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

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.