with splenectomy and splenic dysfunction, such patients do not always respond in the same way as healthy individuals of the same age. In immunocompromised patients, antibody responses are often diminished or absent. Patients with leukaemia, lymphoma, multiple myeloma, chronic renal failure on dialysis, renal transplantation and nephrotic syndrome have significantly impaired antibody responses. HIV-seropositive individuals often have lower responses to pneumococcal vaccine, particularly with lower CD4+ counts, and a number of cases of vaccine failure in these individuals have been noted.

7.3 Duration of antibody level[2,5,31,46,47,51]

Levels of antibody to most pneumococcal antigens remain raised for at least 5 years in healthy adults, and decline after 5 - 10 years. A more rapid decline in antibody levels has been noted in some children who have undergone splenectomy, in the elderly and in patients with nephrotic syndrome, renal disease requiring dialysis, renal transplant, Hodgkin's disease, or multiple myeloma.

7.4 Vaccine efficacy[2,5,6,9,15,33,43,52,55-69]

Numerous studies have been undertaken evaluating the efficacy of the vaccine, including randomised controlled trials and case control and cohort studies, with varying results. A number of the studies have had limitations that may have lessened their ability to demonstrate efficacy. There have been significant concerns of small sample sizes in the prospective studies and concerns of various biases in the retrospective ones. In some of the investigations unexpectedly low rates of bacteraemic infections occurred, confounding the statistical analyses. Also it is important to recognise that while many of these studies tested a polyvalent vaccine, several did not contain the full 23 capsular types.

Randomised controlled trials were conducted in the 1970s among young, healthy goldminers in South Africa who had high rates of pneumococcal pneumonia and bacteraemia. The vaccine was found to be 80 - 90% effective and to reduce the occurrence of radiographically diagnosed pneumonia in these patients significantly. Other prospective studies and even a recent meta-analysis failed to show protection of the vaccine for patients with high-risk conditions. In retrospective and case control studies the effectiveness of the vaccine against invasive disease has ranged between 56% and 81%, and the vaccine is noted to be particularly efficacious at reducing bacteraemic pneumococcal pneumonia in low-risk adults. In some studies

of the elderly and patients with underlying medical illness, or high-risk groups, the vaccine has not been demonstrated to be effective against non-bacteraemic pneumonia. In one of the largest case control studies, the overall efficacy of the vaccine was 56% for preventing infections with serotypes contained in the vaccine and 61% effective in patients with diabetes mellitus, chronic lung disease, chronic heart disease, renal failure and alcoholism. Overall vaccine efficacy of 65 - 84% has been demonstrated among specific groups, e.g. patients with diabetes mellitus, coronary vascular disease, congestive heart failure and COPD and after splenectomy, but effectiveness can often not be confirmed among patients who are immunocompromised, such as these with HIV infection, sickle cell disease, chronic renal failure, immunoglobulin deficiency, lymphoma, leukaemia and multiple myeloma. The vaccine is not effective for the prevention of otitis media or sinusitis.

A review of articles on the efficacy of the pneumococcal vaccine suggests that it is more effective in preventing invasive disease (bacteraemia) than in preventing uncomplicated pneumococcal pneumonia and that failures are more likely to occur in immunocompromised patients and in those whose chronic disease impairs immunological function. It may be better to immunise patients early in the course of chronic disease.

7.5 Vaccine administration[2,51]

The vaccine may be administered by anyone legally allowed to do so. It may be administered intramuscularly or subcutaneously as a single 0.5 ml dose. It may be administered at the same time as influenza vaccination (separate injection in the other arm), and it may also be administered with other vaccines. Since occasional episodes of anaphylaxis occur, adrenalin (1:1000) should be available.

8. RECOMMENDATIONS FOR PNEUMOCOCCAL VACCINE USE

Recommendations for the use of the pneumococcal vaccine are shown in summary (Table I). The levels of evidence for the recommendations are indicated in brackets (refer to p. 1223).

8.1 Immunocompetent persons[2,9,14,31,33,43-46,48,49,70-75]

• **Patients aged 2 - 64 years with splenectomy or splenic dysfunction.** Patients with splenectomy or splenic dysfunction caused by diseases such as sickle cell anaemia should receive the pneumococcal vaccine. In patients in whom splenectomy is planned, pneumococcal vaccine should be administered at least 2 weeks before planned surgery, if possible. Patients with splenectomy or splenic dysfunction should be informed that the vaccine does not guarantee protection against fulminant pneumococcal disease, and should these patients develop unexplained fever or sepsis they should seek immediate medical attention and be treated aggressively with antibiotics. These patients should also be encouraged to wear a Medic Alert tag. One approach recommended for prophylaxis in children homozygote for sickle cell disease is that they should receive pneumococcal vaccine and penicillin prophylaxis. Penicillin prophylaxis should start at the age of 4 - 6 months when splenic dysfunction begins and maternal antibodies wane. Children may then be vaccinated at the age of 2 years. At 5 - 6 years of age, when the risk of pneumococcal infection has markedly decreased, penicillin prophylaxis may not be necessary. The new conjugate pneumococcal vaccines may yet be shown to provide better protection against pneumococcal infections in these patients, but further studies are needed.

Table I. Target groups for the use of the 23-valent pneumococcal polysaccharide vaccine (level of evidence given in brackets)

Immunocompetent individuals (B - except as indicated)

- Persons aged 2 - 64 years with:
  - splenectomy or splenic dysfunction (e.g. sickle-cell anaemia)
  - chronic CSF leak
  - chronic cardiovascular disease, e.g. cardiomyopathy, congestive cardiac failure
  - chronic pulmonary disease, e.g. COPD
  - other chronic medical diseases, e.g. diabetes mellitus, cirrhosis, alcholism
- Persons ≥ 65 years
- Persons living in special environments: e.g. frail-care centres, mines (A), hostels, prisons

Immunocompromised individuals

- Persons ≥ 2 years of age with:
  - leukaemia
  - lymphoma
  - multiple myeloma
  - generalised malignancy
  - chronic renal failure
  - nephrotic syndrome
  - receiving immunosuppressive therapy (including corticosteroids)
  - organ or bone marrow transplant recipients
  - HIV infection - not routinely indicated - see full guideline text

Contraindications to pneumococcal vaccination

- Acute severe febrile illness, until symptoms subside
- Allergy to components of the pneumococcal vaccine
- Revaccination contraindicated in anyone who has had a severe reaction to the first vaccination

• **Patients at increased risk of meningitis due to CSF leaks** caused by congenital abnormality, surgical procedures or skull fractures should receive pneumococcal vaccine.

• **Persons aged 2 - 64 years with chronic underlying illness.** Patients at increased risk for pneumococcal infections due to chronic lung disease, chronic cardiac disease, chronic liver disease and alcoholism, renal failure requiring dialysis, or

diabetes mellitus should be vaccinated.

• **Person aged > 65 years.** Because of rather limited data suggesting that the healthy elderly are at increased risk of pneumococcal infections and concerns that the vaccine may not always be effective in the elderly, not all international guidelines recommend routine vaccination in this group of individuals. Nevertheless, based on evidence of an increased incidence of pneumococcal bacteraemia in the elderly in South Africa, the safety of the vaccine, likely efficacy and studies showing cost-effectiveness in the elderly, routine vaccination of this group of patients is recommended.

• **Persons aged 2 - 65 years living in special environments** or social settings where rapid spread of pneumococcal infections may occur should receive the pneumococcal vaccine. Such spread has been well documented to occur in residents in frail-care centres but may also apply to residents in mining compounds, hostels, prisons, and other such institutions.

The level of evidence for vaccine efficacy in all these cases is level B, except for mine workers, in whom the level is A.

8.2 Immunocompromised individuals[2,76-78]

• Persons with conditions associated with decreased immunological function that markedly increase the risk of pneumococcal disease or its complications should be vaccinated. The level of evidence of vaccine efficacy is level C. Although the vaccine may not be as effective in this situation as it is in immunocompetent individuals, the potential benefits and safety of the vaccine justify its use. The following groups are considered: persons > 2 years with leukaemia, lymphoma, multiple myeloma, generalised malignancy, nephrotic syndrome, organ or bone-marrow transplantation, and persons receiving immunosuppressive chemotherapy, including long-term corticosteroids. Patients who are about to begin chemotherapy or other immunosuppressive therapy should, if possible, receive the vaccine 2 weeks before initiation.

• Although pneumococcal vaccination is recommended routinely and as early as possible by the Centers for Disease Control and Prevention (CDC) for patients who are HIV-seropositive, this is not recommended at the present time in South Africa. The recommendation by the CDC was not based on studies, but based on the premise that while there is not proven efficacy, the potential benefit and safety of the vaccine justify its use in this situation. There is currently insufficient evidence to support this recommendation. Plasma HIV levels have been found to be transiently elevated in some studies in HIV-seropositive individuals following pneumococcal vaccination. The significance of these elevated levels is uncertain. Preliminary data from a recent study in Uganda showed lack of benefit of vaccination of HIV-seropositive individuals with the 23-valent polysaccharide vaccine. These indications are undergoing scrutiny at the current time. As evidence emerges to support these recommendations, changes will be made to the guideline and these will appear promptly on the Internet site (**www.samedical.org/cqc**)

8.3 Revaccination[2,47,51,74]

Routine revaccination of immunocompetent patients who have previously been vaccinated with the 23-valent polysaccharide vaccine is not recommended. Revaccination once after 5 years is recommended for persons ≥ 2 years who are at high risk of serious pneumococcal infection and/or its complications and those who are likely to have a rapid decline in antibody levels, including patients with splenectomy or splenic dysfunction, leukaemia, lymphoma, multiple myeloma, generalised malignancy, chronic renal failure, nephrotic syndrome, organ or bone-marrow transplant, and patients receiving immunosuppressive chemotherapy. If vaccination status is unknown, patients in these categories should have pneumococcal vaccine. Elderly patients > 65 years should receive a second dose of vaccine if they received the vaccine > 5 years previously and were aged < 65 years at the time of the vaccination. Elderly patients with unknown vaccine status should receive one dose of the vaccine. The need for subsequent doses of the vaccine is uncertain at the present time. Revaccination is contraindicated in persons who have a severe reaction to the initial dose of the vaccine.

8.4 Contraindications to pneumococcal vaccination[2]

The vaccine is contraindicated in anyone who has hypersensitivity to any of its components. Immunisation should be delayed in the case of fever, acute infection and relapse of chronic disease, unless withholding the vaccine poses a greater threat. Pneumococcal vaccination is also not recommended in persons who were given the vaccine previously within the past 3 years. Revaccination is contraindicated in anyone who had a severe reaction to the first vaccination. Care should be exercised when administering the vaccine to any person with an allergic condition and to patients with severely compromised cardiac and respiratory function in whom a systemic reaction may pose a serious risk. Safety in pregnancy has NOT been established.

8.5 Side-effects and adverse reactions[2,15,43,48,60]

Local reactions are quite common at the injection site, including pain, erythema, induration and oedema. These are usually mild and transient, lasting < 48 hours. Very rarely an Arthus-like reaction has been reported. This is reversible without side-effects and occurs mainly in persons with high initial levels of pneumococcal antibodies.

Systemic reactions have been observed, especially moderate transient fever. Fever > 39°C occurs rarely. Febrile episodes tend to occur very early after vaccination and resolve within 24 hours. Rarely anaphylactic reactions have been noted.

8.6 Cost effectiveness[2,9,15,79-81]

There are relatively few data on cost-effectiveness of the pneumococcal vaccine, but a recent study in the USA does suggest that the vaccine is cost-saving in terms of prevention of bacteraemia alone. One study has noted that the cost-effectiveness of the pneumococcal vaccine may increase with increasing rates of penicillin resistance. These increased costs are related to increased hospital stay, and this appears to reflect physician concerns of treating cases with penicillin-resistant infections rather than differences in patient morbidity and/or mortality.

8.7 Strategies for implementation[2,7,8,15,27,36]

The vaccine is significantly underutilised in South Africa. A number of recommendations have been made for the successful implementation of pneumococcal vaccination, along the lines discussed under the influenza vaccine. Firstly, it is essential to educate health care workers and the general public about the potential benefits of vaccination. Secondly, individuals in whom vaccination is recommended could be identified in the various settings from outpatient clinics through to acute care hospitals. A hospital-based strategy may be an important route for targeting patients for pneumococcal vaccine. It would potentially encompass a number of elderly individuals as well as patients being discharged from the hospital following pneumococcal pneumonia, a group of patients who are likely to have risk factors for these infections and who are at particular risk for further pneumococcal infections.

8.8 Conjugate pneumococcal vaccines[2,82]

The capsular polysaccharide vaccine is not effective in children < 2 years of age. This is due to the fact that the major antibody response to polysaccharide antigens is in the IgG2 subclass and IgG2 subclass levels and responses do not mature and reach adult levels until the age of 2 years. One promising approach to this problem has been the development and testing of protein conjugate vaccines, which are currently used successfully in the prevention of *Haemophilus influenzae* infections. These vaccines convert the humoral response into a T-cell-dependent response with the added benefit of the development of immunological memory. These vaccines are being tested in children worldwide in phase III studies for efficacy against carriage, otitis media and invasive infections. It is possible that they may also be found to be of benefit in immunocompromised adults with high-risk conditions for pneumococcal infections who respond poorly to the polysaccharide vaccine.

9. DISCLAIMER

This national clinical guideline is for reference and education only and is not intended to be a substitute for the advice of the appropriate health care professional or for independent research and judgement. SAMA relies on the source of the national clinical guideline to provide updates and to notify us if the guideline protocol becomes outdated. SAMA accepts no responsibility or liability arising from any information contained in or any error in or omission from the protocol or from the use of any information contained in it.

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