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8. Plesner AM. Allergic reactions to Japanese encephalitis vaccine. *Immunol Allergy Clin North Am* 2003; **23:** 665–97. Correction. *ibid.* 2004; **24:** 335.

Interactions
As for vaccines in general, p.2202.

Uses and Administration
Two types of inactivated Japanese encephalitis (JE) vaccine containing either the Nakayama or the Beijing-1 strain of the virus and grown in mouse-brain tissue are generally used for active immunisation against encephalitis due to JE virus. The Nakayama strain vaccine produced in Japan was widely available internationally, but production has been stopped. Another inactivated JE vaccine is made in China from the Beijing-3 strain of JE virus and grown in Syrian hamster kidney-cell cultures. This vaccine has been replaced in the Chinese vaccination programme by a live, attenuated JE virus (strain SA 14-14-2) vaccine that is also produced on primary hamster cells. JE vaccines are widely used in China, Japan and other parts of Asia where JE is endemic and may form part of the WHO Expanded Programme on Immunization. Vaccination is recommended for visitors to rural areas of South East Asia and the Far East where infection is endemic and where the visit is to be for more than one month; it is also recommended for shorter visits in individuals likely to be at exceptional risk.

In the UK adults and children over 3 years who are non-immune travellers are usually given 3 doses each of 1 mL of the inactivated mouse-brain vaccine subcutaneously at 0, 7 to 14, and 28 to 30 days; full immunity will take up to one month to develop. A two-dose schedule with doses given 7 to 14 days apart may provide short-term immunity but is less effective; in the USA, an abbreviated dosage schedule with doses at 0, 7, and 14 days is suggested if time is not available for the standard schedule. Children under 3 years of age may be given 3 doses of 0.5 mL; in the USA, the vaccine is not recommended for children under 1 year. Reinforcing doses may be needed but the interval at which they are given varies with the vaccine preparation.

In areas where JE is endemic, primary immunisation with inactivated vaccines has been given according to a different schedule. Although the ages and schedule of subsequent boosters varies in different countries, the same schedule is used for primary immunisation. The first dose is given at age 6 months to 3 years according to the country, but in all cases is followed by a second dose 1 to 4 weeks later and then a third after 1 year. Live attenuated Japanese encephalitis vaccines are also used, in single or 2-dose schedules (see below), in some countries in the Far East where disease is endemic.

◊ Inactivated Japanese encephalitis vaccines have been widely used in Asia for some years. In Japan, the incidence of the disease has decreased since the introduction of nationwide vaccination in the mid-1960s.

A live attenuated vaccine, SA14-14-2, is widely used in China and is replacing the use of inactivated vaccine. Studies[1,2] with the live attenuated vaccine showed that 2 doses given a year apart were 97% effective in an endemic region of rural China. Similar results were obtained when the interval between doses was reduced to 1 to 3 months. A further case-control study[3] in Nepal found that single-dose administration was more than 99% effective.

Other vaccines are under development including recombinant DNA and chimeric vaccines. Recombinant vaccines delivered using poxvirus vectors were also investigated but research appears to have been halted.[4,5]

1. Hennessy S, *et al.* Effectiveness of live-attenuated Japanese encephalitis vaccine (SA14-14-2): a case-control study. *Lancet* 1996; **347:** 1583–6.
2. Tsai TF, *et al.* Immunogenicity of live attenuated SA14-14-2 Japanese encephalitis vaccine—a comparison of 1- and 3-month immunization schedules. *J Infect Dis* 1998; **177:** 221–3.
3. Bista MB, *et al.* Efficacy of single-dose SA 14-14-2 vaccine against Japanese encephalitis: a case control study. *Lancet* 2001; **358:** 791–5.
4. Tauber E, *et al.* Safety and immunogenicity of a Vero-cell-derived, inactivated Japanese encephalitis vaccine: a non-inferiority, phase III, randomised controlled trial. *Lancet* 2007; **370:** 1847–53.
5. Schiøler KL, *et al.* Vaccines for preventing Japanese encephalitis. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2007 (accessed 11/04/08).

Preparations
Proprietary Preparations (details are given in Part 3)
Austral.: JE-Vax; ***Canad.:*** JE-Vax; ***Cz.:*** JE-Vax†; ***Thai.:*** JE-Vaccine; ***USA:*** JE-Vax.

Jellyfish Venom Antisera
Antisuero contra el veneno de la medusa; Jellyfish Antivenins; Jellyfish Antivenoms.

Adverse Effects and Precautions
As for antisera in general, p.2201.

Uses and Administration
An antiserum for use in the management of severe stings by the box jellyfish or sea wasp *Chironex fleckeri* is available in Australia. The preparation contains the specific antitoxic globulins that neutralise the venom of *Chironex fleckeri* and is prepared from the serum of sheep immunised with the venom of the box jellyfish.

Box jellyfish antivenom is usually given by the intravenous route in a dose of 20 000 units. Alternatively, 60 000 units may be injected intramuscularly.

Jellyfish stings. Many stings caused by the box jellyfish *Chironex fleckeri* are of little consequence and can be managed by simple first aid measures; however, some can be rapidly fatal so immediate assessment is vital.[1] Fragments of tentacle adhering to the skin should be inactivated by the application of vinegar or 3 to 10% acetic acid solution. Cardiopulmonary resuscitation may be necessary in severe cases. The antiserum can be effective if given quickly and in adequate dosage,[2,3] although use is mainly reserved for those with cardiorespiratory instability, severe pain refractory to opioid analgesics, or at risk of significant scarring.[1,3] Some experimental evidence suggested that verapamil might be useful for treatment of the cardiotoxic effects of the venom and allow more time for the antiserum to exert its action,[1,4] but is now considered to be contraindicated.[3] Some have suggested that the *Chironex fleckeri* antiserum may be effective for severe envenomation by related species.[3,5]

Irukandji syndrome consists of several hypercatecholaminergic symptoms (such as generalised pain, distress, hypertension, cardiomyopathy, and pulmonary oedema) arising from envenomation with the small box jellyfish *Carukia barnesi*.[1,6] Treatment is essentially symptomatic and supportive. The *Chironex fleckeri* antivenom is not effective.[3,5] Acetic acid may also be helpful for stings by related species (see p.2244).

1. Bailey PM, *et al.* Jellyfish envenoming syndromes: unknown toxic mechanisms and unproven therapies. *Med J Aust* 2003; **178:** 34–7.
2. Fenner PJ, *et al.* Successful use of chironex antivenom by members of the Queensland Ambulance Transport Brigade. *Med J Aust* 1989; **151:** 708–10.
3. Tibballs J. Australian venomous jellyfish, envenomation syndromes, toxins and therapy. *Toxicon* 2006; **48:** 830–59.
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Leishmaniasis Vaccines
Vacunas de la leishmaniasis.

Profile
Vaccines containing *Leishmania* spp. are under investigation in an attempt to prevent cutaneous leishmaniasis.

◊ The inoculation of an infective strain of a *Leishmania* sp. into the skin, a technique known as leishmanisation, has been used to protect against cutaneous leishmaniasis (p.824). Although the technique has been standardised it is not generally recommended since large, slow-healing lesions have occurred in some patients. There is currently no effective vaccine for any form of leishmaniasis. First-generation vaccines containing killed leishmanial promastigotes, with or without BCG as an adjuvant, have been developed and tested in humans. These have conferred some protection against cutaneous disease but it has waned relatively quickly in some cases. They have not been found to confer protection against visceral leishmaniasis. New studies are ongoing investigating the use of alum as an adjuvant. There is also further investigation into second-generation vaccines using different approaches such as the use of surface antigens (gp63 and lipophosphoglycan), promastigote antigen from *L. amazonensis*, enzyme receptor (LACK), Th1-driving adjuvant such as interleukin-12, oligodeoxynucleotides with leishmanial antigens, or recombinant leishmanial antigen (TSA, LmSTI-1), all of which have conferred some protection in *mice*. A glycoprotein-enriched *L. donovani* promastigote vaccine (*Leishmune*®) is available for prophylactic veterinary use in Brazil. DNA constructs encoding gp63 and LACK have also conferred protection against *L. major* in *mice*. A chimeric vaccine has also been developed combining three leishmanial antigens (LeIF, LmSTI-1, and TSA) in monophosphoryl lipid A adjuvant but had, at best, mixed results in trials in *dogs*. Attenuated vaccines prepared by gene deletion have shown promise in *mice*. The saliva of sandflies (the vector) seems to enhance infectivity, and vaccines against salivary or gut antigens of the insect have also been investigated.

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2. Melby PC. Vaccination against cutaneous leishmaniasis: current status. *Am J Clin Dermatol* 2002; **3:** 557–70.
3. Mauel J. Vaccination against Leishmania infections. *Curr Drug Targets Immune Endocr Metabol Disord* 2002; **2:** 201–26.
4. Brodskyn C, *et al.* Vaccines in leishmaniasis: advances in the last five years. *Expert Rev Vaccines* 2003; **2:** 705–17.
5. WHO. State of the art of new vaccines: research & development. Information available at: http://www.who.int/vaccine_research/documents/stateoftheart/en/index.html (accessed 24/03/06)
6. Palatnik-de-Sousa CB. Vaccines for leishmaniasis in the fore coming 25 years. *Vaccine* 2008; **26:** 1709–24.

Leprosy Vaccines
Vacunas de la lepra.

Profile
Vaccines against leprosy including those using *Mycobacterium leprae*, as well as other mycobacteria, are under investigation. A killed vaccine has been developed in India for use as an adjunct to standard multidrug therapy in the treatment of leprosy. Although studies of new vaccines are continuing, BCG vaccine (p.2207) also appears to be effective.

◊ Leprosy vaccines are being studied both to prevent infection with *M. leprae* (immunoprophylaxis) and to prevent disease in infected individuals (immunotherapeutic). Attempts to develop a vaccine against leprosy are based on the assumption that induction of a cell-mediated immune response to *Mycobacterium leprae* will lead to protection against the bacillus. Several vaccines have been studied and include BCG, BCG plus heat-killed *M. leprae*, heat-killed *Mycobacterium w*, and ICRC (Indian Cancer Research Centre) bacillus. The fortuitous finding that BCG vaccine, which is inexpensive and widely available, is effective against leprosy has important implications for leprosy control. Considerable **immunoprophylaxis** against leprosy is afforded by BCG vaccination (see p.2207), and a study in Malawi showed that repeated vaccination provided additional protection.[1] However, the addition of killed *M. leprae* did not produce any further improvement, confirming preliminary results of a study in Venezuela.[2] However, in a report of their sixth meeting,[3] the WHO Technical Advisory Group on the Elimination of Leprosy reported superior vaccine efficacy for BCG plus heat-killed *M. leprae* than with BCG alone in a prophylactic leprosy vaccine study in south India. The study was begun in 1991 and involved 171 400 subjects who received either BCG alone, BCG plus heat-killed *M. leprae*, *Mycobacterium w*, ICRC bacillus, or placebo. Three surveys of the results have since been conducted by way of follow-up; the preliminary findings of the latest of these surveys revealed that the overall efficacy rates for the vaccines were 22% for BCG alone, 67% for BCG plus heat-killed *M.leprae*, 41% for *Mycobacterium w*, and 51% for ICRC bacillus. Within these results, the findings specifically for efficacy in contacts of patients with leprosy were 11% for BCG alone, 88% for BCG plus heat-killed *M. leprae*, 87% for *Mycobacterium w*, and 11% for ICRC bacillus. Further studies are being conducted in Brazil regarding the use of BCG for booster doses in schoolchildren, and also for its use in household contacts.

Beneficial responses have been reported[4-10] from the **immunotherapeutic** use of *Mycobacterium w* vaccine with standard multidrug therapy (p.176) although a small increase in Type 1 lepra reactions has been observed.[9-11] A similar, and possibly identical, vaccine based on the ICRC bacillus has also been evaluated.[12,13] Immunotherapy with BCG and heat killed *M.leprae* has produced beneficial responses when given as an adjunct to chemotherapy.[14] WHO has suggested that the immunotherapeutic use of vaccines may ultimately prove to be more clinically relevant than the immunoprophylactic use,[12] and high compliance with immunotherapy appears to be attainable.[15]

1. Karonga Prevention Trial Group. Randomised controlled trial of single BCG, repeated BCG, or combined BCG and killed Mycobacterium leprae vaccine for prevention of leprosy and tuberculosis in Malawi. *Lancet* 1996; **348:** 17–24.
2. Convit J, *et al.* Immunoprophylactic trial with combined Mycobacterium leprae/BCG vaccine against leprosy: preliminary results. *Lancet* 1992; **339:** 446–50.
3. WHO. Report on the sixth meeting of the WHO Technical Advisory Group on the Elimination of Leprosy: Geneva, February 2004. Available at: http://www.ops-oms.org/English/AD/DPC/CD/lep-TAG-6.pdf (accessed 01/04/08)
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5. Zaheer SA, *et al.* Immunotherapy with Mycobacterium w vaccine decreases the incidence and severity of type 2 (ENL) reactions. *Lepr Rev* 1993; **64:** 7–14.
6. Zaheer SA, *et al.* Addition of immunotherapy with Mycobacterium w vaccine to multi-drug therapy benefits multibacillary leprosy patients. *Vaccine* 1995; **13:** 1102–10.
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8. Talwar GP. An immunotherapeutic vaccine for multibacillary leprosy. *Int Rev Immunol* 1999; **18:** 229–49.
9. De Sarkar A, *et al.* Impact of combined Mycobacterium w vaccine and 1 year of MDT on multibacillary leprosy patients. *Int J Lepr Other Mycobact Dis* 2001; **69:** 187–94.
10. Kaur I, *et al.* Combined 12-month WHO/MDT MB regimen and Mycobacterium w vaccine in multibacillary leprosy: a follow-up of 136 patients. *Int J Lepr Other Mycobact Dis* 2002; **70:** 174–81.
11. Kar HK, *et al.* Reversal reaction in multibacillary leprosy patients following MDT with and without immunotherapy with a candidate for an antileprosy vaccine, Mycobacterium w. *Lepr Rev* 1993; **64:** 219–26.
12. Mangla B. Leprosy vaccine debate in India re-ignited. *Lancet* 1993; **342:** 233.
13. Jayaraman KS. Charges fly over rival leprosy vaccines. *Nature* 1994: **367:** 403.
14. Rada E, *et al.* A follow-up study of multibacillary Hansen's disease patients treated with multidrug therapy (MDT) or MDT + immunotherapy (IMT). *Int J Lepr* 1997; **65:** 320–7.

15. Walia R, *et al.* Field trials on the use of Mycobacterium w vaccine in conjunction with multidrug therapy in leprosy patients for immunotherapeutic and immunoprophylactic purposes. *Lepr Rev* 1993; **64:** 302–11.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Immuvac.

Leptospirosis Vaccines

Leptospira Vaccines; Vacunas de la leptospirosis.

Profile

Leptospirosis vaccines prepared from killed *Leptospira interrogans* are available in some countries. They are used for active immunisation against leptospirosis icterohaemorrhagica (spirochaetal jaundice; Weil's disease) in persons at high risk of contracting the disease.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Spirolept; ***Switz.:*** Spirolept.

Lyme Disease Vaccines

Vacunas de la enfermedad de Lyme.

Profile

Vaccines based on recombinant outer surface proteins of *Borrelia burgdorferi* were developed and used in some countries for active immunisation against Lyme disease in persons at risk of contracting the disease.

Lyme arthritis refractory to treatment with antibacterials has occurred rarely as an immune reaction to vaccine-derived outer surface proteins of *Borrelia burgdorferi*.

Malaria Vaccines

Vacunas del paludismo.

Profile

Malaria vaccines acting against the sporozoite, asexual, and sexual stages of the *Plasmodium falciparum* life cycle are under investigation, as well as multicomponent vaccines consisting of combined antigens from various stages.

Vaccine development. Chemoprophylaxis of malaria is becoming increasingly problematical (see p.594), resulting in the increased desirability of effective malaria vaccines, several of which have been, or are being, studied clinically. The various approaches to malaria vaccine development have been extensively reviewed.[1-15] Malaria vaccines can be categorised into 4 main groups:

- vaccines against pre-erythrocytic forms of the parasite, specifically the sporozoite and liver stages of infection. A sporozoite vaccine could prevent infection either via an antibody response to block invasion of liver cells or via a cell-mediated response to destroy infected liver cells by preventing release of parasites into the bloodstream. The most advanced of these vaccines are derived from the circumsporozoite antigen present on the sporozoite and the main vaccine candidate of this type is RTS,S/AS02A. This vaccine is comprised of the antigenic C-terminus of the circumsporozoite gene from *Plasmodium falciparum* fused to hepatitis B surface antigen and encouraging results in early studies in endemic African areas have been reported.[16] The US military is also investigating the possibility of DNA vaccines for malaria, including a liver-stage DNA candidate encoding the circumsporozoite (CS) protein of *P. falciparum*; however, this vaccine has so far failed to induce antigen-specific antibodies. A multiple-antigen version of this DNA vaccine, known as MuStDo5, encoding 5 different liver-stage antigens including CS is also under investigation. Some workers are investigating the prospect of priming with a DNA vaccine and boosting with recombinant antigen or viral vectors. There is also some development of vaccines that focus on the intracellular liver stage of the parasite, since some antigens expressed by sporozoites or merozoites can also be expressed by liver stage parasites
- vaccines against asexual erythrocytic stages, directed at the merozoite form of the parasite. These vaccines would be expected to reduce the severity and the duration of disease by decreasing the blood-parasite density; this effect correlates with reduced symptoms and risk of death. The most advanced asexual vaccine candidate is merozoite surface protein 1 (MSP-1), which forms part of a complex thought to be involved in erythrocyte invasion; antibodies to MSP-1 have been shown to block parasite entry to erythrocytes *in vitro*. Recombinant MSP-1 has also been shown to protect against lethal parasite challenge in *animal* studies. Several other merozoite surface proteins are also under development (MSP-2, 3, 4, 5, 8, and 9). A vaccine comprising MSP-1 and MSP-2 in combination with *P. falciparum* ring-infected erythrocyte (RESA) has recently shown a 62% reduction in parasite density in children in a study in Papua New Guinea. Two further promising asexual erythrocytic stage vaccine candidates are the apical membrane antigen-1 (AMA-1) and erythrocyte-binding antigen-175 (EBA-175)
- transmission-blocking vaccines to raise antibodies in humans against the gamete stage of the parasite present in the mosquito gut; these antibodies would then be taken up by the biting mosquito from in the blood and block further parasite development in the mosquito, thus rendering it non-infectious. Blocking transmission in this way could reduce infectivity of mosquitoes in that they would carry fewer parasites, and could extend the useful life of a pre-erythrocytic or erythrocytic vaccine by preventing transmission of antibody-resistant mutants. The most advanced candidate vaccines of this type contain the *P. falciparum* surface protein antigens Pfs-25 and Pfs-28 or the *P. vivax* homologues Pvs-25 and Pvs-28. Recombinant forms of these antigens are currently being investigated. Other similar sexual stage vaccines under development include Pfs-48/45 and Pfs-230
- vaccines against the toxins produced by the parasite that contribute to the disease itself. The glycosylphosphatidyl inositol (GPI) anchor, which binds several of the parasite's antigens to the erythrocyte membrane, has been shown to be highly toxic in *mouse* models, but has potential for disease attenuation if it can be detoxified and rendered safe.

A multi-antigen, multistage combination vaccine is thought to be the best approach to effective vaccination against malaria. One such vaccine, SPf66, a synthetic preparation of three antigens from the asexual phase of the parasite in the blood linked by a sporozoite antigen has been studied but little or no evidence for its protective efficacy has been found.[3] Another multicomponent vaccine, NYVAC-Pf7, using a recombinant vaccinia viral vector that expresses 7 proteins from different stages of malarial infection, has also been studied,[17] but results have been disappointing. A further multicomponent vaccine, CDC/NIIMALVAC-1 has provided encouraging preliminary results in *animals* and *in vitro*.[18]

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14. Pinzon-Charry A, Good MF. Malaria vaccines: the case for a whole-organism approach. *Expert Opin Biol Ther* 2008; **8:** 441–8.
15. Tyagi RK, *et al.* Various carrier system(s)-mediated genetic vaccination strategies against malaria. *Expert Rev Vaccines* 2008; **7:** 499–520.
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17. Ockenhouse CF, *et al.* Phase I/IIa safety, immunogenicity, and efficacy trial of NYVAC-Pf7, a pox-vectored, multiantigen, multistage vaccine candidate for Plasmodium falciparum malaria. *J Infect Dis* 1998; **177:** 1664–73.
18. Shi YP, *et al.* Immunogenicity and in vitro protective efficacy of a recombinant multistage Plasmodium falciparum candidate vaccine. *Proc Natl Acad Sci U S A* 1999; **96:** 1615–20.

Measles Immunoglobulins

Inmunoglobulinas contra el sarampión.

ATC — J06BB14.

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

Ph. Eur. 6.2 (Human Measles Immunoglobulin; Immunoglobulinum Humanum Morbillicum). A liquid or freeze-dried preparation containing immunoglobulins, mainly immunoglobulin G (IgG). It is obtained from plasma containing specific antibodies against the measles virus. Normal immunoglobulin may be added. It contains not less than 50 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

Measles immunoglobulins may be used for passive immunisation against measles. They have been used to prevent or modify measles in susceptible persons who have been exposed to infection; in the UK, normal immunoglobulin is usually given.

Preparations

Ph. Eur.: Human Measles Immunoglobulin.

Measles Vaccines

Vacunas del sarampión.

ATC — J07BD01.

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

Ph. Eur. 6.2 (Measles Vaccine (Live); Vaccinum Morbillorum Vivum). A freeze-dried preparation of a suitable live attenuated strain of measles virus grown in cultures of chick-embryo cells or human diploid cells. It is prepared immediately before use by reconstitution from the dried vaccine. The virus concentration is 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 Measles may be used on the label.

USP 31 (Measles Virus Vaccine Live). A bacterially sterile preparation of a suitable live strain of measles virus grown in cultures of chick-embryo cells. It contains not less than the equivalent of 1×10^3 $TCID_{50}$ in each immunising dose, and may contain suitable antimicrobial agents. It should be stored at 2° to 8° and be protected from light.

Adverse Effects

As for vaccines in general, p.2201.

Fever and skin rashes may occur after measles vaccines. The fever generally starts about 1 week after the injection, lasts for about 2 or 3 days, and has sometimes been accompanied by convulsions. More serious effects reported rarely include encephalitis and thrombocytopenia.

◊ Reviews.

1. Duclos P, Ward BJ. Measles vaccines: a review of adverse events. *Drug Safety* 1998; **19:** 435–54.

Incidence of adverse effects. Some brief comments made by the Advisory Committee on Immunization Practices in the USA on adverse effects of standard measles vaccines.[1] An excellent safety record of measles vaccines has been indicated by the experience gained through the use of more than 240 million doses up to 1993. Fever with a temperature of 39.4° or more may develop in 5 to 15% of vaccinees beginning 5-12 days after vaccination and usually lasts several days. Transient rashes have been reported in about 5% of vaccinees. CNS disorders, including encephalitis and encephalopathy, have been reported with a frequency of less than one case per million doses given. The incidence of encephalitis or encephalopathy after vaccination is lower than the incidence rate of encephalitis of unknown origin suggesting that such events after vaccination may be only temporally related to, rather than due to, vaccination.

1. Immunization Practices Advisory Committee. Update: vaccine side effects, adverse reactions, contraindications, and precautions. *MMWR* 1996; **45** (RR 12): 1–35.

Atypical measles. The atypical-measles syndrome has occurred in persons vaccinated against measles and later exposed to the natural infection. The syndrome has been characterised by high fever and atypical rash; abdominal pain has been common and pneumonia almost universal.[1] Although atypical measles has occurred particularly in patients given killed vaccine[1] (no longer used) it has been reported in recipients of live measles vaccines.[2,3]

Measles occurring in patients previously vaccinated with live measles vaccines may be mild and go unrecognised. However, secondary vaccine failure does not appear to be a major problem (see Immunisation Schedules under Uses, below).

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2. Chatterji M, Mankad V. Failure of attenuated viral vaccine in prevention of atypical measles. *JAMA* 1977; **238:** 2635.
3. Henderson JAM, Hammond DI. Delayed diagnosis in atypical measles syndrome. *Can Med Assoc J* 1985; **133:** 211–13.

Effects on hearing. There have been individual case reports of sensorineural hearing loss after measles vaccination.[1,2] Similar reports have been made after vaccination with measles and rubella vaccines (p.2223) and measles, mumps, and rubella vaccines (p.2223).

1. Watson JG. Bilateral hearing loss in a 3-year-old girl following measles immunisation at the age of 15 months. *Int J Pediatr Otorhinolaryngol* 1990; **19:** 189–90.
2. Jayarajan V, Sedler PA. Hearing loss following measles vaccination. *J Infect* 1995; **30:** 184–5.

Effects on the nervous system. ***GUILLAIN-BARRÉ SYNDROME.*** No association was found between measles vaccination and Guillain-Barré syndrome in an analysis of 2296 cases.[1]

1. da Silveira CM, *et al.* Measles vaccination and Guillain-Barré syndrome. *Lancet* 1997; **349:** 14–16.

OPTIC NEURITIS. For a report of optic neuritis in 2 children after being given measles and rubella vaccine, see under Adverse Effects of Measles and Rubella Vaccines, p.2223.

SUBACUTE SCLEROSING PANENCEPHALITIS. Subacute sclerosing panencephalitis (SSPE) is a rare complication of measles infection (p.860) and has been reported in children who have