18 Rubella

Key information

Mode of transmission	By contact with infected nasopharyngeal secretions. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine.
Incubation period	14–23 days, usually 16–18 days.
Period of communicability	7 days before until 7 days after the onset of the rash. Infants with CRS may be infectious for months.
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. For (re-)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Pregnancy	All pregnant women and women planning pregnancy should have their immunisation history checked. A woman is considered to be immune to rubella if she has had 2 documented doses of a rubella-containing vaccine given at least 4 weeks apart and given after age 12 months, regardless of serology. Pregnant non-immune women should avoid contact with known cases of rubella, and should receive MMR after delivery.
Vaccine efficacy/ effectiveness	Highly effective with a 2-dose schedule; protection lasts at least 20 years and may be considerably longer.
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 rubella disease.

18.1 Virology

Rubella is an enveloped RNA virus from the family Togaviridae and the genus *Rubivirus*.

18.2 Clinical features

Clinical features include a transient erythematous rash and lymphadenopathy without respiratory symptoms. Arthritis or arthralgia is relatively common and a classic feature of infection in adults. While usually a mild childhood illness, rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs with a prevalence of approximately 1 in 6,000 cases and may result in residual neurological damage or, occasionally, death. Thrombocytopenia rarely occurs.

Clinical diagnosis is unreliable because the symptoms are often fleeting and can be mimicked by other viruses. In particular, the rash is not diagnostic of rubella. Up to 50 percent of rubella infections are subclinical or asymptomatic. A history of rubella should therefore never be accepted as proof of immunity without laboratory confirmation.

Transmission of rubella is through direct or indirect contact with infected nasopharyngeal secretions and droplets. The incubation period is usually 16 to 18 days (range 14 to 23 days) and infectivity is between seven days before and seven days after the onset of the rash. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine for months after birth and should be considered infectious until they are aged 12 months.

Although the vaccine virus is excreted after vaccination, mostly from the pharynx, transmission to susceptible contacts has not been demonstrated (see section 11.7.2). Therefore, a recently immunised contact is not a risk to a pregnant woman.

Rubella infection during pregnancy can result in fetal infection, causing CRS in a high proportion of cases. Rubella infection in the first eight weeks of pregnancy results in fetal damage in up to 85 percent of infants, and multiple defects are common. The risk of damage declines to 10–20 percent by about 16 weeks' gestation, and after this stage of pregnancy fetal abnormalities are rare.

Infants born with CRS may have cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow. Some infected infants may appear normal at birth, but have nerve deafness detected later.

The frequency of complications and consequences of rubella infection are best described from the 1963/64 US outbreak, involving 12.5 million cases of rubella and 30,000 infants damaged by intrauterine rubella, an incidence rate of 100 per 10,000 pregnancies (see Table 18.1).

Table 18.1: Estimated morbidity and mortality associated with the 1963/64 US rubella epidemic

Total number of cases of rubella: 12,500,000	
Complications of rubella	**Risk per case**
Arthritis or arthralgia	1.3%
Encephalitis	17 per 100,000
Neonatal deaths	17 per 100,000
Complications caused by congenital rubella syndrome (CRS)	**Numbers of cases (% of CRS cases)**
Total number with CRS	20,000
Deaf children	8,055 (40%)
Deaf–blind children	3,580 (18%)
Intellectually handicapped children	1,790 (9%)

Adapted from: Reef S, Plotkin SA. 2013. Rubella vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders. Table 31.7.

Rubella infection can occur (very rarely) in individuals with either naturally acquired or vaccine-induced antibody. Rare cases of CRS have been reported after reinfection during pregnancy.

As with measles, public health measures of accurately diagnosing potential cases of rubella with notification and contact tracing are critical (see section 18.8).

18.3 Epidemiology

18.3.1 Global burden of disease

Humans are the only source of rubella infection. Infection is often asymptomatic. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among 5–9-year-old children, and 80–90 percent of adults were immune to rubella. Extensive outbreaks of rubella occurred every six to nine years, in which many children were affected by CRS. Immunisation against rubella, introduced to prevent the occurrence of CRS, has resulted in a very significant reduction in infection, especially once vaccination was introduced to boys and girls.

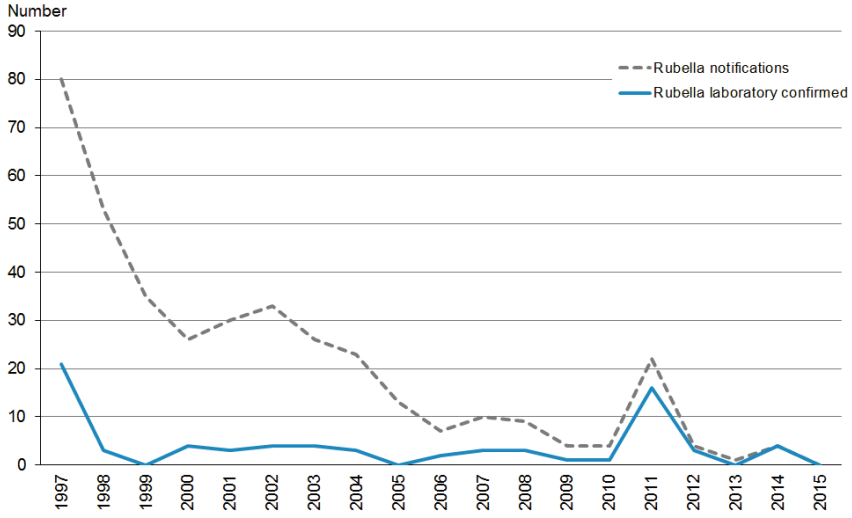
18.3.2 New Zealand epidemiology

Rubella immunisation was introduced in 1970 (see Appendix 1), and rubella has been a notifiable disease since 1996. The last large rubella outbreak in 1995–1996 mostly involved young adult males, who would not have been offered immunisation. This emphasises the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.

Three cases of rubella were notified in 2016, with no notifications in 2015 and four in 2014. All of the 2016 and 2014 cases were imported from overseas (ESR, 14 March 2017).

There have been no reported cases of CRS in New Zealand since 1998.

Figure 18.1: Rubella notifications and laboratory-confirmed cases by year, 1997–2015



Source: ESR

18.4 Vaccines

18.4.1 Available vaccines

Rubella vaccine is one of the components of the live attenuated MMR and MMRV vaccines, considered in sections 11.4.1 and 21.4.1. Single-antigen rubella vaccine is not available in New Zealand.

Funded vaccine

MMR vaccine funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella, and Jeryl Lynn mumps. (See section 11.4.1 for more information.)

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 11.4.1).

18.4.2 Efficacy and effectiveness

The rubella vaccine has been shown to be 90–97 percent effective in an outbreak after a single dose, and this is likely to be higher with a two-dose schedule. One dose of rubella vaccine at 12 months or older induces an antibody response in at least 95 percent of recipients. Studies have found no evidence of waning of protection over decades of follow-up.[1] In 90 percent of recipients, antibodies persisted for at least 16 years; other studies have reported persistence up to 21 years.[1] A few recipients fail to produce antibodies following immunisation, and a small number of individuals lose antibodies, whether derived from natural infection or the vaccine. See also section 11.4.2 for further evidence on the duration of immunity.

18.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[2] 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.

18.4.4 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.[3]

18.5 Recommended immunisation schedule

As in other high-income countries, New Zealand's primary strategy for preventing and eventually eliminating rubella is to vaccinate both boys and girls with two doses of MMR vaccine (Table 18.2).

It is important for vaccinators to be able to explain why boys need rubella vaccine, given that the aim is to prevent rubella in pregnancy. In New Zealand and the UK, where a targeted approach was used and 11-year-old girls were offered rubella immunisation, even with high coverage there were still women of childbearing age who were susceptible to rubella, either because of failure to be vaccinated or vaccine failure. Rubella continued to circulate in New Zealand because children aged under 11 years and males were not vaccinated, and so CRS continued to occur, albeit at a reduced rate.

To prevent all cases of CRS, rubella must not circulate in the community and therefore males must be immunised. Achieving at least 95 percent coverage of two doses of MMR prevents the circulation of rubella (which is much less infectious than measles) and therefore lead to the elimination of rubella.

Table 18.2: 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 MMR vaccine is funded for those who are susceptible to 1 or more of the 3 diseases. See sections 18.5.2 and 18.5.3.

18.5.1 Usual childhood schedule

Two doses of rubella vaccine as MMR are recommended at age 15 months and age 4 years. Over 95 percent of individuals will become immune to rubella after one dose.[4] The second dose is not a booster. Two doses are recommended because the 2–5 percent not protected by the first dose will nearly all be protected by the second. The second dose of vaccine can be given as soon as four weeks after the first dose. (See below for the recommendations for other groups.)

Children who in an outbreak (of measles, mumps or rubella) receive MMR vaccine when aged under 12 months require two further doses administered after age 12 months. 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.

18.5.2 Catch-up

Any individual born on or after 1 January 1969 (see section 11.5.2) who does not have two documented doses of MMR vaccine, given at least four weeks apart with the first dose given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded).

Even if the individual has previously received single-antigen measles vaccine, up to two doses of MMR vaccine (ie, additional doses of measles vaccine) may be given to these individuals to ensure rubella and mumps protection. There are no significant adverse effects from further vaccinating individuals who are already immune to measles, mumps and/or rubella, and no reliance can be placed on a prior clinical history of rubella infection.

Immigrants to New Zealand

The vaccination status of immigrants should be checked as a priority group. Anyone who does not have two documented doses of MMR vaccine, given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded if eligible).

18.5.3 Pregnancy and breastfeeding

Women planning pregnancy

It is particularly important to ensure that women of child-bearing age are immune to rubella.[5] Women who are planning pregnancy should have their immunisation history checked for having received two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months. Non-immune women may receive MMR vaccine before pregnancy, but pregnancy should be avoided for four weeks after the last MMR vaccination.[6, 7]

Pregnant women

MMR vaccine is contraindicated during pregnancy.

> All pregnant women should have their immunisation history checked. A pregnant woman is considered to be immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months, *regardless of serology*. If a pregnant women is non-immune, give one or two doses of MMR vaccine four weeks apart (as appropriate) when not pregnant (funded).

Serological testing for immunity to rubella is not usually performed in New Zealand except as part of routine antenatal care. Improved documentation and effective surveillance showing the rarity of CRS when there is high immunisation coverage has led to some countries, such as England, discontinuing routine antenatal rubella screening.[8] Also, the screening tests used for rubella serology can potentially give inaccurate results and may cause unnecessary stress for women.[8]

In general, it should be remembered that the great majority of New Zealand-born individuals who received all scheduled childhood vaccines will be immune to rubella, and the chance of being exposed in New Zealand to an infectious case is becoming increasingly rare. (If exposure during pregnancy does occur, see the guidelines in section 18.8.3.)

The following groups of women are more likely to be non-immune to rubella:[5]

- women born overseas (especially in Asia, the Pacific Islands, sub-Saharan Africa and South America) who entered New Zealand after the age of routine vaccination
- women over the age of 35 years.

After delivery

If MMR vaccine and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccinees (see section A6.4.1).

Breastfeeding

There is no risk to the mother or child in giving MMR to breastfeeding women.[1]

18.5.4 Immunocompromise

MMR vaccine is contraindicated in immunocompromised children (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised, 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.

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/mm^3 or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[6]

18.6 Contraindications and precautions

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

18.6.1 Contraindications

See section 11.6.1 for specific MMR vaccine contraindications.

The general contraindications that apply to all immunisations are relevant to MMR.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[1, 6] However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.[1]

18.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication for MMR vaccine. See section 11.6.3 for more information, and section 11.6.2 for further precautions.

18.7 Expected responses and AEFIs

See also section 11.7.

18.7.1 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.[6] Rash occurs in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others.[6] The majority of these events are coincidental and not caused by the vaccine.[9] Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

Joint symptoms may be reported in 0.5 percent of young children and 10–25 percent of post-pubertal women.[4] Symptoms begin one to three weeks after immunisation and are usually transient. The prevalence of joint symptoms following rubella immunisation is lower than occurs with natural infection at a corresponding age.[4]

It was previously thought that the rubella vaccine might lead to long-term arthritis. A 2012 Institute of Medicine review concluded that the evidence was inadequate to accept or reject a causal relationship between MMR vaccine and chronic arthritis in women.[10]

18.7.2 AEFIs

ITP and, rarely, neurological disturbances have been reported (see section 11.7.2).

18.8 Public health measures

Rubella (including CRS) is a notifiable disease, and suspected cases should be notified by the clinician on suspicion to the local medical officer of health. Accurate diagnosis requires laboratory confirmation.

The preferred method of diagnosis is by PCR or culture (see the 'Rubella' chapter of the *Communicable Disease Control Manual 2012*[11]). Serology may be useful but can be hard to interpret if the person has received rubella vaccine in the past.

The local medical officer of health will arrange contact tracing and alert the contacts or the public of potential exposure, particularly of pregnant women.

18.8.1 Exclusion of cases of rubella infection

Parents/guardians should be advised that children with suspected rubella should be excluded from early childhood services or school until fully recovered and for seven days after the appearance of the rash. Children with CRS should be considered infectious until they are aged 12 months. Adults should be excluded from work until fully recovered and for seven days after the appearance of the rash.

18.8.2 Management of non-pregnant contacts

The local medical officer of health will advise on contact management. Check the immunisation status of all close contacts.

Rubella-containing vaccine does not provide protection if given after exposure to rubella. However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection. Human normal immunoglobulin does not prevent rubella infection after exposure and should not be used for that purpose.[12]

18.8.3 Management of pregnant contacts

It is critical to accurately document the rubella status of all people who may have rubella and potentially exposed a pregnant woman to the virus. Such people will have travelled overseas or had contact with an infected returned traveller. As described in section 18.3.2, rubella virus does not circulate in New Zealand. Rubella infection in the first half of pregnancy is potentially devastating, and every possible exposure of a pregnant woman should be discussed with the local medical officer of health, obstetrician and microbiologist or infectious diseases physician.

Pregnant contacts with confirmed immunity can be reassured that the likelihood of rubella infection is remote.[11] This applies if:

- she has received at least two documented doses of rubella-containing vaccine, OR
- a previous antibody screening test has detected a protective level of antibodies, and this has been documented, OR
- one dose of vaccine followed by a rubella antibody screening test showing a protective level of antibodies has been documented.[11]

Coordinated care and management

Coordinated care and management are essential (Table 18.3). An obstetrician (or a maternal fetal medicine specialist) and an infectious diseases specialist/microbiologist should be consulted when the diagnosis of possible rubella infection in a pregnant woman is first considered. The clinical picture and all test results should be discussed by all involved in the care of the woman, to enable an accurate interpretation of the serological results before advising the woman about the risk to her fetus and options regarding the continuation of pregnancy.

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, **and who have been exposed to rubella in the first half of pregnancy**, must be investigated serologically and virologically, irrespective of immunisation history or history of previous clinical rubella. Serum should be obtained as soon as possible, with the clinical details included on the request form. The laboratory should be asked to store an aliquot of serum for later testing in tandem with a follow-up sample. These results must be interpreted in conjunction with the time period since exposure, to determine whether or not acute infection has occurred.

It is essential to discuss testing with the local clinical microbiologist before taking samples, to ensure that the right samples are obtained and the best tests performed expeditiously. All requests to laboratories must state the:

- duration of pregnancy and last menstrual period
- date of exposure to possible rubella

- date of blood specimen
- name of the index case who is thought to have rubella.

The use of IG is not recommended for post-exposure prophylaxis of rubella in early pregnancy or any other circumstance. However, IG may be considered if termination of the pregnancy is not an option, but termination must be discussed when maternal infection is confirmed. Although IG has been shown to reduce clinically apparent infection in the mother, there is no guarantee that fetal infection will be prevented.

> It is a legal requirement that all cases of CRS and rubella be notified immediately on suspicion to the local medical officer of health.

For more details on control measures, refer to the 'Rubella' chapter of the *Communicable Disease Control Manual 2012*.[11]

Table 18.3: Suggested roles of health professionals

	Lead maternity carer	Medical officer of health	GP	Obstetrician/ infectious diseases specialist/ maternal fetal medicine specialist
Check rubella status in every pregnancy (2 documented doses of rubella-containing vaccine)	✓			
Investigate initial suspected rubella case and trace contacts		✓		
Coordinate care of exposed non-immune pregnant woman		✓	✓	
Review clinical and laboratory results, and discuss options with the pregnant woman if rubella is confirmed				✓
AFTER delivery – vaccinate any woman who is not immune	✓		✓	

18.9 Variations from the vaccine data sheet

See section 11.9 for variations from the MMR (Priorix) data sheet.

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