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,

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)
Cz.: Mopavac; ***Ger.:*** M-M Vax†.

Measles and Rubella Vaccines

Vacunas del sarampión y la rubéola.
ATC — J07BD53.

Pharmacopoeias. Many pharmacopoeias, including *US*, have monographs.
USP 31 (Measles and Rubella Virus Vaccine Live). Bacterially sterile preparation of suitable live strains of measles virus and live rubella virus. It may contain suitable antimicrobial agents. Each labelled dose provides an immunising dose of each component. It should be stored at 2° to 8° and be protected from light.

Adverse Effects and Precautions

As for vaccines in general, p.2201.
See also under Measles Vaccines, p.2221, and Rubella Vaccines, p.2236.

Incidence of adverse effects. Eight million children aged between 5 and 16 years were immunised with a measles and rubella vaccine in 1994 in the UK. By October 1995 the UK CSM had received reports on 2735 suspected adverse reactions most of which were minor and self-limiting.[1] Serious suspected reactions were rare and generally the number of reported cases was consistent with the background frequency of the particular disorder.

1. Committee on Safety of Medicines/Medicines Control Agency. Adverse reactions to measles rubella vaccine. *Current Problems* 1995; **21:** 9–10. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015633&RevisionSelectionMethod=LatestReleased (accessed 25/05/06)

Effects on hearing. Profound, irreversible sensorineural deafness was reported in a 27-year-old woman after administration of a measles and rubella vaccine.[1] Sensorineural deafness has also been reported after use of measles, mumps, and rubella vaccine (below), and monovalent measles vaccine (p.2221).

1. Hulbert TV, *et al.* Bilateral hearing loss after measles and rubella vaccination in an adult. *N Engl J Med* 1991; **325:** 134.

Effects on the nervous system. Optic neuritis was reported in 2 children given measles and rubella vaccine 2 to 3 weeks previously.[1]

1. Stevenson VL, *et al.* Optic neuritis following measles/rubella vaccination in two 13-year-old children. *Br J Ophthalmol* 1996; **80:** 1110–11.

Interactions

As for vaccines in general, p.2202.
See also under Measles Vaccines, p.2222.

Uses and Administration

Measles and rubella vaccines may be 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

USP 31: Measles and Rubella Virus Vaccine Live.

Proprietary Preparations (details are given in Part 3)
Braz.: Rudi-Rouvax†; ***Chile:*** MoRu-Viraten; ***Ital.:*** MoRu-Viraten†; ***Mex.:*** Moruviraten; ***Thai.:*** Rudi-Rouvax†.

Measles, Mumps, and Rubella Vaccines

Vacunas del sarampión, la parotiditis y la rubéola.
ATC — J07BD52.

Pharmacopoeias. Many pharmacopoeias, including *Eur.* (see p.vii) and *US*, have monographs.
Ph. Eur. 6.2 (Measles, Mumps and Rubella Vaccine (Live); Vaccinum Morbillorum, Parotitidis et Rubellae Vivum). A freeze-dried preparation containing suitable live attenuated strains of measles virus, mumps virus (*Paramyxovirus parotitidis*), and rubella virus. The vaccine is prepared immediately before use by reconstitution from the dried vaccine. It contains in each dose not less than 3.0 log $CCID_{50}$ of infective measles virus, not less than 3.7 log $CCID_{50}$ of infective mumps virus, and not less than 3.0 log $CCID_{50}$ of infective rubella virus. The dried vaccine should be stored at 2° to 8° and be protected from light.
The BP 2008 states that MMR may be used on the label.
USP 31 (Measles, Mumps, and Rubella Virus Vaccine Live). A bacterially sterile preparation of suitable live strains of measles virus, mumps virus, and rubella virus. It may contain suitable antimicrobial agents. Each labelled dose provides an immunising dose of each component. It should be stored at 2° to 8° and be protected from light.

Adverse Effects and Precautions

As for vaccines in general, p.2201.
See also under Measles Vaccines, p.2221, Mumps Vaccines, p.2225, and Rubella Vaccines, p.2236.
Events due to the measles component usually occur 6 to 11 days after vaccination and those due to the mumps and rubella components after 2 to 3 weeks but may occur up to 6 weeks after vaccination.
Adverse effects tend to be less frequent after the second dose of vaccine than after the first dose.
Measles, mumps, and rubella vaccines should not be given to individuals with a confirmed anaphylactic reaction to any antibacterial such as neomycin or kanamycin, that may be used in the manufacturing process.
Recommendations on vaccination in persons with egg allergy are discussed under Hypersensitivity, below.

Incidence of adverse effects. A double-blind placebo-controlled crossover study[1] in 581 pairs of twins showed that the frequency of adverse effects from the use of measles, mumps and rubella (MMR) vaccine was between 0.5 and 4.0%, indicating that adverse reactions are much less common than was previously thought. A study in the USA[2] showed that children given the vaccine at age 4 to 6 years had fewer adverse effects than those given it at 10 to 12 years. A later study[3] based on family reported symptoms was unable to detect any vaccine-related adverse effects when the second dose of MMR vaccine was given at either 4 to 6 years or 10 to 12 years. Vaccine-related adverse effects after the first dose of MMR vaccine were reported in about 17% in those vaccinated between the age of 12 and 20 months.
A further study[4] that assessed the effect of almost 3 million doses of vaccines in 1.8 million individuals revealed that 173 potentially serious reactions were claimed to have been caused by vaccination. There were 77 neurologic, 73 allergic, and 22 miscellaneous reactions recorded, and 1 death reported. However, 45% of the reactions were probably caused by some other factor. It was therefore concluded that serious events caused by MMR vaccine are rare and are greatly outweighed by the risks of the natural diseases.

1. Peltola H, Heinonen OP. Frequency of true adverse reactions to measles-mumps-rubella vaccine: a double-blind placebo-controlled trial in twins. *Lancet* 1986; **i:** 939–42.
2. Davis RL, *et al.* MMR2 immunization at 4 to 5 years and 10 to 12 years of age: a comparison of adverse clinical events after immunization in the vaccine safety datalink project. *Pediatrics* 1997; **100:** 767–71.
3. LeBaron CW, *et al.* Evaluation of potentially common adverse events associated with the first and second doses of measles-mumps-rubella vaccine. *Pediatrics* 2006; **118:** 1422–30.
4. Patja A, *et al.* Serious adverse events after measles-mumps-rubella vaccination during a fourteen-year prospective follow-up. *Pediatr Infect Dis J* 2000; **19:** 1127–34.

Effects on the blood. Thrombocytopenia occurs rarely in children receiving measles, mumps, and rubella vaccine and usually resolves spontaneously. The rubella component is considered to be the most likely cause. An increased incidence of thrombocytopenia after the second dose of the vaccine has been reported in children who developed thrombocytopenia after the first dose.[1] A study[2] by the UK Public Health Laboratory Service has suggested a link between measles, mumps, and rubella vaccine and the occurrence of idiopathic thrombocytopenic purpura, with an absolute risk of 1 in 22 300 of occurrence within 6 weeks of the first dose of the vaccine, and 2 out of every 3 cases attributable to it. Children with idiopathic thrombocytopenic purpura before receiving measles, mumps, and rubella vaccine experienced no vaccine-associated recurrences. A further study[3] of children aged 13 to 24 months and diagnosed with idiopathic thrombocytopenic purpura for the first time between January 1988 and December 1999 similarly found the attributable risk of developing it within 6 weeks of receiving the vaccine to be about 1 in 25 000. As a consequence of these findings, the UK CSM has recommended[4] that children developing idiopathic thrombocytopenic purpura within 6 weeks of vaccination with measles, mumps, and rubella vaccine, or any of its components, should have serological testing before their second dose is due; if this suggests that full immunity is not established, then a second dose should be given.

1. Vlacha V, *et al.* Recurrent thrombocytopenic purpura after repeated measles-mumps-rubella vaccination. *Pediatrics* 1996; **97:** 738–9.
2. Miller E, *et al.* Idiopathic thrombocytopenic purpura and MMR vaccine. *Arch Dis Child* 2001; **84:** 227–9.
3. Black C, *et al.* MMR vaccine and idiopathic thrombocytopaenic purpura. *Br J Clin Pharmacol* 2003; **55:** 107–11.
4. Committee on Safety of Medicines/Medicines Control Agency. MMR vaccine and idiopathic thrombocytopenic purpura. *Current Problems* 2001; **27:** 15. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON007456&RevisionSelectionMethod=LatestReleased (accessed 24/05/06)

Effects on the bones and joints. Arthralgia and arthritis occurring in patients given mumps, measles, and rubella vaccines have generally been attributed to the rubella component.[1] However, arthritis has been reported in an infant after vaccination with measles and mumps vaccine.[2]

1. Benjamin CM, *et al.* Joint and limb symptoms in children after immunisation with measles, mumps, and rubella vaccine. *BMJ* 1992; **304:** 1075–8.
2. Nussinovitch M, *et al.* Arthritis after mumps and measles vaccination. *Arch Dis Child* 1995; **72:** 348–9.

Effects on hearing. Nine cases of sensorineural hearing loss after measles, mumps, and rubella vaccine were reported to the UK CSM between 1988 and 1993.[1] Of these, 3 cases were judged not to have been associated with the vaccine. In the remaining 6, the mumps virus component was considered to be the most likely cause of deafness if the vaccine was to blame, but the risk was considered to be small compared with the risks of natural infection. However, sensorineural deafness has also been reported after measles and rubella vaccine (see above) and monovalent measles vaccine (see p.2221).

1. Stewart BJA, Prabhu PU. Reports of sensorineural deafness after measles, mumps, and rubella immunisation. *Arch Dis Child* 1993; **69:** 153–4.

Effects on the nervous system. Although there have been case reports[1] linking Guillain-Barré syndrome with measles, mumps, and rubella vaccine, a retrospective study[2] that involved 189 patients with the syndrome and about 630 000 recipients of the vaccine could not find a causal association.
Prolonged tonic-clonic seizures were associated with prolonged hemiparesis in a 16-month-old girl 6 days after measles, mumps, and rubella vaccination.[3] There was evidence of transient encephalopathy. However, a causal relationship between measles-containing vaccines and encephalitis is generally considered to be unlikely. Other reported neurological effects after vaccination include gait disturbances,[4,5] and transverse myelitis.[6] However, a retrospective study[7] found no evidence for a causal association between vaccination and acute ataxia and the development of gait disturbances and suggested the original reports represented chance occurrence.
For discussion of meningitis and encephalitis occurring after measles, mumps, and rubella vaccination, see under Adverse Effects of Mumps Vaccines, p.2225.

1. Morris K, Rylance G. Guillain-Barré syndrome after measles, mumps, and rubella vaccine. *Lancet* 1994; **343:** 60.
2. Patja A, *et al.* Risk of Guillain-Barré syndrome after measles-mumps-rubella vaccination. *J Pediatr* 2001; **138:** 250–4.
3. Sackey AH, Broadhead RL. Hemiplegia after measles, mumps, and rubella vaccination. *BMJ* 1993; **306:** 1169.
4. Plesner A-M. Gait disturbances after measles, mumps, and rubella vaccine. *Lancet* 1995; **345:** 316.
5. Plesner AM, *et al.* Gait disturbance interpreted as cerebellar ataxia after MMR vaccination at 15 months of age: a follow-up study. *Acta Paediatr* 2000; **89:** 58–63.
6. Joyce KA, Rees JE. Transverse myelitis after measles, mumps, and rubella vaccine. *BMJ* 1995; **311:** 422.
7. Miller E, *et al.* No evidence of an association between MMR vaccine and gait disturbance. *Arch Dis Child* 2005; **90:** 292–6.

Hypersensitivity. Since the measles and mumps components of measles, mumps, and rubella vaccines are grown in cell cultures of chick embryos the vaccine was formerly contra-indicated in individuals with a history of anaphylactic reactions to egg. In both the UK and USA, serious reactions to egg including anaphylaxis are no longer regarded as absolute contra-indications to vaccination although specialist advice should be obtained and vaccination performed only under controlled conditions. It is generally agreed that the vaccine can be given safely to children with less severe reactions to eggs.
A confirmed anaphylactic reaction to gelatin, kanamycin, or neomycin is a contra-indication to measles, mumps, and rubella vaccines.

Inflammatory bowel disease and autism. A controversial report[1] in 1998 linked measles, mumps, and rubella vaccination with the development of inflammatory bowel disease and behavioural abnormalities including autism. However, there is now overwhelming evidence from studies and analyses that the vaccine does not cause autism.[2-11] Similarly, the link between measles-containing vaccines and inflammatory bowel disease has not been substantiated (see under Precautions for Measles Vaccines, p.2222).

1. Wakefield AJ, *et al.* Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; **351:** 637–41.
2. Peltola H, *et al.* No evidence for measles, mumps, and rubella vaccine-associated inflammatory bowel disease or autism in a 14-year prospective study. *Lancet* 1998; **351:** 1327–8.
3. Roberts R. There is no causal link between MMR vaccine and autism. *BMJ* 1998; **316:** 1824.
4. Taylor B, *et al.* Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. *Lancet* 1999; **353:** 2026–9.
5. Kaye JA, *et al.* Mumps, measles, and rubella vaccine and the incidence of autism recorded by general practitioners: a time trend analysis. *BMJ* 2001; **322:** 460–3. Correction. *ibid.*; 720.
6. Dales L, *et al.* Time trends in autism and in MMR immunization coverage in California. *JAMA* 2001; **285:** 1183–5.
7. Halsey NA, *et al.* Measles-mumps-rubella vaccine and autistic spectrum disorder: report from the new challenges in childhood immunizations conference convened in Oak Brook, Illinois, June 12-13, 2000. Abstract: *Pediatrics* 2001; **107:** 1174. Full version: http://pediatrics.aappublications.org/cgi/content/full/107/5/e84 (accessed 14/12/04)
8. Smeeth L, *et al.* MMR vaccination and pervasive developmental disorders: a case-control study. *Lancet* 2004; **364:** 963–9.
9. Immunization Safety Review Committee. *Immunization safety review: vaccines and autism.* Washington DC: National Academy Press, 2004. Also available at: http://www.nap.edu/catalog/10997 (accessed 15/07/08)
10. 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)
11. Department of Health. *Immunisation Against Infectious Disease* 2006: "The Green Book". Available at: http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/GreenBook/GreenBookGeneralInformation/GreenBookGeneralArticle/fs/en?CONTENT_ID=4097254&chk=isTfGX (accessed 14/04/08)

Interactions

As for vaccines in general, p.2202.
See also under Measles Vaccines, p.2222.