Uses and Administration

Measles, mumps, and rubella vaccines are used for active immunisation against measles, mumps, and rubella. They are used for primary immunisation in children 12 months of age or older and to protect susceptible contacts during an outbreak of measles. For discussion of immunisation schedules, see under Vaccines, p.2202.

In the UK, it is recommended that all children receive two doses of 0.5 mL of a measles, mumps, and rubella vaccine by intramuscular injection (or subcutaneously if there is a bleeding disorder). These are usually given shortly after the first birthday and before school entry, but may be given at any age if routine vaccination has been omitted, allowing 3 months between doses. The combined vaccine may also be used for prophylaxis after exposure to measles provided it is given within 72 hours of contact. However, it is not considered to be effective for postexposure prophylaxis against either mumps or rubella. If the vaccine is given before 12 months of age, re-immunisation will be necessary starting at between 12 and 15 months with a further dose according to national schedules.

Similar schedules are used in the USA.

Preparations

Ph. Eur.: Measles, Mumps, and Rubella Vaccine (Live);
USP 31: Measles, Mumps, and Rubella Virus Vaccine Live.

Proprietary Preparations (details are given in Part 3)
Arg.: MMR II; Trimovax; Triviraten; ***Austral.:*** MMR II†; Priorix; ***Austria:*** Priorix; ***Belg.:*** MMR Vax; Priorix; ***Braz.:*** MMR II†; Priorix†; Trimovax†; Vacina Comb. Contra Sarampo, Caxumba e Rubeola; Vacina Contra Sarampo, Caxumba e Rubeola; Vacina de Virus Vivos de Sarampo, Caxumba e Rubeola; ***Canad.:*** MMR II; Priorix; ***Cz.:*** MMR II; MMRVaxPro; Priorix; Trimovax†; Trivivac; ***Denm.:*** MMR; ***Fin.:*** MMR II; Priorix; ***Fr.:*** MMRVaxPro; Priorix; R.O.R.; ***Ger.:*** MMR Triplovax; MMR Vax; Priorix; ***Gr.:*** MMR II; MMRVaxPro; Priorix; ***Hong Kong:*** MMR II; Priorix; Trimovax; Triviraten†; ***Hung.:*** MMR II; ***India:*** Tresivac; ***Indon.:*** MMR II; Trimovax; ***Irl.:*** MMR II; Priorix; ***Israel:*** MMR II; Priorix; ***Ital.:*** MMR II; Morupar†; Priorix; ***Malaysia:*** MMR II; Priorix; Triviraten†; ***Mex.:*** MMR II; Morupar†; Priorix; ***Neth.:*** Priorix; ***Norw.:*** MMR II; Priorix; ***NZ:*** Priorix; Triviraten; ***Philipp.:*** Morupar†; Priorix; Trimovax; Triviraten; ***Pol.:*** MMR II; Priorix; Trimovax†; ***Port.:*** Priorix; ***Rus.:*** MMR II (ММР II); Priorix (Приорикс); ***S.Afr.:*** Morupar†; Priorix; Trimovax; ***Singapore:*** MMR II; Priorix; ***Spain:*** Priorix; Triviraten†; Vacuna Triple MSD; ***Swed.:*** MMR II; Priorix; ***Switz.:*** MMR II; Priorix; Triviraten; ***Thai.:*** MMR II; Morupar†; Priorix; Trimovax; Triviraten†; ***Turk.:*** MMR II; Priorix; Trimovax; Triviraten; ***UK:*** MMR II; Priorix; ***USA:*** MMR II; ***Venez.:*** Priorix; Trimovax†.

Multi-ingredient: ***NZ:*** MMR II.

Measles, Mumps, Rubella, and Varicella-Zoster Vaccines

ATC — J07BD54.

Profile

Measles, mumps, rubella, and varicella-zoster vaccines are used for active immunisation against measles, mumps, rubella and varicella (chickenpox).

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Priorix-Tetra; ProQuad; ***NZ:*** Priorix-Tetra; ***Port.:*** Priorix-Tetra; ProQuad; ***USA:*** ProQuad.

Meningococcal Vaccines

Vacunas de polisacáridos meningocócicos.

ATC — J07AH01; J07AH02; J07AH03; J07AH04; J07AH05; J07AH06; J07AH07.

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

Ph. Eur. 6.2 (Meningococcal Polysaccharide Vaccine; Vaccinum Meningitidis Cerebrospinalis). It consists of one or more purified capsular polysaccharides obtained from one or more suitable strains of *Neisseria meningitidis* group A, group C, group Y, and group W135; it may contain a single type of polysaccharide or any mixture of the types. It is prepared immediately before use by reconstitution from the stabilised freeze-dried vaccine with a suitable sterile liquid. The freeze-dried vaccine should be stored at 2° to 8° and be protected from light.

The BP 2008 states that Men plus the relevant antigen may be used on the label (for example MenAC).

Ph. Eur. 6.2 (Meningococcal Group C Conjugate Vaccine; Vaccinum Meningococcale Classis C Coniugatum). A liquid or freeze-dried preparation of purified capsular polysaccharide derived from a suitable strain of *Neisseria meningitidis* group C covalently linked to a carrier protein. The vaccine may contain an adjuvant. The freeze-dried vaccine should be stored at 2° to 8° and be protected from light.

The BP 2008 states that MenC(conj) may be used on the label.

Adverse Effects and Precautions

As for vaccines in general, p.2201.

Immunity to the unconjugated serogroup C polysaccharide in meningococcal vaccines may be insufficient to confer adequate protection against infection in infants under about 2 years of age.

Effects on the nervous system. From June 2005 to September 2006, 17 cases of Guillain-Barré syndrome were reported to the Vaccine Adverse Event Reporting System (VAERS) after use of a tetravalent (A, C, W135, and Y) meningococcal conjugate vaccine (Menactra). Whether the cases were caused by the vaccine or were coincidental was unknown.[1,2] The CDC recommends that persons with a history of Guillain-Barré syndrome should not be vaccinated with the tetravalent meningococcal conjugate vaccine.[2]

1. CDC. Guillain-Barré syndrome among recipients of Menactra meningococcal conjugate vaccine - United States, June-July 2005. *MMWR* 2005; **54:** 1023–5.
2. CDC. Update: Guillain-Barré syndrome among recipients of Menactra meningococcal conjugate vaccine— United States, June 2005-September 2006. *MMWR* 2006; **55:** 1120–4. Correction. *ibid.*; 1177.

Pregnancy and the neonate. A study[1] in 157 Asian women given a tetravalent polysaccharide vaccine in the third trimester of pregnancy found that immunisation was safe for both mothers and infants. Infants were provided with significantly increased levels of IgG for 2 to 3 months and of oral IgA for 6 months from breast feeding.

1. Shahid NS, *et al.* Placental and breast transfer of antibodies after maternal immunization with polysaccharide meningococcal vaccine: a randomized, controlled evaluation. *Vaccine* 2002; **20:** 2404–9.

Interactions

As for vaccines in general, p.2202.

Uses and Administration

Meningococcal vaccines are used for active immunisation against *Neisseria meningitidis* infections, which include meningitis and septicaemia. They are preparations of purified polysaccharide antigens from *N. meningitidis* and may be monovalent, containing the antigen of only one serotype of *N. meningitidis* or polyvalent, containing antigens of two or more serotypes. Conjugation of the polysaccharide to a carrier such as diphtheria CRM_{197} protein or to tetanus toxoid protein increases the immunogenicity.

In the UK, primary immunisation is recommended during infancy whereas in the USA routine immunisation is recommended during adolescence or for those at increased risk for meningococcal disease from 2 to 10 years of age. In the UK, a conjugate meningococcal C vaccine is used and is generally given by intramuscular injection with the subcutaneous route reserved for patients with haemophilia or thrombocytopenia. Infants, starting at 2 months of age, are given 3 doses of 0.5 mL at monthly intervals. If primary immunisation is delayed until 5 months of age then 2 doses, one month apart, are sufficient; children over 1 year of age and adults should be given a single dose only. In the USA, routine immunisation with a single dose, given intramuscularly, of a conjugate tetravalent vaccine from groups A, C, Y, and W135 is performed at 11 to 18 years of age if not previously vaccinated. For discussion of immunisation schedules see under Vaccines, p.2202.

Asplenic persons or those who have terminal complement component deficiencies are at higher than normal risk of acquiring meningococcal infection and therefore they should be immunised. Either a conjugate meningococcal C vaccine or a tetravalent vaccine (A, C, Y, and W135, unconjugated or conjugated) may be used depending on availability.

Meningococcal vaccines are also indicated in persons travelling to countries where the risk of infection is high. They should receive a tetravalent meningococcal polysaccharide vaccine (either unconjugated or conjugated) rather than the group C conjugate vaccine, and should be immunised even if they have already received the latter. Vaccination is indicated particularly for visits of 1 month or more and for those backpacking or living or working with local residents. Vaccination is a visa requirement for Hajj pilgrims to Saudi Arabia.

Meningococcal vaccines may be given as an adjunct to chemoprophylaxis in contacts of persons with meningitis (see p.178).

A meningococcal group B vaccine has been developed in New Zealand and contains outer membrane vesicles from *N. meningitidis* group B strain NZ 98/254. It is given for primary immunisation against the New Zealand strain (P1.7-b,4* PorA protein) of group B meningococcal disease. Adults and children over 6 months old are given three doses of 0.5 mL at intervals of 6 weeks intramuscularly; infants less than 6 months old should be given 4 doses, at 6 weeks, 3 months, 5 months, and 10 months of age. Vaccines against other group B meningococci are under investigation (see below).

◊ Reviews.

1. Ruggeberg J, Heath PT. Safety and efficacy of meningococcal group C conjugate vaccines. *Expert Opin Drug Saf* 2003; **2:** 7–19.

Vaccine development. Despite the established use of vaccines against meningococcal groups A, C, W135, and Y, about 60 to 80% of meningococcal infections (p.179) in the UK and the USA are caused by *Neisseria meningitidis* of group B serotype. Unfortunately the purified group B polysaccharide is only poorly immunogenic, even after conjugation with proteins but several avenues of research are being followed in the development of an effective vaccine. These include vaccines based on other outer membrane proteins contained in outer membrane vesicles, in particular the most important outer membrane proteins, PorA, and on lipopolysaccharide derivatives. More recently, group B meningococcal vaccine based on PorA has been developed in New Zealand (see above) and is available for primary immunisation against the New Zealand strain specifically, and has resulted in a marked reduction in incidence in that country. Recombinant technology has been used in the Netherlands to develop both a monovalent PorA vaccine and a hexavalent vaccine containing 6 PorA proteins, including that of the New Zealand strain. Results obtained with the New Zealand PorA antigen in the hexavalent formulation have been poor, but it has been shown to stimulate a satisfactory immune response in infants or small children in the monovalent form. The successful sequencing of the meningococcal genome has allowed discovery of several new proteins and raised potential for the development of new candidate vaccines, including novel surface-located vaccine candidates which are currently in preclinical evaluation.

An intranasal meningococcal group B vaccine is also under development.

References.

1. Katial RK, *et al.* Immunogenicity and safety testing of a group B intranasal meningococcal native outer membrane vesicle vaccine. *Infect Immun* 2002; **70:** 702–7.
2. Jodar L, *et al.* Development of vaccines against meningococcal disease. *Lancet* 2002; **359:** 1499–1508.
3. Vermont CL, van den Dobbelsteen GP. Meningococcal serogroup B infections: a search for a broadly protective vaccine. *Expert Rev Vaccines* 2003; **2:** 673–81.
4. Broker M. Development of new vaccines against meningococcal disease. *Arzneimittelforschung* 2003; **53:** 805–13.
5. Zimmer SM, Stephens DS. Meningococcal conjugate vaccines. *Expert Opin Pharmacother* 2004; **5:** 855–63.
6. Zimmer SM, Stephens DS. Serogroup B meningococcal vaccines. *Curr Opin Investig Drugs* 2006; **7:** 733–9.
7. Holst J. Strategies for development of universal vaccines against meningococcal serogroup B disease: the most promising options and the challenges evaluating them. *Hum Vaccin* 2007; **3:** 290–4.
8. Kelly C, *et al.* A prospective study of the effectiveness of the New Zealand meningococcal B vaccine. *Am J Epidemiol* 2007; **166:** 817–23.
9. McNicholas A, *et al.* Surveillance of vaccine breakthrough cases following MeNZB vaccination. *N Z Med J* 2008; **121:** 38–46.
10. van Alphen L, van den Dobbelsteen G. Meningococcal B vaccine development and evaluation of efficacy. *Hum Vaccin* 2008; **4:** 158–61.
11. WHO: Initiative for Vaccine Research (IVR). Neisseria meningitidis. Information available at: http://www.who.int/vaccine_research/diseases/soa_bacterial/en/index2.html (accessed 13/04/06)

Preparations

Ph. Eur.: Meningococcal Group C Conjugate Vaccine; Meningococcal Polysaccharide Vaccine.

Proprietary Preparations (details are given in Part 3)
Arg.: Antimeningococica A+C; Meningitec†; Menjugate; NeisVac-C; Va-Mengoc-BC; ***Austral.:*** Mencevax ACWY; Meningitec; Menjugate; Menomune; NeisVac-C; ***Austria:*** Mencevax ACWY; Meningitec; Menomune; NeisVac-C; ***Belg.:*** Mencevax ACWY; Meningitec; Meningovax A+C†; Menjugate; NeisVac-C; ***Braz.:*** Va-Mengoc-BC†; Vacina Meningococica A+C; Vacina Meningococica Conjugada Grupo C; ***Canad.:*** Meningitec; Menjugate; Menomune; NeisVac-C; ***Chile:*** Meningo A+C; ***Cz.:*** Menjugate; Menpovax A+C†; NeisVac-C; ***Denm.:*** Meningovax A+C; NeisVac-C; ***Fin.:*** Mencevax ACWY; Meningovax A+C; NeisVac-C; ***Fr.:*** Meningitec; Meninvact; Menjugate; Menomune; NeisVac; ***Ger.:*** Mencevax ACWY; Meningitec; Meningokokken-Impfstoff A + C; Menjugate; NeisVac-C; ***Gr.:*** Meningitec; Meninvact; Menjugate; Menomune; NeisVac-C; Vaccin Meningococcique; ***Hong Kong:*** Mencevax ACWY; Meningococcal A+C†; ***Hung.:*** Mencevax ACWY; Meningitec; Menjugate; NeisVac-C; ***Indon.:*** Mencevax ACWY; ***Irl.:*** Mengivac (A+C)†; Meningitec; Menjugate; ***Israel:*** Mencevax AC†; Mencevax ACWY; ***Ital.:*** Mencevax ACWY; Meningitec; Meninvact; Menjugate; Menomune; NeisVac-C; ***Malaysia:*** Mencevax ACWY; Menomune†; ***Neth.:*** Meningovax A+C; Meninvact; Menjugate; NeisVac-C; ***Norw.:*** Mencevax AC; Meningitec; Meningovax A+C; NeisVac-C; ***NZ:*** Mencevax ACWY; Meningitec; Menomune; MeNZB; ***Philipp.:*** Euro A & C; ***Pol.:*** NeisVac-C; ***Port.:*** Meningitec; Menjugate; NeisVac-C; ***Rus.:*** Mencevax ACWY (Менцевакс АСWY); ***S.Afr.:*** Imovax Meningo A & C; Mencevax; ***Singapore:*** Mencevax ACWY; Menomune; ***Spain:*** Mencevax AC; Meningitec; Meninvact†; Menjugate; NeisVac-C; Vacuna Antimeningococica A+C; ***Swed.:*** Meningitec†; Meningovax A+C; NeisVac-C; ***Switz.:*** Mencevax ACWY; Meningitec; Menjugate; NeisVac-C; ***Thai.:*** Meningococcal A+C†; Menomune; ***Turk.:*** Imovax Meningo A+C; ***UK:*** ACWY Vax; Mengivac (A+C)†; Meningitec; Menjugate; NeisVac-C; ***USA:*** Menactra; Menomune; ***Venez.:*** Imovax Meningo A+C†; Mencevax ACWY†.