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