14: Immunological products and VACCINES

In this chapter, immunisation is discussed under the following headings:

14.1 Active immunity
14.2 Passive immunity
14.3 Storage and reconstitution of immunological products
14.4 Prevention and treatment of disease
14.5 Immunoglobulins
14.6 Vaccination programmes for children
14.7 International travel

14.1 Active immunity

Vaccines are designed to produce specific protection against a given disease. They may consist of

1. an attenuated form of an infective agent, as in the vaccines which are used against virus diseases such as rubella and measles, or BCG used against tuberculosis,
2. inactivated preparations of the virus or bacteria, as in influenza, pertussis (whooping-cough), or typhoid vaccines, or
3. extracts of or exotoxins produced by a micro-organism, as in tetanus vaccine.

Vaccines stimulate the production of protective antibody and other immune mechanisms. They are given by injection, with the exception of live attenuated poliomyelitis vaccine, which is given by mouth, and BCG vaccine which is given intracutaneously (intradermally).

In the case of vaccines consisting of living agents, immunisation is generally achieved with a single dose, but 3 doses are required in the case of oral poliomyelitis vaccine. Live virus multiplies in the body and usually produces a durable immunity but not always as long as that of the natural infection.

Inactivated vaccines usually require a primary series of doses of vaccine to produce an adequate antibody response and in most cases reinforcing or 'booster' injections are required. The duration of immunity following the use of inactivated vaccines varies from months to many years.

The health departments of the UK have issued a memorandum, *Immunisation against Infectious Disease* (1984) giving information on immune mechanisms, precautions, dosage intervals, storage, reconstitution, etc.

SIDE-EFFECTS. Some vaccines such as poliomyelitis vaccines produce virtually no reactions, while others, as in the case of measles vaccine, may produce a very mild form of the disease. Some of the inactivated vaccines may produce mild discomfort at the site of injection and mild fever and malaise. Occasionally there are more serious untoward reactions which should always be reported in the usual way to the Committee on Safety of Medicines.

CONTRA-INDICATIONS. Most vaccines may have some contra-indications to their use, and the manufacturer's leaflet accompanying the vaccine should always be consulted. In general, vaccines should not be given to individuals if they have a febrile illness or if any active infection is present or suspected.

Various viral vaccines contain small quantities of antibiotics used in their production, such as neomycin or polymixin or both. Vaccine may need to be withheld from individuals who are known to be sensitive to the antibiotic which it contains.

Live virus vaccines, especially rubella vaccine, should never be routinely offered to pregnant women because of possible harm to the fetus. They should not be given to individuals with impaired immune responsiveness, whether occurring naturally or as a result of radiotherapy or treatment with corticosteroids or other immunosuppressive drugs. They should not be given to those suffering from malignant conditions or other tumours of the reticulo-endothelial system. When two live virus vaccines are required they should be given either simultaneously at different sites or with an interval of at least 3 weeks.

14.2 Passive immunity

Defence or immediate protection against certain infective organisms can be obtained by injecting preparations made from the plasma of immune individuals with adequate levels of antibody to the disease for which protection is sought.

Antibodies of human origin are usually termed immunoglobulins. The term antiserum is applied to material prepared in animals. Because of the serum sickness reactions that may follow injections of antisera, this therapy has been replaced wherever possible by the use of immunoglobulins, as in the case of tetanus. Tetanus vaccine or tetanus vaccine, adsorbed should also be given to commence a course of active immunisation (section 14.4.14).

Diphtheria antitoxin prepared in horses is still used, and serum sickness is common after administration of this preparation. (Reactions are theoretically possible after injection of human immunoglobulins but must be extraordinarily uncommon.)

14.3 Storage and reconstitution of immunological products

Care must be taken to store all vaccines and other immunological products under the conditions recommended by the manufacturer in the literature accompanying the vaccine, otherwise the preparation may become denatured and totally ineffec-

tive. **Refrigerated storage** is usually necessary; many vaccines need to be stored at 2° to 8° and not allowed to freeze. Opened multidose vials which have not been fully used should be discarded within one hour if no preservative is present (most live virus vaccines) or within 3 hours or at the end of a session when vaccines containing a preservative are used; this category includes poliomyelitis vaccine (oral).

Particular attention must be paid to the instructions on the use of diluents where these are provided (usually with freeze-dried preparations of the vaccines), and ampoules of vaccine should always be adequately shaken before use to ensure uniformity of the material to be injected.

14.4 Prevention and treatment of disease

14.4.1 Anthrax
14.4.2 Cholera
14.4.3 Diphtheria
14.4.4 Hepatitis B
14.4.5 Influenza
14.4.6 Measles
14.4.7 Mumps
14.4.8 Pertussis (whooping-cough)
14.4.9 Pneumococcal pneumonia
14.4.10 Poliomyelitis
14.4.11 Rabies
14.4.12 Rubella
14.4.13 Smallpox
14.4.14 Tetanus
14.4.15 Tuberculosis
14.4.16 Typhoid
14.4.17 Typhus
14.4.18 Yellow fever

AVAILABILITY OF VACCINES AND OTHER IMMUNOLOGICAL PRODUCTS. Anthrax, rabies (human diploid cell), smallpox (freeze-dried), and yellow fever vaccines, botulinum antitoxin, and snake and scorpion venom antitoxins are available from local designated holding centres. *The Health Service Supply Purchasing Guide*, section D pp. 1101–1199 gives details of current arrangements with names, addresses, and telephone numbers of holding centres. **Poliomyelitis vaccine (inactivated)** is available on request to the Department of Health and Social Security, Room 421, 14 Russell Square, London WC1B 5EP, telephone 01-636 6811, extn 3117 3236. Most other vaccines and other immunological products are available commercially.

Enquiries for vaccines not available commercially should be made to the Department of Health and Social Security, address and telephone number above. In Scotland information about availability of vaccines can be obtained from the Chief Administrative Pharmaceutical Officer of the local Health Board. In Wales enquiries should be directed to the Welsh Office, Cathays Park, Cardiff, telephone 0222 825111, extn 4658 and in Northern Ireland to the Department of Health and Social Services, Dundonald House, Belfast, telephone 0232 63939.

14.4.1 Anthrax

An inactivated bacterial vaccine is available for anyone subject to heavy exposure to anthrax, such as those exposed to infected hides and carcasses and to imported bonemeal, fishmeal, and feeding stuffs. The vaccine is prepared from a culture of *Bacillus anthracis* and, following the primary course of injections, reinforcing doses should be given at about yearly intervals.

PoM **Anthrax Vaccine**

Dose: initial course 3 doses of 0.5 ml by intramuscular or deep subcutaneous injection at intervals of 3 weeks followed by a 4th dose after an interval of 6 months

Reinforcing doses: 0.5 ml annually

Availability—section 14.4

14.4.2 Cholera

Vaccines against cholera contain killed Inaba and Ogawa serotypes and may also contain the El Tor biotype that became prevalent in 1961. Although an international certificate of vaccination is still required for entry to some countries, it is now recognised that while cholera vaccine may provide some individual protection for about 6 months it cannot control the spread of the disease. Reinforcing injections are recommended every 6 months for those living in endemic areas.

Patients who travel in a country where cholera exists should be warned that attention to the hygiene of food and water is still essential, even after vaccination.

PoM **Cholera Vaccine** Cho/Vac. Price 1-ml amp = **D**; 1.5-ml amp = **E**; 10-ml vial = **E**, 50-ml vial = **J**

Dose: first dose, as specified on the label, usually 0.5 ml by deep subcutaneous or intramuscular injection; CHILD 1–5 years 0.1 ml; 6–10 years 0.3 ml; second dose after at least a week and preferably 4 weeks 1 ml (or 0.2 ml by intracutaneous injection); CHILD 1–5 years 0.3 ml, 6–10 years 0.5 ml (or 1–10 years 0.1 ml by intracutaneous injection)

14.4.3 Diphtheria

Protection against diphtheria is essentially due to the presence in the blood stream of antitoxin, the production of which is stimulated by toxoid vaccines prepared from the toxin of *Corynebacterium diphtheriae*. This toxoid is more effective if adsorbed onto a mineral carrier, and adsorbed diphtheria vaccines are generally used for the routine immunisation of babies and given in the form of a triple vaccine, Adsorbed Diphtheria, Tetanus, and Pertussis Vaccine. A dose of Poliomyelitis Vaccine, Live (Oral) is generally given at the time of each of the doses of the triple vaccine (see schedule, section 14.6). Adsorbed Diphtheria and Tetanus Vaccine is used in place of the

triple vaccine when it is decided not to immunise against whooping-cough.

A reinforcing dose of adsorbed diphtheria and tetanus vaccine is recommended at the age of school entry.

Further reinforcing doses of diphtheria vaccine are not recommended except in the case of those who work in units where there is a potentially high risk of infection such as those employed in infectious disease units, hospitals for the mentally handicapped, or microbiology laboratories. A special vaccine is available for this purpose. The small quantity of diphtheria toxoid present in the preparation is sufficient to recall immunity in individuals previously immunised against diphtheria but whose immunity may have diminished with time. It is insufficient to cause the reactions that may occur when diphtheria vaccine of conventional formulation is used in adults. Diphtheria vaccine for adults (adsorbed) may be given without prior Schick testing.

Mixed vaccines

PoM **Diphtheria and Tetanus Vaccine** DT/Vac/FT. A mixture of diphtheria formol toxoid and tetanus formol toxoid. Price 5-ml vial = **E**

Dose: reinforcing dose for children, 0.5 ml or as stated on the label by intramuscular or deep subcutaneous injection

PoM **Diphtheria and Tetanus Vaccine, Adsorbed** DT/Vac/Ads. Prepared from diphtheria formol toxoid and tetanus formol toxoid with a mineral carrier (aluminium hydroxide, aluminium phosphate, or calcium phosphate). Used for primary immunisation of children (see schedule, section 14.6) and reinforcing doses. Price 0.5-ml amp = **C**; 5-ml vial = **E**

Dose: 0.5 ml or as stated on the label by intramuscular or deep subcutaneous injection

PoM **Diphtheria, Tetanus, and Pertussis Vaccine** DTPer/Vac. A mixture of diphtheria formol toxoid, tetanus formol toxoid, and pertussis vaccine. Used for reinforcing doses in children. Price 0.5-ml amp = **C**; 5-ml vial = **E**

Dose: 0.5 ml or as stated on the label by intramuscular or deep subcutaneous injection

PoM **Diphtheria, Tetanus, and Pertussis Vaccine, Adsorbed** DTPer/Vac/Ads. Prepared from diphtheria formol toxoid, tetanus formol toxoid, and pertussis vaccine with a mineral carrier (aluminium hydroxide, aluminium phosphate, or calcium phosphate). Used for primary immunisation of children (see schedule, section 14.6). Price 0.5-ml amp = **C**

Dose: 0.5 ml or as stated on the label by intramuscular or deep subcutaneous injection

PoM **Trivax®** (Wellcome)

Diphtheria, tetanus, and pertussis vaccine. For primary vaccination of children (see schedule, section 14.6). Price 0.5-ml amp = **C**; 5-ml vial = **F**

Dose: 0.5 ml by intramuscular or deep subcutaneous injection

PoM **Trivax-AD®** (Wellcome)

Diphtheria, tetanus, and pertussis vaccine, adsorbed. For primary vaccination of children (see schedule, section 14.6). Price 0.5-ml amp = **C**; 5-ml vial = **F**

Dose: 0.5 ml by intramuscular or deep subcutaneous injection

Single vaccines

PoM **Diphtheria Vaccine, Adsorbed** Dip/Vac/Ads. Prepared from diphtheria formol toxoid with a mineral carrier (aluminium hydroxide, aluminium phosphate, or calcium phosphate). Used for primary immunisation of children who do not require immunisation against tetanus or whooping-cough; also in reduced dosage for Schick-positive adults and children over 10 years. Price 0.5-ml amp = **C**

Dose: the volume stated on the label by intramuscular or deep subcutaneous injection

Adult vaccine

PoM **Diphtheria Vaccine for Adults, Adsorbed.** Dip/Vac/Ads for Adults. For primary immunisation and reinforcement in patients over 10 years of age. Price 0.5-ml amp = **E**

Dose: primary immunisation, three doses each of 0.5 ml by intramuscular or deep subcutaneous injection separated by intervals of 1 month; reinforcement, 0.5 ml

Available from distributor (Regent)

Antisera

PoM **Diphtheria Antitoxin** Dip/Ser. For passive immunisation (after exposure) and treatment of diphtheria

Dose: prophylactic 500 to 2000 units by subcutaneous or intramuscular injection; therapeutic 10 000 to 30 000 units by intramuscular injection; *or* 40 000 to 100 000 units by intravenous injection in 2 divided doses with an interval of ½–2 hours

Available from distributor (Regent) or stocks may be held by hospital pharmacies

14.4.4 Hepatitis B

Hepatitis B vaccine is an alum adsorbed, inactivated hepatitis B virus surface antigen (HBsAg) vaccine prepared from the plasma of human carriers. The vaccine is used in individuals at high risk of contracting hepatitis B.

In the UK high-risk groups include health care personnel and patients in units where there is a high incidence of hepatitis B or a direct risk of contact with contaminated human blood, and also certain family contacts of carriers. Similar persons in indirect contact with a source of infection and at a lower risk would be considered a lower priority group. Another group for whom vaccination is recommended is infants born to hepatitis B carriers or HBsAg-positive mothers, particularly if they are e antigen-positive or are without anti-e antibody. Active immunisation combined with hepatitis B immunoglobulin is started immediately after delivery, but the precise details of dosage and optimal spacing of doses for active-passive immunisation have yet to be defined. More detailed guidance is given in DHSS circular

CMO(82)13/CNO(82)11. Vaccination does not eliminate the need for commonsense precautions for avoiding the risk of infection from known carriers by the routes of infection which have been clearly established. Accidental inoculation of hepatitis B virus-infected blood into a wound, incision, needle-prick, or abrasion may lead to infection, whereas it is unlikely that indirect exposure to a carrier will do so.

Specific hyperimmune immunoglobulin (HBIG) is available for those accidentally infected (section 14.5.2).

▼ PoM H-B-Vax® (Morson)

A suspension of hepatitis B surface antigen 20 micrograms/ml adsorbed onto alum. Price 1-ml vial = J

Dose: by intramuscular injection, 3 doses of 1 ml, the second 1 month and the third 6 months after the first dose; CHILD birth to 10 years 3 doses of 0.5 ml

14.4.5 Influenza

While most viruses are antigenically stable, the influenza viruses A and B (especially A) are constantly altering their antigenic structure as indicated by changes in the haemagglutinins (H) and neuraminidases (N) on the surface of the viruses. It is essential that influenza vaccines in use contain the H and N components of the prevalent strain or strains.

The recommended virus strains for vaccine production are grown in the allantoic cavity of developing chick embryos (and are therefore **contra-indicated** in those who are sensitive to eggs or feathers). The allantoic fluid is purified and the vaccines containing the haemagglutinin and neuraminidase of the strain expected to become prevalent are harvested. The World Health Organization makes recommendations every year as to what strains should be included in the vaccines and 3 strains are advised for the 1985–6 season; A/Philippines/2/82 (H_3N_2), A/Chile/1/83(H_1N_1), and B/USSR/100/83. If the H and N of the anticipated strain are different from that of recent strains it may be that 2 doses of vaccine will be required; on the other hand the value of annual immunisation with vaccine prepared from related strains is doubtful. Children under the age of 13 who are in high risk categories should receive 2 doses of influenza vaccine, inactivated (surface antigen) with an interval of 4–6 weeks.

Since the influenza vaccines will not control epidemics they are recommended only for those at high risk, particularly the elderly, those with chronic disease of the cardiovascular, respiratory, renal, and endocrine systems, and for those living in closed institutions where opportunites for contact and spread are great. In non-pandemic years immunisation is not recommended for Health Service staff, except for those at special risk.

Purified surface-antigen vaccines should be used in children aged 4–12 years; older children and adults may be vaccinated with surface-antigen or whole or split virus vaccine.

Drug interactions: see Appendix 1 (section 3).

PoM **Influenza Vaccine, Inactivated** Flu/Vac

Used for active immunisation against influenza (see notes above)

Dose: 0.5 ml by deep subcutaneous or intramuscular injection

PoM **Influenza Vaccine, Inactivated (Surface Antigen)** Flu/Vac/SA. Used for active immunisation against influenza (see notes above)

Dose: 0.5 ml by deep subcutaneous or intramuscular injection

PoM **Fluvirin®** (Evans)

Inactivated influenza vaccine, surface antigen (purified). Price 0.5-ml syringe = F; 5- and 25-ml vial (both) = J

Dose: 0.5 ml by deep subcutaneous or intramuscular injection

PoM **Influvac Sub-unit®** (Duphar)

Inactivated influenza vaccine, surface antigen. Price 0.5-ml amp or syringe = F; 5- and 25-ml vial (both) = J

Dose: 0.5 ml by deep subcutaneous or intramuscular injection

PoM **MFV-Ject®** (Servier)

Inactivated influenza vaccine (split virus vaccine). Price 0.5-ml syringe = F; 5- and 25-ml vial (both) = J

Dose: 0.5 ml by subcutaneous or intramuscular injection

14.4.6 Measles

Measles vaccine consists of a live attenuated strain of measles virus grown in chick-embryo fibroblast-tissue cultures (since it contains virtually no residual egg protein it is contra-indicated only in those known to suffer from severe hypersensitivity to egg protein with a history of the anaphylactoid type). It should be offered to all children in the second year of life and may be expected to produce a durable immunity.

Administration of this vaccine to children may be associated with a mild measles-like syndrome with a measles-like rash and pyrexia which come on about a week after the injection of the vaccine. Much less commonly, convulsions and, rarely, encephalitis have been reported as being associated with measles vaccines. Convulsions in babies are relatively common and may occur by chance following any immunisation procedure; they are certainly much less frequently associated with measles vaccine than with other conditions leading to febrile episodes.

Serious neurological complications following the vaccine are extremely rare, perhaps of the order of 1 in 87 000 vaccinees and probably about 12–20 times less common than such complications associated with natural infections of measles, but it is difficult to get exact figures because of variable criteria of what is diagnosed as a serious neurological condition. Subacute sclerosing panencephalitis follows natural measles infection at a rate of approximately 5 to 10 cases for every million children who have developed measles. This condition may be associated with live measles vaccine at a rate of 0.5–1.0 case per million doses of vaccine distributed, and so it appears that mea-

sles vaccination to some extent protects against subacute sclerosing panencephalitis.

Unfortunately, measles vaccine is taken up by only about 50% of those eligible. This is said to be due to the fact that some doctors and parents do not consider that measles is now a serious disease. It is possible that, when there is a partial coverage of the susceptible members of population with vaccine, wild measles virus does not spread so readily, which means that in vaccinated communities, many children will grow up susceptible and may be subject to an attack of measles as adolescents or adults when the disease may be more serious.

Measles vaccine may also be used in the control of outbreaks and should be offered to school and playstreet contacts within 3 days of exposure to infection.

Because of the generally poor uptake of this vaccine in the second year of life, it would seem wise to offer the vaccine also to children at entry to playgroup, nursery, or primary school. Again it would seem sensible to offer vaccine to any child entering secondary school who has not had either a natural infection or a previous dose of vaccine.

Children with a personal history of convulsions, or whose parents or siblings (first-degree relatives) have a history of idiopathic epilepsy should be given measles vaccine only with simultaneous administration of specially diluted normal immunoglobulin (obtainable from hospital pharmacies or the Blood Products Laboratory, Dagger Lane, Elstree, Herts, telephone 01-953 6191) supplied for use with measles vaccine.

Children with partially or totally impaired immune responsiveness should not receive live vaccines. See section 14.1 for further contra-indications. If they have been exposed to measles infection they should be given normal immunoglobulin (section 14.5.1).

PoM **Measles Vaccine, Live** Meas/Vac(Live). Freeze-dried stabilised aqueous suspension of an approved strain of live attenuated measles virus grown in culture of chick-embryo cells. Used for active immunisation against measles (see schedule, section 14.6)

▼ PoM **Attenuvax®** (Morson)
Measles vaccine, live, Enders' Edmonston strain. Price single-dose vial (with diluent) = D
Dose: 0.5 ml by subcutaneous injection

PoM **Mevilin-L®** (Evans)
Measles vaccine, live, Schwarz strain. Price single-dose vial (with diluent) = D
Dose: 0.5 ml by subcutaneous or intramuscular injection

PoM **Rimevax®** (SK&F)
Measles vaccine, live, Schwarz strain. Price single-dose vial (with diluent) = D
Dose: 0.5 ml by subcutaneous or intramuscular injection

14.4.7 Mumps

Mumps vaccine consists of a live attenuated strain of virus grown in chick-embryo tissue culture. Since mumps and its complications are very rarely serious there is little indication for the routine use of mumps vaccine. See section 14.1 for contra-indications.

PoM **Mumpsvax®** (Morson)
Mumps vaccine (Jeryl Lynn strain) Single-dose vial with syringe containing solvent. Price complete unit = F
Dose: adults and children over 1 year, 0.5 ml by subcutaneous injection

14.4.8 Pertussis (whooping-cough)

Pertussis vaccine is usually given combined with diphtheria and tetanus vaccine starting after the third month of life (see schedule, section 14.6) but may also be given as a simple vaccine.

Pertussis-containing vaccines may give rise to local reactions at the site of injection, mild pyrexia, and irritability. With some vaccines available in the early 1960s persistent screaming and collapse were reported but these reactions are rarely observed with the vaccines now available.

Convulsions and encephalopathy have been reported as rare complications, but such conditions may arise from other causes and be falsely attributed to the vaccine. A 3-year study of children aged 2 months–3 years who were admitted to hospitals in Great Britain suffering from serious neurological illness of the type likely to be attributed to whooping-cough vaccine has been carried out. Out of the first 1000 cases notified to the study, only 35 children had received pertussis vaccine within 7 days before becoming ill. Of these 35 children, 32 had no previous neurological abnormality and on follow-up of these children 1 year later, 2 had died and 9 had developmental retardation, while 21 were normal.

It is advisable to postpone vaccination if the child is suffering from any acute febrile illness, particularly if it is respiratory, until fully recovered. Minor infections without fever or systemic upset are not regarded as contra-indications. Vaccination should not be carried out in children who have

(1) a history of any severe local or general reaction, *including a neurological reaction*, to a preceding dose; or
(2) a history of cerebral irritation or damage in the neonatal period, or who have suffered from fits or convulsions.

There are certain groups of children in whom whooping-cough vaccination is not absolutely contra-indicated but who require special consideration as to its advisability. These groups are

(1) children whose parents or siblings have a history of idiopathic epilepsy;
(2) children with developmental delay thought to be due to a neurological defect; and
(3) children with neurological disease.

For these groups the risk of vaccination may be higher than in normal children but the effects of whooping-cough may be more severe, so that the benefits of vaccination would also be greater. The balance of risk and benefit should be assessed with special care in each individual case.

Allergy, according to a substantial body of medical opinion, is not a contra-indication to the administration of pertussis vaccine, but doctors should use their own discretion in the individual case.

PoM **Pertussis Vaccine** Per/Vac. A sterile suspension of killed *Bordetella pertussis*. Used for active immunisation against whooping-cough when simultaneous immunisation against diphtheria and tetanus is not required (see schedule, section 14.6). Price 0.5-ml amp = C
Dose: 0.5 ml or as specified on the label by intramuscular or deep subcutaneous injection

14.4.9 Pneumococcal pneumonia

A polyvalent pneumonia vaccine is available for the immunisation of persons for whom the risk of contracting pneumococcal pneumonia is unusually high, for example patients who have had a splenectomy. It is effective in a single dose if the types of pneumonia in the community are reflected in the polysaccharides contained in the vaccine. Studies with other pneumococcal vaccines suggest that protection may last for 5 years. Revaccination should not be carried out after less than 3 years or there may be a high level of frequent and severe local reactions. The vaccine should not be given to children under 2 years, in pregnancy, or when there is infection. It should be used with caution in cardiovascular or respiratory disease. Hypersensitivity reactions may occur.

PoM **Pneumovax®** (Morson)
For details, contact manufacturer

14.4.10 Poliomyelitis

There are two types of poliomyelitis vaccine, namely poliomyelitis vaccine, inactivated, and poliomyelitis vaccine, live (oral). The oral vaccine, consisting of a mixture of attenuated strains of virus types 1, 2, and 3 is at present generally used.

INITIAL COURSE. **Poliomyelitis vaccine, live (oral)** is given on 3 occasions, usually at the same time as routine immunisation against diphtheria, tetanus, and pertussis (see schedule, section 14.6).

REINFORCEMENT. A reinforcing dose of oral poliomyelitis vaccine is recommended at school entry at which time children should also receive a reinforcing dose of diphtheria and tetanus vaccine. Oral poliomyelitis vaccine is also recommended at school leaving at the same time as a dose of tetanus vaccine.

Unimmunised parents who are having their babies immunised should be offered vaccine at the same time because of a very small risk of infection of parents from vaccine virus which may have increased in neurovirulence following replication in the gut of their baby. Contact vaccine-associated poliomyelitis such as this is rare, and so is vaccine-associated poliomyelitis in those who actually received the vaccine. These adverse effects occur about once in one or more millions of vaccinated persons.

Contra-indications to the use of oral poliomyelitis vaccine include diarrhoea and hypogammaglobulinaemia. See section 14.1 for further contra-indications.

TRAVELLERS. Travellers to areas other than Australia, New Zealand, Northern Europe, and North America should be given a full course of oral poliomyelitis vaccine if they have not been immunised in the past. Those who have received immunisation should be given a single booster dose of oral poliomyelitis vaccine.

At the present time **poliomyelitis vaccine (inactivated)** may be used for those in whom poliomyelitis vaccine (oral) is contra-indicated because of pregnancy or immunosuppressive disorders.

PoM **Poliomyelitis Vaccine, Inactivated** Pol/Vac (Inact). An inactivated suspension of suitable strains of poliomyelitis virus, types 1, 2, and 3. Used for active immunisation when the oral vaccine is contra-indicated, as in pregnancy or immunosuppressive disorders.
Dose: 0.5 ml or as stated on the label by deep subcutaneous or intramuscular injection; for primary immunisation 3 doses are required (see schedule, section 14.6)
Availability—section 14.4

PoM **Poliomyelitis Vaccine, Live (Oral)** Pol/Vac (Oral). A suspension of suitable live attenuated strains of poliomyelitis virus, types 1, 2, and 3. Used for active immunisation. Available in single-dose and 10-dose containers
Dose: 3 drops or as stated on the label; for primary immunisation 3 doses are required (see schedule, section 14.6)
Available from District Health Authorities

14.4.11 Rabies

Since the time of Pasteur there have been a number of rabies vaccines in which the virus has been grown in nervous tissue of various animals. All of these vaccines have been associated with a greater or lesser degree of postvaccinal allergic encephalomyelitis. Other vaccines made from virus grown in animal tissue cultures or in embryonated duck eggs have tended to be of low antigenicity as measured by the levels of circulating antibodies achieved.

A human diploid cell vaccine has now been developed. This vaccine has been shown to be life saving in trials carried out in Iran in people who had been bitten by infected wolves. It should be offered prophylactically to those at high risk—those working in quarantine stations, animal handlers, veterinary surgeons, and field workers who may be exposed to bites of wild animals. A detailed list is given in Health Circular HC(77)29. For prophylactic use the vaccine produces a good antibody response when given in a 2-dose schedule with an interval of one month between doses and a reinforcing dose after an interval of 6–12 months with further reinforcing doses every 3 years when required.

For post-exposure treatment of previously unvaccinated patients a course of injections should be started as soon as possible after exposure (days 0, 3, 7, 14, 30, and 90). The course may be discontinued if it is proved that the patient was not at risk. There are no known contra-indications to this diploid cell vaccine and its use should be considered whenever a patient has been attacked by an animal in a country where rabies is endemic, even if there is no direct evidence of rabies in the attacking animal.

Staff in attendance on a patient who is highly suspected of, or known to be suffering from, rabies should be offered vaccination. Four intracutaneous doses of 0.1 ml of human diploid cell vaccine (Merieux) given on the same day at different sites has been suggested for this purpose in the *Memorandum on Rabies*.

Advice on the use of rabies vaccine for pre-exposure prophylaxis and on the use of vaccine and immunoglobulin (section 14.5.2) for post-exposure use is given in Department of Health and Social Security, *Memorandum on Rabies*, London, HMSO, 1977. Advice on post-exposure vaccination and treatment of rabies is available from the Duty Medical Officer, Central Public Health Laboratory, Colindale Avenue, Colindale, London NW9 5HT, telephone 01-200 4400.

PoM **Rabies Vaccine** Rab/Vac. An inactivated suspension of suitable strains of rabies virus grown in cell cultures

Available in accordance with Health Circular HC(77)29 from the Central Public Health Laboratory, London; Regional Public Health Laboratories in Birmingham, Cardiff, Leeds, Liverpool, and Newcastle; and the Area Public Health Laboratory, Exeter on a named-patient basis

▼ PoM **Merieux Inactivated Rabies Vaccine®** (Servier)

Freeze-dried human diploid cell rabies vaccine prepared from Wistar strain PM/WI 38 1503-3M. For prevention and treatment of rabies. Price single-dose vial with syringe containing diluent = J

Dose: prophylactic, 1 ml by deep subcutaneous injection, followed by a second dose after 1 month and a third after 6–12 months; also further reinforcing doses every 3 years depending on the risk of infection

Therapeutic, 1 ml on the first, third, seventh and fourteenth day and after 1 and 3 months

14.4.12 Rubella

The introduction of a vaccine to protect a fetus as yet not conceived was a totally new idea. Rubella (German measles) as a childhood disease is of little moment, but rubella infection in the pregnant woman greatly increases the risk of congenital malformations in the fetus which is more severe the earlier in pregnancy the infection occurs.

Rubella vaccines are prepared in tissue-culture cells of rabbit kidney or duck embryo, or human diploid cell lines. **Contra-indications** with regard to sensitivities or antibiotics vary from one vaccine to another and as always the literature accompanying the package should be consulted. But the main contra-indication at present applying to all of the available vaccines is pregnancy. See section 14.1 for further contra-indications.

Rubella vaccine is recommended for prepubertal girls aged 10 to 13 years and for women of childbearing age (see schedule, section 14.6) as well as those who might put pregnant women at risk of infection (for example nurses and doctors in obstetric units). It is recommended practice to offer vaccine to those women who are found to be seronegative to rubella virus.

The important point is that women offered vaccine should **not** become pregnant for 3 months after immunisation. If this cannot be assured then vaccine should at present be withheld. At the same time more and more evidence is accumulating which suggests that rubella vaccine virus may present less risk to the fetus than was originally thought compared with the serious risk of wild rubella virus in pregnant women. For short-term interim contraception at the time of vaccination medroxyprogesterone acetate (section 7.3.2) may be suitable.

In addition to offering vaccine to schoolgirls and those at special risk, vaccine is also being offered to previously unvaccinated and seronegative post-partum women. Again they must avoid pregnancy for 3 months. Immunising susceptible post-partum women a few days after delivery is important as far as the overall reduction of congenital abnormalities in the UK is concerned, for about 60% of these abnormalities occur in the babies of multiparous women.

In the long term it is hoped that the routine immunisation of schoolgirls will produce an immune adult female population but in order to prevent congenital abnormalities due to rubella it may require 100% acceptance of vaccine and this has rarely been achieved with other vaccines. Acceptance amongst schoolgirls might be greater if the effort was concentrated among 10-year-olds, but even so, with a high acceptance rate the efficacy of this programme will not be evident until the end of the century. At the same time the damage which is done by wild rubella virus must be kept in perspective, for it is responsible for perhaps only about 1% of all congenital abnormalities.

Susceptible pregnant women who are exposed to rubella and who refuse therapeutic abortion may be offered normal immunoglobulin injection (section 14.5.1).

PoM **Rubella Vaccine, Live** Rub/Vac (Live). A freeze-dried suspension of a suitable live attenuated strain of rubella virus grown in suitable cell cultures. Used for active immunisation against rubella (see schedule, section 14.6 and notes above). Price 0.5-ml amp = E; 5-ml vial = J

Dose: 0.5 ml by subcutaneous injection. Not to be given to any woman who may be pregnant. Advise women not to become pregnant within 3 months of vaccination

C = 51-100p, D = 101-180p, E = 181-300p, F = 301-450p, G = 451-650p, H = 651-900p, I = 901-1200p, J = over 1200p.

PoM **Almevax®** (Wellcome)
Rubella vaccine, live, prepared from Wistar RA 27/3 strain propagated in human diploid cells. Price single-dose amp with diluent = **E**; 10-dose vial with diluent = **J**

PoM **Cendevax®** (SK&F)
Rubella vaccine, live, prepared from Cendehill strain propagated in primary rabbit kidney cells. Price single-dose vial with diluent = **E**; 10-dose vial with diluent = **J**

▼ PoM **Meruvax II®** (Morson)
Rubella vaccine, live, prepared from Wistar RA27/3 strain propagated in human diploid cells. Price single-dose vial with diluent = **D**

14.4.13 Smallpox

Smallpox vaccination is no longer required routinely in the UK and other countries because global eradication of smallpox has now been achieved. The vaccine is offered to a small number of doctors and other health workers who may be called upon to deal with suspected cases of smallpox. Otherwise the only requirement for smallpox vaccination is for a few workers in institutions dealing with pox viruses. Contra-indications to elective smallpox vaccine are pregnancy, babies under 1 year, any illness at the time of vaccination, eczema in the vaccinees or in members of their households; the vaccine is also contra-indicated in patients with impaired immune responsiveness, whether occurring naturally or as a result of radiotherapy or treatment with corticosteroids or other immunosuppressive drugs. See section 14.1 for further contra-indications.

PoM **Smallpox Vaccine** Var/Vac. Consists of a suspension of live vaccinia virus grown in the skin of living animals, supplied in freeze-dried form with diluent
Dose: 0.05 ml by multiple pressure inoculation or through a single linear scratch not more than 2–3 mm long

Available from Regional Public Health Laboratories in Birmingham, Bristol, Cambridge, Cardiff, Leeds, Liverpool, Manchester, Newcastle, Oxford, and Sheffield; and the Area Public Health Laboratory at Whipps Cross Hospital, London

14.4.14 Tetanus

Tetanus vaccine stimulates the production of the protective antitoxin. It is offered routinely to babies in combination with diphtheria vaccine (DT/Vac/Ads) and more usually also combined with killed *Bordetella pertussis* organisms as Diphtheria, Tetanus, and Pertussis Vaccine (DT Per/Vac) or as an adsorbed vaccine (DT Per/Vac/Ads), see schedule, section 14.6. In general, adsorption on aluminium hydroxide, aluminium phosphate, or calcium phosphate improves the antigenicity of diphtheria and tetanus toxoids. The combined vaccines are described under Diphtheria (section 14.4.3).

Of the monovalent tetanus vaccines the adsorbed tetanus vaccine is to be preferred to the plain vaccine. Adsorbed vaccine may be given in reduced dosage to patients who have previously reacted abnormally to the vaccine but only when they are considered to be at high risk. Adsorbed vaccine must not be given intracutaneously.

In children, the triple vaccine or a course of adsorbed diphtheria and tetanus vaccine not only gives protection against tetanus in childhood but also gives the basic immunity for subsequent reinforcing doses of tetanus vaccine at school entry and at school leaving and also when a potentially tetanus-contaminated injury has been received. Normally, tetanus vaccine should not be given unless more than 5 years have elapsed since the last reinforcing dose of tetanus toxoid because of the possibility that hypersensitivity reactions may develop.

Active immunisation is important for persons in older age groups for they may never have had the routine courses of immunisation when younger. In these persons a course of tetanus vaccine (adsorbed) may be given.

For serious, potentially contaminated wounds antitetanus immunoglobulin injection (section 14.5.2) should be selectively used in addition to wound toilet, adsorbed tetanus vaccine, and benzylpenicillin or another anaerobicidal antibiotic.

PoM **Tetanus Vaccine** Tet/Vac/FT. Tetanus formol toxoid. Used for active immunisation against tetanus (see notes). Price 0.5-ml amp = **C**; 5-ml vial = **E**
Dose: 0.5 ml or as stated on the label, by intramuscular or deep subcutaneous injection followed after 6–12 weeks by a second dose and after a further 4–12 months by a third

PoM **Tetanus Vaccine, Adsorbed** Tet/Vac/Ads. Prepared from tetanus formol toxoid with a mineral carrier (aluminium hydroxide, aluminium phosphate, or calcium phosphate). Price 0.5-ml amp = **B**; 5-ml vial = **E**
Dose: as for Tetanus Vaccine

PoM **Merieux Tetavax®** (Servier)
Tetanus formol toxoid adsorbed onto aluminium hydroxide. Price 0.5-ml amp = **B**; 0.5-ml single-dose syringe = **C**; 5-ml vial = **E**
Dose: 0.5 ml by deep subcutaneous or intramuscular injection followed after 6–8 weeks by a second dose and after a further 4–6 months by a third

14.4.15 Tuberculosis

BCG (Bacillus Calmette-Guérin) is a live attenuated strain derived from bovine *Mycobacterium tuberculosis* which stimulates the development of hypersensitivity to *M. tuberculosis*. Vaccine is given by intracutaneous injection or the percutaneous vaccine may be given by multiple puncture. 0.1 ml of the vaccine (reconstituted immediately before use) is injected intracutaneously just above the insertion of the deltoid muscle raising a wheal of about 8 mm in diameter. If it is injected too high, too far forward, or too far backward, the adjacent lymph glands may become involved

and tender. After about 1 week a small swelling appears at the injection site which progresses to a papule or to a benign ulcer about 10 mm in diameter after 3 weeks and heals in 6–12 weeks. No dressing should be used unless there is much discharge from the ulcer.

Normally, BCG is offered routinely to tuberculin-negative children of 10–13 years. BCG vaccination should also be strongly recommended to those living in crowded conditions in urban communities and to all immigrants and their children from countries with a high incidence of tuberculosis. They should be tuberculin tested before vaccination with the exception of newborn babies who should be vaccinated without delay. With babies great care must be taken to ensure that the inoculation is given intracutaneously in a dose of 0.05 ml: if BCG is accidentally given subcutaneously to babies it may give rise to a troublesome persistent local reaction. See section 14.1 for contra-indications.

PoM **Bacillus Calmette-Guérin Vaccine.** BCG Vaccine. Dried Tub/Vac/BCG. A freeze-dried preparation of live bacteria of a strain derived from the bacillus of Calmette and Guérin. Used for active immunisation

Dose: 0.1 ml (infants under 3 months 0.05 ml) by intracutaneous injection

Available from District Health Authorities

PoM **Bacillus Calmette-Guérin Vaccine, Percutaneous** Tub/Vac/BCG(Perc). A preparation of live bacteria of a strain derived from the bacillus of Calmette and Guérin. Used for active immunisation (see notes) and administered by the percutaneous route by multiple puncture with a suitable instrument. **Not** for intracutaneous (intradermal) injection.

Dose: 0.02 ml by percutaneous administration

Available on direct application from the manufacturer (Glaxo)

DIAGNOSTIC REAGENTS. In the *Mantoux test* the initial dose is 1 unit of tuberculin PPD in 0.1 ml by intracutaneous injection and in subsequent tests 10 and finally 100 units in 0.1 ml are given. In the *Heaf test* (multiple puncture) a solution containing 100 000 units in 1 ml is used. For the *Tine*, *Imotest*, and other similar tests a special device impregnated with tuberculin is used.

PoM **Tuberculin PPD.** Prepared from the heat-treated products of growth and lysis of the appropriate species of mycobacterium, and containing 100 000 units/ml. Price 1-ml vial = **E**; 5-ml vial = **I**. Also available diluted 1 in 100 (1000 units/ml), 1 in 1000 (100 units/ml), and 1 in 10 000 (10 units/ml). Price 1 ml (all) = **C**

Dose: see notes above

Available from District Health Authorities

14.4.16 Typhoid

Typhoid vaccination is no substitute for personal precautions in avoiding typhoid fever in countries where the disease is endemic; green salads and uncooked vegetables should be avoided and only fruits which can be skinned should be eaten. Only suitable bottled water or water treated with sterilising tablets should be used for drinking purposes.

Typhoid vaccine (monovalent typhoid vaccine) is used and because it contains no paratyphoid components it is less likely to produce the local and systemic reactions which have, in the past, been so commonly associated with TAB. These local reactions which consist of swelling, pain, and tenderness appear about 2–3 hours after the subcutaneous or intramuscular injection of the vaccine. Systemic reactions which consist of fever, malaise, and headache may also occur and usually last for about 48 hours after injection. If severe reactions are experienced after the first dose intracutaneous injection may be preferred for the second dose, as these reactions are virtually absent when this route is used. Normally, 2 doses should be given at 4–6 weeks interval for primary immunisation, with reinforcing doses about every 2 or 3 years on continued exposure.

PoM **Typhoid Vaccine** Typhoid/Vac. A suspension of killed *Salmonella typhi* organisms. Used for active immunisation against typhoid. Price 1.5-ml vial = **E**

Dose: 0.5 ml by deep subcutaneous or intramuscular injection; CHILD 1–10 years 0.25 ml Second dose after 4–6 weeks, 0.5 ml (or 0.1 ml by intracutaneous injection); CHILD 1–10 years 0.25 ml (or 0.1 ml by intracutaneous injection)

14.4.17 Typhus

The vaccine consists of formalin-inactivated *Rickettsia prowazekii* grown in the yolk sac of embryonated hens' eggs and is effective against louse-borne typhus. This vaccine is not necessary for travellers visiting countries where the disease is endemic if they will be staying in urban accommodation but it could be of value for those living in close personal contact with the indigenous population of such areas. However the vaccine is no longer distributed in the United Kingdom but may be obtained on a named patient basis from the Commonwealth Serum Laboratories, Parkville 3052, Victoria, Australia.

14.4.18 Yellow Fever

Yellow fever vaccine consists of a live attenuated yellow fever virus (17D strain) grown in developing chick embryos. It is available only at designated centres, but should not be given to children under 9 months of age since it may cause them to develop encephalitis. Vaccine should not be given to individuals who are pregnant, have impaired immune responsiveness, or who are sensitive to eggs. See section 14.1 for further contra-indications. Reactions are few. The immunity which probably lasts for life is officially accepted for 10 years starting from 10 days after primary vaccination and for a further 10 years immediately after revaccination.

PoM **Yellow Fever Vaccine, Live** Yel/Vac. A suspension of chick embryo proteins containing attenuated 17D strain virus. Used for active immunisation against yellow fever

Dose: the volume indicated on the label by subcutaneous injection

Available from designated Yellow Fever Vaccination centres only

PoM **Arilvax®** (Wellcome)

Freeze-dried yellow fever vaccine, live. 1-, 5-, and 10-dose vials (with diluent)

14.5 Immunoglobulins

The injection of immunoglobulins produces immediate protection. Normally, when foreign immunoglobulins are injected, antibodies develop and this presents problems of hypersensitivity; these properties of horse and other animal sera have led to virtual abandonment of animal immunoglobulins for passive protection and human immunoglobulins have taken their place.

There are essentially two types of human immunoglobulin preparation: human **normal immunoglobulin** (HNIG, gamma globulin) prepared from the plasma of at least 1000 donors, and **specific immunoglobulins** for tetanus, rabies, vaccinia, etc. which are prepared by pooling the blood of convalescent patients or of immunised donors who have recently been specifically boosted.

Normal immunoglobulin and the specific immunoglobulins are available from the Public Health Laboratory Service laboratories and Regional Blood Transfusion Centres in England and Wales with the exception of antitetanus immunoglobulin which is distributed through Regional Blood Transfusion Centres to hospital pharmacies or blood transfusion departments and is also available to general medical practitioners, and antirabies immunoglobulin which is available from the Central Public Health Laboratory, London (section 14.4.11).

In Scotland all immunoglobulins are available from Blood Transfusion Centres. Antitetanus immunoglobulin is distributed by Blood Transfusion Centres to hospitals and general medical practitioners on demand. Normal immunoglobulin injection and antitetanus immunoglobulin injection are also available commercially.

14.5.1 Normal immunoglobulin

HEPATITIS A (infective hepatitis). At the time of writing there are no suitable techniques available for growing hepatitis A virus in quantities which would make vaccine preparation possible. Control depends on good hygiene and many studies have also shown the value of normal immunoglobulin in the prevention and control of outbreaks of this disease. It is recommended for controlling infection in contacts in closed institutions and also, under certain conditions, in school and home contacts and for travellers going to areas where the disease is highly endemic. The usual prophylactic dose by intramuscular injection for adults and children is 0.02–0.04 ml/kg. This usually gives immunological protection for 3 months; for greater than 3 months periods of exposure or in areas of high endemicity, the dose is 0.06–0.12 ml/kg, repeated every 4–6 months on continued exposure.

MEASLES. Normal immunoglobulin may be used to modify or prevent measles in the few babies in whom an attack of measles must be avoided and in children in whom live measles vaccine is contraindicated; specially diluted normal immunoglobulin should be used to moderate the reactions to measles vaccine in children with a personal history of convulsions, or whose parents or siblings (first-degree relatives) have a history of idiopathic epilepsy (section 14.4.6).

RUBELLA. Normal immunoglobulin may lessen the likelihood of infection and fetal damage in pregnant women exposed to rubella for whom therapeutic abortion is unacceptable. The usual dose is 20 ml. It is not recommended for routine prophylaxis; see section 14.4.12.

PoM **Normal Immunoglobulin Injection** (HNIG). Immunoglobulin prepared from pools of at least 1000 donations of human plasma, available in liquid form or as a freeze-dried preparation for reconstitution. It is administered by intramuscular injection. Used for the protection of susceptible contacts against hepatitis A virus (infectious hepatitis), measles and, to a lesser extent, rubella. Special forms for intravenous administration are available for replacement therapy for patients with congenital agammaglobulinaemia and hypogammaglobulinaemia who are not able to tolerate repeated intramuscular injections. Live virus vaccine should not be given until 3 months after a dose of normal immunoglobulin injection. If a live virus vaccine has been given normal immunoglobulin injection should not be given for at least 2 weeks, except in special circumstances, e.g. the concomitant administration of measles vaccine with a specially diluted normal immunoglobulin is recommended for children with personal history of convulsions, or whose parents or siblings (first-degree relatives) have a history of idiopathic epilepsy (section 14.4.6). Rubella vaccine may be administered in the postpartum period with anti-D (Rh_0) immunoglobulin injection

PoM **Gammabulin®** (Immuno)

Normal immunoglobulin injection. Price 2-ml vial = **E**; 5-ml vial = **G**; 10-ml vial = **I**; 320-mg vial with 2 ml water for injections = **F**

▼ PoM **Intraglobin®** (Biotest Folex)

Normal immunoglobulin injection. Powder for reconstitution. Price 250 mg = **G**; 500 mg = **I**; 2.5 g = **J** (all with solvent)

PoM **Kabiglobulin** (KabiVitrum)

Normal immunoglobulin injection. Price 2-ml amp = **F**; 5-ml amp = **H**

▼ PoM **Sandoglobulin®** (Sandoz)

Normal immunoglobulin injection. Price 3- and

6-g bottle with 100- and 200-ml bottle, respectively, sodium chloride intravenous infusion 0.9% (both) = J. Transfer needle and giving set with each pack

14.5.2 Specific immunoglobulins

HEPATITIS B. A vaccine is now available for those at high risk of infection (section 14.4.4) but specific antihepatitis B virus immunoglobulin (HBIG) may be available for the prevention of infection in laboratory and other personnel who have accidentally become contaminated with hepatitis B virus and for pregnant women and babies born to mothers who have become infected with this virus in pregnancy.

RABIES. Following exposure to a suspected rabid animal, specific antirabies immunoglobulin, if possible of human origin, should be injected at the site of the bite and also given intramuscularly. Rabies vaccine (section 14.4.11) should also be given.

PoM **Antirabies Immunoglobulin Injection.** Used for protection of persons who have been bitten by rabid animals or otherwise exposed to infection
Dose: 20 units/kg by intramuscular injection and infiltration around wounds

TETANUS. Antitetanus immunoglobulin of human origin (HTIG) should be selectively used in addition to wound toilet, vaccine, and benzylpenicillin (or another anaerobicidal antibiotic) for the more seriously contaminated wounds but is rarely required for those who have an established immunity in whom protection may be achieved by a reinforcing dose of vaccine. The administration of antitetanus immunoglobulin should be considered for patients not known to have received active immunisation (a) whose wound was sustained more than 6 hours before treatment was received and (b) with puncture wounds or wounds potentially heavily contaminated with tetanus spores, septic, or with much devitalised tissue. A dose of adsorbed tetanus vaccine should be given at the same time as the antitetanus immunoglobulin and the course of vaccine (section 14.4.14) subsequently completed.

PoM **Antitetanus Immunoglobulin Injection** (HTIG). Used for the protection of unimmunised persons when there is a specific risk of tetanus
Dose: by intramuscular injection, prophylactic 250 units, therapeutic 30–300 units/kg
PoM **Humotet®** (Wellcome)
Antitetanus immunoglobulin injection 250 units/ml. Price 1-ml vial = J

VACCINIA. Antivaccinia immunoglobulin is available for the prevention and treatment of the complications of smallpox vaccination, as when vaccination is necessary in an individual for whom there are contra-indications to vaccination. It is also used in familial and other close contacts exposed to smallpox.

PoM **Antivaccinia Immunoglobulin Injection.** Used to treat patients with generalised vaccinia or with localised vaccinial infection that endangers the eye
Dose: by intramuscular injection, 1.5–2 g; CHILD under 1 year 500 mg, 1–6 years 1 g, and 7–14 years 1.5 g

OTHER SPECIFIC IMMUNOGLOBULINS. These include antivaricella/zoster immunoglobulin, antiherpes simplex immunoglobulin and are in limited supply. Others are under study, but their availability and evaluation requires the cooperation of general practitioners to provide blood from patients who are convalescent from these and other specific viral infections in order to prepare specific immunoglobulin preparations.

14.5.3 Anti-D (Rh_0) immunoglobulin

Anti-D immunoglobulin is available to prevent a rhesus-negative mother from forming antibodies to fetal rhesus-positive cells which may pass into the maternal circulation during childbirth or abortion. It must be injected within 72 hours of the birth or abortion. The objective is to protect any further child from the hazard of haemolytic disease.

PoM **Anti-D (Rh_0) Immunoglobulin Injection.** See notes above
Dose: for rhesus-negative women, 250–500 units by intramuscular injection following the birth of a rhesus-positive infant; after transfusion, up to 5000 units

14.6 Vaccination programmes for children

A schedule promulgated by the Department of Health and Social Security proposes that the course of adsorbed diphtheria, tetanus and pertussis vaccine, together with poliomyelitis vaccine (oral) should commence at 3 months. The schedule CMO(78)15—in Scotland SHHD/CAMO(78)18, on vaccination and immunisation procedures is set out in the Table. The principal points are as follows:

1. The basic course of triple vaccine, or diphtheria and tetanus vaccine, together with oral poliomyelitis vaccine should commence at the age of 3 months. The intervals between the 3 doses of the basic course should remain the same as those previously recommended, that is 6–8 weeks between the first and second doses and 4–6 months between the second and third doses.
2. An alternative basic course which completes the protection against pertussis at an earlier age is described but for use only in the event of a whooping-cough epidemic. If this alternative is followed a booster dose of diphtheria

Table: Schedule of vaccination and immunisation procedures (children and adults)

Age	Vaccine	Interval	Notes
During the first year of life	DTPer/Vac/Ads *and* Pol/Vac (Oral) (1st dose)		The first doses should be given at 3 months of age. If pertussis vaccine is contra-indicated or the parents decline, DT/Vac/Ads should be given
	DTPer/Vac/Ads *and* Pol/Vac (Oral) (2nd dose)	Preferably after an interval of 6–8 weeks	
	DTPer/Vac/Ads *and* Pol/Vac (Oral) (3rd dose)	Preferably after an interval of 4–6 months	
During the second year of life	Meas/Vac (Live)		
At school entry or entry to nursery school	DT/Vac/Ads *and* Pol/Vac (Oral)	Preferable to allow an interval of at least 3 years after completing basic course	
Between 10 and 13 years of age	Tub/Vac/BCG	Leave an interval of not less than 3 weeks between BCG and rubella vaccination	For tuberculin-negative children. For tuberculin-negative contacts at any age
Between 10 and 13 years of age (girls only)	Rub/Vac (Live)		All girls of this age should be offered rubella vaccine, regardless of a past history of an attack of rubella
On leaving school or before employment or entering further education	Pol/Vac (Oral) *or* Pol/Vac (Inact); *and* Tet/Vac/Ads		
Adult life	Pol/Vac (Oral) *or* Pol/Vac (Inact) for previously unvaccinated adults	3 doses with an interval of 6–8 weeks between the first and second doses and of 4–6 months between the second and third	For travellers to countries where polio is endemic. Unvaccinated parents of a child being given oral vaccine should also be offered a course of Pol/Vac (Oral)
	Rub/Vac (Live) for susceptible women of child-bearing age		Adult females of child-bearing age should be tested for rubella antibodies and those sero-negative offered rubella vaccination. Pregnancy must first be excluded and the patient warned not to become pregnant for 3 months after immunisation
	Active immunisation against tetanus (Tet/Vac/Ads) for previously unvaccinated adults	For previously unvaccinated adults: 2 doses at an interval of 6–8 weeks followed by a third dose 6 months later	

and tetanus vaccine is necessary at 12–18 months of age to achieve a satisfactory level of immunity to these diseases.

3. It is recommended that a vaccine containing a pertussis component should not normally be offered after the age of 6 years.

Recently, some parents, who had chosen not to include a pertussis component in the basic immunisation of their infants, have changed their minds because of the greater prevalence of whooping-cough. The Joint Committee on Vaccination and Immunisation has advised that 3 doses of pertussis vaccine can be given at monthly intervals to provide protection in these cases. Where the basic course against diphtheria and tetanus is incomplete triple vaccine may be used to begin or complete the course against whooping-cough so that the infant is not given more injections than necessary.

Poliomyelitis vaccine, live (oral) is usually issued in 10-dose containers (although single-dose

containers are also available). The vaccine should be stored unopened at 4° but once the containers are opened the vaccine may lose its potency however it is stored. For this reason any vaccine remaining in the containers at the end of an immunisation session should be discarded. There is particular need to conserve supplies of vaccines, which in any case are expensive. As far as possible immunisation sessions should therefore be arranged to avoid undue wastage of vaccines, although it is recognised that it will not always be possible to muster those to be vaccinated in groups of 10. The practicability of dispensing vaccines in smaller doses is being considered.

14.7 International travel

No particular immunisation is required for travellers to the United States, Northern Europe, Australia, or New Zealand. In Southern Europe and particularly in those areas surrounding the Mediterranean, in Africa, the Middle East, Asia, and South America, certain special precautions are required. Mention is made of the personal precautions which should be taken in the prevention of **typhoid** (section 14.4.16); these also apply to **cholera** (section 14.4.2) and other diarrhoeal diseases (including travellers' diarrhoea). Immunisation against typhoid is indicated for travellers to those countries where typhoid is endemic, and it would seem that the monovalent typhoid vaccine is acceptable, although it has not been subjected to detailed double-blind trials. Long-term travellers to areas that have a high incidence of **poliomyelitis** (section 14.4.10) or **tuberculosis** (section 14.4.15) should be immunised with the appropriate vaccine; in the case of poliomyelitis previously vaccinated adults may be given a reinforcing dose of oral poliomyelitis vaccine. Overland travellers to Asia and Africa and others at high risk may be given **normal immunoglobulin injection** (section 14.5.1) for protection against hepatitis A.

Cholera vaccine is no substitute for personal hygiene but has some protective value for about 6 months in preventing individual infections. It is required for travellers by some countries and must be certified on an International Certificate. Stamped certificates supplied to general medical practitioners by Family Practitioner Committees (in Scotland by Health Boards) do not require to be authenticated by health authorities.

International Certificates of vaccination against **yellow fever** (section 14.4.18) are still required for travel to much of Africa and South America. The Health Departments of the UK have issued a leaflet, *Protect your health abroad* (SA 35), which can be obtained from travel agents, from local authorities, or DHSS Leaflets Unit, PO Box 21, Stanmore, Middx HA7 1AY; it gives information on vaccination centres, etc. for overseas travellers.

Vaccination requirements change from time to time, and information on the current requirements for any particular country may be obtained from the Department of Health and Social Security, Fleming House, London SE1 6BY, telephone 01-407 5522; Scottish Home and Health Department, St. Andrew's House, Edinburgh EH1 3DE, telephone 031 5568501; Welsh Office, Cathays Park, Cardiff, telephone Cardiff 825111; Department of Health and Social Services, Dundonald House, Upper Newtownards Road, Belfast, telephone 0232 63939; or from the embassy or legation of the appropriate country.