months of age. The 23-valent pneumococcal polysaccharide vaccine should be given to high-risk groups between the ages of 2 and 18 years in addition to previously administered 7-valent pneumococcal conjugate vaccine. The 23-valent vaccine is also used in at-risk adults similarly to that outlined for the UK above.

◊ Reviews.

1. Sheikh A, *et al.* Pneumococcal vaccine for asthma. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 22/04/05).
2. Davies EG, *et al.* Pneumococcal vaccines for sickle cell disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 22/04/06).
3. Straetemans M, *et al.* Pneumococcal vaccines for preventing otitis media. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2004 (accessed 22/04/05).
4. Bernatoniene J, Finn A. Advances in pneumococcal vaccines: advantages for infants and children. *Drugs* 2005; **65:** 229–55.
5. Moberley SA, *et al.* Vaccines for preventing pneumococcal infection in adults. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 10/06/08).

Preparations

Ph. Eur.: Pneumococcal Polysaccharide Conjugate Vaccine (Adsorbed); Pneumococcal Polysaccharide Vaccine.

Proprietary Preparations (details are given in Part 3)
Arg.: Imovax Pneumo†; Neumak†; Pneumo 23; Pneumovax 23; Prevenar; Prote-Neu; ***Austral.:*** Pneumovax 23; Prevenar; ***Austria:*** Pneumo 23; Pnu-Imune†; Prevenar; ***Belg.:*** Pneumo 23; Pneumovax 23†; Pneumune†; Prevenar; ***Braz.:*** Pneumo 23†; Pneumovax 23†; Vacina Pneumococica Conjugada 7-valate; Vacina Pneumococica Polivalente; Vacina Pneumococica Polivalente Pneumo 23; ***Canad.:*** Pneumo 23; Pneumovax 23; Prevnar; ***Chile:*** Pneumo 23; Prevenar; ***Cz.:*** Pneumo 23; Prevenar; ***Denm.:*** Pneumo Novum; Pneumovax; Prevenar; ***Fin.:*** Pneumovax; Prevenar; ***Fr.:*** Pneumo 23; Prevenar; ***Ger.:*** Pneumopur†; Pneumovax 23; Prevenar; ***Gr.:*** Pneumo 23; Pneumovax 23; Pnu-Imune 23†; Prevenar; ***Hong Kong:*** Pneumo 23; Pneumovax 23; Prevenar; ***Hung.:*** Pneumo 23; Pneumovax 23; Prevenar; ***Indon.:*** Pneumo 23; Prevenar; ***Irl.:*** Pneumovax II; Pnu-Imune†; Prevenar; ***Israel:*** Pneumo 23; Pneumovax 23; Prevnar; ***Ital.:*** Pneumo 23; Pneumopur†; Pneumovax; Pnu-Imune 23†; Prevenar; Streptopur; ***Malaysia:*** Pneumo 23; Pneumovax 23†; Prevenar; ***Mex.:*** Pnu-Imune 23†; Prevenar; Pulmovax; ***Neth.:*** Pneumo 23; Pneumovax 23; Prevenar; ***Norw.:*** Pneumovax; Pnu-Imune†; Prevenar; ***NZ:*** Pneumo 23; Pneumovax 23; Prevenar; ***Philipp.:*** Pneumo 23; Prevenar; ***Pol.:*** Pneumo 23; Pneumovax 23; Prevenar; ***Port.:*** Pneumo 23; Pneumovax 23; Pnu-Imune†; Prevenar; ***S.Afr.:*** Imovax Pneumo 23; Pneumovax 23; Prevenar; ***Singapore:*** Pneumo 23; Pneumovax 23; Prevenar; ***Spain:*** Pneumo 23; Pnu-Inmune†; Prevenar; ***Swed.:*** Pneumo 23; Pneumovax†; Pnu-Imune†; Prevenar; ***Switz.:*** Pneumovax 23; Pnu-Imune 23†; Prevenar; ***Thai.:*** Pneumo 23; Pneumovax 23†; Prevnar; ***Turk.:*** Pneumo 23; ***UK:*** Pneumovax II; Prevenar; ***USA:*** Pneumovax 23; Prevnar; ***Venez.:*** Imovax Neumo 23†; Prevenar.

Poliomyelitis Vaccines

Polio Vaccines; Poliovirus Vaccines; Vacunas de la poliomielitis.
ATC — J07BF01; J07BF02; J07BF03.

NOTE. Inactivated poliomyelitis vaccines are sometimes termed Salk Vaccine and live (oral) poliomyelitis vaccines are sometimes termed Sabin Vaccine.

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

Ph. Eur. 6.2 (Poliomyelitis Vaccine (Inactivated); Vaccinum Poliomyelitidis Inactivatum). A liquid preparation of suitable strains of poliomyelitis virus, types 1, 2, and 3, grown in suitable cell cultures and inactivated by a suitable method. Permitted antibacterials may be used in its production and it may contain preservatives. It should be stored at 2° to 8° and be protected from light.
The BP 2008 states that IPV may be used on the label.

Ph. Eur. 6.2 (Poliomyelitis Vaccine (Oral); Vaccinum Poliomyelitidis Perorale; Poliomyelitis Vaccine, Live (Oral) BP 2008). A liquid preparation of suitable live attenuated strains of poliomyelitis virus, types 1, 2, or 3, grown in suitable, approved cell cultures; it may contain any one of the 3 virus types or combinations of them. The trivalent vaccine is standardised for virus titre which is not less than 6.0 log $CCID_{50}$ for type 1, not less than 5.0 log $CCID_{50}$ for type 2, and not less than 5.5 log $CCID_{50}$ for type 3 per dose. Permitted antibacterials may be used in its production. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
The BP 2008 states that OPV may be used on the label.

USP 31 (Poliovirus Vaccine Inactivated). A sterile aqueous suspension of poliomyelitis virus, types 1, 2, and 3, grown separately in cultures of monkey kidney tissue and inactivated. Suitable antimicrobial agents may be used during production. It should be stored at 2° to 8°.

Adverse Effects

As for vaccines in general, p.2201.

Vaccine-associated paralytic poliomyelitis has been reported rarely in recipients of oral poliomyelitis vaccines and in contacts of recipients (see below).

Carcinogenicity. Some poliomyelitis vaccines given in the 1950s and 1960s were found to be contaminated with Simian virus (SV40) from the monkey cell cultures used in the manufacturing process.[1] Once the contamination was realised, steps were taken to eliminate it from future vaccines. However, SV40 is believed to possess biological properties consistent with cancer-causing viruses and epidemiological studies have consequently been conducted to assess whether vaccine recipients have subsequently developed cancer. Although these studies did not find any increased cancer risk, a report by the USA Institute of Medicine in 2002 concluded that these studies were sufficiently flawed to preclude any conclusion being reached. Studies have also assessed the risk to offspring of women given these vaccines during pregnancy (see below). Vaccines now in use do not contain SV40 as they are not manufactured using monkey cell cultures.

1. Stratton K, *et al.*, eds., Institute of Medicine of the National Academies. SV40 contamination of polio vaccine and cancer. *Immunization Safety Review*. Washington D.C.: National Academies Press, 2003. Also available at: http://www.nap.edu/openbook.php?isbn=0309086108 (accessed 15/07/08)

Effects on the nervous system. There have been several case reports of the isolation of poliovaccine virus from the CSF after use of oral poliomyelitis vaccine. A 7-year-old girl who had previously been vaccinated with inactivated poliomyelitis vaccine in infancy received oral vaccine and developed prolonged headache, vomiting, and fever but no paralysis;[1] poliovirus was subsequently isolated from her CSF 34 days after she had received the oral vaccine, and it was concluded that her previous immunisations had been ineffective. In a further report,[2] poliovirus was isolated from the CSF of 2 infants with ventriculoperitoneal shunts who had developed aseptic meningitis without paralysis following oral poliomyelitis vaccination. A neurovirulent variant of Sabin type 2 oral poliomyelitis vaccine virus was detected in both the CSF and stools of an infant with transient hypogammaglobulinaemia who developed meningoencephalitis, retinitis, and irreversible hearing loss after oral poliomyelitis vaccination.[3] A 6-year-old girl given oral poliomyelitis vaccine at 1 and 2 years developed acute disseminated encephalomyelitis and a mutated form of poliovirus was isolated from her CSF;[4] it was thought that she had been infected with the mutated virus from extrafamilial contacts and that the cause of her condition may have been related to her HLA type.

1. Rantala H, *et al.* Poliovaccine virus in the cerebrospinal fluid after oral polio vaccination. *J Infect* 1989; **19:** 173–6.
2. Gutierrez K, Abzug MJ. Vaccine-associated poliovirus meningitis in children with ventriculoperitoneal shunts. *J Pediatr* 1990; **117:** 424–7.
3. Inaba H, *et al.* Polio vaccine virus-associated meningoencephalitis in an infant with transient hypogammaglobulinemia. *Scand J Infect Dis* 2001; **33:** 630–1.
4. Ozawa H, *et al.* Acute disseminated encephalomyelitis associated with poliomyelitis vaccine. *Pediatr Neurol* 2000; **23:** 177–9.

GUILLAIN-BARRÉ SYNDROME. A small cluster of cases of Guillain-Barré syndrome was seen[1] in children after a mass oral poliomyelitis vaccination campaign in Finland in 1985. An increased frequency of Guillain-Barré syndrome was also seen in adults. However, a direct link with poliovaccine virus infection could not be established and no link between Guillain-Barré syndrome and oral polio vaccine was found by a subsequent, epidemiological study in California.[2]

1. Uhari M, *et al.* Cluster of childhood Guillain-Barré cases after an oral poliovaccine campaign. *Lancet* 1989; **ii:** 440–1.
2. Rantala H, *et al.* Epidemiology of Guillain-Barré syndrome in children: relationship of oral polio vaccine administration to occurrence. *J Pediatr* 1994; **124:** 220–3.

VACCINE-ASSOCIATED PARALYTIC POLIOMYELITIS. Although generally considered safe and effective, in extremely rare cases the live attenuated virus in oral poliomyelitis vaccines can cause vaccine-associated paralytic poliomyelitis (VAPP) in either the vaccine recipient or in a close contact. There is no such risk associated with inactivated poliomyelitis vaccines. The incidence of VAPP is about 1 case in every 2.5 million doses of vaccine and may be increased in immunocompromised patients. A case control study[1] identified intramuscular injections given within 30 days of vaccination as a risk factor in the development of VAPP. This phenomenon, known as provocation paralysis or provocation poliomyelitis, has been described with the wild virus[2] and has been recognised as a factor in vaccine-associated paralysis in the UK and USA.[3] Paralytic poliomyelitis in contacts of vaccine recipients can be further reduced by ensuring that parents without evidence of previous immunisation receive the vaccine at the same time as their children. The benefits of oral poliomyelitis vaccination are considered to greatly outweigh the small risk involved, however, and many countries where the risk of wild virus-caused poliomyelitis has been reduced to zero are now considering combined immunisation schedules with both oral and inactivated poliomyelitis vaccines.

1. Strebel PM, *et al.* Intramuscular injections within 30 days of immunization with oral poliovirus vaccine—a risk factor for vaccine-associated paralytic poliomyelitis. *N Engl J Med* 1995; **332:** 500–6.
2. Anonymous. Provocation paralysis. *Lancet* 1992; **340:** 1005–6.
3. Wyatt HV. Vaccine-associated poliomyelitis. *Lancet* 1994; **343:** 610.

Precautions

As for vaccines in general, p.2202.

Poliomyelitis vaccine may contain trace amounts of antibacterials such as neomycin, polymyxin B, and streptomycin and should be used with caution in patients with severe hypersensitivity to these antibacterials.

Oral poliomyelitis vaccines should not be given to patients with diarrhoea or vomiting.

Because the vaccine virus of oral poliomyelitis vaccines is excreted in the faeces for up to 6 weeks, the contacts of recently vaccinated babies and infants should be advised of the need for strict personal hygiene, particularly hand washing after napkin changing, in order to reduce the possibility of infection in unimmunised contacts. Unimmunised adults can be immunised at the same time as their children.

Immunocompromised patients are at increased risk of developing vaccine-associated paralytic poliomyelitis. Oral poliomyelitis vaccines should not be given to immunocompromised patients or their household contacts and in these persons an inactivated vaccine should be used. Asymptomatic HIV-positive persons may receive oral poliomyelitis vaccines but faecal excretion of the vaccine virus may continue for longer than in uninfected individuals. For symptomatic HIV-positive persons the use of inactivated poliomyelitis vaccine may be considered.

Intramuscular injections given after the oral vaccine may also increase the risk of vaccine-associated paralytic poliomyelitis (see above).

Pregnancy. Live vaccines such as *oral poliomyelitis vaccines* are generally contra-indicated in pregnancy because of a theoretical risk to the fetus. Population-wide mass vaccination programmes become impossible, however, if pregnant mothers and women of child-bearing age are to be excluded.[1] In February 1985, mass vaccination with live oral poliomyelitis vaccine was started during a poliomyelitis outbreak in Finland.[1] Pregnant women were advised to take the vaccine. An analysis of all reported congenital malformations in the years 1982 to 1986 suggested that oral poliomyelitis vaccine had no harmful effects on fetal development as measured by overall prevalence of malformations or by the incidence of either CNS or orofacial defects. The results did not, however, exclude an effect measurable by other criteria of fetal development.

The incidence of spontaneous abortions was measured during a mass poliomyelitis vaccination campaign in Israel.[2] The number of spontaneous abortions did not differ between controls and women vaccinated during the first trimester of pregnancy; the percentage of spontaneous abortions in relation to live births was also similar. Microscopic examination of placentas from spontaneous abortions indicated no effect of oral poliomyelitis vaccine on the frequency or type of pathological changes. In addition, subsequent epidemiological study[3] found no increases in congenital malformations or in premature births during the period of and immediately following the vaccination campaign compared with those born before the campaign.

The Collaborative Perinatal Project (CPP) in the USA[4] followed up 50 897 pregnancies to examine risk factors for the development of malignancies in offspring born between 1959 and 1966. In 18 342 children whose mothers were vaccinated during pregnancy with *inactivated poliomyelitis vaccines*, there were 14 malignancies (7.6 per 10 000), while in 32 555 non-exposed children there were 10 malignancies (3.1 per 10 000). There were 7 tumours derived from neural tissue in the exposed children (3.8 per 10 000) and one in non-exposed children (0.3 per 10 000). Thus there was an excess of neural tumours but not of leukaemias or other malignancies in children exposed *in utero* to inactivated poliomyelitis vaccine. No malignancies occurred among the children born to 3056 women who received oral poliomyelitis vaccine. Serum samples collected from mothers on entry into the CPP and at delivery were subsequently analysed[5] for the presence of antibodies to Simian virus 40 (SV40). None of the serum samples from 8 mothers of infants with neural tumours had antibodies to SV40. Two of the 7 mothers of infants with leukaemia had SV40 antibodies, but only one had conversion during pregnancy. None of the samples from the 7 mothers of children with other types of cancer had antibodies. Three of 36 controls had antibodies, but in both the first and second samples. The association between administration of inactivated poliomyelitis vaccine to mothers and neural tumours in their offspring could not be attributed to contamination of vaccine with SV40. A later analysis[6] of 54 796 children enrolled in the CPP found an increased risk of neural tumours and of haematological malignancy in children whose mothers had received pre-1963 poliomyelitis vaccine, but concluded that this was unlikely to have been due to transmission of SV40.

1. Harjulehto T, *et al.* Congenital malformations and oral poliovirus vaccination during pregnancy. *Lancet* 1989; **i:** 771–2.
2. Ornoy A, *et al.* Spontaneous abortions following oral poliovirus vaccination in first trimester. *Lancet* 1990; **i:** 800.
3. Ornoy A, Ben Ishai P. Congenital anomalies after oral poliovirus vaccination during pregnancy. *Lancet* 1993; **341:** 1162.
4. Heinonen OP, *et al.* Immunization during pregnancy against poliomyelitis and influenza in relation to childhood malignancy. *Int J Epidemiol* 1973; **2:** 229–35.
5. Rosa FW, *et al.* Absence of antibody response to simian virus 40 after inoculation with killed-poliovirus vaccine of mothers of offspring with neurologic tumors. *N Engl J Med* 1988; **318:** 1469.
6. Engels EA, *et al.* Poliovirus vaccination during pregnancy, maternal seroconversion to simian virus 40, and risk of childhood cancer. *Am J Epidemiol* 2004; **160:** 306–16.

Interactions

As for vaccines in general, p.2202.

Normal immunoglobulins. Although the use of live vaccines and immunoglobulins at the same time is generally not recommended, normal immunoglobulin had no effect on the antibody response to oral poliomyelitis vaccine when the 2 preparations were given together to 50 subjects.[1]

1. Green MS, *et al.* Response to trivalent oral poliovirus vaccine with and without immune serum globulin in young adults in Israel in 1988. *J Infect Dis* 1990; **162:** 971–4.

Uses and Administration

Poliomyelitis vaccines are used for active immunisation against poliomyelitis. For discussion of immunisation schedules, see under Vaccines, p.2202. Both live (oral) poliomyelitis vaccines and inactivated poliomyelitis vaccines are available. The oral vaccine stimulates the formation of antibodies both in the blood and in the mucosal tissues of the gastrointestinal tract.

In the UK, an inactivated poliomyelitis vaccine containing the 3 types of poliovirus (trivalent) is recommended for the primary immunisation of all age groups, given as a course of 3 doses at intervals of 4 weeks. It is given intramuscularly as a combined diphtheria, tetanus, pertussis (acellular component), poliomyelitis (inactivated), and Haemophilus influenzae vaccine. For children who received primary immunisation during infancy, reinforcing doses are recommended at school entry (diphtheria, tetanus, pertussis, and poliomyelitis) and before leaving school (diphtheria, tetanus, and poliomyelitis). Further reinforcing doses are necessary only in adults exposed to infection including travellers to countries where poliomyelitis is epidemic or endemic and healthcare workers in contact with poliomyelitis cases. A single dose is given, repeated every 10 years if necessary.

In the USA, the recommended schedule consists of four doses of inactivated vaccine given at 2 months, 4 months, 6 to 18 months, and 4 to 6 years of age.

On the occurrence of a single case of paralytic poliomyelitis from wild virus, a single dose of the oral vaccine is recommended for all persons in the neighbourhood, regardless of whether they have previously been immunised. A primary course should be completed in previously unimmunised individuals.

Choice of vaccine. Two types of poliomyelitis vaccine are available: live attenuated oral poliomyelitis vaccine (OPV) and inactivated (killed) poliomyelitis vaccine (IPV) given by injection. Both vaccines are highly effective against all 3 types of poliovirus but there are advantages and disadvantages associated with their use.

The *advantages* of OPV are:

- it produces an immune response in both the blood and in the lining of the gut, thus preventing both spread of infection to the CNS and multiplication of the virus in the gastrointestinal tract and hence transmission via the stools and saliva
- it is given orally and is therefore easy to give without specialist training
- it is relatively inexpensive, an important consideration in developing countries in particular.

The *disadvantage* of OPV is:

- it causes very rare cases of vaccine-associated paralytic poliomyelitis (VAPP).

The *advantage* of IPV is:

- it is not a live vaccine and as such carries no risk of VAPP.

The *disadvantages* of IPV are:

- it confers very little immunity in the gastrointestinal tract, hence when an individual immunised with IPV is infected with wild poliovirus the virus can still multiply in the intestines and be shed in the stools, thus risking continued transmission
- trained health workers are required to give it by injection
- it costs far more than OPV.

Poliomyelitis has now been eradicated from most countries in the world (see below) and hence many, including the UK and the USA, consider it appropriate to use IPV exclusively for routine immunisation. However, the Global Polio Eradication Initiative will continue to use OPV where necessary until global eradication is achieved, at which time it has stated that the use of OPV should cease as soon as possible while population immunity against poliomyelitis and surveillance sensitivity for paralysis remain high, and be replaced by routine use of IPV.[1]

1. WHO. Framework for national policy makers in OPV-using countries: cessation of routine oral polio vaccine (OPV) use after global polio eradication. Geneva: WHO, 2005. Also available at: http://www.polioeradication.org/content/publications/OPVCessationFrameworkEnglish.pdf (accessed 12/10/05)

Eradication of infection. In 1988, WHO announced the goal of eradicating poliomyelitis by the year 2000. Other bodies joined the project which became known as the Global Polio Eradication Initiative.[1] Although the goal was not achieved in 2000, very considerable progress has been made. In 1988, wild poliovirus was endemic in 125 countries and more than 1000 children became paralysed every day. In 2005, only 4 countries still had endemic poliomyelitis. However, some countries are experiencing re-infection (11 by the end of August 2005) and in 2005, for the first time, case numbers were higher in these re-infected countries than in those where the disease is endemic. This illustrates the vulnerability of countries considered free of poliomyelitis when resultant low routine immunisation coverage puts children at risk. The global incidence of polio remained unchanged from 2005 to 2006.[2] A renewed goal was set of global polio eradication by the year 2008.

1. Global Polio Eradication Initiative. Information available at: http://www.polioeradication.org (accessed 25/04/06)
2. CDC. Progress towards interruption of wild poliovirus transmission—worldwide, January 2006–May 2007. *MMWR* 2007; **56:** 682–5. Also available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5627a3.htm (accessed 15/04/08)

Preparations

Ph. Eur.: Poliomyelitis Vaccine (Inactivated); Poliomyelitis Vaccine (Oral); ***USP 31:*** Poliovirus Vaccine Inactivated.

Proprietary Preparations (details are given in Part 3)
Arg.: Imovax Polio; Sabin; ***Austral.:*** Enpovax HDC†; Ipol; ***Belg.:*** Imovax Polio; Sabin†; ***Braz.:*** Imovax Polio†; IPV; Vacina Poliomielitica†; ***Cz.:*** Imovax Polio; IPV-Virelon; ***Fin.:*** Imovax Polio; ***Fr.:*** Imovax Polio; ***Ger.:*** IPV Merieux; IPV-Virelon; ***Gr.:*** Imovax Polio†; Poliorix; Vaccine Antipoliomyelitique/Merieux†; ***Hong Kong:*** Imovax Polio; ***Indon.:*** Imovax Polio; ***Israel:*** Imovax Polio; Polio Sabin; Polioral; ***Ital.:*** Imovax Polio; Polio Sabin†; Poliral†; Poliovax-IN; ***Malaysia:*** Polioral†; ***Mex.:*** Polio Sabin; Polioral; ***Norw.:*** Imovax Polio; ***NZ:*** Imovax Polio; Ipol; ***Philipp.:*** Polio Sabin; Polioral; Poliorix; ***Pol.:*** Imovax Polio; Polio Sabin; ***S.Afr.:*** OPV-Merieux; Polioral; ***Singapore:*** Imovax Polio†; ***Spain:*** Vac Antipolio Or†; Vac Polio Sabin; Vac Poliomielitica; ***Swed.:*** Imovax Polio; ***Switz.:*** Poliorix; ***Thai.:*** Polio Sabin; Polioral; ***Turk.:*** Buccapol; Polio Sabin; Poliorix; ***USA:*** Ipol; ***Venez.:*** Imovax Polio†; Vacuna Sabin†.

Pseudomonas Vaccines

Vacunas de pseudomonas.

Profile

A number of candidate *Pseudomonas aeruginosa* vaccines are under investigation for the prevention of pseudomonal infections in a variety of disease states.

◊ *Pseudomonas aeruginosa* is notably resistant to many antibacterials and there has consequently been considerable interest in developing an effective vaccine against it.[1-4] However, clinical results have tended to be disappointing, and together with improvements in antibacterial management have meant that no such vaccine is yet available for clinical use.

Early attempts in the 1960s at developing a vaccine focused on cell wall components (lipopolysaccharides). Multivalent lipopolysaccharide vaccines were tested in *animals* and in patients, including burns patients and patients with various forms of cancer and acute and chronic lung disease but, despite some positive results, these vaccines never gained clinical acceptance because of problems associated with the use of lipopolysaccharides. Vaccines designed at targeting the toxic exoproduct of *Ps. aeruginosa*, exotoxin A, produced mixed results at best; there has also been interest in exotoxin A toxoid in combination with other protective immunogens and in multicomponent and conjugate vaccines. There was brief interest in ribosomes and ribosomal RNA vaccines but these fell out of favour.

The discovery that motility was associated with *Ps. aeruginosa* virulence prompted research into the use of flagella as protective immunogens. The organism normally has two types of flagellum and a divalent vaccine has been tested, but with only modest benefit. There has also been some interest in development of vaccines against pili, bacterial appendages used for attachment.

Some investigators tried the use of high-molecular-weight polysaccharides as potential vaccine candidates but interest in this area has declined. Another defunct area of research is the use of pseudomonal alginate and mucoid exopolysaccharide; these were suggested for use in cystic fibrosis patients but did not progress beyond *animal* studies.

From the 1980s, there was considerable interest in the use of a variety of outer membrane proteins to develop a vaccine, partly because outer membrane proteins are exposed on the cell surface and at least one, protein F, is common to all serotypes. Encouraging results were obtained in *animal* models of infected burns and of chronic lung disease. Preliminary studies in healthy humans yielded large and sustained increases in antibody titres and found outer membrane proteins to be well tolerated. Multicomponent vaccines have been developed consisting of toxoids of known pseudomonal virulence factors such as proteases, elastases, and exotoxin A. Conjugate vaccines have been shown to be effective in *animal* models and to elicit a high antibody titre in cystic fibrosis patients.

In recent years, attention has also turned to the development of DNA vaccines, and to the use of some novel immunological approaches such as the use of pooled monoclonal antibodies directed against a variety of *Ps. aeruginosa* virulence antigens and of epitopes of pseudomonal elastase. In addition, research has shown that both active and passive immunisation with the purified type III translocation protein (PcrV) from *Ps. aeruginosa* is effective in *mouse* models of lung infection and burns, although results of combined active and passive immunisation in clinical studies were disappointing. Finally, there has been interest in obtaining immunological protection by presenting *Pseudomonas* antigens via mucous membranes, particularly in the gastrointestinal tract or intranasally.

1. Keogan MT, Johansen HK. Vaccines for preventing infection with Pseudomonas aeruginosa in people with cystic fibrosis. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 1999 (accessed 03/06/05).
2. Cachia PJ, Hodges RS. Synthetic peptide vaccine and antibody therapeutic development: prevention and treatment of Pseudomonas aeruginosa. *Biopolymers* 2003; **71:** 141–68.
3. Holder IA. Pseudomonas vaccination: a historical overview. *Vaccine* 2004; **22:** 831–9.
4. Döring G, Pier GB. Vaccines and immunotherapy against Pseudomonas aeruginosa. *Vaccine* 2008; **26:** 1011–24.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Psaeva†; ***Pol.:*** Pseudovac.

Q Fever Vaccines

Vacunas de la fiebre Q.

Profile

A Q fever vaccine consisting of a purified killed suspension of *Coxiella burnetii* is available in Australia. It is prepared from Phase I Henzerling strain of *C. burnetii* grown in the yolk sacs of embryonated eggs. A single 0.5-mL subcutaneous dose is given for active immunisation in individuals at high risk of Q fever. These include abattoir workers, veterinarians, farmers and others exposed to farm animals, and laboratory workers handling potentially infected tissue.

Before immunisation, patients should be tested for their serum antibody titre and a skin test performed; giving the vaccine to persons already sensitised to Q fever antigens may cause serious hypersensitivity reactions.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Q-Vax.

Rabies Antisera

Antisuero de la rabia.
ATC — J06AA06.

Profile

Rabies antisera have been used to provide passive immunisation against rabies but the use of rabies immunoglobulins (see below) is preferred.

Rabies Immunoglobulins

Inmunoglobulinas contra la rabia.
ATC — J06BB05.

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

Ph. Eur. 6.2 (Human Rabies Immunoglobulin; Immunoglobulinum Humanum Rabicum). A liquid or freeze-dried preparation containing human immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma from donors immunised against rabies and contains specific antibodies that neutralise the rabies virus. Normal immunoglobulin may be added. It contains not less than 150 international units/mL. The liquid preparation should be stored, protected from light, in a colourless, glass container. The freeze-dried preparation should be stored, protected from light, in a colourless, glass container, under vacuum or under an inert gas.

USP 31 (Rabies Immune Globulin). A sterile solution of globulins derived from plasma or serum from selected adult human donors who have been immunised with rabies vaccine and have developed high titres of rabies antibody. It contains 10 to 18% of protein of which not less than 80% is monomeric immunoglobulin G. It has a potency of 150 international units/mL. It contains glycine as a stabilising agent, and a suitable preservative. A solution diluted to contain 1% of protein has a pH of 6.4 to 7.2. It should be stored at 2° to 8°.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Uses and Administration

Rabies immunoglobulins are used for passive immunisation against rabies. They are combined with active immunisation by rabies vaccines (see below) in postexposure treatment for the prevention of rabies in previously unimmunised persons who have been bitten by rabid animals or animals suspected of being rabid. There are 2 types of immunoglobulin available: human rabies immunoglobulin (HRIG) and pepsin-digested or highly purified equine rabies immunoglobulin (ERIG). The recommended dose of HRIG is 20 international units/kg; for ERIG products it is 40 international units/kg. The recommended dose should be infiltrated in and around the cleansed wound; if infiltration of the whole volume is not possible, any remaining immunoglobulin should be given intramuscularly (in the anterolateral thigh and not the gluteal region) at a different site to that at which the vaccine was given.

Preparations

Ph. Eur.: Human Rabies Immunoglobulin;
USP 31: Rabies Immune Globulin.

Proprietary Preparations (details are given in Part 3)
Arg.: Imogam Rabia; ***Austral.:*** Imogam; ***Austria:*** Berirab; ***Canad.:*** BayRab†; Hyperrab; Imogam; ***Cz.:*** Favirab; Imogam Rabies†; ***Fr.:*** Imogam Rage; ***Ger.:*** Berirab; Tollwutglobulin; ***Hong Kong:*** BayRab; Rabumant†; ***India:*** Berirab-P; Carig; ***Indon.:*** Imogam; ***Israel:*** BayRab; Berirab; Imogam