fever, and lymphadenopathy; arthralgia and arthritis may also occur. Thrombocytopenia (including idiopathic thrombocytopenic purpura) has been reported rarely.

Effects on bones and joints. Although acute arthralgia or arthritis occurs in up to 30% of women after rubella vaccination,[1] a retrospective analysis found no evidence of an increased risk of chronic arthropathies.[2]

1. Tingle AJ, *et al.* Randomised double-blind placebo-controlled study on adverse effects of rubella immunisation in seronegative women. *Lancet* 1997; **349:** 1277–81.
2. Ray P, *et al.* Risk of chronic arthropathy among women after rubella vaccination. *JAMA* 1997; **278:** 551–6.

Effects on hearing. For a report of irreversible sensorineural deafness associated with use of measles and rubella vaccine, see p.2223.

Effects on the nervous system. For a report of optic neuritis in 2 children after use of measles and rubella vaccine, see under Adverse Effects of Measles and Rubella Vaccines, p.2223.

Precautions

As for vaccines in general, p.2202.

Rubella vaccines should not be given during pregnancy. In the UK it is recommended that patients should be advised not to become pregnant within 1 month of vaccination. However, no case of congenital rubella syndrome has been reported after the inadvertent use of rubella vaccines shortly before or during pregnancy and there is no evidence that the vaccines are teratogenic. Inadvertent use of rubella vaccines during pregnancy should not therefore result in a recommendation to terminate the pregnancy. There is no risk to a pregnant woman from contact with recently vaccinated persons as the vaccine virus is not transmitted.

Rubella vaccines are not generally recommended for children below the age of 1 year in whom maternal antibodies might prevent a response.

Vaccines may contain traces of neomycin and/or polymyxin and should therefore not be given to individuals with a history of anaphylaxis to these antibacterials.

Pregnancy. Since 1971 the US CDC has followed up women who received rubella vaccines within 3 months before or after conception.[1] Up to 1979 vaccines containing either the Cendehill or HPV-77 strains of rubella virus were available. None of the 290 infants born to the 538 women who had received these vaccines had defects indicative of congenital rubella syndrome; this included 94 live-born infants of women who were known to be susceptible to rubella before receiving the vaccine. In 1979 a rubella vaccine containing the Wistar RA 27/3 strain was introduced. None of 212 infants born live to 254 women known to be susceptible to rubella and who had received the RA 27/3 rubella vaccine from 1979 to 1988 had defects indicative of congenital rubella syndrome. These results are consistent with experiences in Germany[2] and the UK.[3,4] However, because of evidence that rubella vaccine viruses can cross the placenta and infect the fetus a theoretical risk to the fetus cannot be completely ruled out.[1] Thus in both the UK and USA pregnancy is considered a contraindication to rubella vaccination, and patients are also advised not to become pregnant within one month of vaccination. However, in neither country is termination of pregnancy recommended if the vaccine is inadvertently given during pregnancy.

1. Anonymous. Rubella vaccination during pregnancy—United States, 1971–1988. *JAMA* 1989; **261:** 3374–83.
2. Enders G. Rubella antibody titers in vaccinated and nonvaccinated women and results of vaccination during pregnancy. *Rev Infect Dis* 1985; **7** (suppl 1): S103–S107.
3. Sheppard S, *et al.* Rubella vaccination and pregnancy: preliminary report of a national survey. *BMJ* 1986; **292:** 727.
4. Tookey PA, *et al.* Rubella vaccination in pregnancy. *Commun Dis Rep* 1991; **1** (review 7): R86–R88.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Rubella vaccines are used for active immunisation against rubella (German measles). The symptoms of rubella infection are generally mild except in the early stages of pregnancy when it leads to fetal damage in most infants.

For primary immunisation combined measles, mumps, and rubella vaccine (p.2223) is usually given. For discussion of immunisation schedules, see under Vaccines, p.2202.

Women of child-bearing age should also be vaccinated with the combined vaccine if they are seronegative; women who are found to be seronegative during pregnancy should be vaccinated in the early postpartum period. Effective precautions against pregnancy must be observed for at least one month after vaccination. To avoid the risk of transmitting rubella to pregnant patients, all health service staff, both male and female, should be screened and those found to be seronegative should be vaccinated.

In the USA and in many other countries, a single-antigen rubella vaccine is available although combined vaccines are usually preferred.

Preparations

Ph. Eur.: Rubella Vaccine (Live);
USP 31: Rubella Virus Vaccine Live.

Proprietary Preparations (details are given in Part 3)
Arg.: Imovax Rubeola†; Rudivax; ***Austral.:*** Ervevax; Meruvax II; ***Austria:*** Ervevax; Rubeaten; ***Braz.:*** Rudivax†; ***Cz.:*** Ervevax†; Rudivax†; ***Denm.:*** Meruvax†; ***Fr.:*** Rudivax; ***Ger.:*** Rubellovac†; ***Gr.:*** Vaccin Rubeole; ***Hong Kong:*** Rudivax†; ***India:*** R-Vac; ***Irl.:*** Ervevax†; ***Israel:*** Rudivax; ***Ital.:*** Ervevax†; Gunevax†; Rudivax†; ***Malaysia:*** Ervevax†; Gunevax†; ***Mex.:*** Ervevax; Gunevax†; ***NZ:*** Ervevax; ***Port.:*** Rubeaten†; Rudivax; ***Rus.:*** Ervevax (Эрвевакс); ***S.Afr.:*** Rudivax; ***Spain:*** Vac Antirrubeola†; ***Swed.:*** Meruvax†; ***Switz.:*** Ervevax†; Meruvax; Rubeaten; ***Thai.:*** Gunevax†; Rudivax†; ***UK:*** Almevax; ***USA:*** Meruvax II; ***Venez.:*** Imovax Rubeola†.

Rubella and Mumps Vaccines

Vacunas de la rubéola y la parotiditis.

ATC — J07BJ51.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

See also under Mumps Vaccines, p.2225, and Rubella Vaccines, above.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Rubella and mumps vaccines have been used for active immunisation although for primary immunisation a combined measles, mumps, and rubella vaccine (p.2223) is usually used. For discussion of immunisation schedules, see under Vaccines, p.2202.

Preparations

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

Schistosomiasis Vaccines

Bilharzia Vaccines; Vacunas de la esquistosomiasis.

Profile

Vaccines against schistosomiasis are under development.

◊ Despite attempts since the 1960s, development of an effective vaccine against schistosomiasis has proved difficult.[1,2] The worms themselves are not thought to be responsible for the disease but the eggs elicit a powerful and damaging immune response when they are trapped in tissue.

As only the very young in endemic areas will not have been exposed to schistosomiasis a protective antigen for a candidate vaccine must be one that will attack the adult parasite without cross reacting with egg antigens thus increasing the risk of developing chronic disease in those already affected. Most antigen vaccine candidates tested to date have at best resulted in 50 to 60% protection in animal models although repeated immunisation with irradiated cercariae in *murine* models has resulted in almost 80% protection. Consequently it has been questioned whether sterilising immunity should be the aim. It might be more realistic to develop a vaccine which can reduce the overall worm burden and the fecundity of surviving worms, thus reducing the number of eggs released and deposited in the liver. This in turn would lead to lower rates of infection by reducing the numbers of miracidia available to infect snails. Such a vaccine would, however, only be effective in terms of infection and morbidity rates after a considerable period of time, probably more than 20 years. Alternatively, vaccine candidates that specifically attack particular stages of the parasite life cycle might be feasible. A number of potential vaccine candidate antigens have been identified although the only vaccine candidate to have progressed to phase I and II clinical studies is the glutathione-*S*-transferase antigen from *S. haematobium*, Sh28 GST, and these studies are currently ongoing. Use of antigens with recombinant cytokines in order to enhance immune response, or with the B subunit of cholera toxin in order to suppress harmful inflammatory responses, is also being investigated. There is also some suggestion that it might be possible to develop a multicomponent vaccine consisting of multiple antigens that will give protection against different stages in the parasite cycle.[1]

1. Lebens M, *et al.* Current status and future prospects for a vaccine against schistosomiasis. *Expert Rev Vaccines* 2004; **3:** 315–28.
2. McManus DP, Loukas A. Current status of vaccines for schistosomiasis. *Clin Microbiol Rev* 2008; **21:** 225–42.

Scorpion Venom Antisera

Antisuero contra el veneno de escorpión; Scorpion Antivenins; Scorpion Antivenoms.

Adverse Effects and Precautions

As for antisera in general, p.2201.

Uses and Administration

Some scorpion stings are dangerous and even fatal. The use of a scorpion venom antiserum suitable for the species of scorpion can prevent symptoms, provided that it is given with the least possible delay; other general supportive measures and symptomatic treatment are also needed. The effectiveness of scorpion venom antisera is disputed by some clinicians.

Scorpion stings. Scorpion stings are common throughout the tropics, but the most dangerous and potentially fatal species are found in India, North Africa and the Middle East, the southern states of North America and Mexico, Latin America and the Caribbean, and southern Africa. Local symptoms after scorpion stings include intense pain and swelling. Systemic symptoms result from excitation of nerve and muscle cells by the venom; the pattern of symptoms depends upon the species of scorpion. Symptoms such as hypersalivation, vomiting, and diarrhoea are generally followed by adrenergic features, with release of catecholamines producing hypertension, toxic myocarditis, arrhythmias, heart failure, and pulmonary oedema. The cardiotoxic effects are prominent features of stings in India, North Africa, and the Middle East. Neurotoxic effects such as fasciculations, spasms, and respiratory paralysis are seen with stings from North American species. Stings by the black scorpion of Trinidad may also produce pancreatitis.

Pain is treated with local infiltration or peripheral nerve block with local anaesthetics; opioid analgesics may be necessary, but are regarded as dangerous after stings by some North American species. An appropriate antiserum may be given as soon as possible after envenomation, although the effectiveness of some antisera has been questioned and in some countries they are no longer considered of benefit. Supportive treatment for cardiotoxic effects includes alpha blockers, calcium-channel blockers, and ACE inhibitors. The use of cardiac glycosides, beta blockers, and atropine is controversial. Phenobarbital has been suggested for neurotoxic effects.

References.

1. el Amin EO, *et al.* Scorpion sting: a management problem. *Ann Trop Paediatr* 1991; **11:** 143–8.
2. Bond GR. Antivenin administration for Centruroides scorpion sting: risks and benefits. *Ann Emerg Med* 1992; **21:** 788–91.
3. Warrell DA, Fenner PJ. Venomous bites and stings. *Br Med Bull* 1993; **49:** 423–39.
4. Müller GJ. Scorpionism in South Africa: a report of 42 serious scorpion envenomations. *S Afr Med J* 1993; **83:** 405–11.
5. Gateau T, *et al.* Response to specific centruroides sculpturatus antivenom in 151 cases of scorpion stings. *Clin Toxicol* 1994; **32:** 165–71.
6. Sofer S, *et al.* Scorpion envenomation and antivenom therapy. *J Pediatr* 1994; **124:** 973–8.
7. Karalliedde L. Animal toxins. *Br J Anaesth* 1995; **74:** 319–27.
8. Abroug F, *et al.* Serotherapy in scorpion envenomation: a randomised controlled trial. *Lancet* 1999; **354:** 906–9.
9. Isbister GK, *et al.* Scorpion stings in Australia: five definite stings and a review. *Intern Med J* 2004; **34:** 427–30.
10. Gazarian KG, *et al.* Immunology of scorpion toxins and perspectives for generation of anti-venom vaccines. *Vaccine* 2005; **23:** 3357–68.
11. Bencheikh RS, *et al.* Conduite à tenir devant une piqûre de scorpion au Maroc. *Ann Fr Anesth Reanim* 2008; **27:** 317–22.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Alacramyn.

Shigella Vaccines

Dysentery Vaccines; Shigellosis Vaccines; Vacunas contra Shigella.

Profile

Shigella vaccines have been under investigation since the 1960s but early prototypes were unsatisfactory. Live attenuated oral vaccines, parenteral conjugated vaccines, and intranasal vaccines are now also under development.

◊ Natural or experimental exposure to *Shigella* antigens has been shown to induce clinical immunity, and there has been some work towards developing an effective vaccine.[1,2] There have been 3 main approaches to vaccination under investigation.[1] Firstly, workers at the USA National Institutes of Health have developed a series of vaccines in which the O antigen of *S. sonnei*, *S. flexneri* 2a strain, or *S. dysenteriae* type 1 is conjugated to *Pseudomonas aeruginosa* recombinant exoprotein A. These vaccines are given intramuscularly and have elicited strong immune responses in adults and children tested, and some have reached phase III studies. A second approach has been to deliver *Shigella* lipopolysaccharide intranasally in proteasomes, which are purified outer membrane proteins that form a multimolecular vesicular complex around the antigen; these vaccines are being tested in phase I studies. The third approach is the use of live attenuated oral vaccines, attenuated by creating deletions in genes that govern vital metabolic processes within the organism or by mutating genes that encode specific virulence factors.

A major challenge in the development of a shigella vaccine is to provide protection against all of the numerous serotypes that appear epidemiologically important. Most experts agree that for a shigella vaccine to be totally effective globally it must protect against *S. dysenteriae* type 1, *S. sonnei*, and all 15 classical *S. flexneri* serotypes. However, it has been shown that a composite of 3 *S. flexneri* serotypes (2a, 3a, and 6) can provide cross protection against the remaining 12. Hence the ultimate plan is to develop a pentavalent vaccine comprising these 3 *S. flexneri* serotypes together with *S. sonnei* and *S. dysenteriae* type 1.[1] Shigella vaccines have been licensed for use in China.[2]

1. Kotloff KL. Progress in Shigella vaccine development. In: de Quadros CA, ed. *Vaccines: Preventing Disease and Protecting Health*. Washington D.C., 2004: 130–9.

2. Kweon MN. Shigellosis: the current status of vaccine development. *Curr Opin Infect Dis* 2008; **21:** 313–8.

Smallpox Vaccines

Vacunas de la viruela.

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

Ph. Eur. 6.2 (Smallpox Vaccine (Live)). A liquid or freeze-dried preparation of live vaccinia virus grown in the membranes of the chick embryo, in cell cultures, or in the skin of living animals. The cell culture medium may contain suitable antibacterials at the lowest effective concentration. Store at 2° to 8° and protect from light. The liquid vaccine should not be allowed to freeze.

USP 31 (Smallpox Vaccine). A suspension or solid containing a suitable strain of the living virus of vaccinia grown in the skin of bovine calves; it may contain a suitable preservative. The liquid vaccine should be stored below 0° and the dried vaccine at 2° to 8°.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Both first and second generation live smallpox vaccines have been associated with a high incidence of adverse effects. The most common adverse effects are injection site reactions, fatigue, fever, headache, malaise, myalgia, erythema, and generalised rash. Rarely there may be generalised vaccinial infection, or severe skin or CNS infection resulting in encephalitis, encephalomyelitis, encephalopathy, necrotising skin infection (progressive vaccinia, vaccinia necrosum), eczema vaccinatum, and erythema multiforme (including Stevens-Johnson syndrome). Fatalities have occurred, particularly from post-vaccination encephalitis and progressive vaccinia. Inadvertent contamination of other body sites (such as the face, mouth, nose, lips, and genitalia) from the site of vaccination also occurs frequently; autoinoculation of the eye (ocular vaccinia) may result in blindness. Benign and malignant lesions have also been reported at the vaccination site.

There have been reports of myocarditis or pericarditis or both, including some fatalities, associated with smallpox vaccination. Smallpox vaccination is not recommended for infants under 12 months of age, for persons with a history of eczema or other skin conditions, those who are immunocompromised, for pregnant women, or for women who breast feed. Household contacts of these groups should also not be vaccinated. Vaccination is best avoided in persons with known cardiac disease.

◊ References.

1. CDC. Smallpox vaccination and adverse reactions: guidance for clinicians. *MMWR* 2003; **52** (RR-04): 1–28. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5204.pdf (accessed 05/11/07)
2. CDC. Notice to readers: supplemental recommendations on adverse events following smallpox vaccine in the pre-event vaccination program: recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2003; **52** (RR-07): 1–16. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5207.pdf (accessed 05/11/07)
3. Fulginiti VA, *et al.* Smallpox vaccination: a review, part II. Adverse events. *Clin Infect Dis* 2003; **37:** 251–71.
4. CDC. Update: adverse events following civilian smallpox vaccination—United States, 2003. *MMWR* 2004; **53:** 106–7. Correction. *ibid.*; 133. Also available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5305a4.htm (accessed 06/11/07)
5. Sejvar JJ, *et al.* Neurologic adverse events associated with smallpox vaccination in the United States, 2002–2004. *JAMA* 2005; **294:** 2744–50. Corrections. *ibid.*; 3092 and **298:** 1864.
6. Casey CG, *et al.* Surveillance guidelines for smallpox vaccine (vaccinia) adverse reactions. *MMWR* 2006; **55** (RR-1): 1–16. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5501.pdf (accessed 05/11/07)

Uses and Administration

After the global eradication of smallpox in 1980, vaccination against smallpox (using first generation vaccinia virus vaccine) has been indicated for those considered to be at high risk such as laboratory workers handling certain orthopoxviruses, and key emergency, healthcare, and military personnel who may have to respond to a bioterrorist release of smallpox. A second generation smallpox vaccine has been licensed in the USA for inclusion to the National Stockpile for vaccination of those considered to be at high risk for smallpox infection. Persons at high risk and who have received primary vaccination against smallpox, should be re-vaccinated every 10 years. Vaccination is not recommended for persons working with highly attenuated strains of orthopoxviruses.

WHO considers that mass vaccination against smallpox is currently not appropriate, although individuals who may be at risk of exposure to smallpox or those with confirmed infection may be vaccinated.

Recombinant vaccinia viruses are being investigated as vectors of foreign antigens, for example in a candidate AIDS vaccine (p.2203).

Vaccine development. Smallpox[1] is an acute contagious and sometimes fatal disease caused by variola virus, a member of the Poxviridae family and of the orthopoxvirus genus. There is substantial cross-protection between poxviruses of the same genus; the very effective first generation smallpox vaccine used in the global vaccination programme was created from an orthopoxvirus, vaccinia. In 1980 WHO declared smallpox to have been globally eradicated.

There has since been concern that smallpox may be used as a terrorist weapon (although WHO considers this risk to be extremely low in most countries). Therefore, research into safer vaccines against smallpox has continued. First generation vaccine was produced from vaccinia strains grown on the skin of live animals or calf lymph. Despite purification processes, the vaccine contained some bacteria, animal proteins, and adventitious animal viruses, and produced a high incidence of adverse effects, some of which were extremely serious (see Adverse Effects and Precautions, above). Second generation vaccines are single clones of vaccinia isolated from the set of genetically related viruses that made up the first generation ones; they are grown in tissue culture (rather than on animal skin or calf lymph) and are free of bacteria and adventitious animal viruses. A second generation vaccine has been found to be effective and is licensed in the USA for inclusion to the National Stockpile. However, this vaccine still has a high incidence of adverse effects. Third generation vaccines are in the early stages of development. They are being developed from vaccinia strains attenuated by serial passage on non-human tissue or by genetic manipulation, and are expected to be safer than either first or second generation vaccines. Interest has also been shown in monoclonal variola antibodies for passive immunisation.[1,2]

Stocks of smallpox (variola) virus are being kept in a few secure laboratories in the USA and Russia. Since the eradication of smallpox, WHO maintains a stockpile of smallpox vaccine, and recommends vaccination for people with occupational exposure to fully potent orthopoxviruses, such as certain laboratory and healthcare workers. Because of concern that smallpox may be used for bioterrorism, WHO and several countries have increased the number of doses kept in stock.[1] Policies for the use of smallpox vaccine, including bioterrorism preparedness, have been developed in many countries such as the USA[3,4] and UK[5,6] with some countries recommending vaccination for key emergency and military personnel.

1. Moore ZS, *et al.* Smallpox. *Lancet* 2006; **367:** 425–35.
2. Metzger W, Mordmueller BG. Vaccines for preventing smallpox. Available in the Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 14/09/07).
3. CDC. Vaccinia (smallpox) vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2001. *MMWR* 2001; **50** (RR-10): 1–25. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5010.pdf (accessed 25/05/06)
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Preparations

Ph. Eur.: Smallpox Vaccine (Live);
USP 31: Smallpox Vaccine.

Proprietary Preparations (details are given in Part 3)
USA: ACAM2000; Dryvax.

Snake Venom Antisera

Antisuero contra el veneno de serpiente; Snake Antivenins; Snake Antivenoms.

ATC — J06AA03.

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

Ph. Eur. 6.2 (Viper Venom Antiserum, European; Immunoserum Contra Venena Viperarum Europaearum). A preparation containing the specific antitoxic globulins that have the power of neutralising the venom of one or more species of viper (*Vipera ammodytes*, *V. aspis*, *V. berus*, or *V. ursinii*). The globulins are obtained by fractionation of the serum of animals that have been immunised against the venom or venoms. Each mL neutralises the venoms in not less than 100 mouse LD_{50} of *V. ammodytes*, 100 of *V. aspis*, 50 of *V. berus*, or 50 of *V. ursinii*. It should be stored at 2° to 8°, and not be allowed to freeze.

The BP 2008 states that the only poisonous snake native to the British Isles is the adder or common viper, *Vipera berus*. In a geographical region where other species of snake (including elapids) are found, antisera able to neutralise the venoms of the species of snake indigenous to the region should be used. When the preparation is intended to neutralise the venom or venoms of one or more snakes other than vipers, the title Snake Venom Antiserum is used.

USP 31 (Antivenin (Crotalidae) Polyvalent). A sterile freeze-dried preparation of specific venom-neutralising globulins obtained from the serum of healthy horses immunised against 4 species of pit vipers, *Crotalus atrox* (western diamondback), *Crotalus adamanteus*, *Crotalus durissus terrificus* (South American rattlesnake), and *Bothrops atrox* (South American fer de lance). One dose neutralises the venoms in not less than 180 mouse LD_{50} of *C. atrox*, 1320 of *C. durissus terrificus*, and 780 of *B. atrox*. It may contain a suitable preservative. It should be preserved in single-dose containers and stored at a temperature not exceeding 40°.

USP 31 (Antivenin (Micrurus Fulvius)). A sterile freeze-dried preparation of specific venom-neutralising globulins obtained from the serum of healthy horses immunised against venom of *Micrurus fulvius* (eastern coral snake). One dose neutralises the venom in not less than 250 mouse LD_{50} of *M. fulvius*. It may contain a suitable preservative. It should be preserved in single-dose containers and stored at a temperature not exceeding 40°.

Adverse Effects and Precautions

As for antisera in general, p.2201.

Serum sickness is not uncommon and anaphylactic reactions may occur.

Anaphylaxis. Conjunctival or cutaneous hypersensitivity testing failed to predict early (anaphylactic) reactions to the antivenom given in a study of patients in Nigeria with systemic envenoming by the saw-scaled or carpet viper (*Echis carinatus*) and in Thailand with local or systemic envenoming by green pit vipers (*Trimeresurus albolabris* and *T. macrops*), the monocellate Thai cobra (*Naja kaouthia*), or the Malayan pit viper (*Calloselasma rhodostoma*). It was considered that conventional hypersensitivity testing has no predictive value for the occurrence of allergic reactions to antivenom and that it is not justifiable to delay treatment for 20 or 30 minutes to read the results of these tests. Although the rate at which antiserum can be given is more easily controlled by intravenous infusion, this method has serious practical disadvantages in the rural tropics where most cases of snake bite occur and an advantage of the intravenous push injection is that the person giving the antiserum must remain with the patient during the period when most severe anaphylactic reactions develop.

Pretreatment with low-dose subcutaneous adrenaline may reduce the incidence of anaphylaxis and other acute adverse reactions to the antiserum.[1] However, premedication with adrenaline, antihistamines, and corticosteroids, although widely practiced, is controversial. In one study,[2] prophylaxis with promethazine was ineffective in preventing anaphylaxis from antiserum against *Bothrops* envenomation.

1. Premawardhena AP, *et al.* Low dose subcutaneous adrenaline to prevent acute adverse reactions to antivenom serum in people bitten by snakes: randomised, placebo controlled trial. *BMJ* 1999; **318:** 1041–3.
2. Fan HW, *et al.* Sequential randomised and double blind trial of promethazine prophylaxis against early anaphylactic reactions to antivenom for bothrops snake bites. *BMJ* 1999; **318:** 1451–2.

Uses and Administration

Venomous snakes comprise the Viperidae (vipers), Elapidae (cobras, kraits, and mambas), and the Hydrophiidae (sea snakes).

The venom of snakes is a complex mixture chiefly of proteins, many of which have enzymatic activity, and may provoke local inflammatory reactions. The venom may have profound effects on tissue, blood vessels and other organs, blood cells, coagulation, and myotoxic or neurotoxic effects with sensory, motor, cardiac, renal, and respiratory involvement.

Snake venom antisera are the only specific treatment available for venomous snake bites, but can produce severe adverse reactions. They are generally only used if there are clear indications of systemic involvement, severe local involvement, or, in regions where supplies are not limited, in patients at high risk of systemic or severe local involvement. Adrenaline should be available in case of anaphylactic reactions to the antiserum; premedication with adrenaline, corticosteroids, and/or antihistamines is widely practiced but is regarded as controversial.

In Great Britain, the only indigenous poisonous snake is the adder, *Vipera berus*; its bite is rarely fatal but European Viper Venom Antiserum (or Zagreb antivenom) may sometimes be indicated as part of the overall treatment. The usual dose for adults and children is 10 mL by intravenous injection over 10 to 15 minutes or by intravenous infusion over 30 minutes after diluting in 5 mL/kg body-weight of sodium chloride 0.9%; the dose may be repeated after about 1 to 2 hours if symptoms of systemic envenoming persist.

In the USA, a polyvalent crotalidae antiserum against *Bothrops atrox*, *Crotalus adamanteus*, *C. atrox*, and *C. durissus terrificus*, and an antiserum against the North American coral snake, *Micrurus fulvius*, are available. In Australia, polyvalent antisera against the brown snake, death adder, taipan, and tiger snake, together with either the king brown snake or black snake, are available. A variety of polyvalent and monovalent antisera are also available as appropriate to the indigenous species of snakes in many other countries.