4.9 MEASLES

4.9.1 Virology

Measles is a paramyxovirus, genus *Morbillivirus*. It is an RNA virus with six structural proteins, three complexed to the RNA and three associated with the viral envelope. Two of the envelope proteins, the F (fusion) protein and the H (haemagglutinin) protein, are the most important in pathogenesis. The measles virus can survive for up to 2 hours in air, but is rapidly inactivated by heat, light and extremes of pH.1,2

4.9.2 Clinical features

Measles is a highly infectious, acute viral illness spread by respiratory secretions, including aerosol transmission.1 It is infectious from the beginning of the prodromal period and for up to 4 days after the appearance of the rash. The incubation period is usually 10 to 14 days. The prodrome, lasting 2 to 4 days, is characterised by fever and malaise, followed by a cough, coryza and conjunctivitis. The maculopapular rash typically begins on the face and upper neck, and then becomes generalised.

Measles is often a severe disease, frequently complicated by otitis media (in approximately 9%), pneumonia (in approximately 6%) and diarrhoea (in approximately 8%).1,2 Acute encephalitis occurs in 1 per 1000 cases, and has a mortality rate of 10 to 15%, with a high proportion of survivors suffering permanent brain damage.3 Subacute sclerosing panencephalitis (SSPE) is a late complication of measles, occurring on average 7 years after infection in approximately 0.5 to 1 per 100 000 measles cases.1 SSPE causes progressive brain damage and is always fatal. Complications from measles are more common and more severe in the chronically ill, in children <5 years of age, and in adults.2

Approximately 60% of deaths from measles are attributed to pneumonia, especially in the young, while complications from encephalitis are more frequently seen in adults.1,2 Measles infection during pregnancy can result in miscarriage and premature delivery, but has not been associated with congenital malformation.5 There is no specific therapy for acute measles infection.

4.9.3 Epidemiology

In March 2014, the World Health Organization (WHO) declared that endemic measles has been eliminated from Australia, with the absence of a circulating endemic measles strain for several years.4 However, measles cases in Australia continue to occur, particularly in returning non-immune travellers and their contacts, with measles outbreaks of limited size and duration following importation.5 In 2005 and 2007, measles notifications and hospitalisations were the lowest recorded in Australia.6,8 However, there has been a recent increase in imported measles cases in Australia and subsequent outbreaks,6 highlighting the importance of continued high 2-dose vaccine coverage. To ensure herd immunity and maintenance of elimination, 2-dose vaccine coverage in each new birth cohort should optimally be ≥95%.10 A decline in vaccination rates has resulted in a resurgence in endemic transmission in a number of European countries, including the United Kingdom.11 In 2009, the Australian Childhood Immunisation Register recorded that 94.0% of children aged 2 years had received at least 1 dose of measles-containing vaccine and 80.3% of children aged 5 years had received 2 doses.12 However, improvements have occurred since that time, with 2-dose coverage at 92.2% in children aged 5 years in 2013.13

National serosurveys in early 1999 (evaluating the 1998 National Measles Control Campaign) and in 2000 showed that those most at risk of measles infection in Australia were infants <12 months of age, 1 to <2-year olds due to delayed vaccine uptake, and persons born in the late 1960s to mid-1980s (especially the 1978–1982 birth cohort).14-16 Young adults are recognised to be at a greater risk of measles infection as many missed being vaccinated as infants (when vaccine coverage was low), while during their childhood a 2nd dose was not yet recommended and disease exposure was decreasing. They may also have missed catch-up vaccinations during their school years as part of either the Measles Control Campaign (which only targeted primary school-aged children) or the Young Adult Measles Control Campaign (which did not result in high coverage).17 A high proportion of recent measles cases in Australia have been in unvaccinated young adults.9,18 Since the Measles Control Campaign, there have been no deaths recorded from measles, with the last measles death recorded in 1995.6,8,19 Since 1998, 2 deaths have been attributed to SSPE in Australia, 1 in 1999 and 1 in 2004.7,20

Global elimination of measles

The WHO is overseeing efforts to eliminate measles worldwide through immunisation and surveillance strategies.21 In 2000, measles was the fifth leading cause of childhood morbidity and mortality worldwide. There were an estimated 770 000 deaths, with more than half of these occurring in Africa.22 Following extensive vaccination campaigns, there was a 78% reduction to 164 000 deaths worldwide in 2008, with the majority of deaths reported in Southeast Asia.23 In 2003, measles elimination, defined as the absence of endemic measles virus transmission, was included as a regional goal under the Expanded Programme on Immunization (EPI) for the WHO Western Pacific Region, with a target date set for 2012.24 Considerable progress has been made with an 86% decline in measles cases in the region.24 However, achieving elimination requires continued strengthening of immunisation and surveillance efforts, particularly identification of measles virus genotypes to confirm the absence of an endemic strain. Globally, a number of countries...
have formally declared measles elimination, including Australia, with plans for achieving measles control and elimination across all WHO regions under continual development.

4.9.4 Vaccines

Monovalent measles vaccine is not available in Australia. Measles vaccination is provided using either measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccines. Two combination vaccines containing live attenuated measles, mumps, rubella and varicella viruses (MMRV) are registered in Australia.

Measles immunity induced by 1-dose vaccination provides long-term immunity in most recipients. However, approximately 5% of recipients fail to develop immunity to measles after 1 dose. Following a 2nd vaccine dose, approximately 99% of subjects overall will be immune to measles. Measles vaccine effectiveness studies have found the measles-containing vaccines to be 90 to 95% effective in developed country settings with high vaccination coverage and low incidence of measles. A Cochrane review reported 1-dose vaccine effectiveness to be 95% however, effectiveness has been demonstrated to be lower, particularly by region (e.g. Asia, Africa) in 1-dose recipients.

Combination MMRV vaccines have been shown in clinical trials, predominantly conducted in children 12 months to 6 years of age, to produce similar rates of seroconversion to all four vaccine components compared with MMR and monovalent varicella vaccines administered concomitantly at separate injection sites. In one comparative study assessing seroresponses to a single MMRV vaccine dose in 12–14-month-old children, the seroresponse rates to measles, mumps and rubella were similar, but varicella seroresponses were lower in Priorix-tetra recipients than in ProQuad recipients. However, the clinical significance of this is not clear, particularly for MMRV given after MMR vaccine. Information on adverse events related to MMR and MMRV vaccines is provided in 4.9.11 Adverse events below, and also in 4.22 Varicella (for MMRV).

Combination measles-mumps-rubella (MMR) vaccines

- **M-M-R II** – bioCSL Pty Ltd (live attenuated measles virus [Enders’ attenuated Edmonston strain], mumps virus [Jeryl Lynn B level strain] and rubella virus [Wistar RA 27/3 strain]). Lyophilised pellet in a monodose vial with separate diluent. Each 0.5 mL reconstituted dose contains ≥1000 tissue culture infectious dose 50% (TCID50) of measles virus, ≥12 500 TCID50 of mumps virus, and ≥1000 TCID50 of rubella virus; 14.5 mg sorbitol; 1.9 mg sucrose; 14.5 mg hydrolysed porcine gelatin; ≤0.3 mg recombinant human albumin; <1 ppm fetal bovine serum; 25 μg neomycin.

- **Priorix** – GlaxoSmithKline Australia Pty Ltd (live attenuated measles virus [Schwarz strain], mumps virus [RIT 4385 strain, derived from the Jeryl Lynn strain] and rubella virus [Wistar RA 27/3 strain]). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10¹⁴ cell culture infectious dose 50% (CCID50) of measles virus, ≥10³⁷ CCID50 of mumps virus, and ≥10¹⁰ CCID50 of rubella virus; lactose; neomycin; sorbitol; mannitol.

Combination measles-mumps-rubella-varicella (MMRV) vaccines

- **Priorix-tetra** – GlaxoSmithKline Australia Pty Ltd (live attenuated measles virus [Schwarz strain], mumps virus [RIT 4385 strain, derived from the Jeryl Lynn strain], rubella virus [Wistar RA 27/3 strain] and varicella-zoster virus [Oka strain]). Lyophilised pellet in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10²⁵ CCID50 of measles virus, ≥10³⁴ CCID50 of mumps virus, ≥10¹³ CCID50 of rubella virus, and ≥10¹³ plaque-forming units (PFU) of varicella-zoster virus; lactose; neomycin; sorbitol; mannitol.

- **ProQuad** – bioCSL Pty Ltd (live attenuated measles virus [Enders’ attenuated Edmonston strain], mumps virus [Jeryl Lynn B level strain], rubella virus [Wistar RA 27/3 strain] and varicella-zoster virus [Oka/Merck strain]). Lyophilised powder in a monodose vial with a pre-filled diluent syringe. Each 0.5 mL reconstituted dose contains ≥10¹⁰ TCID50 of measles virus, ≥10⁵ TCID50 of mumps virus, ≥10¹⁰ TCID50 of rubella virus, and ≥10⁹ PFU of varicella-zoster virus; 20 mg sucrose; 11 mg hydrolysed porcine gelatin; 2.5 mg urea; 16 mg sorbitol; 0.38 mg monosodium L-glutamate; 0.25 mg recombinant human albumin; 5 μg neomycin; residual components of MRC-5 cells; 0.5 μg bovine serum albumin.

4.9.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5. Store at +2°C to +8°C. Do not freeze. Protect from light.

Both MMR and MMRV vaccines must be reconstituted by adding the entire contents of the diluent container to the vial containing the pellet and shaking until the pellet is completely dissolved.

Reconstituted Priorix (MMR), M-M-R II (MMR) and Priorix-tetra (MMRV) vaccines should be used as soon as practicable. If storage is necessary, hold at +2°C to +8°C for not more than 8 hours.
Reconstituted ProQuad (MMRV) vaccine should be used immediately. If storage is necessary, hold at +20°C to +25°C for not more than 1 hour or at +2°C to +8°C for not more than 2.5 hours.

**4.9.6 Dosage and administration**

The dose of Priorix (MMR) vaccine for both children and adults is 0.5 mL, to be given by either SC or IM injection.

The dose of M-M-R II (MMR) vaccine for both children and adults is 0.5 mL, to be given by SC injection.

For children <14 years of age, the dose of MMRV vaccine is 0.5 mL, to be given by SC injection. Priorix-tetra may also be given by IM injection.

MMRV vaccines are not recommended for use in persons aged ≥14 years.

When 2 doses of MMR-containing vaccine are required, the minimum interval between doses is 4 weeks.

**Co-administration with other vaccines**

MMR or MMRV vaccines can be given at the same time as other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever) or other inactivated vaccines (including DTPa, hepatitis B, Hib, IPV, MenCCV, hepatitis A and pneumococcal conjugate vaccine),

using separate syringes and injection sites. If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines, they should be given at least 4 weeks apart.

If MMR vaccine is given at the same time as monovalent varicella vaccine (VV), they should be given using separate syringes and injection sites. MMR vaccine and monovalent VV should not be mixed together prior to injection.

Separate administration of measles, mumps or rubella vaccine is not available as an alternative to MMR vaccine, although a monovalent varicella vaccine is available (refer to 4.22 Varicella).

**Interchangeability of MMR-containing vaccines**

In general, the two brands of MMR vaccine can be considered interchangeable, that is, the 2nd MMR dose does not have to be of the same brand as the 1st. The same principle applies to the two available MMRV vaccines, although they are not routinely recommended in a 2-dose schedule.

**4.9.7 Recommendations**

For additional recommendations associated with MMRV administration to prevent varicella disease, refer to 4.22 Varicella.

**Infants aged <12 months**

MMR-containing vaccines are not routinely recommended for infants <12 months of age. However, MMR vaccine can be given to children from as early as 9 months of age in certain circumstances, including travel to highly endemic areas and during outbreaks (refer to ‘Travellers’ below, and 4.9.12 Public health management of measles).

Two doses of measles-containing vaccine should be administered at ≥12 months of age (refer to ‘Children’ below). This is because maternal antibodies to measles are known to persist in many infants until approximately 11 months of age and may interfere with active immunisation before 12 months of age. However, there is some evidence that a dose provided at ≥11 months (but prior to 12 months) of age is sufficiently immunogenic; as such, doses given in this timeframe may not need to be repeated in all circumstances (refer also to Table 2.1.5 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances).

**Children**

Two doses of measles-containing vaccine are recommended for all children. The 1st dose should be given at 12 months of age as MMR vaccine. MMRV vaccines are not recommended for use as the 1st dose of MMR-containing vaccine in children <4 years of age, due to a small but increased risk of fever and febrile seizures when given as the 1st MMR-containing vaccine dose in this age group (refer to 4.9.11 Adverse events and Table 4.9.1 below).

The 2nd dose of measles-containing vaccine is recommended to be given routinely at 18 months of age as MMRV vaccine. This is to commence from July 2013 once MMRV vaccine(s) are available under the NIP (refer to Table 4.9.1 below). The recommended age for administration of the 2nd dose of measles-containing vaccine will be moved down from 4 years of age, to provide earlier 2-dose protection against measles, mumps and rubella, and to improve vaccine uptake (refer to 4.9.3 Epidemiology above).

Catch-up vaccination of children who did not receive the 2nd dose of MMR-containing vaccine at 18 months of age can occur at the 4-year-old schedule point, until all relevant children have reached 4 years of age. Use of MMRV vaccine at the 4-year-old schedule point is preferred when varicella vaccination is also indicated (refer to 4.22 Varicella).

Children >12 months of age who have received 1 dose of MMR vaccine can be offered their 2nd dose of MMR-containing vaccine early (if at least 4 weeks after the 1st dose has elapsed) if they are considered at risk of coming in contact with measles. (refer to 4.9.12 Public health management of measles below).
If MMRV vaccine is inadvertently administered as dose 1 of MMR-containing vaccine, the dose does not need to be repeated (providing it was given at ≥12 months of age; refer to Table 2.1.5 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances). However, parents/carers should be advised regarding the small but increased risk of fever and febrile seizures (compared with that expected following MMR vaccine).

Table 4.9.1: Recommendations for measles vaccination with (a) measles-mumps-rubella (MMR) (currently available), and (b) once measles-mumps-rubella-varicella (MMRV) vaccines are available from July 2013

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Schedule point (age)</th>
<th>12 months</th>
<th>18 months</th>
<th>4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Only monovalent varicella vaccine available</td>
<td>MMR</td>
<td>VV</td>
<td>MMR*</td>
<td></td>
</tr>
<tr>
<td>(b) When MMRV vaccine available (from July 2013)</td>
<td>MMR</td>
<td>MMRV</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

* The 2nd dose of MMR-containing vaccine is recommended to be provided at 18 months of age to improve 2-dose coverage and protection against measles in young children. However, until June 2013, the 2nd dose of MMR vaccine is included under the NIP schedule for administration at 4 years of age. From July 2013, the 2nd dose of MMR vaccine will move to the 18-month NIP schedule point and be provided as MMRV vaccine.

Adults and adolescents

Persons born before 1966

No vaccination is required for persons born before 1966 (unless serological evidence indicates otherwise), as circulating virus and disease were prevalent before this time, suggesting most persons would have acquired immunity from natural infection. However, confirmed cases of measles have occurred in persons born before 1966 and, if doubt exists, it may be more expedient to offer vaccination than serological testing. (Refer also to ‘Serological testing for immunity to measles’ below.)

Persons born during or since 1966

All persons born during or since 1966 who are ≥18 months of age (or, until catch-up following the move of the 2nd NIP dose of measles-containing vaccine to 18 months of age is completed, are ≥4 years of age) should have documented evidence of 2 doses of MMR-containing vaccine (administered at least 4 weeks apart and with both doses administered at ≥12 months of age; refer to ‘Children’ above) or have serological evidence of protection for measles, mumps and rubella.

It is recommended that all adolescents and young adults have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine (refer to 4.9.3 Epidemiology above).

MMRV vaccines are not recommended for use in persons ≥14 years of age, due to a lack of data on safety and immunogenicity/efficacy in this age group. If a dose of MMRV vaccine is inadvertently given to an older person, this dose does not need to be repeated.

Healthcare workers and other occupations

All adolescents and adults (born during or since 1966) should have their vaccination records reviewed to ensure they have received 2 doses of MMR vaccine. This is important for all persons, but especially those working in certain occupations, such as healthcare workers, staff working in early childhood education and care, staff of long-term care facilities and staff of correctional facilities. Those who were born during or since 1966 and are non-immune, or who have only received 1 dose of MMR vaccine, should be vaccinated and have documented evidence of 2 doses of MMR vaccine or serological evidence of immunity to measles (refer to ‘Adults and adolescents’ above). (Refer also to 3.3 Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.)

Travellers

It is especially important that all persons born during or since 1966 have been given 2 doses of measles-containing vaccine (administered at least 4 weeks apart, with both doses administered at ≥12 months of age; refer to ‘Children’ above) before embarking on international travel if they do not have evidence of previous receipt of 2 doses of MMR vaccine or serological evidence of protection for measles, mumps and rubella (refer to ‘Adults and adolescents’ above).

Infants travelling to countries in which measles is endemic, or where measles outbreaks are occurring, may be given MMR vaccine from as young as 9 months of age, after an individual risk assessment. In these cases, 2 further doses of
MMR vaccine are still required. The next dose of MMR vaccine should be given at 12 months of age or 4 weeks after the 1st dose, whichever is later. This should be followed by the routine administration of the next dose of measles-containing vaccine, as MMRV vaccine, at 18 months of age.

**Serological testing for immunity to measles**

Serological testing for immunity to measles, mumps, rubella or varicella is not recommended before or after routine administration of the 2-dose childhood schedule of these vaccines.

However, serological testing for measles can be performed in cases where a history of natural immunity or 2 doses of vaccine administration is uncertain (refer to ‘Adults and adolescents’ above). Serology is indicated in special situations, such as pre-pregnancy planning (refer also to 4.18 Rubella, 4.22 Varicella and 3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants). Serological tests to investigate immunity to measles are generally sensitive at detecting antibody produced by both prior natural infection and vaccination, although sensitivity varies by assay and the clinical setting (e.g. time since vaccination). Interpretation of the results of serological testing may be enhanced by discussion with the laboratory that performed the test, ensuring that relevant clinical information is provided. An alternative to serological testing is presumptive administration of MMR vaccine dose(s). There is no known increase in adverse events from vaccinating those with pre-existing immunity to one or more of the vaccine components (refer to 4.9.11 Adverse events below).

**4.9.8 Pregnancy and breastfeeding**

MMR-containing vaccines are contraindicated in pregnant women. Pregnancy should be avoided for 28 days after vaccination. MMR vaccines can be given to breastfeeding women. (Refer also to 4.18 Rubella.) MMRV vaccines are not recommended for use in persons aged ≥14 years. There is no risk to pregnant women from contact with recently vaccinated persons. The vaccine virus is not transmitted from vaccinated persons to susceptible contacts. Refer also to 4.18 Rubella, 4.22 Varicella and 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

**4.9.9 Contraindications**

**Anaphylaxis to vaccine components**

MMR and MMRV vaccines are contraindicated in persons who have had:

- anaphylaxis following a previous dose of any MMR-containing vaccine
- anaphylaxis following any vaccine component.

Refer to 4.9.11 Adverse events below for persons with a known egg allergy.

**Persons who are immunocompromised**

Measles-, mumps- and rubella-containing vaccines contain live attenuated vaccine viruses and are contraindicated in persons who are immunocompromised. Thus, MMR-containing vaccines are contraindicated in the following groups:

- Persons immunocompromised due to HIV/AIDS. MMR vaccination of asymptomatic HIV-infected persons >12 months of age with an age-specific CD4+ count of ≥15% may be considered (refer to ‘HIV-infected persons’ in 3.3.3 Vaccination of immunocompromised persons). Since studies have not been performed using combination MMRV vaccines in asymptomatic HIV-infected persons or persons with an age-specific CD4+ count of ≥15%, it is recommended that only MMR vaccine (and monovalent VV, refer to 4.22 Varicella) be considered for use in this setting.
- Persons with other medical conditions associated with significant immunocompromise (refer to 3.3.3 Vaccination of immunocompromised persons).
- Persons receiving high-dose systemic immunosuppressive therapy, such as chemotherapy, radiation therapy or oral corticosteroids. MMR-containing vaccines are contraindicated in persons taking high-dose oral corticosteroids for more than 1 week (in children equivalent to >2 mg/kg per day prednisolone, and in adults >60 mg per day) (refer to 3.3.3 Vaccination of immunocompromised persons). Those who have been receiving high-dose systemic steroids for more than 1 week may be vaccinated with live attenuated vaccines after corticosteroid therapy has been discontinued for at least 1 month (refer to 4.9.10 Precautions below and 3.3.3 Vaccination of immunocompromised persons).

Refer also to 3.3 Groups with special vaccination requirements and 4.22 Varicella for more information.
Pregnant women
Refer to 4.9.8 Pregnancy and breastfeeding above.

4.9.10 Precautions

Vaccination with other live attenuated parenteral vaccines
If MMR or MMRV vaccine is not given simultaneously with other live attenuated parenteral vaccines (e.g. varicella, BCG, yellow fever), the vaccines should be given at least 4 weeks apart.

Vaccination after immunoglobulin or blood product administration
Administration of MMR or MMRV vaccine should be delayed after administration of immunoglobulin-containing products. After receipt of immunoglobulin-containing blood products, the expected immune response to measles, mumps, rubella and varicella vaccination may be impaired.28,38,50 MMR-containing vaccines should not be given for between 3 and 11 months following the administration of immunoglobulin-containing blood products. The interval between receipt of the blood product and vaccination depends on the amount of immunoglobulin in each product, and is indicated in 3.3 Groups with special vaccination requirements, Table 3.3.6 Recommended intervals between either immunoglobulins or blood products and MMR, MMRV or varicella vaccination.28 For further information, refer to 3.3.4 Vaccination of recent recipients of normal human immunoglobulin and other blood products.

Recent blood transfusion with washed red blood cells is not a contraindication to MMR or MMRV vaccines. MMR vaccine should be administered concomitantly with, or at any time in relation to, anti-D immunoglobulin, but at a separate injection site. Anti-D immunoglobulin does not interfere with the antibody response to vaccine.

Immunoglobulin or blood product administration after vaccination
Immunoglobulin-containing products should not be administered for 3 weeks following vaccination with measles-containing vaccines, unless the benefits exceed those of vaccination. If immunoglobulin-containing products are administered within this interval, the vaccinated person should either be revaccinated later at the appropriate time following the product (as indicated in Table 3.3.6), or be tested for immunity 6 months later and then revaccinated if seronegative.

Rh (D) immunoglobulin (anti-D) may be given at the same time in different sites with separate syringes or at any time in relation to MMR vaccine, as it does not interfere with the antibody response to the vaccine.

HIV-infected persons
MMR vaccine can be given to asymptomatic HIV-infected persons >12 months of age with an age-specific CD4+ count of ≥15%.51 (refer to 3.3 Groups with special vaccination requirements, Table 3.3.4 Categories of immunocompromise in HIV-infected persons, based on age-specific CD4+ counts and percentage of total lymphocytes). This is because the risk posed by measles infection is considered to be greater than the likelihood of adverse events from vaccination.49 MMR vaccine is contraindicated in immunocompromised HIV-infected persons (refer to 4.9.9 Contraindications above).

As there are no data available on the safety, immunogenicity or efficacy of MMRV vaccines in HIV-infected children, MMRV vaccine should not be administered as a substitute for MMR vaccine when vaccinating these children.28,50

Persons receiving immunosuppressive therapy
MMR-containing vaccines may be given to persons on low-dose systemic corticosteroid therapy (e.g. children on doses of ≤2 mg/kg per day for less than 1 week, and those on lower doses of 1 mg/kg per day or alternate-day regimens for longer periods). Persons receiving high-dose corticosteroids can receive MMR-containing vaccines after corticosteroid therapy has been discontinued for at least 1 month (refer to 4.9.9 Contraindications above).49 Some experts suggest withholding lower doses of steroids 2 to 3 weeks prior to vaccination with live viral vaccines, if this is possible.49,50 (Refer also to 3.3.3 Vaccination of immunocompromised persons.)

Household contacts of persons who are immunocompromised
Household contacts of persons who are immunocompromised, should ensure that they are age-appropriately vaccinated against, or are immune to, measles, as well as mumps, rubella and varicella. MMR-containing vaccines can be safely administered to household contacts, as measles, mumps and rubella vaccine viruses are not transmissible from vaccinated persons to others.28 If using MMRV vaccine, refer to 4.22 Varicella for information regarding varicella vaccine virus transmission.

Persons receiving long-term aspirin or salicylate therapy
There is no need to avoid salicylates before or after MMR or MMRV vaccination. Persons receiving long-term salicylate therapy (aspirin) can be vaccinated with MMRV, if indicated, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination with a varicella-containing vaccine (refer to 4.22 Varicella).
Persons with a history of thrombocytopenia

Thrombocytopenia is a rare adverse event following MMR vaccination (refer also to 4.9.11 Adverse events below).\textsuperscript{1,52,53} In children with a past history of an episode(s) of idiopathic thrombocytopenia purpura (ITP), the risk of vaccine-associated thrombocytopenia occurring following a dose of MMR vaccine has been uncertain.\textsuperscript{28,53} However, a recent systematic review concluded that MMR vaccination, either as a 1st or 2nd dose, did not lead to a recurrence of ITP.\textsuperscript{54}

Personal or close family history of seizures or convulsions

Children with a personal or close family history of seizures or convulsions should be given MMR or MMRV vaccine, provided the parents/careers understand that there may be a febrile response 5 to 12 days after vaccination.\textsuperscript{28} Advice should be given regarding the management of fever following vaccination with paracetamol and other measures (refer to 2.3.2 Adverse events following immunisation). Due to an increased risk of fever and febrile convulsions in 1st dose recipients of MMRV vaccine, MMRV vaccines are only recommended for use as the 2nd dose of MMR-containing vaccine (refer to 4.9.7 Recommendations above and 4.9.11 Adverse events below).

Tuberculin skin testing following MMR vaccination

Measles virus inhibits the response to tuberculin and tuberculin-positive persons may become tuberculin-negative for up to a month after measles infection.\textsuperscript{28,55} As such, tuberculin skin testing (Mantoux test) may be unreliable for at least 4 weeks after the administration of measles-containing vaccines. There are no studies on the effect of MMR or MMRV vaccination on the results of interferon-gamma release assays (IGRAs).\textsuperscript{56}

4.9.11 Adverse events

If using MMRV vaccine, additional adverse events relating to the varicella vaccine component are outlined in 4.22 Varicella.

Adverse events following administration of MMR-containing vaccines are generally mild and well tolerated.\textsuperscript{2} Adverse events are much less common after the 2nd dose of MMR or MMRV vaccine than after the 1st dose. Fever (with malaise and/or a rash, which is non-infectious) may occur after MMR vaccination, most commonly between 7 to 10 days (range 5 to 12 days) after vaccination and lasting about 2 to 3 days. This coincides with the period of peak measles vaccine virus replication. High fever (>39.4°C) occurs in approximately 5 to 15% of MMR vaccine recipients, and rash occurs in approximately 5%.\textsuperscript{2,28} There is also an increased risk for febrile seizures in the same time period of approximately 1 case per 3000 doses.\textsuperscript{28}

It is recommended that vaccine recipients or their parents/careers be advised about possible symptoms in the period 5 to 12 days after vaccination, and given advice on their management, including the use of paracetamol for fever (refer to 2.3.2 Adverse events following immunisation).

Higher rates of fever were observed in clinical trials of both MMRV vaccines, particularly following dose 1, when compared with giving MMR vaccine and monovalent VV at the same time but at separate sites.\textsuperscript{31-34} Two post-marketing studies in the United States identified an approximately 2-fold increased risk of fever and febrile convulsions in 1st dose recipients of MMRV vaccine, who were predominantly 12–23 months of age, in the period 7 to 10 days\textsuperscript{57} (or 5 to 12 days)\textsuperscript{28} after vaccination, compared with recipients of separate MMR and VV vaccines. MMRV vaccination resulted in 1 additional febrile seizure for every 2300 doses compared to separate MMR and VV vaccination.\textsuperscript{57} An increase in fever or febrile convulsions has not been identified after the 2nd dose of MMRV vaccine in the United States, although most 2nd dose recipients were aged 4–6 years, an age at which the incidence of febrile convulsions is low.\textsuperscript{59} These post-marketing studies were in children who received ProQuad; however, it is anticipated that this side effect profile would be similar in Priorix-tetra recipients.

A varicelliform rash may occur after MMRV vaccination (refer to 4.22.11 Adverse events in 4.22 Varicella). The appearance of a rash after monovalent varicella vaccine occurs in less than 5% of vaccine recipients (usually within 5 to 26 days), and similar rates are observed with the use of MMRV vaccine.\textsuperscript{60} Anaphylaxis following the administration of MMR vaccine is very rare (less than 1 in 1 million doses distributed).\textsuperscript{28} Although no cases of anaphylaxis were reported in MMRV vaccine clinical trials, the incidence is likely to be similar to that occurring with use of MMR vaccine. Anaphylaxis after vaccination is likely due to anaphylactic sensitivity to gelatin or neomycin, not egg allergy. Although measles and mumps (but not rubella or varicella) vaccine viruses are grown in chick embryo tissue cultures, it is now recognised that measles- and mumps-containing vaccines contain negligible amounts of egg ovalbumin (refer to 4.9.13 Variations from product information below and 3.3.1 Vaccination of persons who have had an adverse event following immunisation).

Persons with egg allergy can be safely given MMR or MMRV vaccine.\textsuperscript{1,61} Skin testing is not required prior to vaccine administration.

Thrombocytopenia (usually self-limiting) has been very rarely associated with the rubella or measles component of MMR vaccine, occurring in 3 to 5 per 100 000 doses of MMR vaccine administered.\textsuperscript{1,28,52,53} This is considerably less
frequent than after natural measles, mumps and rubella infections. Any association with MMRV vaccine is expected to be similar.

It is uncertain whether encephalopathy occurs after measles vaccination. If it does, it is at least 1000 times less frequent than as a complication from natural infection.2,28

Other rare adverse events attributed to MMR vaccine include transient lymphadenopathy and arthralgia (refer to 4.18 Rubella). Parotitis has been reported rarely (refer to 4.11 Mumps).28

Autism, autistic spectrum disorder and inflammatory bowel disease are not associated with the MMR vaccine. There has been no credible scientific evidence to support this claim and most proponents of the link have retracted this claim.62,63 There is now a substantial body of evidence to refute it64-67 (refer to Appendix 4 Commonly asked questions about vaccination).

4.9.12 Public health management of measles

Measles is a notifiable disease in all states and territories in Australia. The public health management of measles is described in *Measles: national guidelines for public health units*40 (www.health.gov.au/cdnasongs) and is given urgent public health priority. Refer to the national guidelines for current case definitions, testing and post-exposure prophylaxis of contacts.

Further instructions about the public health management of measles can also be obtained from state/territory public health authorities (refer to Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

MMR vaccine (and MMRV in some instances) is recommended for post-exposure prophylaxis within 72 hours of a non-immune individual being exposed to measles. Refer to Table 4.9.2 for detailed information. Administration of normal human immunoglobulin (NHIG), rather than MMR or MMRV, is recommended in some settings (refer to Part 5 Passive immunisation and Table 4.9.2).40 Post-exposure prophylaxis should be given on the direction of public health authorities.

Children >12 months of age who have received 1 dose of measles-containing vaccine can be offered their 2nd dose early (if at least 4 weeks after the 1st dose has elapsed) if they are considered at risk of coming in contact with measles40 (refer to 4.9.7 Recommendations above and Table 4.9.2). If varicella vaccination is also indicated, MMRV vaccine can be used, although MMRV vaccine is not routinely recommended as the 1st dose of MMR-containing vaccine in children aged <4 years (refer to 4.9.7 Recommendations above). If a child receives the 2nd dose of measles-containing vaccine early, they are considered to have completed their vaccination schedule and therefore do not require another dose at 18 months of age or beyond, provided that the 2 doses were given at ≥12 months of age and at least 4 weeks apart.

Table 4.9.2: Post-exposure prophylaxis required within 72 hours of first exposure for persons exposed to measles (adapted from Measles: national guidelines for public health units)40

<table>
<thead>
<tr>
<th>Age or immune status</th>
<th>Measles-mumps-rubella (MMR) vaccination history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 doses MMR or unknown</td>
</tr>
<tr>
<td></td>
<td>1 dose MMR</td>
</tr>
<tr>
<td></td>
<td>2 doses MMR</td>
</tr>
<tr>
<td>Immunocompromised (any age)</td>
<td>Normal human immunoglobulin (NHIG) 0.5 mL/kg to maximum of 15 mL</td>
</tr>
<tr>
<td>Birth to 5 months</td>
<td>NHIG 0.2 mL/kg only if mother has had &lt;2 doses of MMR and no history of past measles infection or negative maternal IgG (otherwise no NHIG)</td>
</tr>
<tr>
<td>6 to 8 months</td>
<td>NHIG* 0.2 mL/kg</td>
</tr>
<tr>
<td>Age Range</td>
<td>Vaccine Recommendations</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td>9 to 11 months</td>
<td>MMR now, then repeat dose at 12 months of age or 4 weeks later (whichever is later)†</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>12 months to &lt;18 months</td>
<td>MMR†</td>
</tr>
<tr>
<td>≥18 months and born during or since 1966</td>
<td>MMR if not pregnant‡§ If pregnant: check IgG if time; offer NHIG (0.2 mL/kg to maximum of 15 mL)¶</td>
</tr>
</tbody>
</table>

* NHIG is required because maternal antibody will have partially waned and vaccination is not as reliably effective in this age group compared with older infants.
† The 2nd scheduled dose of MMR-containing vaccine (MMRV) should then be given at 18 months of age, with a minimum interval of 4 weeks after the previous dose of MMR vaccine (refer to 4.9.7 Recommendations above).
‡ A subsequent dose of MMR-containing vaccine (MMR or MMRV) should be provided at least 4 weeks after the 1st valid dose (a valid dose is one given at ≥12 months of age) to complete a 2-dose vaccine schedule (refer to 4.9.7 Recommendations above).
§ In children aged ≥4 to <14 years, MMRV vaccine could also be used as dose 1 if the child has not been previously immunised against varicella (refer to 4.9.7 Recommendations above).
¶ Consult public health authority (and/or obstetrician or GP) about interpretation of IgG results and use of NHIG.

### 4.9.13 Variations from product information

The product information for MMR and MMRV vaccines recommends that women of child-bearing age should be advised not to become pregnant for 3 months after vaccination. The ATAGI instead recommends avoiding pregnancy for 28 days after vaccination.41

The product information for Priorix, M-M-R II, Priorix-tetra and ProQuad states that persons with a history of anaphylactic or anaphylactoid reactions to egg should not be vaccinated. The ATAGI recommends instead that either Priorix, M-M-R II, Priorix-tetra or ProQuad can be given in this situation.28

The product information for Priorix-tetra states that it should be given by SC injection. The ATAGI recommends that it may also be given by IM injection.

The product information for ProQuad states that this vaccine is indicated for vaccination in individuals 12 months through 12 years of age. The product information for Priorix-tetra states that this vaccine can be used in persons from 9 months of age. The ATAGI recommends instead that both MMRV vaccines can be given to persons up to 14 years of age. The ATAGI also recommends that MMRV vaccine should not be used routinely as the 1st dose of MMR-containing vaccine in children aged <4 years.

The product information for both MMRV vaccines states that salicylates should be avoided for 6 weeks after vaccination, as Reye syndrome has been reported following the use of salicylates during natural varicella infection. The ATAGI recommends instead that non-immune persons receiving long-term salicylate therapy can receive varicella-containing vaccine, as the benefit is likely to outweigh any possible risk of Reye syndrome occurring after vaccination.

### References

A full reference list is available on the electronic Handbook or website www.immunise.health.gov.au.

4. World Health Organization (WHO), Western Pacific Region. Four Western Pacific countries and areas are the first in their Region to be measles-free. 2014. Available at: http://www.wpro.who.int/mediacentre/releases/2014/20140320/en/ (accessed Mar 2015).


recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. MMWR. Recommendations and Reports 2009;58(RR-11):1-166.


