

11 Rubella

11.1 Introduction

Rubella has probably afflicted humans for centuries, but its often mild symptoms and the similarity of its rash to many other infections prevented recognition of the disease as a separate entity until the late 18th century. George Maton gave a clear description of the disease in 1814. Henry Veale named the illness 'rubella' half a century after he observed an outbreak in India. The viral nature of the infection was demonstrated by Hess in 1914 and confirmed by Hiro and Tasaka in 1938, when they inoculated children with the filtered nasal washings of infectious cases. In 1941 Gregg published his classic account of *Congenital Cataract Following German Measles in the Mother*. The virus was not isolated in tissue culture until 20 years later in 1962. The first effective live attenuated virus vaccine, based on the Cendehill strain, was released for use in 1969 following a major outbreak of rubella, starting in Europe in 1962/63 and spreading to the United States (US) in 1964/65, with many cases of the congenital rubella syndrome. A triple vaccine containing attenuated measles, mumps and rubella viruses has been in use in the US since the early 1970s. The RA27/3 strain has been used since 1979 because of its superior immunogenicity and lower rate of reactions.

11.2 The illness

Rubella is a common childhood disease that can affect adults and, like measles, often occurs in epidemics. It is most common in children of early school age. Clinical features include a transient erythematous rash, lymphadenopathy (particularly in the posterior auricular and suboccipital nodes), without respiratory symptoms. In adults, arthritis or arthralgia may occur. Rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs more frequently than the previously estimated 1 in 6000 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. A history of 'rubella' should never be accepted without confirmation by positive serology. The incubation period is 14–21 days, usually 16–18, and infectivity is from seven days before until seven days after the onset of the rash. Transmission is primarily via respiratory secretions.

Maternal rubella 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 the congenital rubella syndrome (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. Infants with CRS may excrete the virus for a year or more after birth.

The risks from rubella 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 100,000 pregnancies (see Table 11.1 below, and Table 9.1).

Table 11.1: Estimated morbidity/mortality associated with 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 CRS	20,000
Deaf children	8055 (40%)
Deaf-blind children	3580 (18%)
Intellectually handicapped children	1790 (9%)

Source: Plotkin SA, Reef S. 2004. Rubella vaccine. In: SA Plotkin, WA Orenstein (eds). *Vaccines* (4th edition). Philadelphia: WB Saunders Company, Table 26–6, p.712.

The risk of rubella infection increases in later pregnancies because parous women with older children are more likely to be exposed to rubella from their children. 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.

11.3 Epidemiology

Humans are the only source of rubella infection. Asymptomatic infection is common. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among five to nine 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 significant reduction, especially where there is extensive use of the rubella vaccine.

New Zealand epidemiology

Outbreaks of rubella continue to occur in New Zealand. Although rubella immunisation was offered from 1979 to all girls in year 7 (form 1), it was not offered to boys until 1992, allowing spread in the community. There were 100 cases

reported between August 1989 and February 1990, some among pregnant women, and there were three cases of CRS reported. The outbreaks of rubella in 1993 and a larger one in 1995 have mostly involved young adult males, who would not have been offered immunisation. These outbreaks emphasise 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.

Rubella has been a notifiable disease since 1996. In 2003 there were 26 cases of rubella notified, of which three cases were laboratory confirmed; and in 2004 there were 25 cases notified, of which three were laboratory confirmed. It is important that suspected cases are notified and are laboratory confirmed so that public health control programmes can limit spread (see section 11.8). (See Figure 11.1 for notifications and laboratory confirmed cases of rubella.)

There have been no cases of CRS in New Zealand newborns reported to the New Zealand Paediatric Surveillance Unit between 1998 and 2004.

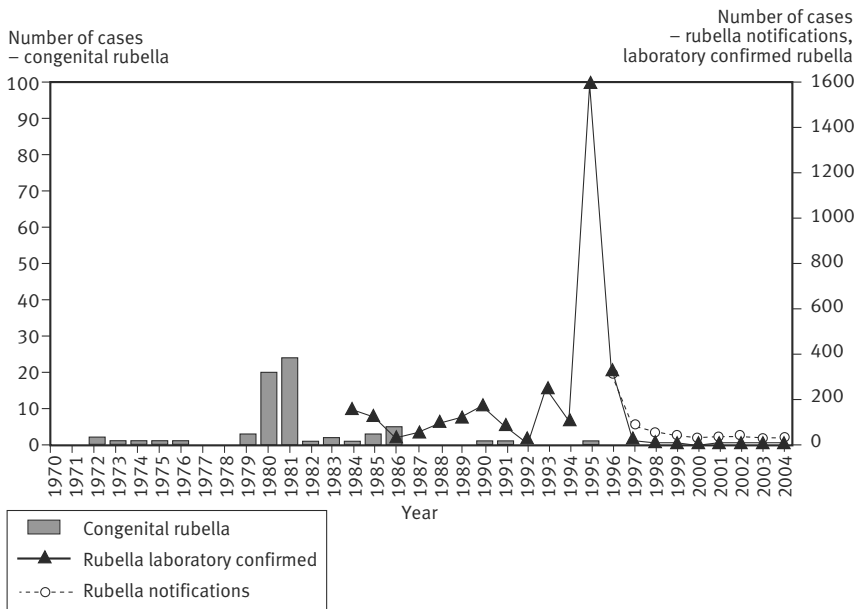
History of the New Zealand Immunisation Schedule

Immunisation with an attenuated rubella vaccine (Cendehill strain) was first offered to all four year old New Zealand children in 1970, the rationale being to prevent transmission of the wild virus in five to nine year old children, who were the main sufferers from clinical disease. At the same time the Department of Health delivered a school based programme, which succeeded in immunising 95 percent of children five to nine years of age. The acceptance rate of the preschool entry dose of rubella was only about 40 percent, and many practitioners did not feel it was appropriate to immunise males.

In 1979 the immunisation policy for rubella was altered to offer the vaccine to girls of 11 years of age, in year 7 (form 1). The aim was to immunise females before they attained childbearing age. In 1990 MMR was introduced at 15 months for all children and rubella vaccine continued to be offered to girls in form 1. Since 1992 two doses of rubella vaccine – as measles, mumps and rubella (MMR) vaccine – have been offered to all children, the first dose in the second year of life and the second dose at 11 years of age. This was changed in 2001, maintaining the first dose of MMR at 15 months and changing the second to four years of age, before school entry. The aim of this strategy was to prevent rubella epidemics, reduce the background incidence of rubella and continue to protect women before childbearing, therefore eventually abolishing CRS (see Figure 11.1). In 2001 there was an MMR school catch-up programme throughout the country for all children between five and 10 years of age who would no longer receive an MMR dose in year 7.

In 2006 the rubella schedule will continue as two doses of MMR vaccine offered at age 15 months and four years. All young women should be screened to check their rubella immunity. The MMR vaccine is available and publicly funded for all susceptible adult women. All women are screened for rubella immunity during pregnancy, and susceptible women are offered MMR vaccine after delivery.

Figure 11.1: Notifications of congenital rubella, 1970–2004, notifications of rubella 1996–2004, and laboratory confirmed cases, 1984–2004



11.4 Vaccines

The rubella vaccine is one of the components of the MMR vaccine, which is considered in section 9.4. Single antigen rubella vaccine is no longer available in New Zealand.

Efficacy

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. A recent review found no evidence of waning in protection over decades of follow-up.^{1,2} In 90 percent of recipients antibodies persisted for 16 years, other studies have reported persistence up to 21 years.³ 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.

Serological testing

Women should be screened for the rubella antibody in their early reproductive years before pregnancy, in the antenatal period of every pregnancy, and at their request when pregnancy is planned (see sections 11.5 and 11.8).

Although it has been considered that a rubella antibody level of greater than 10 IU/mL indicates protection is likely, reinfection with rubella can occur even with antibody levels above 15 IU/mL and the risk is expected to be greater with rubella antibody levels of 10–15 IU/mL or lower. However, CRS is less likely after reinfection with rubella in pregnancy compared with a primary infection (see section 11.2). It is estimated that the incidence of CRS is 5 percent after reinfection with rubella in the first trimester, and negligible later in pregnancy.⁴

It is therefore recommended that pregnant women with a rubella antibody level below 15 IU/mL be counselled to avoid contact with cases of rubella. If the antibody level is below 25 IU/mL, the woman should be offered MMR after delivery if she has not already received two doses of a rubella containing vaccine.

A pregnant woman with low anti-rubella antibody levels should have her serology repeated if she comes into contact with someone with a rash. If a rise in titre is detected, the results should be discussed with an expert (see section 11.8). Women exposed to rubella during pregnancy should be tested as in section 11.8. Reinfection with rubella is associated with a rise in IgG but not a rise in IgM.⁵

Although the vaccine virus is excreted, mostly from the pharynx, extensive efforts to identify transmission to susceptible contacts have failed (see section 9.4). A recently immunised contact is not a risk to a pregnant woman.

If an individual has no documented history of immunisation with MMR vaccine they should be given a dose of MMR vaccine rather than performing serology. There are no undue adverse effects from 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. (See also section 9.5.)

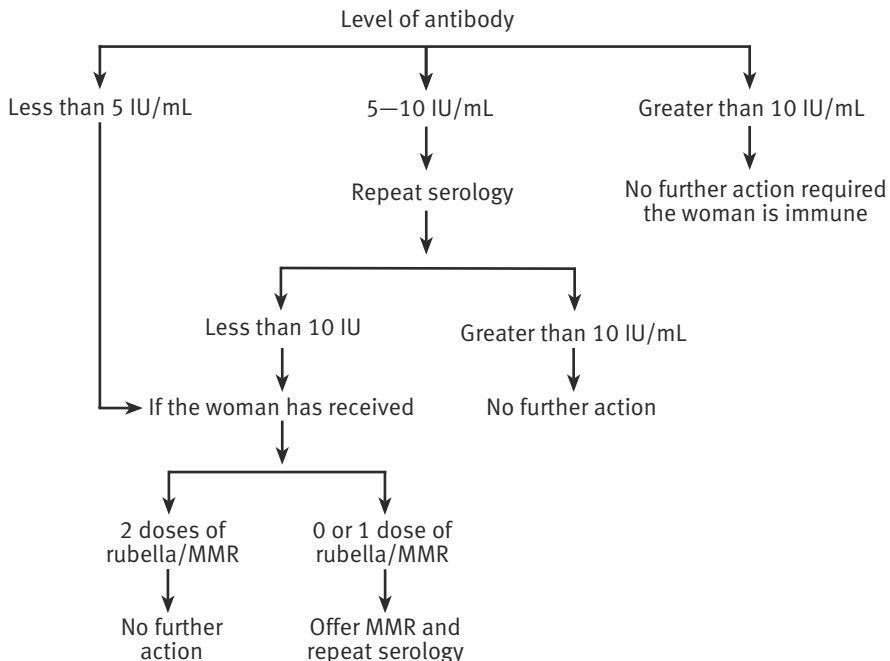
Dosage

The correct dose is all of the reconstituted MMR vaccine (about 0.5 mL) given by subcutaneous injection in the deltoid area to all age groups. (See section 2.3 for needle sites and sizes.)

11.5 Recommended immunisation schedule

Two doses of rubella vaccine (as MMR) are recommended at 15 months and four years of age, before school entry. Two doses are recommended because the 2–5 percent who fail to be 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.)

Figure 11.2: Guide to rubella immunisation for women with low levels of antibodies



It is important for vaccinators to be able to explain why boys need rubella vaccine, given that the primary aim is to prevent rubella in pregnancy. In New Zealand and the United Kingdom (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 child bearing age who were susceptible to rubella, either because of failure to be vaccinated or vaccine failure. Rubella continued to circulate in New Zealand because no one under age 11 and males were not vaccinated and CRS continued to occur, although 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 MMR should prevent the circulation of rubella, which is less infectious than measles, and therefore lead to the elimination of rubella and CRS.

At risk groups from rubella

1 Non-pregnant susceptible women

MMR should be offered (and is publicly funded) to all women to protect against all three diseases. If the woman is already immune, the vaccine virus will not replicate and any boosting of rubella antibodies will increase the duration of protection for any future babies.

It is important to ensure that all women of childbearing age have been screened for rubella antibodies and, if not immune, vaccinated prior to pregnancy. Opportunities for screening arise at any health service encounter. Every effort must be made to identify and immunise seronegative women. All women should be informed of the result of their antibody test. Note that female immigrants may not have been immunised, and may be at risk (see below).

2 Women born between 1965 and 1967

These women are at risk of rubella because they were too young for the initial 1970 campaign targeted at children four to nine years of age, and too old to be immunised in year 7 (form 1) during 1979 (see section 11.3). This cohort is less likely to develop natural immunity in childhood because of high coverage in the proximate cohorts, and they may be at increased risk of susceptibility to rubella.⁶ It is important that these women have their rubella antibody status checked and, if not immune, be offered rubella immunisation.

3 Pregnant susceptible women

All women should be routinely tested for rubella antibodies during the antenatal period. Women found to be seronegative on antenatal screening should be immunised (publicly funded) after delivery (with MMR vaccine) before they leave the supervision of the lead maternity carer.

If MMR vaccine and anti-D immunoglobulin are required after delivery, both the vaccine and anti-D immunoglobulin 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 immunoglobulin 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. Rubella serology should be checked six to eight weeks later to ensure that seroconversion has occurred, with immunisation repeated if it has not. MMR may be given to women who are breastfeeding.

4 Immigrants to New Zealand

The rubella status of immigrants should be checked as a priority group. While most industrialised countries have for many years included rubella vaccination on their immunisation schedules, rubella has not been a component of the immunisation schedules in most non-industrialised countries such as the Pacific Islands. Surveys of susceptibility to rubella in women of childbearing age have found rates greater than 25 percent in India, Israel, Malaysia, Nigeria, Singapore, Sri-Lanka and Thailand, and rates of 10–25 percent in many African, Middle Eastern and South American countries. Immigrants from non-industrialised countries should be offered two doses of MMR vaccine (four weeks apart).

5 Health care workers and students

Health care workers and students should all (both male and female) be screened for rubella antibodies and immunised with at least one dose of MMR if seronegative, to avoid risk to their patients. Health care workers without a documented history of two doses of MMR vaccine should be given one dose of MMR.

11.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses

Mild reactions after immunisation with the rubella or MMR vaccines include fever, sore throat, lymphadenopathy, rash, arthralgia and arthritis (see section 9.6). The incidence of these side effects is age related. Joint symptoms may occur in 0–3 percent of infants and 12–20 percent of adult women. Symptoms begin one to three weeks after immunisation and are usually transient. The incidence of joint symptoms following rubella immunisation is at a lower rate than occurs with natural infection at a corresponding age.

It was previously thought that the rubella vaccine might lead to long term arthritis. However, two large controlled studies found no supporting evidence of this.^{7,8} Another study did find a slight increase in risk from rubella vaccine, but this was of borderline statistical significance.⁹ A review of the available evidence concluded that the rubella vaccine does not cause chronic arthritis.¹⁰

Thrombocytopenia and, rarely, neurological disturbances have been reported (see section 9.6 for information on adverse events and reimmunisation).

Adverse events following immunisation

Anaphylaxis to a previous dose of MMR is a contraindication to a further dose of MMR. (See also section 9.6 for further information on the MMR vaccine.)

Any severe or unexpected reactions should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at <http://carm.otago.ac.nz>. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

11.7 Contraindications

The general contraindications, which apply to all immunisations, are relevant to MMR (see sections 1.9 and 9.7).

Rubella vaccines contain traces of neomycin and/or polymyxin. Previous anaphylactic reactions to these substances contraindicate rubella vaccine.

The MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for 28 days after immunisation.¹¹ However, inadvertent immunisation with a rubella containing vaccine in early pregnancy is no longer considered an indication for abortion. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, UK and Germany.¹²

11.8 Control measures

It is recommended that when a diagnosis of rubella is suspected, the diagnosis should be confirmed by laboratory testing (IgM) and the case notified to the medical officer of health to enable control measures to be put in place to halt an outbreak. All cases of CRS should also be notified to the local medical officer of health.

Parents/caregivers should be advised that children with rubella should be excluded from early childhood services or school for seven days after the appearance of the rash. Children with congenital rubella should be considered infectious until they are one year of age.

Unimmunised contacts need not be excluded from early childhood services or school but should be given advice about MMR and the National Immunisation Schedule. Female staff of childbearing age should ensure they are immune to rubella. Pregnant women known to be susceptible to rubella must avoid contact with known or suspected cases.

Management of a pregnant woman who has been exposed to rubella

All women should have been routinely tested for the presence of rubella antibodies before pregnancy and early in every pregnancy. If this result is available and the woman is known to be immune, she may be reassured that her fetus is at little risk (see sections 11.2 and 11.5).

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, and who may have been exposed to rubella, must be investigated serologically irrespective of immunisation history, clinical rubella or previous positive rubella antibody. The rash is not diagnostic and infection can occur without clinical symptoms.

Serological testing

The pregnant woman should be tested for rubella antibodies as soon as possible after exposure. Request the laboratory to store (frozen) an aliquot of serum for later testing in tandem with a follow-up sample.

If the first sample is antibody positive, then a full assessment of the serological status is needed. These results must be interpreted in conjunction with the time lapse since exposure to determine whether or not acute infection has occurred.

If the woman is rubella antibody negative and remains asymptomatic, a second blood specimen should be obtained 28 days after the exposure date. However, a second blood specimen should be obtained as soon as possible if the woman

develops clinical symptoms suggestive of rubella. A third blood specimen may be necessary seven days after the onset of symptoms.

It is essential that all requests to laboratories state the:

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

Ideally, a virologist or infectious disease specialist should be consulted when the diagnosis is first considered. The clinical picture and all test results should be discussed by the virologist and the specialist to enable accurate interpretation of serological results before advising the woman about the risk to her fetus.

Management

This is well covered in the 2003 *Red Book*,¹³ which includes the following advice.

The routine use of immune globulin (IG) for post exposure prophylaxis of rubella in early pregnancy is not recommended. Administration of IG should be considered only if termination of the pregnancy is not an option. Limited data indicate that IG in a dose of 0.55 mL/kg may decrease clinically apparent infection in an exposed susceptible person from 87 percent to 18 percent compared with placebo. However, the absence of clinical signs in a woman who has received intramuscular IG does not guarantee that fetal infection has been prevented. Infants with congenital rubella have been born to mothers who were given IG shortly after exposure.

Live rubella virus vaccine given after exposure has not been demonstrated to prevent illness but theoretically can prevent illness if administered within three days of exposure. Immunization of exposed, nonpregnant persons may be indicated because if the current exposure does not result in infection, the immunization will protect the individual in the future. Immunization of a person who is incubating natural rubella or who is already immune is not associated with increased risk of adverse effects (p. 538).

For more details on control measures, refer to *Control of Communicable Diseases Manual*.¹⁴

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