source of infection. In contrast to food-borne botulism, in infant botulism low doses of toxin continue to be released into the gut for some time. Treatment is with intensive supportive care; equine botulism antitoxin used in adults is not generally used for infant botulism because of its serious adverse effects (including serum sickness and anaphylaxis), its short half-life, and the possibility of life-long sensitisation to equine proteins.[4] A human-derived intravenous botulism immunoglobulin (BIG-IV) is available in the USA for the treatment of patients under 1 year of age with infant botulism caused by toxin type A or B. Clinical studies[4] reported that treatment with BIG-IV within 7 days of hospital admission reduced the length of hospital stay and severity of illness in infant botulism type A or B; treatment given within 3 days was more effective than treatment given 4 to 7 days after admission.

1. Robinson RF, Nahata MC. Management of botulism. *Ann Pharmacother* 2003; **37:** 127–31.
2. Health Protection Agency. Guidelines for action in the event of a deliberate release: botulism (issued April 2007). Available at: http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1194947315628 (accessed 15/07/08)
3. Sobel J. Botulism. *Clin Infect Dis* 2005; **41:** 1167–73.
4. Arnon SS, *et al.* Human botulism immune globulin for the treatment of infant botulism. *N Engl J Med* 2006; **354:** 462–71.

Preparations

Ph. Eur.: Botulinum Antitoxin;
USP 31: Botulism Antitoxin.

Proprietary Preparations (details are given in Part 3)
USA: BabyBIG.

Multi-ingredient: ***Cz.:*** Bosea†.

Bovine Colostrum

Calostro bovino.

Profile

Bovine colostrum has been used similarly to antisera and human immunoglobulin preparations to provide passive immunity against infectious diseases. Hyperimmune bovine colostra have been prepared from cows previously immunised with specific antigens. In particular, these specific hyperimmune bovine colostra have been tried in cryptosporidiosis and in the prevention of rotavirus diarrhoea in infants. They may also have potential for use against *Helicobacter pylori*, *Shigella* spp., and measles.

◊ Reviews.

1. Kelly GS. Bovine colostrums: a review of clinical uses. *Altern Med Rev* 2003; **8:** 378–94. Correction. *ibid.* 2004; **9:** 69.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Travelan.

Multi-ingredient: ***Indon.:*** Stimox; Vistrum; ***Ital.:*** Colostrum; ***UK:*** BioXtra†.

Brucellosis Vaccines

Vacunas de la brucelosis.

ATC — J07AD01.

Profile

A brucellosis vaccine prepared from an antigenic extract of *Brucella abortus* has been used for active immunisation against brucellosis (p.165) in persons at high risk of contracting the disease.

Campylobacter Jejuni Vaccines

Vacunas contra el Campylobacter jejuni.

Profile

An oral vaccine is under development to provide active immunisation against *Campylobacter jejuni* infection.

Cholera Vaccines

Vacunas del cólera.

ATC — J07AE01; J07AE02.

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

Ph. Eur. 6.2 (Cholera Vaccine; Vaccinum Cholerae). A sterile homogeneous suspension of a suitable killed strain or strains of *Vibrio cholerae*. It consists of a mixture of equal parts of vaccines prepared from smooth strains of 2 main serological types, Inaba and Ogawa of the classical biotype with or without the El Tor biotype. A single strain or several strains of each type may be included. All strains must contain, in addition to their type O antigens, the heat-stable O antigen common to the Inaba and Ogawa types. If more than one strain each of Inaba and Ogawa are used they may be selected to contain other O antigens. It contains not less than 8000 million *V. cholerae* per dose, which does not exceed 1 mL. It contains not more than 0.5% of phenol. It should be stored at 2° to 8° and protected from light.

The BP 2008 states that Cholera may be used on the label.

Ph. Eur. 6.2 (Cholera Vaccine, Freeze-dried; Vaccinum Cholerae Cryodesiccatum). Cholera vaccine that is freeze-dried and reconstituted immediately before use by the addition of a suitable sterile liquid. Phenol may not be used in the preparation of the dried vaccine. It should be stored at 2° to 8° and be protected from light.

Ph. Eur. 6.2 (Cholera Vaccine (Inactivated, Oral); Vaccinum Cholerae Perorale Inactivatum). A homogeneous suspension of inactivated suitable strains of *Vibrio cholerae* serogroup O1, representing serotypes and biotypes of epidemic strains. The vaccine may contain the B subunit of cholera toxin (CTB). Just prior to ingestion, one dose of vaccine suspension is mixed with a suitable buffer as stated on the label. Store at 2° to 8 °. Protect from light.

The BP 2008 states that Dried/Cholera may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Slight swelling, erythema, and tenderness occasionally occur at the injection site. Fever and malaise have been reported and general reactions, including anaphylaxis and hypersensitivity reactions, have occurred. Neurological and psychiatric reactions have occasionally occurred.

Gastrointestinal disturbances, headache, dizziness, and respiratory symptoms have followed use of oral cholera vaccine.

Interactions

As for vaccines in general, p.2202.

The oral cholera vaccine available in the UK is acid labile; consequently food should not be consumed for 1 hour before and after use.

Uses and Administration

Injectable inactivated whole-cell cholera vaccines have been used for active immunisation against cholera but are not considered to be very effective and the immunity conferred is short-lived. They have no role in the management of contacts of cases or in controlling the spread of infection.

Oral vaccines containing either live attenuated or inactivated strains are available in some countries and appear to be more effective than parenteral vaccines (see below). In the UK, an oral vaccine containing inactivated strains of *Vibrio cholerae* O1 and recombinant cholera toxin B subunit is available for use in adults and children aged over 2 years who are travelling to areas of risk. The vaccine is given as a suspension, in doses of 3 mL, mixed with sodium hydrogen carbonate solution. Adults and children aged over 6 years are given two doses, and children aged 2 to 6 years three doses, in each case at weekly intervals. Immunisation should be complete at least 1 week prior to potential exposure. Booster doses may be given after 2 years in adults and children over 6 years, or after 6 months in children aged 2 to 6 years, if continuous protection is required. Oral vaccines containing a live attenuated form of the *V. cholerae* strain CVD 103-HgR are available in some countries. They are effective against the O1 serogroup of cholera, but do not afford protection against the O139 serogroup. They may be given to adults and children aged over 2 years who are travelling to areas of risk and are given as a single-dose suspension in sodium hydrogen carbonate solution. Immunisation should be carried out at least 1 week before potential exposure. When necessary revaccination is recommended every 6 months.

The WHO International Health Regulations do not require cholera vaccination for travellers as the introduction of cholera into any country cannot be prevented by cholera vaccination. However, travellers may still be asked for evidence of immunisation at some borders.

Oral cholera vaccines. Since parenteral cholera vaccines are not considered to be very effective, providing at best 50% protection and confer immunity lasting only 3 to 6 months, attention has turned towards oral vaccines that stimulate intestinal immunity.[1] Both killed and live attenuated oral vaccines have been developed, and both types have been shown to be non-toxic and immunogenic.

Killed vaccines contain inactivated whole *Vibrio cholerae* O1 either alone or with B subunit component of cholera toxin. These vaccines typically produce a protective efficacy of about 60 to 70% and both modify established infections and prevent new ones. Although the vaccines are effective in areas where the El Tor biotype predominates, they are more effective against classical strains. Immunity particularly against El Tor may be less sustained in children under 5 years of age than in older children and adults. The main drawback is the need to give two or more doses at 1- to 2-week intervals to achieve a protective effect. The protective effect is rapidly established but diminishes over time and booster doses are necessary to maintain a high level of immunity.

A live attenuated vaccine is now available containing CVD 103-HgR in which the genes encoding the toxic A subunit are deleted by recombinant techniques.[2,3] This vaccine is effective 8 days after a single dose but less so against El Tor than against classical strains. It is not effective against *V. cholorae* O139.

Live oral vaccines effective against El Tor are now being developed,[4,5] and promising responses have also been reported with a live attenuated O139 vaccine.[6]

The efficacy and cost-effectiveness of oral vaccines to control cholera outbreaks in refugee populations is uncertain.

1. Ryan ET, Calderwood SB. Cholera vaccines. *Clin Infect Dis* 2000; **31:** 561–5.
2. Tacket CO, *et al.* Randomized, double-blind, placebo-controlled, multicentered trial of the efficacy of a single dose of live oral cholera vaccine CVD 103-HgR in preventing cholera following challenge with Vibrio cholerae O1 El tor inaba three months after vaccination. *Infect Immun* 1999; **67:** 6341–5.
3. Richie E, *et al.* Efficacy trial of single-dose live oral cholera vaccine CVD 103-HgR in North Jakarta, Indonesia, a cholera-endemic area. *Vaccine* 2000; **18:** 2399–2410.
4. Tacket CO, *et al.* Volunteer studies investigating the safety and efficacy of live El Tor Vibrio cholerae O1 vaccine strain CVD 111. *Am J Trop Med Hyg* 1997; **56:** 533–7.
5. Sack DA, *et al.* Evaluation of Peru-15, a new live oral vaccine for cholera, in volunteers. *J Infect Dis* 1997; **176:** 201–5.
6. Coster TS, *et al.* Safety, immunogenicity, and efficacy of live attenuated Vibrio cholerae O139 vaccine prototype. *Lancet* 1995; **345:** 949–52.

Preparations

Ph. Eur.: Cholera Vaccine; Cholera Vaccine (Inactivated, Oral); Freeze-dried Cholera Vaccine.

Proprietary Preparations (details are given in Part 3)
Arg.: Orochol; ***Austral.:*** Dukoral; Orochol†; ***Braz.:*** Vacina Oral Contra Colera e Diarreia Causada Por ETEC; ***Canad.:*** Dukoral; Mutacol†; ***Cz.:*** Dukoral; ***Denm.:*** Dukoral; ***Fin.:*** Dukoral; ***Fr.:*** Dukoral; ***Hong Kong:*** Orochol†; ***Ital.:*** Dukoral; ***Malaysia:*** Dukoral; ***Neth.:*** Dukoral; ***Norw.:*** Dukoral; ***NZ:*** Dukoral; ***Philipp.:*** Dukoral; Orochol; ***Port.:*** Dukoral; ***S.Afr.:*** Dukoral; ***Singapore:*** Dukoral; ***Spain:*** Dukoral; ***Swed.:*** Dukoral; ***Switz.:*** Orochol; ***Thai.:*** Dukoral; ***Turk.:*** Dukoral; ***UK:*** Dukoral.

Contraceptive Vaccines

Vacunas anticonceptivas.

Profile

Various approaches to development of a contraceptive vaccine are under investigation. A synthetic contraceptive vaccine that stimulates the production of an antibody against human chorionic gonadotrophin has been studied in human trials.

◊ Reviews.

1. Delves PJ. The development of contraceptive vaccines. *Expert Opin Invest Drugs* 2002; **11:** 1225–37.
2. Aitken RJ. Immunocontraceptive vaccines for human use. *J Reprod Immunol* 2002; **57:** 273–87.
3. McLaughlin EA, *et al.* Contraceptive vaccines. *Expert Opin Biol Ther* 2003; **3:** 829–41.
4. Ferro VA, Mordini E. Peptide vaccines in immunocontraception. *Curr Opin Mol Ther* 2004; **6:** 83–9.

Crimean-Congo Haemorrhagic Fever Immunoglobulins

Inmunoglobulinas contra la fiebre hemorrágica de Congo-Crimea.

Profile

Preparations containing antibodies against Crimean-Congo haemorrhagic fever have been used for passive immunisation against the disease.

◊ References.

1. Vassilenko SM, *et al.* Specific intravenous immunoglobulin for Crimean-Congo haemorrhagic fever. *Lancet* 1990; **335:** 791–2.
2. Ergonul O. Treatment of Crimean-Congo hemorrhagic fever. *Antiviral Res* 2008; **78:** 125–31.

Crimean-Congo Haemorrhagic Fever Vaccines

Profile

An inactivated vaccine against Crimean-Congo haemorrhagic fever, derived from *mouse* brains, is used in parts of eastern Europe.

Cytomegalovirus Immunoglobulins

Inmunoglobulinas contra el citomegalovirus.

ATC — J06BB09.

Description. Cytomegalovirus immunoglobulins containing high levels of specific antibody against CMV have been prepared from human plasma.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Interactions

As for immunoglobulins in general, p.2201.

Uses and Administration

Cytomegalovirus immunoglobulins are used for passive immu-

nisation against CMV infection. They are used prophylactically, especially in patients undergoing certain transplant procedures. In transplants from CMV-seropositive donors into seronegative recipients, prophylactic use of cytomegalovirus immunoglobulin with ganciclovir should also be considered.

In the USA, a cytomegalovirus immunoglobulin G is available for use in recipients of heart, kidney, liver, lung, and pancreas transplants, and for CMV-seronegative recipients of these organs other than kidney from CMV-seropositive donors. The dosage schedule for kidney transplant recipients is 150 mg/kg by intravenous infusion within 72 hours of transplantation, then 100 mg/kg once every 2 weeks for 4 doses, then 50 mg/kg every 4 weeks for 2 doses. The rate of infusion should start at 15 mg/kg per hour increasing gradually to a maximum rate of 60 mg/kg per hour. For recipients of transplants other than kidney, the recommended dosage schedule is 150 mg/kg within 72 hours of transplantation and then once every 2 weeks for 4 further doses, then 100 mg/kg every 4 weeks for 2 doses. In the UK, cytomegalovirus immunoglobulin is available on a named patient basis for prophylaxis in patients receiving immunosuppressive treatment.

The name sevirumab is applied to a χ-chain human monoclonal cytomegalovirus immunoglobulin G1.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: CytoGam†; Megalotect; ***Austral.:*** CMV Immunoglobulin; ***Austria:*** Cytoglobin; Cytotect; ***Belg.:*** Ivegam-CMV; ***Chile:*** Cytotect; ***Cz.:*** Cytotect; ***Ger.:*** Cytoglobin; Cytotect; ***Gr.:*** Megalotect; ***Hong Kong:*** Cytotect; ***Hung.:*** Cytotect; ***Irl.:*** Megalotect†; ***Israel:*** Megalotect; ***Ital.:*** Cytotect; Immunoendocig†; Uman-Cig†; ***Neth.:*** Megalotect; ***Pol.:*** Cytotect; ***Port.:*** Megalotect; ***S.Afr.:*** Megalotect†; ***Singapore:*** Megalotect; ***Switz.:*** Cytotect; ***Thai.:*** Megalotect; ***Turk.:*** Cytotect; ***USA:*** CytoGam.

Cytomegalovirus Vaccines

Vacunas contra el citomegalovirus.

Profile

Several vaccines for active immunisation against CMV infection are under investigation, including some produced by recombinant technology. A live attenuated cytomegalovirus vaccine containing human CMV Towne strain has been investigated in humans since the late 1970s, particularly for the prevention of CMV infection in renal transplant recipients. However, there have been doubts over its safety.

◊ Several promising candidate vaccines against human CMV infection are under development, of which 5 have been or are being tested in humans.[1] Firstly, attenuated CMV (Towne strain) vaccine has been tried but found to be erratic in efficacy and loses segments of its genetic material; to overcome this a second, more robust, vaccine has been designed consisting of a chimera between the attenuated CMV and wild-type virus. The third vaccine developed, known as ALVAC, consists of a canarypox vector with either a glycoprotein B envelope or a core antigen from CMV pp65, a protein found to be recognised by CD8+ T lymphocytes during naturally acquired infection. Fourthly, a protein sub-unit vaccine consisting of a recombinant envelope glycoprotein has been found to be safe and to induce a neutralising antibody response. Finally, the fifth vaccine developed is a mixture of synthetic peptides incorporating a T helper epitope known as CD8+ cytotoxic T cell epitope and a lipid tail. Currently, the attenuated cytomegalovirus vaccine, the protein sub-unit vaccine, and the recombinant vector vaccine have been or are being tested in CMV-negative subjects, and the chimeric vaccine has been tested in CMV-positive patients as a precursor to testing in CMV-negative persons.[1]

Further vaccine candidates that have been proposed include DNA vaccines and a vaccine based on recombinant technology.[1] Some commentators[2] have suggested that reduction or prevention of cytomegalovirus disease may be a more realistic goal for a vaccine than prevention of infection.

1. Arvin AM, *et al.* Vaccine development to prevent cytomegalovirus disease: report from the National Vaccine Advisory Committee. *Clin Infect Dis* 2004; **39:** 233–9.
2. Khanna R, Diamond DJ. Human cytomegalovirus vaccine: time to look for alternative options. *Trends Mol Med* 2006; **12:** 26–33.

Dengue Fever Vaccines

Vacunas del dengue.

Profile

Live attenuated vaccines under study for active immunisation against dengue fever contain dengue virus types 1, 2, 3, and 4 alone or in various combinations. WHO considers that protection against only one or two dengue viruses might actually increase the risk of more serious disease. The ultimate aim is to produce a vaccine active against all types of dengue virus.

Recombinant vaccines are also under investigation.

◊ References.

1. Velzing J, *et al.* Induction of protective immunity against dengue virus type 2: comparison of candidate live attenuated and recombinant vaccines. *Vaccine* 1999; **17:** 1312–30.
2. Kanesa-Thasan N, *et al.* Safety and immunogenicity of attenuated dengue virus vaccines (Aventis Pasteur) in human volunteers. *Vaccine* 2001; **19:** 3179–88.
3. Rothman AL, *et al.* Induction of T lymphocyte responses to dengue virus by a candidate tetravalent live attenuated dengue virus vaccine. *Vaccine* 2001; **19:** 4694–99.
4. Sabchareon A, *et al.* Safety and immunogenicity of tetravalent live-attenuated dengue vaccines in Thai adult volunteers: role of serotype concentration, ratio, and multiple doses. *Am J Trop Med Hyg* 2002; **66:** 264–72.
5. Sun W, *et al.* Vaccination of human volunteers with monovalent and tetravalent live-attenuated dengue vaccine candidates. *Am J Trop Med Hyg* 2003; **69** (suppl 6): 24–31.
6. Sabchareon A, *et al.* Safety and immunogenicity of a three dose regimen of two tetravalent live-attenuated dengue vaccines in five- to twelve-year-old Thai children. *Pediatr Infect Dis J* 2004; **23:** 99–109.
7. Monath TP. Dengue and yellow fever—challenges for the development and use of vaccines. *N Engl J Med* 2007; **357:** 2222–5.
8. Edelman R. Dengue vaccines approach the finish line. *Clin Infect Dis* 2007; **45** (suppl 1): S56–60.
9. Hatch S, *et al.* Dengue vaccine: opportunities and challenges. *IDrugs* 2008; **11:** 42–5.

Dental Caries Vaccines

Vacunas de la caries dental.

Profile

Dental caries vaccines consisting of purified proteins from *Streptococcus mutans* or *Str. sobrinus* are under investigation. Monoclonal antibodies are also being studied for local passive immunisation.

◊ Several *animal* studies of candidate vaccines for the prevention of dental caries have shown that immunisation with protein antigens from *Streptococcus mutans* or *Str. sobrinus* can induce salivary IgA antibodies which inhibit both sucrose-dependent or sucrose-independent accumulation of these organisms on tooth surfaces. It is thought that candidate vaccines for study in humans could be given by mucosal application since children are already naturally exposed to the antigens involved during the first years of life. Infection with *Str. mutans* normally occurs from the age of about 18 months and the intention is therefore to vaccinate 1-year-old children in order to intercept colonisation. However, progress towards a vaccine for active immunisation against dental caries requires further clinical evaluation. Passive administration of salivary antibodies to *Str. mutans* has also provided some protection in preclinical studies and small scale studies in humans.[1-4]

1. Koga T, *et al.* Immunization against dental caries. *Vaccine* 2002; **20:** 2027–44.
2. Smith DJ. Caries vaccines for the twenty-first century. *J Dent Educ* 2003; **67:** 1130–9.
3. Russell MW, *et al.* A caries vaccine? The state of the science of immunization against dental caries. *Caries Res* 2004; **38:** 230–5.
4. Smith DJ, Mattos-Graner RO. Secretory immunity following mutans streptococcal infection or immunization. *Curr Top Microbiol Immunol* 2008; **319:** 131–56.

Diphtheria Antitoxins

Antitoxinas diftéricas.

ATC — J06AA01.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.
Ph. Eur. 6.2 (Diphtheria Antitoxin; Immunoserum Diphtherici). A sterile preparation containing the specific antitoxic globulins that have the power of neutralising the toxin formed by *Corynebacterium diphtheriae*. It has a potency of not less than 1000 international units/mL when obtained from horse serum and not less than 500 international units/mL when obtained from other mammals. It should be stored at 2° to 8°, and not be allowed to freeze.
The BP 2008 states that Dip/Ser may be used on the label.

Adverse Effects and Precautions

As for antisera in general, p.2201.

Uses and Administration

Diphtheria antitoxins neutralise the toxin produced by *Corynebacterium diphtheriae* locally at the site of infection and in the circulation.

Diphtheria antitoxin is used for passive immunisation in suspected cases of diphtheria and should be given without waiting for bacteriological confirmation of the infection. An antibacterial is usually given concomitantly (see p.168). Diphtheria antitoxin is generally not used for the prophylaxis of diphtheria because of the risk of provoking a hypersensitivity reaction. Contacts of a diphtheria case should be promptly investigated, given antibacterial prophylaxis and active immunisation with a suitable diphtheria-containing vaccine as appropriate (see below), and kept under observation.

A test dose of diluted diphtheria antitoxin should always be given intradermally to exclude hypersensitivity. In the UK, diphtheria antitoxin is given by intravenous infusion for the treatment of diphtheria of mild to moderate severity in the following recommended doses: for nasal diphtheria, 10 000 to 20 000 units; for tonsillar diphtheria, 15 000 to 25 000 units; for pharyngeal or laryngeal diphtheria, 20 000 to 40 000 units. In cases of combined disease, or when diagnosis is delayed, 40 000 to 60 000 units should be given, and, in severe disease, doses up to 100 000 units used. For most cutaneous infections, diphtheria antitoxin is insufficiently absorbed and is therefore not given; however, if the ulcer is sufficiently large (more than 2 cm^2) and especially if it is membranous, then 20 000 to 40 000 units may be given. Higher doses have been used in some countries.

Preparations

Ph. Eur.: Diphtheria Antitoxin.

Diphtheria Vaccines

Vacunas de la difteria.

ATC — J07AF01.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii), have monographs.
Ph. Eur. 6.2 (Diphtheria Vaccine (Adsorbed); Vaccinum Diphtheriae Adsorbatum). A preparation of diphtheria formol toxoid adsorbed on a mineral carrier. The formol toxoid is prepared from the toxin produced by the growth of *Corynebacterium diphtheriae*. The mineral carrier may be hydrated aluminium phosphate or aluminium hydroxide and the resulting mixture is approximately isotonic with blood. The antigenic properties are adversely affected by certain antimicrobial preservatives, particularly those of the phenolic type. It contains not less than 30 international units per dose. It should be stored at 2° to 8°, not be allowed to freeze, and be protected from light.
Ph. Eur. 6.2 (Diphtheria Vaccine (Adsorbed, Reduced Antigen Content); Vaccinum Diphtheriae, Antigeniis Minutum, Adsorbatum). It is an adsorbed diphtheria vaccine containing not less than 2 international units per dose.
The BP 2008 states that for a vaccine for use in the UK, the amount of toxoid used is adjusted so that the final vaccine contains not more than 2.0 flocculation equivalents per dose.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Local reactions may occur but are generally not severe in young children; the frequency and severity of reactions is reported to be less in children under 2 years of age than in older children and adults. If diphtheria vaccines or vaccines containing a diphtheria component need to be given to children over the age of 10 years or to adults, vaccines with a reduced content of diphtheria toxoid and intended for adults and adolescents should be used. For further details see Uses and Administration, below.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Diphtheria vaccines are used for active immunisation against diphtheria. The non-adsorbed vaccine has poor immunogenic properties and its effects are enhanced if given as an adsorbed preparation. For primary immunisation combined diphtheria vaccines, usually diphtheria, tetanus, and pertussis vaccines (p.2210) or diphtheria, tetanus, pertussis, poliomyelitis, and haemophilus influenzae vaccines (p.2212), are used. A single-component diphtheria vaccine has sometimes been used, for example in the event of contact with an infected patient or a carrier. For discussion of immunisation schedules, see under Vaccines, p.2202.

Individuals coming into contact with a case of diphtheria or carrier of a toxigenic strain, or those travelling to an endemic or epidemic area should receive a complete primary course or a reinforcing dose according to age and immunisation history; those not previously immunised should receive a primary course of immunisation, and those previously immunised should receive a single reinforcing dose of a diphtheria-containing vaccine. Contacts of a case of diphtheria or carrier of a toxigenic strain should in addition receive a prophylactic course of a suitable antibacterial (see p.168). Individuals at repeated risk of exposure to infection may be offered booster doses every 10 years.

Schick testing (p.2384) to ascertain immune status is no longer considered necessary before giving diphtheria vaccine to adults provided that a low dose is given; antibody testing is used to check immunity in those regularly exposed to diphtheria.

In some countries, booster doses of a diphtheria and tetanus vaccine are recommended every 10 years (see under Diphtheria and Tetanus Vaccines, p.2210).

Conjugation to diphtheria toxoid has been used to increase the immunogenicity of other vaccines (see Haemophilus Influenzae Vaccines, p.2213).