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