

11 Measles

Key information

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| Mode of transmission | By direct contact with infectious droplets or by airborne spread. Measles is one of the most highly communicable of all infectious diseases. |
| Incubation period | About 10 days, but may be 7–18 days from exposure to onset of fever. The incubation period may be longer in those given IG after exposure. |
| Period of communicability | From 5 days before to 5 days after rash onset, counting the day of rash onset as day 1. |
| Herd immunity threshold | To prevent recurrent outbreaks of measles, 95 percent of the population must be immune. |
| Funded vaccine | MMR vaccine (Priorix) is a live attenuated vaccine. |
| Dose, presentation, route | 0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection. |
| Funded vaccine indications and schedule | Children at ages 15 months and 4 years. Adults who are susceptible to one or more of measles, mumps and rubella. Susceptible adults are: <ul style="list-style-type: none"> • individuals born from 1 January 1969 with no documented history of 2 doses of measles-containing vaccine after age 12 months • individuals with no documented measles IgG antibody. For (re-)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine). |
| Vaccine efficacy/effectiveness | Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations. |
| Egg allergy | Egg allergy, including anaphylaxis, is not a contraindication for MMR vaccine. |
| Adverse events to vaccine | MMR vaccine is generally well tolerated. The risk of adverse reactions to MMR vaccine is low compared to the risk of complications from measles disease. |

Continued overleaf

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| Public health measures | Notify the local medical officer of health immediately on suspicion. Prevent measles transmission through exclusion and use of personal protective equipment. Promote immunisation to susceptible individuals. Management of contacts of measles cases should be discussed with the medical officer of health. |
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11.1 Virology

The measles virus is an RNA virus, from the genus *Morbillivirus*, in the family Paramyxoviridae. Humans are the only natural host for the measles virus. The virus is rapidly inactivated by sunlight, heat and extremes of pH.¹

11.2 Clinical features

Measles is transmitted by direct contact with infectious droplets and also by airborne spread. It is one of the most highly communicable of all infectious diseases, with an approximate basic reproductive number of 12–18 in high-income countries² (see section 1.2.1). There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik's spots on the buccal mucosa. The characteristic maculopapular rash classically appears first behind the ears on the third to seventh day, spreads over three to four days from the head and face, over the trunk to the extremities. It lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is about 10 days, but may be 7 to 18 days from exposure to onset of fever. It may be longer in those given IG after exposure. Measles is highly infectious from five days before to five days after rash onset, counting the day of rash onset as day one.

Complications are common, occurring in 10 percent of cases, and include otitis media, pneumonia, croup and diarrhoea. Encephalitis has been reported in 1 in every 1,000 cases, of whom some 15 percent die and a further 25–35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and

idiopathic thrombocytopenic purpura (ITP or immune thrombocytopenia).

Sub-acute sclerosing panencephalitis, a rare degenerative central nervous system disease resulting from persistent measles virus infection, is fatal. Sub-acute sclerosing panencephalitis typically occurs 7 to 11 years after wild-type measles virus infection.³ This complication has virtually disappeared where there is widespread measles immunisation.

The case fatality rate for reported cases of measles in the US is 1–3 per 1,000.³ Measles is particularly severe in the malnourished, children with vitamin A deficiency, and in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash, and have a much higher case fatality rate. Measles during pregnancy can cause miscarriage, stillbirth and preterm delivery.¹

Measles is also serious in healthy children: over half of all the children who died from measles in the UK between 1970 and 1983 were previously healthy.⁴ No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

11.3 Epidemiology

11.3.1 Global burden of disease

Mortality and morbidity

From 2000 to 2015, the annual reported measles incidence decreased by 75 percent worldwide, from 146 to 36 cases per million population, due to increased vaccine coverage. Annual estimated measles deaths decreased by 79 percent, from 651,600 cases to 134,200.⁵

Although measles mortality rates have fallen significantly,⁶ measles remains an important vaccine-preventable cause of death among children throughout the world, particularly in low-income countries. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year.

Measles elimination

When a country is verified by the Measles Regional Verification Commission as having eliminated measles, it means that the country interrupted transmission of the endemic strain of circulating measles virus for a period of 36 months. Importations of measles virus may have occurred during this period, but circulation of the imported strains of measles virus was interrupted within 12 months of the importation.⁷

In May 2012 the 194 member states of the World Health Assembly endorsed the *Global Vaccine Action Plan 2011–2020*,⁸ which aims to eliminate measles in at least four WHO regions by 2015 and in five WHO regions by 2020. In September 2016, the Region of the Americas was the first WHO region to be declared free of measles. New Zealand has not yet been verified as having eliminated measles.

11.3.2 New Zealand epidemiology

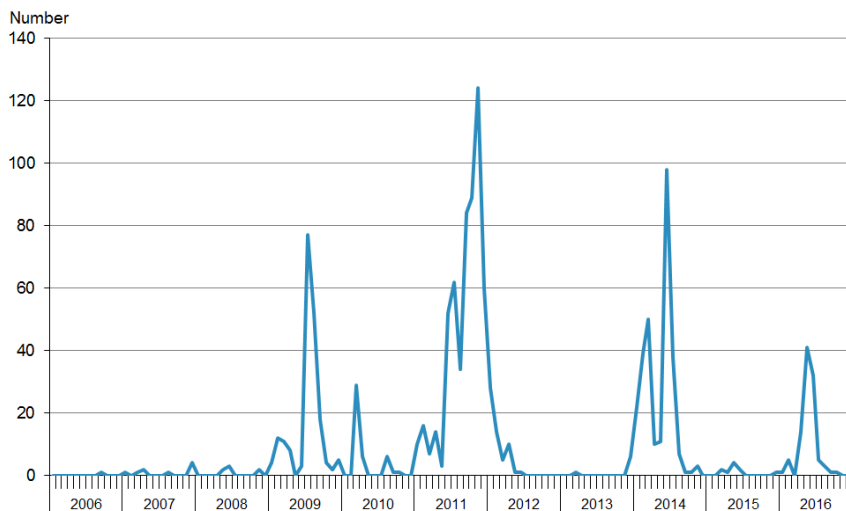
Measles vaccine was introduced in 1969 and moved to a two-dose schedule (as MMR vaccine) in 1992. Measles became a notifiable disease in 1996. The current two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information about the history of the Schedule).

The most recent measles epidemics occurred in 1991 (the number of cases was estimated to be in the tens of thousands) and 1997 (2,169 cases identified).

Smaller outbreaks occurred in 2009, 2011, 2014 and 2016 (see Figure 11.1). The largest outbreak was in 2011 and mainly affected Auckland, with 489 confirmed or probable cases. It started with an unimmunised child who became infected on a family trip to England, then developed measles when back in Auckland. Many of the secondary cases were in unimmunised high school children and young adults. The outbreak officially ended in July 2012.⁹

Importation of measles by non-immune people who had travelled overseas was also linked to the measles outbreaks in New Zealand in 2014 and 2016 (see also section 11.5.5).

Figure 11.1: Number of measles notifications by month reported, January 2006 to December 2016



Note: 2016 data is provisional.

Source: ESR

To eliminate measles epidemics, modelling suggests that New Zealand needs to achieve a coverage level of greater than 90 percent for both doses of MMR.¹⁰ If this coverage level is achieved and maintained, the length of time between epidemics will increase and may lead to the elimination of measles. As at 31 December 2016, the 5-year-old immunisation coverage rate, which includes two doses of measles-containing vaccine, was 88.6 percent – close to the target. However, previous years of low vaccine coverage have resulted in sufficient numbers of non-immune adolescents and young adults to permit outbreaks to occur.

11.4 Vaccines

11.4.1 Available vaccines

The measles vaccine is only available as one of the components of MMR vaccine. This vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses.

Funded vaccine

Each 0.5 mL dose of the reconstituted MMR vaccine (Priorix, GSK) contains:

- not less than $10^{3.0}$ CCID₅₀ of the attenuated line of Schwarz strain measles, propagated in chick embryo tissue culture
- not less than $10^{3.7}$ CCID₅₀ of RIT 4385 mumps strain, derived from the Jeryl Lynn strain and propagated in chick embryo tissue culture
- not less than $10^{3.0}$ CCID₅₀ of the Wistar RA 27/3 rubella strains, propagated in MRC₅ human diploid cells
- lactose, amino acids supplement, mannitol, sorbitol and neomycin sulphate as excipients, and water for injection.

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change. It contains:

- Attenuvax (Measles Virus Vaccine Live, MSD), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture
- Mumpsvax (Mumps Virus Vaccine Live, MSD), the Jeryl Lynn (B level) strain of mumps virus propagated in chick embryo cell culture
- Meruvax II (Rubella Virus Vaccine Live, MSD), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.

Two quadrivalent measles, mumps, rubella and varicella vaccines (MMRV, see chapter 21) are also registered but not currently available in New Zealand:

- ProQuad (MSD), which contains further attenuated Enders' Edmonston (Moraten) strain measles, RA 27/3 rubella, Jeryl Lynn mumps and Varicella Virus Vaccine Live (Oka/Merck)
- MMRV (Priorix-Tetra, GSK) contains not less than $10^{3.0}$ CCID₅₀ of the Schwarz measles, not less than $10^{4.4}$ CCID₅₀ of the RIT 4385 mumps, not less than $10^{3.0}$ CCID₅₀ of the Wistar RA 27/3 rubella and not less than $10^{3.3}$ PFU of the varicella virus strains.

11.4.2 Efficacy and effectiveness

Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations.¹¹ Outbreaks and epidemics continue to occur where low immunisation rates and/or sufficient numbers of susceptible members of communities are present. A 2012 Cochrane review of the safety and effectiveness of MMR vaccine concluded that a single dose of MMR vaccine is at least 95 percent effective in preventing clinical measles and 92 percent effective in preventing secondary cases among household contacts aged 6 months and older.¹² This was a systematic review of clinical trials and studies, which involved approximately 14.7 million children.

Seroconversion to all three viruses of MMR vaccine occurs in 85–100 percent of recipients. ‘Primary vaccine failure’ refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate an immune response. This occurs in 5–10 percent of recipients after the first dose and is rare after a second dose. More than 99 percent of people who receive two MMR doses (given at least four weeks apart, and the first dose given after age 12 months) develop serologic evidence of immunity to measles.³ Two doses are required for measles control and elimination in populations.³ The second MMR dose is not a booster, it is given to address primary vaccine failure.

Measles vaccination may have nonspecific effects, reducing mortality from other infectious diseases. Infection with the measles virus may cause immune memory loss and predispose people to opportunistic infections for up to three years.¹³ Population-level data from the UK, US and Denmark indicates that when measles was common, measles virus infections could have been implicated in as many as half of all childhood deaths from infectious disease.¹³ The authors suggest that the reduction in measles infections was the main factor in reducing overall childhood infectious disease mortality after the introduction of vaccination.

Duration of immunity

Even though antibody levels decline over time, secondary vaccine failure (ie, vaccine failure due to waning of protective immunity) has only rarely been documented for measles and rubella, but recently there have been outbreaks thought to be due to declining vaccine-induced mumps immunity.¹⁴

In Finland in 1982 a cohort was recruited at the start of the national MMR vaccination programme to study the persistence of vaccine-induced antibodies. By the mid-1990s Finland had eliminated measles, mumps and rubella, and there was little opportunity for natural boosting to occur. The follow-up of this cohort has shown that while antibodies wane over time, 20 years after the second MMR dose immunity to rubella was secure, 95 percent of people remained sero-positive for measles and immunity to mumps declined, with 74 percent being sero-positive.¹⁵ The antibody avidity also decreased over time, by 8 percent for measles and 24 percent for mumps.¹⁶

Waning of both the concentration and the avidity of antibodies might contribute to measles and mumps infections occurring in individuals who have received two doses of MMR.

See section 21.4.2 for efficacy and effectiveness data for VV.

11.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.¹⁷ Store at +2°C to +8°C. Do not freeze.

MMR vaccine must be reconstituted only with the diluents supplied by the manufacturer. Use MMR vaccine as soon as possible after reconstitution. If storage is necessary, reconstituted MMR vaccine can be stored at +2°C to +8°C for up to eight hours.

11.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by subcutaneous injection (see section 2.2.3).

Co-administration with other vaccines

MMR vaccine can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR vaccine (Priorix and MMR II) may be used interchangeably for completion of a course.¹⁸

11.5 Recommended immunisation schedule

Table 11.1: Recommended MMR vaccine schedule

| | Schedule |
|------------------------------------------------------------|----------------------------------------|
| Usual childhood schedule ^a | 2 doses: at ages 15 months and 4 years |
| Catch-up ^b for children, adolescents and adults | 2 doses: at least 4 weeks apart |

- a If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 15 months and 4 years.
- b For those born from 1 January 1969 who do not have documented evidence of two doses of an MMR-containing vaccine given after age 1 year, or who do not have serological evidence of protection for measles, mumps and rubella. See section 11.5.2.

11.5.1 Usual childhood schedule

MMR vaccine is recommended irrespective of a history of measles, mumps or rubella infection or measles immunisation. A clinical history does not reliably indicate immunity unless confirmed by serology. There are no known ill effects from vaccinating children, even if they have had serologically confirmed infection with any of the viruses.

Measles vaccine is recommended as MMR at age 15 months and at age 4 years. Two doses of measles vaccine are recommended because nearly all of the 5–10 percent who fail to be protected by the first dose will be protected by the second. The second dose of measles vaccine can be given as soon as four weeks after the first dose.

MMR vaccine may be given to children aged 12 months or older whose parents/guardians request it, and no opportunity should be missed to achieve immunity. If MMR is given early (ie, at 12 months of age), the vaccinator may also give the other scheduled 15-month vaccinations. This would reduce the risk of the child not returning for the other 15-month vaccinations.

MMR vaccine when aged under 12 months

MMR may be recommended for infants aged 6–12 months during measles outbreaks if cases are occurring in the very young (see section 11.8). These children still require a further two doses of MMR at ages 15 months and 4 years because their chance of protection from measles is lower when the vaccine is given when they are aged under 12 months. Any recommendations will be made by the local medical officer of health and the Ministry of Health based on local epidemiology. Note: Some immigrant children may have received a measles-containing vaccine when aged under 12 months.

11.5.2 Catch-up

Two doses of MMR (at least four weeks apart) are recommended and funded for any child, adolescent or adult who is known to be susceptible to one or more of the three diseases.

Adults born in New Zealand before 1969 are considered to be immune to measles as circulating virus and disease was prevalent prior to the introduction of measles vaccine in 1969.

Adults born from 1 January 1969

All individuals born in 1969 or later who do not have documented evidence of two doses of an MMR-containing vaccine given after age 1 year (even if they have received two doses of a measles-containing vaccine) or who do not have serological evidence of protection for measles, mumps and rubella should be considered susceptible.

This particularly applies to:

- a student in post-secondary education
- a health care worker with patient contact
- those in institutional care and those who care for them
- a susceptible international traveller visiting a country in which measles is endemic.

Some adults may have received one dose of measles vaccine and one dose of MMR during one of the catch-up campaigns (eg, the 1997 campaign, when all those aged up to 10 years were offered MMR vaccine). They will have therefore received the recommended two doses of measles, but only one of mumps and rubella. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended and funded. These individuals can receive a second dose of MMR (ie, a third dose of measles vaccine) without any concerns. It is important that women of childbearing age are immune to rubella (see chapter 18).

All persons born from 1 January 1969 with only one documented dose of prior MMR should receive a further dose of MMR; if there are no documented doses of prior MMR, then two doses should be administered, at least four weeks apart.

11.5.3 Immunocompromise

Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immunocompromised individual (see section 11.7.2). See also 'Household contacts' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

(Re-)vaccination following immunosuppression

MMR vaccine is funded for (re-)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.3).

MMR vaccine is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if the CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR vaccine from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR vaccine if the CD4+ lymphocyte count is 200 cells/mm³ or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).³

11.5.4 Pregnancy and breastfeeding

MMR vaccine is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.^{1, 3}

MMR vaccine can be given to breastfeeding women.

(See also sections 4.1 and 18.5.3.)

11.5.5 Travel

International travel is an important factor in reintroducing measles into New Zealand, and so vaccination with a measles-containing vaccine should be considered for all children and adults travelling overseas if they have not previously been adequately vaccinated.

Measles remains endemic in many countries, including areas in Europe, Asia, the Pacific and Africa. Of the 159 measles cases reported in the US from January to April 2015, 153 (96 percent) were import-associated.¹⁹ Travel was also linked to the measles outbreaks in New Zealand in 2011, 2014 and 2016.

11.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

11.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR vaccine (eg, children with an acute febrile illness should have their immunisation deferred).

Anaphylaxis following a previous dose of MMR or any of the vaccine components is a contraindication to a further dose of MMR. Individuals who have anaphylaxis after receiving MMR should be serologically tested for immunity and referred to, or discussed with, a specialist if non-immune to rubella or measles.

MMR is contraindicated for:

- those with proven anaphylaxis (but not contact dermatitis) to neomycin
- immunocompromised individuals (ie, those with significantly impaired cell-mediated immunity, including those with untreated malignancy, altered immunity as a result of drug therapy [including high-dose steroids], or receiving high-dose radiotherapy) (see section 4.3)
- individuals who have received another live vaccine, including BCG, within the previous four weeks (see chapter 20)
- pregnant women – pregnancy should be avoided for four weeks after immunisation
- individuals who have received IG or a blood transfusion during the preceding 11 months (see Table A6.1 in Appendix 6 for the length of time to defer measles vaccine after specific blood products)
- those with severe immune deficiency from HIV, because vaccine-related pneumonitis (from the measles component) has been reported³ – discuss vaccination of individuals with HIV infection with their specialist.

11.6.2 Precautions

Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response. Children with current ITP should have the timing of vaccination discussed with the specialist responsible for their care.

Women of childbearing age should be advised to avoid pregnancy for the next four weeks^{1, 3} after MMR vaccination (see section 18.5.3).

Measles vaccination may temporarily suppress tuberculin skin test (TST/Mantoux) reactivity, so if required, TST should be placed on the same day as MMR vaccination or postponed for four to six weeks after vaccination.³ TST is not a prerequisite for measles vaccination. An individual with active TB should be established on treatment before administering MMR vaccine.

11.6.3 Egg allergy

The measles and mumps components of the MMR vaccine are manufactured in chick embryo cell culture, so there may be trace amounts of egg protein in the vaccine. However, egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. Various studies have confirmed children with egg allergy can be vaccinated safely.^{3, 20, 21} Other components of the vaccine may be responsible for allergic reactions.²² Individuals with egg allergy may therefore be safely vaccinated in primary care.²³

11.7 Expected responses and AEFIs

11.7.1 Expected responses

A fever of 39.4°C or more occurs in 5–15 percent of children 6 to 12 days after immunisation and generally lasts one to two days.³ Rash occurs in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others.³ The majority of these events are coincidental and not caused by the vaccine.²⁴ Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccinees, most often 10 to 14 days after immunisation.²⁵ The rubella vaccine can cause a mild rash, fever, lymphadenopathy and joint pain between one and three weeks after immunisation.²⁶ There were no persisting sequelae associated with the administration of three million doses of MMR to 1.5 million children in Finland.^{24, 27}

11.7.2 AEFIs

Temporally related reactions, including febrile seizures, nerve deafness, aseptic meningitis, encephalitis, rash, pruritus, and purpura, may follow immunisation rarely; however, causality has not been established.²⁸

Vaccine virus transmission

MMR vaccine viruses have been regarded as being non-transmissible from vaccinees. There are two poorly documented case reports of transmission: one of rubella and one of a mumps vaccine strain from a vaccine that is no longer in production.²⁹ Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.^{30, 31} There have been no confirmed cases of disease transmission from MMR vaccine viruses.

Idiopathic thrombocytopenic purpura (ITP)

MMR vaccine is the only childhood vaccine with an elevated risk of ITP, which occurs in 1 in 22,000 to 40,000 people, 15 to 35 days after immunisation.³ A review of data from 1.8 million children in the US found 197 cases of ITP, with an incidence risk ratio of 5.48 (95% CI: 1.61–18.64) in the 1 to 42 days after vaccination.³² If ITP occurs, measles, mumps and rubella serology should be measured, and if the individual is immune to all three infections, a second dose is not required. However, if the individual is susceptible to any of the three infections, a second dose should be administered.^{33, 34, 35} The risk of thrombocytopenia is higher after the first dose of vaccine than after the second dose.³

11.7.3 Adverse outcomes not linked to MMR

There have been multiple epidemiological studies published from the UK,³⁶ Finland³⁷ and elsewhere^{38, 39} confirming that there is no link between MMR vaccine and the development of autism in young children (see section 3.2.4 for further discussion on this issue).

11.8 Public health measures

It is a legal requirement that all cases of measles be notified immediately on suspicion to the local medical officer of health – do not wait for a laboratory confirmation.

11.8.1 Diagnosis

A single case of measles should be considered an outbreak and result in a suitable outbreak response. Practitioners should have a low index of suspicion for notification, and all suspected clinical cases should be isolated immediately and notified to the medical officer of health.

The standard clinical case definition for measles is ‘an illness characterised by all of the following: generalised maculopapular rash, starting on the head and neck; fever (at least 38°C if measured) present at the time of rash onset; cough or coryza or conjunctivitis or Koplik’s spots present at the time of rash onset’.

It is important that the diagnosis be laboratory confirmed, as many viral infections can mimic measles. In the first instance, a nasopharyngeal and throat swab should be taken for viral identification by PCR. Further testing should be discussed with a clinical microbiologist. For instructions on measles specimen collection and transport, see the National Measles Laboratory website (www.measles.co.nz).

11.8.2 Prophylaxis

Management of contacts of a measles case should be discussed with the local medical officer of health.

MMR vaccine

There is evidence that a single dose of MMR vaccine when given to an unvaccinated person within 72 hours of first contact with an infectious person may reduce the risk of developing disease.¹ If there is doubt about vaccination status, MMR should still be given. MMR will not exacerbate the symptoms of measles if a person is already incubating the

disease, but in these situations, any measles-like illness occurring shortly after vaccination is likely to be due to infection.

If MMR vaccine is not given within 72 hours of first exposure, it should still be offered at any interval in order to offer protection from future exposures, unless the vaccine is contraindicated.

In an outbreak affecting infants, the use of MMR vaccine for infants aged 6–14 months should be considered. If MMR vaccine is given to an infant aged under 12 months, two more doses are still required after age 12 months and at least four weeks apart. This is because the seroconversion rate is lower when MMR is administered to an infant aged under 12 months. In an outbreak affecting young children, the second MMR vaccine does not have to be delayed until 4 years of age but can be given at any time from four weeks after the first dose.

Human normal immunoglobulin prophylaxis for contacts

Human normal immunoglobulin is recommended for measles-susceptible individuals in whom the vaccine is contraindicated (see section 11.6) and susceptible pregnant contacts. For these individuals, human normal immunoglobulin is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure. All other susceptible contacts should be offered MMR as post-exposure prophylaxis (as described above). Infants aged under 6 months where there is evidence of maternal immunity do not require any prophylaxis, but will still need the scheduled MMR doses at ages 15 months and 4 years.

Human normal immunoglobulin may be recommended for the following contacts of measles cases as soon as possible and up to six days after exposure:

- immunocompromised or immune-deficient people
- susceptible pregnant women
- immune-competent infants aged under 6 months where there is no evidence of maternal immunity (presence of maternal antibody, or documentation of two MMR doses or previous history of measles infection)
- immune-competent children aged between 6 and 15 months, who are outside the 72-hour exposure window for MMR vaccine.

The recommended doses as follows.

- Immune-competent infants aged under 15 months should receive 0.6 mL/kg intramuscularly, to a maximum volume of 5 mL.
- Pregnant women and immunocompromised or immune-deficient people should receive 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, recommended as three 5 mL injections.

Prophylaxis with intravenous immunoglobulin

IVIG (Intragam P) can be considered for immunosuppressed and immune-deficient measles contacts (who may, for example, have a central venous catheter), individuals with reduced muscle bulk, or in those people for whom large doses are required (see Appendix 6 for more information about passive immunisation).

The recommended dose of IVIG is 0.15 g/kg. See the guidance from the Health Protection Agency for further information (www.gov.uk/government/publications/measles-post-exposure-prophylaxis).

If there are further queries, these can be directed to the New Zealand Blood Service medical team via the DHB blood bank.

11.8.3 Exclusion

Exclusion of measles cases or contacts should be discussed with the local medical officer of health.

Parents/guardians should be advised that children who are suspected or confirmed measles cases should be excluded from early childhood services, school or community gatherings until at least five days after the appearance of the rash.

Immune contacts (ie, children aged 12 months to under 4 years who have received one dose of measles-containing vaccine after their first birthday and children aged 4 years and older who have received two doses) need not be excluded from these settings. Non-immune (susceptible) contacts should be excluded because of the risk of developing the disease themselves, and the risk of passing on the disease during the prodromal phase to other susceptible children. Advise

susceptible contacts to avoid attending school, early childhood services or community gatherings, and to avoid contact with other susceptible individuals, until 14 days after the last exposure to the infectious case.

Given that post-exposure MMR vaccination cannot guarantee protection, susceptible contacts who have received their first MMR vaccination within the 72-hour period after first exposure should also be excluded for 14 days after the last exposure to the infectious case (unless they subsequently meet the criteria for immunity). Contacts who have previously received one documented dose of MMR and then receive their second dose of MMR within 72 hours after first exposure can go back to school or work. If contacts receive their second MMR more than 72 hours after exposure, they should be excluded for 14 days after the last exposure to a person with measles.

Individuals who have received IG prophylaxis should also be excluded for 14 days after the last exposure to the infectious case.

Acceptable evidence of immunity is:

- anyone born before 1 January 1969
- documentation of previous immunity or previous infection
- children aged 12 months to under 4 years who have documentation of at least one dose of measles-containing vaccine after their first birthday
- individuals aged 4 years and older who have documentation of two doses of measles-containing vaccine, given at least one month apart and given after 12 months of age.

For more details on control measures, refer to the 'Measles' chapter of the *Communicable Disease Control Manual 2012*.⁴⁰

11.9 Variations from the vaccine data sheet

The vaccine data sheet recommends a single dose of MMR vaccine. However, as 5–10 percent of recipients fail to seroconvert after the first dose (see section 11.4.2), the Ministry of Health recommends and funds a second dose of MMR vaccine. Two doses are required for measles control and elimination;³ the second MMR dose is not a booster.

The vaccine data sheet states that pregnancy should be avoided for three months after vaccination. The Ministry of Health advises that women of childbearing age should avoid pregnancy for the next four weeks^{1, 3} after MMR vaccination.

The vaccine data sheet states that individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur. However, various studies have confirmed that egg-allergic children can be vaccinated safely.^{3, 20, 21} The Ministry of Health recommends that individuals with egg allergy, including anaphylaxis, may be safely vaccinated in primary care (see section 11.6.3).

References

1. Strebel PM, Papania MJ, Fiebelkorn AP, et al. 2013. Measles vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.
2. Fine PEM, Mulholland K. 2013. Community immunity. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.
3. American Academy of Pediatrics. 2015. Measles. In: Kimberlin DW, Brady MT, Jackson MA, et al (eds). *Red Book: 2015 Report of the Committee on Infectious Diseases* (30th edition). Elk Grove Village, IL: American Academy of Pediatrics.
4. Miller CL. 1985. Deaths from measles in England and Wales, 1970–83. *British Medical Journal* 290(6466): 443–4.

5. Patel MK, Gacic-Dobo M, Strebel PM, et al. 2016. Progress toward regional measles elimination – worldwide, 2000–2015. *Morbidity and Mortality Weekly Report* 65(44): 1228–33. URL: <https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6544a6.pdf> (accessed 14 November 2016).
6. GBD 2015 Child Mortality Collaborators. 2016. Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 388(10053): 1725–74. URL: [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(16\)31575-6/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31575-6/fulltext) (accessed 14 November 2016).
7. World Health Organization. 2015. *Measles Verification Q & A – March 2015*. URL: http://www.wpro.who.int/mediacentre/releases/2015/final_rvc_measlesverificationqa.pdf?ua=1 (accessed 5 August 2016).
8. World Health Organization. 2013. *Global Vaccine Action Plan 2011–2020*. URL: www.who.int/immunization/global_vaccine_action_plan/GVAP_doc_2011_2020/en/ (accessed 27 August 2013).
9. Auckland Regional Public Health Service. 2012. *Measles*. URL: www.arphs.govt.nz/health-information/communicable-disease/measles (accessed 26 October 2013).
10. Roberts MG. 2004. *A Mathematical Model for Measles Vaccination*. Unpublished report to the Ministry of Health, New Zealand.
11. Zahraei SM, Gouya MM, Mokhtari Azad T, et al. 2011. Successful control and impending elimination of measles in the Islamic Republic of Iran. *Journal of Infectious Diseases* 204(Suppl 1): S305–11.
12. Demicheli V, Rivetti A, Debalini MG, et al. Vaccines for measles, mumps and rubella in children. *Cochrane Database of Systematic Reviews* 2012, Issue 2, Art. No. CD004407. DOI: 10.1002/14651858.CD004407.pub3 (accessed 27 August 2013).
13. Mina MJ, Metcalf CJE, de Swart RL, et al. 2015. Long-term measles-induced immunomodulation increases overall childhood infectious disease mortality. *Science* 348(6235): 694–99. DOI: 10.1126/science.aaa3662 (accessed 17 November 2016).

14. Albertson JP, Clegg WE, Reid HD, et al. 2016. Mumps outbreak at a university and recommendation for a third dose of Measles-Mumps-Rubella vaccine — Illinois, 2015–2016. *Morbidity and Mortality Weekly Report* 65(29): 731–4. URL: <https://www.cdc.gov/mmwr/volumes/65/wr/pdfs/mm6529a2.pdf> (accessed 20 October 2016).
15. Davidkin I, Jokinen S, Broman M, et al. 2008. Persistence of measles, mumps and rubella antibodies in an MMR vaccinated cohort: a 20-year follow-up. *Journal of Infectious Diseases* 197(7): 950–6.
16. Kontio M, Jokinen S, Paunio M, et al. 2012. Waning antibody levels and avidity: implications for MMR vaccine-induced protection. *Journal of Infectious Diseases* 206(10): 1542–8.
17. Ministry of Health. 2017. *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*. URL: www.health.govt.nz/coldchain (accessed 14 February 2017).
18. Department of Health and Ageing. 2016. Measles. In: *The Australian Immunisation Handbook* (10th edition; updated August 2016). URL: <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-9> (accessed 20 October 2016).
19. Clemmons NS, Gastanaduy PA, Parker Fiebelkorn A, et al. 2015. Measles — United States, January 4–April 2, 2015. *Morbidity and Mortality Weekly Report* 64(14): 373–6. URL: <http://www.cdc.gov/mmwr/pdf/wk/mm6414.pdf> (accessed 5 August 2016).
20. James JM, Burks W, Roberson P, et al. 1995. Safe administration of measles vaccine to children allergic to eggs. *New England Journal of Medicine* 332(19): 1262–6.
21. Khakoo GA, Lack G. 2000. Recommendations for using MMR vaccine in children allergic to eggs. *British Medical Journal* 320(7239): 929–32.
22. Fox A, Lack G. 2003. Egg allergy and MMR vaccination. *British Journal of General Practice* 53(495): 801–02. URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1314715/pdf/14601358.pdf> (accessed 7 November 2016).
23. Clark AT, Skypala I, Leech SC, et al. 2010. British Society for Allergy and Clinical Immunology guidelines for the management of egg allergy. *Clinical & Experimental Allergy* 40(8): 1116–29. URL: <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2222.2010.03557.x/epdf> (accessed 9 November 2016).

24. Peltola H, Heinonen OP. 1986. Frequency of true adverse reactions to measles-mumps-rubella vaccine. *The Lancet* 327(8487): 939–42.
25. Rubin SA, Plotkin SA. 2013. Mumps vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.
26. American Academy of Pediatrics. 2015. Rubella. In: Kimberlin DW, Brady MT, Jackson MA, et al (eds). *Red Book: 2015 Report of the Committee on Infectious Diseases* (30th edition). Elk Grove Village, IL: American Academy of Pediatrics.
27. Peltola H, Patja A, Leinikki P, et al. 1998. No evidence for measles mumps and rubella vaccine-associated inflammatory bowel disease or autism in a 14-year prospective study. *The Lancet* 351(9112): 1327–8.
28. American Academy of Pediatrics. 2015. Mumps. In: Kimberlin DW, Brady MT, Jackson MA, et al (eds). *Red Book: 2015 Report of the Committee on Infectious Diseases* (30th edition). Elk Grove Village, IL: American Academy of Pediatrics.
29. Wolf J, Eisen JE, Fraimow HS. 1993. Symptomatic rubella reinfection in an immune contact of a rubella vaccine recipient. *Southern Medical Journal* 86(1): 91–3.
30. Morfin F, Beguin A, Lina B, et al. 2002. Detection of measles vaccine in the throat of a vaccinated child. *Vaccine* 20(11–12): 1541–3.
31. Reef SE, Plotkin SA. 2013. Rubella vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.
32. O’Leary ST, Glanz JM, McClure DL, et al 2012. The risk of immune thrombocytopenic purpura after vaccination in children and adolescents. *Pediatrics* 129(2): 248–55.
33. Beeler J, Varricchio F, Wise R. 1996. Thrombocytopenia after immunisation with measles vaccines: review of the vaccine adverse events reporting system (1990 to 1994). *Pediatric Infectious Disease Journal* 15(1): 88–90.
34. Miller E, Waight P, Farrington CP, et al. 2001. Idiopathic thrombocytopenic purpura and MMR vaccine. *Archives of Disease in Childhood* 84(3): 227–9.
35. Stowe J, Kafatos G, Andrews N, et al. 2008. Idiopathic thrombocytopenic purpura and the second dose of MMR. *Archives of Disease in Childhood* 93(2): 182–3.
36. Miller E. 2002. MMR vaccine: review of benefits and risks. *Journal of Infection* 44(1): 1–6.

37. Makela A, Nuorti JP, Peltola H. 2002. Neurologic disorders after measles-mumps-rubella vaccination. *Pediatrics* 110(5): 957–63.
38. Health Canada. 2001. Does measles-mumps-rubella (MMR) vaccination cause inflammatory bowel disease and autism? *Canada Communicable Disease Report* 27(8): 65–72.
39. Davis RL, Kramarz P, Bohlke K, et al. 2001. Measles-mumps-rubella and other measles-containing vaccines do not increase the risk for inflammatory bowel disease. *Archives of Pediatric & Adolescent Medicine* 155(3): 354–9.
40. Ministry of Health. 2012. *Communicable Disease Control Manual 2012*. URL: <http://www.health.govt.nz/publication/communicable-disease-control-manual-2012> (accessed 15 November 2016).