

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 Germany² 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 contra-indication 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. Tooke 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 (Эрвевак); **S.Afr.:** Rudivax; **Spain:** Vac Antirubeola†; **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 Antivenens; 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.