ma; Gammagard; Globuman†; Intraglobin F; Octagam; Pentaglobin; Venoglobulin-S†; ***Hung.:*** Gammagard; Gammanorm; Humaglobin; Intratect; Octagam; Pentaglobin; Vivaglobin; ***India:*** Gamafine; ***Indon.:*** Gamimune N; Gammaraas; ***Irl.:*** Intraglobin; ***Israel:*** Beriglobin P; Endobulin†; Flebogamma; Gammagard†; Intraglobin F; Omr-IgG; Sandoglobulin; Venoglobulin; Vigam; ***Ital.:*** Biaven; Endobulin; Flebogamma; Gamma-Venin P†; Gammagard; Globuman†; Haimaven†; Ig Gamma†; Ig Vena; Intraglobin; Isiven; Pentaglobin; Sandoglobulina; Uman-Gamma†; Venimmun†; ***Jpn:*** Venilon; Venoglobulin; ***Malaysia:*** Flebogamma; Gammagard†; Globuman†; Intraglobin F†; IV-Globulin; Pentaglobin†; Venoglobulin-S†; Vigam; ***Mex.:*** Beriglobina P; Gamma-Venin P; Gammagard†; Isiven†; Octagam; Pentaglobin; Sandoglobulina; Seroglubin†; Vigam; ***Neth.:*** Endobuline†; Flebogamma; Gammagard; Gammanorm; GammaQuin; Ivegam; Octagam; Subcuvia; Vivaglobin; ***Norw.:*** Gammaglobulin†; Gammanorm; Octagam; ***NZ:*** Intragam; Octagam; Sandoglobulin; ***Philipp.:*** Gamimune N; Gammagard; IV-Globulin S; ***Pol.:*** Endobulin; Gamma-Globulina; Gammagard; Intraglobin F; Intratect; Kiovig; Pentaglobin; Sandoglobulin; Subcuvia; Venimmun; ***Port.:*** Flebogamma; Gammagard; Gammanorm; Gamunex; Globuman†; Ig Vena; Octagam; Sandoglobulina; Subcuvia; Vivaglobin; ***Rus.:*** Gamimune N (Гамимун Н); Humaglobin (Хумаглобин)†; Immunovenin (Иммуновенин)†; Octagam (Октагам); ***S.Afr.:*** Beriglobin; Endobulin†; Intragam; Intraglobin F; Pentaglobin; Polygam; ***Singapore:*** Flebogamma; Gammagard†; Intraglobin F; Pentaglobin; Venoglobulin†; Vigam†; ***Spain:*** Beriglobina P; Endobulin; Flebogamma; Gammagard; Gammaglobulina; Globuman†; Octagamocta; ***Swed.:*** Beriglobin; Endobulin; Gammagard; Gammanorm; Gammonativ; Octagam; Polyglobin†; Subcuvia; Xepol; ***Switz.:*** Beriglobin; Endobulin; Gammagard; Globuman; Intraglobin F; Octagam; Pentaglobin; Redimune; ***Thai.:*** Flebogamma; Gammaraas; Globuman†; Ig Vena; Intraglobin; Octagam; Pentaglobin; Venoglobulin-S†; Vigam; ***Turk.:*** Biseko; Endobulin; Flebogamma; Gamimune N; Gammar; Globuman; IG Vena NIV; Intraglobin; Isiven; Octagam; Pentaglobin; Subcuvia; Tegeline; Vigam; ***UK:*** Flebogamma; Gammabulin†; Gammagard; Kiovig; Octagam; Sandoglobulin; Subcuvia; Subgam; Vigam; Vivaglobin; ***USA:*** Carimune; Flebogamma; Gamastan; Gamimune N†; Gammagard; Gammar-P†; Gamunex; Iveegam†; Octagam; Panglobulin†; Polygam; Privigen; Venoglobulin†; Vivaglobin; ***Venez.:*** Flebogamma; Sandoglobulina†; Venoglobulina†.

Multi-ingredient: ***Arg.:*** Biotaer Gamma†; Histaglobin; ***Austria:*** Histaglobin; ***Chile:*** Pentaglobin; ***Cz.:*** Histaglobin†; ***Ger.:*** Histadestal; ***India:*** Histaglobulin; ***Pol.:*** Histaglobulina; ***S.Afr.:*** Histaglobin.

Pertussis Immunoglobulins

Inmunoglobulinas contra la tos ferina.

ATC — J06BB13.

Pharmacopoeias. Many pharmacopoeias, including *US*, have monographs.

USP 31 (Pertussis Immune Globulin). A sterile solution of globulins derived from the plasma of adult human donors who have been immunised with pertussis vaccine. It may contain glycine as a stabilising agent, and a suitable preservative. It should be stored at 2° to 8°.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Interactions

As for immunoglobulins in general, p.2201.

Uses and Administration

Pertussis immunoglobulins have been used for passive immunisation against pertussis (whooping cough) and to prevent or modify pertussis in susceptible persons who have been exposed to infection.

Preparations

USP 31: Pertussis Immune Globulin.

Pertussis Vaccines

Vacunas de la tos ferina.

ATC — J07AJ01; J07AJ02.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.

Ph. Eur. 6.2 (Pertussis Vaccine (Adsorbed); Vaccinum Pertussis Adsorbatum). A sterile suspension of inactivated whole cells of one or more strains of *Bordetella pertussis* in saline to which hydrated aluminium phosphate or aluminium hydroxide has been added. It may contain a suitable antimicrobial preservative. The estimated potency is not less than 4 units per dose. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

The BP 2008 states that wP may be used on the label.

Ph. Eur. 6.2 (Pertussis Vaccine (Acellular, Component, Adsorbed); Vaccinum Pertussis sine Cellulis ex Elementis Praeparatum Adsorbatum). A preparation of individually prepared and purified antigenic components of *Bordetella pertussis* adsorbed on a mineral carrier such as aluminium hydroxide or hydrated aluminium phosphate. It contains either a suitably prepared pertussis toxoid or a pertussis toxin-like protein free from toxic properties produced by expression of a genetically modified form of the corresponding gene. It may also contain filamentous haemagglutinin, pertactin, and other defined antigens such as fimbrial-2 and fimbrial-3 antigens. The final vaccine contains not more than 100 units of bacterial endotoxin per dose. It may contain a suitable antimicrobial preservative. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

The BP 2008 states that aP may be used on the label.

Ph. Eur. 6.2 (Pertussis Vaccine (Acellular, Co-purified, Adsorbed); Vaccinum Pertussis Sine Cellulis Copurificatum Adsorbatum). A preparation of antigenic components of *Bordetella pertussis* adsorbed on a mineral carrier such as aluminium hydroxide or hydrated aluminium phosphate. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.

The BP 2008 states that aP may be used on the label.

Adverse Effects

As for vaccines in general, p.2201.

Local reactions may occur at the site of injection of pertussis vaccines or pertussis-containing vaccines and use may be followed by fever and irritability. Local reactions and fever occur less frequently with the acellular vaccine than with whole-cell vaccine, especially in children over 6 months of age and adults. However, booster doses of acellular pertussis-containing vaccines are associated with an increased risk of injection site reactions.

Severe reactions which have been reported include persistent screaming and generalised collapse but these effects were generally associated with an earlier type of vaccine and the reactions are stated to be rarely observed with the currently available vaccines.

Rare neurological adverse reactions have included convulsions and encephalopathy. There has been much debate, however, on the causal role of pertussis vaccine in such reactions (see below for detailed discussion). It should be remembered that neurological complications occur more frequently as a consequence of pertussis infection than from vaccination.

Asthma. A higher incidence of asthma was reported in 243 children who had received whole-cell pertussis vaccine than in 203 children who had not.[1] However, follow-up of a large Swedish study[2] showed no difference in the incidence of wheezing or allergic reactions between children who had received diphtheria, tetanus, and whole-cell pertussis vaccines and those who had not. A later prospective study[3] also found no evidence that whole-cell pertussis vaccination increased the risk of wheezing illness in young children. Furthermore, no association was found between pertussis vaccination in infancy and development of asthma in children aged up to 7 years in a later study of the same group of children.[4]

1. Odent MR, *et al.* Pertussis vaccination and asthma: is there a link? *JAMA* 1994; **272:** 592–3.
2. Nilsson L, *et al.* Lack of association between pertussis vaccination and symptoms of asthma and allergy. *JAMA* 1996; **275:** 760.
3. Henderson J, *et al.* Pertussis vaccination and wheezing illnesses in young children: prospective cohort study. *BMJ* 1999; **318:** 1173–6.
4. Maitra A, *et al.* Pertussis vaccination in infancy and asthma or allergy in later childhood: birth cohort study. *BMJ* 2004; **328:** 925–6.

Effects on the nervous system. There has been continuing debate over several decades concerning the perceived link between pertussis vaccination and brain damage. Anxiety among both the public and health care professionals in the UK in the mid-1970s over the safety of whole-cell pertussis vaccines led to a fall in the acceptance rates for infant vaccination and major epidemics of pertussis in 1977/79 and 1981/83. Since that time confidence has been restored and, with the introduction of acellular vaccines, the vast majority of infants now receive the vaccine before their second birthday. Comparison of whole-cell vaccines with acellular vaccines has since confirmed that the latter are associated with a greatly reduced incidence of serious neurological disorders.[1]

The consensus of opinion now seems to be that there is a temporal, but not necessarily causal, relationship between whole-cell pertussis vaccine and acute neurological illness that may occasionally lead to long-term dysfunction, and that risks of not immunising are greater than the potential risks associated with the vaccine.

The difficulty in ascertaining whether a causal relationship exists between whole-cell pertussis vaccine (usually given as diphtheria, tetanus, and pertussis (DTP) vaccine) and acute neurological reactions arises partly because primary vaccination is given at an age when neurological dysfunction with other causes is often first manifested. The observed temporal relationship may be entirely coincidental, may result from indirect factors such as pyrexia after vaccination, or may represent a direct effect of DTP vaccine. Much of the evidence is based on large epidemiological studies,[2-7] in particular the National Childhood Encephalopathy Study (NCES)[8] from the UK and its 10-year follow-up.[9] Serious acute neurological illnesses reported to the NCES[8] were found to be more common in infants immunised within 7 days (relative risk 2.4), and especially within 72 hours of onset, than in unimmunised children. For previously normal children, irrespective of outcome, the risk was estimated as 1 in 110 000 injections. In a subset of cases diagnosed as infantile spasms,[10] no link with vaccination was found overall, but there was a small excess of cases of infantile spasm in previously normal children who had received either DTP or diphtheria and tetanus vaccines during the previous 7 days (relative risk 2.0-2.5) followed by a corresponding deficit during the next 3 weeks. This suggested that vaccination may trigger the onset of spasms in a child with an underlying predisposition.

In 1991, the USA Institute of Medicine reviewed the available data, including the NCES results, and concluded that a causal relationship between the whole-cell pertussis component of DTP vaccine and acute encephalopathy probably existed, with an estimated excess risk of 0 to 10.5 per million vaccinations.[11] They concurred with the conclusion that a causal relationship between vaccination and infantile spasm was unlikely.

The NCES 10-year follow-up found that children who had had a serious acute neurological illness (excluding infantile spasms) had an increased risk of death or long-term dysfunction, but the risk was no greater in children given DTP vaccine in the 7 days before the original acute illness.[9] The National Vaccines Advisory Committee concluded that the results were insufficient to determine whether DTP vaccine influenced the development of chronic neurological dysfunction, and this conclusion has been accepted by both the Advisory Committee on Immunization Practices[12] and the American Academy of Pediatrics.[13]

1. Geier DA, Geier MR. An evaluation of serious neurological disorders following immunization: a comparison of whole-cell pertussis and acellular pertussis vaccines. *Brain Dev* 2004; **26:** 296–300.
2. Pollock TM, Morris J. A 7-year survey of disorders attributed to vaccination in North West Thames Region. *Lancet* 1983; **i:** 753–7.
3. Pollock TM, *et al.* Symptoms after primary immunisation with DTP and with DT vaccine. *Lancet* 1984; **ii:** 146–9.
4. Walker AM, *et al.* Neurologic events following diphtheria-tetanus-pertussis immunization. *Pediatrics* 1988; **81:** 345–9.
5. Shields WD, *et al.* Relationship of pertussis immunization to the onset of neurologic disorders: a retrospective epidemiologic study. *J Pediatr* 1988; **113:** 801–5.
6. Griffin MR, *et al.* Risk of seizures and encephalopathy after immunization with the diphtheria-tetanus-pertussis vaccine. *JAMA* 1990; **263:** 1641–5.
7. Gale JL, *et al.* Risk of serious acute neurological illness after immunization with diphtheria-tetanus-pertussis vaccine: a population-based case-control study. *JAMA* 1994; **271:** 37–41.
8. Miller DL, *et al.* Pertussis immunisation and serious acute neurological illness in children. *BMJ* 1981; **282:** 1595–9.
9. Miller D, *et al.* Pertussis immunisation and serious acute neurological illnesses in children. *BMJ* 1993; **307:** 1171–6.
10. Bellman MH, *et al.* Infantile spasms and pertussis immunisation. *Lancet* 1983; **i:** 1031–4.
11. Howson CP, Fineberg HV. Adverse events following pertussis and rubella vaccines: summary of a report of the Institute of Medicine. *JAMA* 1992; **267:** 392–6.
12. CDC. Update: vaccine side effects, adverse reactions, contraindications, and precautions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1996; **45** (RR-12): 1–45. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr4512.pdf (accessed 25/05/06)
13. Committee on Infectious Disease, American Academy of Pediatrics. The relationship between pertussis vaccine and central nervous system sequelae: continuing assessment. *Pediatrics* 1996; **97:** 279–81.

Precautions

As for vaccines in general, p.2202. The precautions and contra-indications to the use of pertussis vaccines have sometimes been more stringent than is now considered necessary because of the controversy about their potential adverse effects, especially neurotoxicity (see under Adverse Effects, above). In the UK it is now recommended that immunisation should continue with acellular pertussis vaccine even when episodes of fever (irrespective of severity), hypotonic-hyporesponsive episodes, persistent crying or screaming, or severe local reactions (irrespective of extent) have occurred after a preceding dose. Children who have had a local or general reaction to a whole-cell pertussis vaccine should complete their immunisation with acellular pertussis vaccine.

Whether or not children with a personal or family history of convulsions or epilepsy or who have suffered cerebral damage in the neonatal period should receive pertussis vaccines appears to have been the most difficult question to resolve in the past. In the UK it is now considered that a family history of seizures is not a contra-indication to immunisation. When a child has a history of seizures associated with fever, but no evidence of neurological deterioration, immunisation should proceed as normal; advice on the prevention of fever should be given at the time of immunisation (see Fever and Hyperthermia, p.10 for comments on the prevention of fever after immunisation). Similarly when there is a history of seizures not associated with fever, but no evidence of neurological deterioration, immunisation should proceed as normal. If a seizure associated with fever occurs within 72 hours of immunisation, further immunisation should be deferred until the condition is stable if no underlying cause is found and the child has not recovered completely within 24 hours. Immunisation should also be carried out in children with a history of cerebral damage in the neonatal period unless there is evidence of an evolving neurological abnormality. In children with a neurological problem that is still evolving it is recommended that immunisation should be deferred until the condition is stable. If a child develops encephalopathy or encephalitis within 7 days of immunisation, further immunisation should be deferred until the condition is stable if no underlying cause is found and the child has not recovered completely within 7 days.

A personal or family history of hypersensitivity reactions is not generally considered to be a contra-indication to the use of pertussis vaccines, and neither are stable neurological conditions such as spina bifida, congenital brain abnormality, or perinatal hypoxic ischaemic encephalopathy.

Interactions
As for vaccines in general, p.2202.

Uses and Administration
Pertussis vaccines are used for active immunisation against pertussis (whooping cough) (p.185). Acellular pertussis vaccines have taken the place of whole-cell vaccines in several countries including the UK and the USA.

For primary immunisation combined pertussis vaccines, usually diphtheria, tetanus, and pertussis vaccines (p.2210) or diphtheria, tetanus, pertussis, poliomyelitis, and haemophilus influenzae vaccines (p.2212) are used. For pre-school boosters diphtheria, tetanus, pertussis, and poliomyelitis vaccines (p.2211) are sometimes given. For discussion of immunisation schedules, see below.

Immunisation schedules. Pertussis is a common, highly infectious, respiratory disease, mainly affecting children, and for which there is no effective treatment. WHO estimates that 20 to 40 million cases of pertussis occur annually and that the disease is responsible for 200 000 to 400 000 deaths each year. The highest incidence of pertussis occurs in developing countries where immunisation is low.

Combined vaccines are now used in most countries but both the strength of the pertussis component and production methods vary, leading to vaccines of different potencies. The considerably higher cost of acellular over whole-cell pertussis vaccines means that the latter are still used widely in developing countries.

Depending upon the country, the age at which a child is given the first dose of a combined vaccine varies from 5 weeks to 6 months. (For summaries of immunisation schedules in the UK and USA, see under Vaccines, p.2202.) In countries with a high incidence of pertussis, WHO recommends that immunisation should start at 6 weeks of age and that the schedule involve 3 doses at monthly intervals followed by a booster dose at 18 months to 6 years of age. In the UK and USA, booster doses should be given after the end of the primary series of 3 injections before entry to school. Several reports have described the use of a 2-dose widely-spaced primary immunisation schedule and this would indeed simplify procedures in developing countries; however, the limitation of such a schedule is the long period of risk between doses without adequate protection and unless the interval can be shortened to 4 weeks, the wide use of such a schedule is not advisable in endemic areas.

Vaccine development. Dissatisfaction with whole-cell vaccines in the 1970s because of adverse reactions led to reduced uptake and a resurgence of pertussis in several countries. In Japan, research into less reactogenic pertussis vaccines resulted in the introduction of acellular vaccines for routine vaccination in the early 1980s. Acellular pertussis vaccines can contain a variety of pertussis components:

- pertussis toxin (PT; also formerly known as lymphocytosis-promoting factor, LPF)
- filamentous haemagglutinin (FHA)
- pertactin (PRN)
- fimbrial agglutinogens (FIM) 2 and 3

The acellular vaccines commonly used are a 3-component vaccine containing PT/FHA/PRN and a 5-component vaccine containing PT/FHA/PRN/FIM2/FIM3. The vaccine used in combination vaccines for primary immunisation in the UK is the 5-component vaccine. The 3-component vaccine does not provide the same level of protection against whooping cough in primary immunisation. Both 3-component and 5-component vaccines may be used in combination vaccines for pre-school boosting. The combination vaccine used for pre-school boosting that contains 5-component pertussis vaccine does not provide the recommended strength of diphtheria to be used for primary immunisation.

Acellular vaccines are now recommended in the UK and USA for both primary immunisation in infants and for the booster doses in young children before school entry. Whole-cell vaccines are still, however, widely used in other countries, particularly in the developing world.

Preparations
Ph. Eur.: Pertussis Vaccine (Acellular Component, Adsorbed); Pertussis Vaccine (Acellular, Co-purified, Adsorbed); Pertussis Vaccine (Adsorbed).

Proprietary Preparations (details are given in Part 3)
Ger.: Pac Merieux†; ***Neth.:*** Acellulair.

Pigbel Vaccines
Vacunas de la enteritis necrotizante.

Profile
A vaccine against pigbel (necrotising enteritis), a disease occurring mainly in children in the highlands of Papua New Guinea, is used for active immunisation against the disease. The vaccine consists of an adsorbed *Clostridium perfringens* type C toxoid.

◊ An immunisation programme, in which pigbel vaccine was given to children at 2, 4, and 6 months of age and, initially, to older children, was introduced in Papua New Guinea in 1980.[1] A survey found a sustained overall fall in the incidence of severe pigbel in children coincident with the increased induced immunity. However, protection may be relatively short-lived and boosters may be necessary for full protection of young children.

1. Lawrence GW, *et al.* Impact of active immunisation against enteritis necroticans in Papua New Guinea. *Lancet* 1990; **336:** 1165–7.

Plague Vaccines
Vacunas de la peste.
ATC — J07AK01.

Adverse Effects and Precautions
As for vaccines in general, p.2201.

Interactions
As for vaccines in general, p.2202.

Uses and Administration
Plague vaccines have been used for active immunisation against plague in those occupationally exposed to the organism and in some field workers in infected areas. They may reduce morbidity and mortality in bubonic plague but their activity against pneumonic plague is unknown.

Pneumococcal Vaccines
Vacunas neumocócicas.
ATC — J07AL01; J07AL02.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.
Ph. Eur. 6.2 (Pneumococcal Polysaccharide Vaccine; Vaccinum Pneumococcale Polysaccharidum). A mixture of purified polysaccharide capsular antigens from 23 differing serotypes of *Streptococcus pneumoniae*. Each 0.5-mL dose contains 25 micrograms of each of the 23 polysaccharide types. An antimicrobial preservative may be added. The vaccine has a pH of 4.5 to 7.4. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
The BP 2008 states that Pneumo may be used on the label.
Ph. Eur. 6.2 (Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed); Vaccinum Pneumococcale Polysaccharidicum Coniugatum Adsorbatum). A solution of purified immunochemically different capsular polysaccharides obtained from *Streptococcus pneumoniae* serotypes individually conjugated to a carrier protein. The vaccine may be adsorbed on a suitable adjuvant or adsorbant. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
The BP 2008 states that Pneumo(conj) may be used on the label.

Adverse Effects and Precautions
As for vaccines in general, p.2201. Unless otherwise stated, the information below refers to the unconjugated polyvalent vaccine.

Revaccination of adults is not routinely recommended because of the increased incidence and severity of adverse reactions.

Pneumococcal vaccination is relatively ineffective in patients with multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, especially during treatment, and in chronic alcoholism. In patients with Hodgkin's disease the use of pneumococcal vaccines is not recommended in those who have received extensive chemotherapy or nodal irradiation. Pneumococcal vaccines should be given at least 2 weeks (and preferably 4 to 6 weeks) before starting immunosuppressive therapy or be delayed until at least 3 months after completion of therapy.

A satisfactory response to the unconjugated polyvalent pneumococcal vaccines is not obtained in children less than 2 years of age and therefore immunisation of this age group with this vaccine is not recommended. However, a pneumococcal conjugate vaccine is available that may be given to infants from 2 months of age.

Effects on the blood. Relapses have occurred on rare occasions in patients with stabilised idiopathic thrombocytopenic purpura at 2 to 14 days after vaccination against pneumococcal infections, lasting for up to 2 weeks. One such case was reported[1] following revaccination less than 2.5 years after an uneventful primary vaccination with pneumococcal vaccine.

1. Neil VS. Long term management after splenectomy: revaccination may cause relapse. *BMJ* 1994; **308:** 339.

Effects on the kidneys. Glomerulonephritis was described[1] in a splenectomised patient after use of pneumococcal vaccine. It was postulated that high antibody titres from a recent pneumococcal infection could have contributed. Minimal change nephrotic syndrome with mild interstitial nephritis following pneumococcal vaccination was suggested as the cause of oedema of the face and legs, visual disturbance suggestive of uveitis, and massive proteinuria in a 67-year-old woman who had been vaccinated about 4 months earlier.[2]

1. Tan SY, Cumming AD. Vaccine related glomerulonephritis. *BMJ* 1993; **306:** 248.
2. Kikuchi Y, *et al.* Minimal change nephrotic syndrome, lymphadenopathy and hyperimmunoglobulinemia after immunization with a pneumococcal vaccine. *Clin Nephrol* 2002; **58:** 68–72.

Effect of nutritional status. An impaired antibody response to pneumococcal vaccine was reported[1] in elderly patients with low serum concentrations of vitamin B_{12}.

1. Fata FT, *et al.* Impaired antibody responses to pneumococcal polysaccharide in elderly patients with low serum vitamin B12 levels. *Ann Intern Med* 1996; **124:** 299–304.

Interactions
As for vaccines in general, p.2202.

Uses and Administration
Of the many serotypes of *Streptococcus pneumoniae* the 23 from which antigens are obtained for the most commonly available pneumococcal vaccine are considered to cause up to 96% of pneumococcal disease.

Pneumococcal vaccines are used for active immunisation in those at increased risk from infection with the types of *Streptococcus pneumoniae* contained in the vaccine. Pneumococcal vaccines may be in the form of an unconjugated 23-valent polysaccharide vaccine (suitable only for patients over 2 years of age) or as a conjugate vaccine containing 7 serotypes (suitable for infants aged 2 months to 5 years).

In the UK, it is recommended that immunisation should be considered in all persons aged 65 and over; persons who have undergone splenectomy and those with splenic dysfunction, including that due to sickle-cell anaemia and coeliac disease; patients with immunodeficiency or immunosuppression due to disease or treatment, including HIV infection at all stages; persons with chronic cardiac, pulmonary, hepatic, or renal impairment, including nephrotic syndrome, or diabetes mellitus; persons with CSF shunts; children under 5 years old who have previously had invasive pneumococcal disease such as meningitis or septicaemia; and persons with cochlear implants.

An antibody response develops by the third week, and usually lasts about 5 years. The antibody response is less reliable and declines more rapidly in young children and persons with impaired immune function.

A single dose of 0.5 mL of the 23-valent vaccine, containing 25 micrograms of each of the 23 polysaccharide types, is given to at-risk adults and children over 5 years of age by intramuscular injection (or subcutaneously if there are bleeding disorders). The vaccine should be given at least 2 weeks (but preferably 4 to 6 weeks) before elective splenectomy, chemotherapy, or other immunosuppressive treatment. Revaccination is not generally recommended except, after 5 years, in patients likely to have rapidly declining antibody concentrations (for example, those with asplenia or splenic dysfunction and those with nephrotic syndrome).

The 7-valent pneumococcal conjugate vaccine is given by intramuscular injection. In the UK it is recommended that at-risk infants under 6 months should be given 3 single doses of 0.5 mL at intervals of 1 month, starting at 2 months of age, with a fourth dose given in the second year of life; those aged 6 to 11 months should receive 2 doses at least one month apart with a third dose given in the second year of life; and those aged 12 to 60 months should receive 2 doses at least two months apart. The 23-valent pneumococcal polysaccharide vaccine should also be given to the highest risk children (those with asplenia or splenic dysfunction and those with nephrotic syndrome) after their second birthday and at least 2 months after the final dose of conjugate vaccine.

In the USA, three doses of the 7-valent pneumococcal conjugate vaccine are recommended as part of the routine primary immunisation schedule at 2, 4, and 6