

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.<sup>1</sup> 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](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.<sup>1</sup> 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.<sup>1</sup>

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; **Thal.:** 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, Parotiditis et Rubellae Vivum). A freeze-dried preparation containing suitable live attenuated strains of measles virus, mumps virus (*Paramyxovirus parotidis*), 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<sub>50</sub> of infective measles virus, not less than 3.7 log CCID<sub>50</sub> of infective mumps virus, and not less than 3.0 log CCID<sub>50</sub> 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<sup>1</sup> 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<sup>2</sup> 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<sup>3</sup> 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<sup>4</sup> 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, Heineonen 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.<sup>1</sup> A study<sup>2</sup> 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<sup>3</sup> 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<sup>4</sup> 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. Vlach A, *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 thrombocytopenic 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](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 vaccine have generally been attributed to the rubella component.<sup>1</sup> However, arthritis has been reported in an infant after vaccination with measles and mumps vaccine.<sup>2</sup>

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.<sup>1</sup> 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<sup>1</sup> linking Guillain-Barré syndrome with measles, mumps, and rubella vaccine, a retrospective study<sup>2</sup> 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.<sup>3</sup> 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,<sup>4,5</sup> and transverse myelitis.<sup>6</sup> However, a retrospective study<sup>7</sup> 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<sup>1</sup> 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.<sup>2–11</sup> 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. Smith 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=isTfXG](http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/GreenBook/GreenBookGeneralInformation/GreenBookGeneralArticle/fs/en?CONTENT_ID=4097254&chk=isTfXG) (accessed 14/04/08)

## Interactions

As for vaccines in general, p.2202.

See also under Measles Vaccines, p.2222.

The symbol † denotes a preparation no longer actively marketed