Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Synagis; ***Austral.:*** Synagis; ***Belg.:*** Synagis; ***Braz.:*** Synagis; ***Canad.:*** Synagis; ***Chile:*** Synagis; ***Cz.:*** Synagis; ***Denm.:*** Synagis; ***Fin.:*** Synagis; ***Fr.:*** Synagis; ***Ger.:*** Synagis; ***Gr.:*** Synagis; ***Hong Kong:*** Synagis; ***Hung.:*** Synagis; ***Irl.:*** Synagis; ***Israel:*** Abbosynagis; ***Ital.:*** Synagis; ***Malaysia:*** Synagis; ***Mex.:*** Synagis; ***Neth.:*** Synagis; ***Norw.:*** Synagis; ***NZ:*** Synagis; ***Pol.:*** Synagis; ***Port.:*** Synagis; ***S.Afr.:*** Synagis; ***Singapore:*** Synagis†; ***Spain:*** Synagis; ***Swed.:*** Synagis; ***Switz.:*** Synagis; ***Turk.:*** Synagis; ***UK:*** Synagis; ***USA:*** RespiGam; Synagis; ***Venez.:*** Synagis.

Respiratory Syncytial Virus Vaccines

Vacunas del virus sincitial respiratorio.

Profile

Vaccines containing RSV protein subunit are being studied for active immunisation.

◊ Development of an effective and safe vaccine against RSV has been hampered by a number of factors.[1-3] The target population for a vaccine is mainly young infants who may not respond adequately to vaccination owing to the antigenic diversity of RSV, immunological immaturity, or the presence of maternal antibodies. In the early 1960s, a formalin inactivated respiratory syncytial virus vaccine known as FI-RSV (also sometimes called Lot 100) was tested in infants and children aged 2 months to 7 years but failed to protect against subsequent infection with wild-type virus; it also led to a catastrophically exaggerated clinical response to wild-type virus in infants who were naive to RSV before vaccination, resulting in hospitalisation for the majority of recipients and 2 fatalities. Since that time, a number of candidate vaccines have subsequently been developed including live attenuated virus and viral protein subunit vaccines.[1,2] Several of the live attenuated vaccine candidates have been investigated in humans but results have generally been disappointing. More recently, genetically engineered live attenuated vaccine candidates have been generated, and some are currently being investigated in clinical studies.[1,2]

Subunit vaccines are composed of the F and G glycoproteins from RSV since these are the glycoproteins that induce antibody responses.[1,2] They are most likely to be of use in older persons and in high-risk children and might also be used for maternal immunisation. A chimeric FG fusion protein vaccine was evaluated in phase I studies but is no longer in development.

1. Durbin AP, Karron RA. Progress in the development of respiratory syncytial virus and parainfluenza virus vaccines. *Clin Infect Dis* 2003; **37:** 1668–77.
2. Kneyber MCJ, Kimpen JLL. Advances in respiratory syncytial virus vaccine development. *Curr Opin Investig Drugs* 2004; **5:** 163–70.
3. Power UF. Respiratory syncytial virus (RSV) vaccines—two steps back for one leap forward. *J Clin Virol* 2008; **41:** 38–44.

Rift Valley Fever Vaccines

Vacunas de la fiebre del valle del Rift.

Profile

An inactivated rift valley fever vaccine has been developed for the active immunisation of persons at high risk of contracting the disease.

Rotavirus Vaccines

Vacunas de rotavirus.

ATC — J07BH01; J07BH02.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

The most common adverse effects reported in subjects receiving rotavirus vaccines (attenuated human strain or pentavalent reassortant rotavirus vaccine) are fever, fatigue, irritability, and gastrointestinal disturbances. Otitis media, nasopharyngitis, bronchospasm, and haematochezia (blood in the stools) have also been reported with the pentavalent vaccine. A few cases of Kawasaki disease have been reported with the pentavalent vaccine but no causal relationship has been established.

There has been much debate on the causal role of rotavirus vaccines for intussusception (see below); cases have been reported during post-marketing use.

The UK licensed product information for the attenuated human strain vaccine contraindicates the use of this vaccine in children with a history of intussusception or with congenital conditions of the gastrointestinal tract, while the US licensed product information for pentavalent vaccine advises that it be used with caution. Caution is also generally advised in those with gastrointestinal illnesses or growth retardation and use may be postponed in children suffering from diarrhoea or vomiting. Use of a rotavirus vaccine should be carefully considered before being given to infants with a close family contact who is immunocompromised; if given precautions should be taken to avoid transmission of any excreted vaccine virus.

Intussusception. A live oral tetravalent vaccine (RRV-TV) became available in the USA in August 1998 but was withdrawn from the market by the manufacturer in October 1999 after reports of intussusception (a condition when part of the intestine prolapses into the lumen of an adjacent part causing an obstruction). From September 1998 until July 1999, 15 patients with intussusception had been reported to the Vaccine Adverse Event Reporting System (VAERS), 12 of whom developed symptoms within a week of vaccination.[1] While this evidence was considered inconclusive, further studies were expected to clarify the risks associated with routine use of this vaccine. One such study,[2] in which 429 infants with intussusception were retrospectively analysed, found that 74 (17.2%) had received RRV-TV compared with 226 of 1763 controls (12.8%) and concluded that there was evidence of a causal relationship with the vaccine. Another retrospective study,[3] however, found that there was no evidence of an increase in hospital admissions due to intussusception during the period of RRV-TV availability and recommended that a large, randomised, double-blind vaccine trial be performed to determine the absolute risk. Further analysis of the incidence of intussusception associated with RRV-TV has prompted discussion as to whether the absolute risk might in fact be sufficiently low that withholding the vaccine results in greater mortality than would be caused by intussusception.[4] Reassessment of the data on RRV-TV and intussusception has suggested that the risk for intussusception was age-dependent; relative risk for intussusception following the first dose of RRV-TV increased with increasing age.[5,6] However, WHO Global Advisory Committee on Vaccine Safety found that there was insufficient evidence available to determine whether use of RRV-TV before 60 days of age was associated with a lower risk for intussusception but confirmed the association of a high risk of intussusception in infants immunised after day 60.[7] Such considerations have implications for the ongoing evaluation of other candidate live attenuated rotavirus vaccines in that, should cases of intussusception occur, a decision might be required as to what constitutes an acceptable rate.[4]

From February 2006 until February 2007, 35 patients with confirmed intussusception had been reported to VAERS following vaccination with the pentavalent reassortant vaccine; 17 of whom developed symptoms within 21 days of vaccination, including 11 that occurred within 7 days of vaccination. However, this number of cases is not higher than the age adjusted background rates for intussusception.[8]

1. CDC. Intussusception among recipients of rotavirus vaccine—United States, 1998-1999. *MMWR* 1999; **48:** 577–81.
2. Murphy TV, *et al.* Intussusception among infants given an oral rotavirus vaccine. *N Engl J Med* 2001; **344:** 564–72. Correction. *ibid.*; 1564.
3. Simonsen L, *et al.* Effect of rotavirus vaccination programme on trends in admission of infants to hospital for intussusception. *Lancet* 2001; **358:** 1224–9.
4. Murphy BR, *et al.* Reappraisal of the association of intussusception with the licensed live rotavirus vaccine challenges initial conclusions. *J Infect Dis* 2003; **187:** 1301–8.
5. Rothman KJ, *et al.* Age dependence of the relation between reassortant rotavirus vaccine (RotaShield) and intussusception. *J Infect Dis* 2006; **193:** 898.
6. Simonsen L, *et al.* More on RotaShield and intussusception: the role of age at the time of vaccination. *J Infect Dis* 2005; **192** (suppl 1): S36–S43.
7. WHO. Global Advisory Committee on Vaccine Safety, 1–2 December 2005. *Wkly Epidem Rec* 2006; **81:** 15–19.
8. CDC. Postmarketing monitoring of intussusception after RotaTeq vaccination—United States, February 1, 2006–February 15, 2007. *MMWR* 2007; **56:** 218–22.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Several live oral rotavirus vaccines for use in the prevention of childhood diarrhoea have been developed and some are now licensed.

A live attenuated oral monovalent rotavirus vaccine (based on the human RIX4414 strain) is available in some countries. Two doses are given, the first at 6 weeks of age onwards and the subsequent dose at least 4 weeks later; the course should preferably be given before 16 weeks of age, but must be completed by the age of 24 weeks. A live oral pentavalent reassortant rotavirus vaccine (based on human and bovine strains) is available in the USA. Three doses are given, the first at 6 to 12 weeks of age and the two subsequent doses at 4- to 10-week intervals; the third dose should not be given after 32 weeks of age.

A live oral tetravalent rotavirus vaccine (RRV-TV) was formerly available in the USA but was withdrawn by the manufacturer in October 1999 after reports of intussusception associated with its use.

◊ References.

1. Vesikari T, *et al.* Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine. *N Engl J Med* 2006; **354:** 23–33.
2. Ruiz-Palacios GM, *et al.* Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Engl J Med* 2006; **354:** 11–22.
3. Buttery JP, Kirkwood C. Rotavirus vaccines in developed countries. *Curr Opin Infect Dis* 2007; **20:** 253–8.
4. Cunliffe N, Nakagomi O. Introduction of rotavirus vaccines in developing countries: remaining challenges. *Ann Trop Paediatr* 2007; **27:** 157–67.
5. Dennehy PH. Rotavirus vaccines: an overview. *Clin Microbiol Rev* 2008; **21:** 198–208.

Vaccine development. Rotaviruses are an important cause of severe diarrhoea in both developed and developing countries (see Gastro-enteritis, p.850); rates of illness are similar in both and improvement in water quality and general hygiene does not have much effect on viral transmission. The disease infects almost all children before the age of 5 years but is most severe among children 3 to 35 months of age.[1,2] Human rotavirus diarrhoea is caused by group A, B, or C rotaviruses.[3] While an initial infection does not produce complete immunity, it does appear to be protective against further severe gastroenteritis. Vaccination therefore aims to produce a similar effect.[1,2] Development of a suitable vaccine has been made difficult by the diversity of rotaviruses.[3] Initial attempts at vaccine development used single bovine or rhesus monkey strains but these were associated with variable efficacy and adverse effects.[4-6]

To overcome these problems reassortant rotavirus (RRV) strains were constructed. These combined animal rotavirus strains with human rotavirus genes coding for serotype-specific antigens, enabling polyvalent vaccines to be produced against the major rotavirus serotypes causing disease. A number of such candidate vaccines are under development[7] and some are now licensed.[8] Guidelines have been developed in the USA for the use of rotavirus vaccine.[1,2]

1. CDC. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006; **55** (RR-12): 1–13. Also available at: http://www.cdc.gov/mmwr/PDF/rr/rr5512.pdf (accessed 19/06/07)
2. American Academy of Pediatrics Committee on Infectious Diseases. Prevention of rotavirus disease: guidelines for use of rotavirus vaccine. *Pediatrics* 2007; **119:** 171–82. Also available at: http://pediatrics.aappublications.org/cgi/reprint/119/1/171 (accessed 19/06/07)
3. Anonymous. Puzzling diversity of rotaviruses. *Lancet* 1990; **335:** 573–5.
4. Levine MM. Modern vaccines: enteric infections. *Lancet* 1990; **335:** 958–61.
5. Bernstein DI, *et al.* Evaluation of WC3 rotavirus vaccine and correlates of protection in healthy infants. *J Infect Dis* 1990; **162:** 1055–62.
6. Flores J, *et al.* Protection against severe rotavirus diarrhoea by rhesus rotavirus vaccine in Venezuelan infants. *Lancet* 1987; **i:** 882–4.
7. Glass RI, *et al.* The future of rotavirus vaccines: a major setback leads to new opportunities. *Lancet* 2004; **363:** 1547–50.
8. Heaton PM, Ciarlet M. Vaccines: the pentavalent rotavirus vaccine: discovery to licensure and beyond. *Clin Infect Dis* 2007; **45:** 1618–24.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Rotarix; RotaTeq; ***Austral.:*** Rotarix; RotaTeq; ***Belg.:*** Rotarix; ***Chile:*** Rotarix; ***Cz.:*** Rotarix; RotaTeq; ***Fr.:*** Rotarix; RotaTeq; ***Gr.:*** Rotarix; RotaTeq; ***Hung.:*** Rotarix; RotaTeq; ***Malaysia:*** Rotarix; RotaTeq; ***Mex.:*** Rotarix; ***NZ:*** Rotarix; RotaTeq; ***Philipp.:*** Rotarix; ***Pol.:*** Rotarix; RotaTeq; ***Port.:*** Rotarix; RotaTeq; ***Singapore:*** Rotarix; ***Thai.:*** Rotarix; ***UK:*** Rotarix; ***USA:*** Rotarix; RotaTeq; ***Venez.:*** Rotarix.

Rubella Immunoglobulins

Inmunoglobulinas contra la rubéola.

ATC — J06BB06.

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

Ph. Eur. 6.2 (Human Rubella Immunoglobulin; Immunoglobulinum Humanum Rubellae). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma containing specific antibodies against the rubella virus. Normal immunoglobulin may be added. It contains not less than 4500 international units/mL. Both the liquid and freeze-dried preparations should be stored, protected from light, in a colourless, glass container. The freeze-dried preparation should be stored under vacuum or under an inert gas.

Adverse Effects and Precautions

As for immunoglobulins in general, p.2201.

Interactions

As for immunoglobulins in general, p.2201.

Uses and Administration

Rubella immunoglobulins may be used for passive immunisation against rubella (German measles). They have been used to prevent or modify rubella in susceptible persons.

Preparations

Ph. Eur.: Human Rubella Immunoglobulin.

Rubella Vaccines

Vacunas de la rubéola.

ATC — J07BJ01.

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

Ph. Eur. 6.2 (Rubella Vaccine (Live); Vaccinum Rubellae Vivum). A freeze-dried preparation of a suitable live attenuated strain of rubella virus grown in human diploid cell cultures. It is reconstituted immediately before use. The cell-culture medium may contain a permitted antibacterial at the smallest effective concentration, and a suitable stabiliser may be added to the bulk vaccine. The final vaccine contains not less than 3.0 log $CCID_{50}$ per dose. The dried vaccine should be stored at 2° to 8° and be protected from light.

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

USP 31 (Rubella Virus Vaccine Live). A bacterially sterile preparation of a suitable live strain of rubella virus grown in cultures of duck-embryo tissue or human tissue. It contains the equivalent of not less than 1×10^3 $TCID_{50}$ in each immunising dose. It should be stored at 2° to 8° and be protected from light.

Adverse Effects

As for vaccines in general, p.2201.

Generally, adverse effects have not been severe. Those occurring most commonly are skin rashes, pharyngitis,

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.