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]

1. Webster D, Hill AVS. Progress with new malaria vaccines. *Bull WHO* 2003; **81:** 902–9.
2. Moorthy VS, *et al.* Malaria vaccine developments. *Lancet* 2004; **363:** 150–6.
3. Graves P, Gelband H. Vaccines for preventing malaria (SPf66). Available in The Cochrane Library; Issue 2. Chichester: John Wiley; 2006.
4. 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)
5. Graves P, Gelband H. Vaccines for preventing malaria (pre-erythrocytic). Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 10/06/08).
6. Graves P, Gelband H. Vaccines for preventing malaria (blood-stage). Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 10/06/08).
7. Tetteh KK, Polley SD. Progress and challenges towards the development of malaria vaccines. *BioDrugs* 2007; **21:** 357–73.
8. Matuschewski K, Mueller AK. Vaccines against malaria - an update. *FEBS J* 2007; **274:** 4680–7.
9. Mikolajczak SA, *et al.* Preerythrocytic malaria vaccine development. *Curr Opin Infect Dis* 2007; **20:** 461–6. Correction. *ibid.*; 656.
10. Genton B, Reed ZH. Asexual blood-stage malaria vaccine development: facing the challenges. *Curr Opin Infect Dis* 2007; **20:** 467–75.
11. Saul A. Mosquito stage, transmission blocking vaccines for malaria. *Curr Opin Infect Dis* 2007; **20:** 476–81.
12. Sharma S, Pathak S. Malaria vaccine: a current perspective. *J Vector Borne Dis* 2008; **45:** 1–20.
13. Vekemans J, Ballou WR. Plasmodium falciparum malaria vaccines in development. *Expert Rev Vaccines* 2008; **7:** 223–40.
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.
16. Alonso PL, *et al.* Duration of protection with RTS,S/ASO2A malaria vaccine in prevention of Plasmodium falciparum disease in Mozambican children: single-blind extended follow-up of a randomised controlled trial. *Lancet* 2005; **366:** 2012–12.
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).

1. Anonymous. The atypical-measles syndrome. *Lancet* 1979; **i:** 962–3.
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

received measles vaccine but have no history of clinical disease. Nevertheless mass measles vaccination has been effective in reducing the incidence of SSPE in both developing and industrialised countries,[1,2] and the risks of remaining unimmunised are considered to be greater than those arising from immunisation.

1. Anonymous. SSPE in the developing world. *Lancet* 1990; **336:** 600.
2. Immunization Practices Advisory Committee. Update: vaccine side effects, adverse reactions, contraindications, and precautions. *MMWR* 1996; **45** (RR 12): 1–35.

Effects on the skin. Stevens-Johnson syndrome was associated with measles vaccination in a 10-month-old infant.[1]

1. Hazir T, *et al.* Stevens-Johnson syndrome following measles vaccination. *J Pakistan Med Assoc* 1997; **47:** 264–5.

High-titre vaccines and mortality. After reports of excess mortality in children, especially among girls, who received high-titre Edmonston-Zagreb (EZ) measles vaccine,[1] WHO reversed its recommendation for the use of this vaccine in its Expanded Programme on Immunization in developing countries.[2,3] Subsequent study[4] of children who had received high-titre EZ vaccine showed adverse effects on the nutritional status in either sex, confirming a generally deleterious effect of the vaccine. Others, however, have argued that the problems associated with the use of EZ vaccine have been exaggerated.[5,6] A review[6] pointed out that excess mortality was not seen in all studies, and concluded that the problem was unlikely to be due to the vaccine itself.

1. Knudsen KM, *et al.* Child mortality following standard, medium or high titre measles immunization in West Africa. *Int J Epidemiol* 1996; **25:** 665–73.
2. Anonymous. High-titre measles vaccines dropped. *Lancet* 1992; **340:** 232.
3. WHO. Expanded Programme on Immunization; safety of high-titre measles vaccines. *Wkly Epidem Rec* 1992; **67:** 357–61.
4. Garenne M. Effect of Edmonston-Zagreb high-titre vaccine on nutritional status. *Lancet* 1994; **344:** 261–2.
5. Bennett JV, *et al.* Edmonston-Zagreb measles vaccine: a good vaccine with an image problem. *Pediatrics* 1999; **104:** 1123–4.
6. Aaby P, *et al.* High-titer measles vaccination before 9 months of age and increased female mortality: do we have an explanation? *Semin Pediatr Infect Dis* 2003; **14:** 220–32.

Precautions

As for vaccines in general, p.2202.

Measles vaccines are not generally recommended for children below the age of 1 year in whom maternal antibodies might prevent a response, but they have been given to younger infants when the risk of measles is particularly high (see Immunisation Schedules, under Uses, below, for further discussion).

Hypersensitivity. For discussion of precautions to be taken on giving measles vaccines to children allergic to egg, see Measles, Mumps, and Rubella Vaccines, p.2223.

Immunocompromised patients. For a discussion of the use of live vaccines in immunocompromised patients including those with HIV infection, see Precautions on p.2202.

As with other live vaccines, measles vaccine is generally not recommended for use in patients with impaired immunity, although combined measles, mumps, and rubella vaccine may be given to HIV-positive individuals unless they have severe immunosuppression or other contra-indications. WHO and UNICEF[1] recommend that children with suspected or confirmed HIV infection should receive a dose of measles vaccine at 6 months of age in addition to the scheduled dose at 9 months. Immunocompromised patients who come into contact with measles should be given normal immunoglobulin. Specific measles immunoglobulins (p.2221) have been used in some countries. Although measles vaccines have been given to immunocompromised patients without causing adverse effects[2] there have been some reports of severe reactions; disseminated measles infection was reported in a child with severe congenital immunodeficiency,[3] and fatal giant-cell pneumonitis was reported in an adult with AIDS.[4]

1. WHO. *EPI vaccines in HIV-infected individuals: 5 October 2001*. Available at: http://www.who.int/vaccines-diseases/diseases/HIV.shtml (accessed 22/06/04)
2. Krasinski K, Borkowsky W. Measles and measles immunity in children infected with human immunodeficiency virus. *JAMA* 1989; **261:** 2512–16.
3. Monafo WJ, *et al.* Disseminated measles infection after vaccination in a child with a congenital immunodeficiency. *J Pediatr* 1994; **124:** 273–6.
4. Angel JB, *et al.* Vaccine-associated measles pneumonitis in an adult with AIDS. *Ann Intern Med* 1998; **129:** 104–6.

Inflammatory bowel disease. Measles vaccination has been suggested as a possible factor in the development of inflammatory bowel disease.[1] However a case-control study involving 140 patients with inflammatory bowel disease provided no support for this hypothesis,[2] and measles virus has not been detected in biopsy specimens from patients with inflammatory bowel disease.[3] Later reviews[4-6] concluded that there is no evidence of any association between measles-containing vaccines and inflammatory bowel disease. A suggested link between measles vaccine-associated inflammatory bowel disease and autism is now refuted (see p.2223).

1. Thompson NP, *et al.* Is measles vaccination a risk factor for inflammatory bowel disease? *Lancet* 1995; **345:** 1071–4.
2. Feeney M, *et al.* A case-control study of measles vaccination and inflammatory bowel disease. *Lancet* 1997; **350:** 764–6.
3. Afzal MA, *et al.* Absence of measles-virus genome in inflammatory bowel disease. *Lancet* 1998; **351:** 646–7.
4. Davis RL, Bohlke K. Measles vaccination and inflammatory bowel disease: controversy laid to rest? *Drug Safety* 2001; **24:** 939–46.
5. Seagroatt V, Goldacre MJ. Crohn's disease, ulcerative colitis, and measles vaccine in an English population, 1979-1998. *J Epidemiol Community Health* 2003; **57:** 883–7.
6. Demicheli V, *et al.* Vaccines for measles, mumps and rubella in children. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 02/05/06).

Interactions

As for vaccines in general, p.2202

Vitamin A. Supplementation with vitamin A (see Deficiency States, p.1973) is now included as part of WHO's Expanded Programme on Immunization. There has been conflicting evidence of the effects of such supplementation on the response to measles vaccination. One study[1] reported a reduced immune response if vaccination occurs at 6 months (before the age at which measles vaccination is usually given in the EPI) while others[2,3] generally found no significant change in seroconversion or immune response in children vaccinated at 9 months (the age at which vaccination is generally started).

1. Semba RD, *et al.* Reduced seroconversion to measles in infants given vitamin A with measles vaccination. *Lancet* 1995; **345:** 1330–2.
2. Benn CS, *et al.* Randomised trial of effect of vitamin A supplementation on antibody response to measles vaccine in Guinea-Bissau, West Africa. *Lancet* 1997; **350:** 101–5.
3. Cherian T, *et al.* Effect of Vitamin A supplementation on the immune response to measles vaccination. *Vaccine* 2003; **23:** 2418–20.

Uses and Administration

Measles vaccines are used for active immunisation against measles. Measles strains currently used in vaccines are usually the more attenuated Enders' attenuated Edmonston strain or the Schwarz strain. A high-potency measles vaccine prepared from the Edmonston-Zagreb strain of measles virus was formerly used but was stopped because of evidence of increased mortality (see High-titre Vaccines and Mortality, under Adverse Effects, above).

For primary immunisation a combined measles, mumps, and rubella vaccine (p.2223) is usually used. For discussion of immunisation schedules, see below.

Measles vaccines are not generally recommended for children below the age of 1 year in whom maternal antibodies might prevent a response. However, they have been given to infants at 6 to 9 months of age in developing countries and in the USA in certain circumstances (such as during measles outbreaks) (see also Immunisation Schedules, below).

Single-antigen measles vaccines have also been used for prophylaxis after exposure to measles provided they are given within 72 hours of contact.

Administration. Several alternative routes of administration of measles vaccines have been investigated in an attempt to overcome some of the disadvantages of subcutaneous or intramuscular injection.[1] Aerosol administration has produced good responses in children over 9 months of age, although this route was not so effective in younger children.[2,3] Aerosol administration could be potentially useful for mass immunisation campaigns, a suggestion confirmed in a randomised study.[4]

Oral vaccines against measles, produced in edible plants, are under investigation.[5,6]

Work is currently underway to develop oral and/or nasal vaccines that will be suitable in infants less than 9 months of age, a time when they are vulnerable due to waning maternal antibodies.

1. Cutts FT, *et al.* Alternative routes of measles immunization: a review. *Biologicals* 1997; **25:** 323–38.
2. Hiremath GS, Omer SB. A meta-analysis of studies comparing the respiratory route with the subcutaneous route of measles vaccine administration. *Hum Vaccin* 2005; **1:** 30–6.
3. Low N, *et al.* Immunogenicity and safety of aerosolized measles vaccine: systematic review and meta-analysis. *Vaccine* 2008; **26:** 383–98.
4. Dilraj A, *et al.* Response to different measles vaccine strains given by aerosol and subcutaneous routes to schoolchildren: a randomised trial. *Lancet* 2000; **355:** 798–803.
5. Webster DE, *et al.* Appetising solutions: an edible vaccine for measles. *Med J Aust* 2002; **176:** 434–7.
6. Muller CP, *et al.* Immunogenic measles antigens expressed in plants: role as an edible vaccine for adults. *Vaccine* 2003; **21:** 816–19. Correction. *ibid.*; 3093.

Immunisation schedules. In the developed world measles vaccine (usually as measles, mumps, and rubella vaccine) is usually given in the second year of life. As a result of concern that measles vaccine would not elicit an appropriate immune response in young infants due to the persistence of maternal antibodies in circulation, vaccination has generally not been attempted in children under 12 months old. However, infants born to vaccinated mothers tend to have lower levels of maternal antibodies and are susceptible to measles infection at under 12 months of age; vaccination has been shown to be effective at 6 to 9 months of age in such children,[1-3] although antibody titres were lower in infants vaccinated at 6 months of age than in those vaccinated later.[1,4]

In the UK and USA, routine vaccination is given at between 12 and 15 months, with a second dose given at between 4 and 6 years (see the immunisation schedules summarised under Vaccines, p.2202). Similar schedules are used in other countries. There is evidence that these 2-dose strategies will produce high levels of immunity in the community. During an outbreak of measles, vaccination may be given as early as 6 months of age;[5] revaccination is recommended in any child who is vaccinated before their first birthday. Vaccine may be given to non-immune persons of any age considered to be at risk of infection even if their immune status is uncertain.

For discussion of immunisation schedules in the developing world, see under Expanded Programme on Immunization, below.

1. Johnson CE, *et al.* Measles vaccine immunogenicity in 6- versus 15-month-old infants born to mothers in the measles vaccine era. *Pediatrics* 1994; **93:** 939–44.
2. Carson MM, *et al.* Measles vaccination of infants in a well-vaccinated population. *Pediatr Infect Dis J* 1995; **14:** 17–22.
3. Markowitz LE, *et al.* Changing levels of measles antibody titers in women and children in the United States: impact on response to vaccination. *Pediatrics* 1996; **97:** 53–8.
4. Gans HA, *et al.* Deficiency of the humoral immune response to measles vaccine in infants immunized at age 6 months. *JAMA* 1998; **280:** 527–32.
5. De Serres G, *et al.* Effectiveness of vaccination at 6 to 11 months of age during an outbreak of measles. *Pediatrics* 1996; **97:** 232–5.

EXPANDED PROGRAMME ON IMMUNIZATION. Measles remains a leading cause of death among young children, despite the availability of a safe and effective vaccine for the past 40 years. WHO estimated 454 000 people, the majority of them children, died from measles and measles complications in 2004.

In the developed world measles vaccine (usually as measles, mumps, and rubella vaccine) is usually given in the second year of life. If given earlier, passively-acquired maternal antibodies against measles may interfere with development of protective immunity.

In the developing world, protection given by maternal antibodies is often rapidly lost and in hyperendemic areas, such as urban and peri-urban areas, clinical measles may occur in children as young as 5 to 6 months of age. Immunisation against measles is part of WHO's Expanded Programme on Immunization. The first dose of measles vaccine is given to children at the age of 9 months or shortly thereafter. A 'second opportunity' for immunisation is provided to all children (either through routine immunisation campaigns or by targeted supplementary activities depending on local need). This assures measles immunity in children who failed to receive a previous dose of measles vaccine, as well as in those who were vaccinated but failed to develop immunity following vaccination (about 10 to 15% of those children vaccinated at 9 months of age).

Immunisation for travellers. WHO recommends that all travellers from the age of 6 months who have not been immunised should be offered measles vaccine. Infants who are travelling to areas where measles is endemic and who receive the first dose of measles vaccine between the ages of 6 to 8 months should also receive the scheduled primary immunisation doses later.[1]

It is generally recommended that individuals with at least a moderate degree of immune deficiency should receive measles vaccine even when travelling to areas with a low risk of contracting the disease.[1]

1. WHO. *International travel and health* 2008 ed. Available at: http://www.who.int/ith/en/ (accessed 13/04/08)

Preparations

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

Proprietary Preparations (details are given in Part 3)
Arg.: Lirugen†; ***Austral.:*** Rimevax; ***Braz.:*** Rouvax†; ***Cz.:*** Movivac; ***Denm.:*** Attenuvax†; ***Fr.:*** Rouvax; ***Ger.:*** Masern-Impfstoff Merieux; ***Gr.:*** Rouvax†; ***India:*** M-Vac; ***Israel:*** Rimevax†; Rouvax; ***Ital.:*** Morbilvax†; Rouvax†; ***Malaysia:*** Rimevax†; ***Mex.:*** Rimevax; ***Neth.:*** Attenuvax†; ***NZ:*** Rimevax; ***Philipp.:*** Rouvax; ***Pol.:*** Rouvax; ***S.Afr.:*** Diplovax; Morbilvax; Rimevax; Rouvax; ***Spain:*** Amunovax†; Rimevax; ***Switz.:*** Attenuvax; Moraten; Rimevax†; ***Thai.:*** Morbilvax†; Rouvax†; ***Turk.:*** Rouvax; ***USA:*** Attenuvax; ***Venez.:*** Imovax Sarampion†.

Measles and Mumps Vaccines

Vacunas del sarampión y la parotiditis.
ATC — J07BD51.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

See also under Measles Vaccines, p.2221, and Mumps Vaccines, p.2225.

Effects on the bones and joints. For a reference to arthritis occurring after measles and mumps vaccine, see under Adverse Effects and Precautions of Measles, Mumps, and Rubella Vaccines, p.2223.

Interactions

As for vaccines in general, p.2202.

See also under Measles Vaccines, p.2222.

Uses and Administration

Measles and mumps vaccines may be used for active immunisation although for primary immunisation a combined measles,