20 Rubella

Rubella vaccine introduced in 1971
MMR introduced in 1988

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

Contents

Key changes

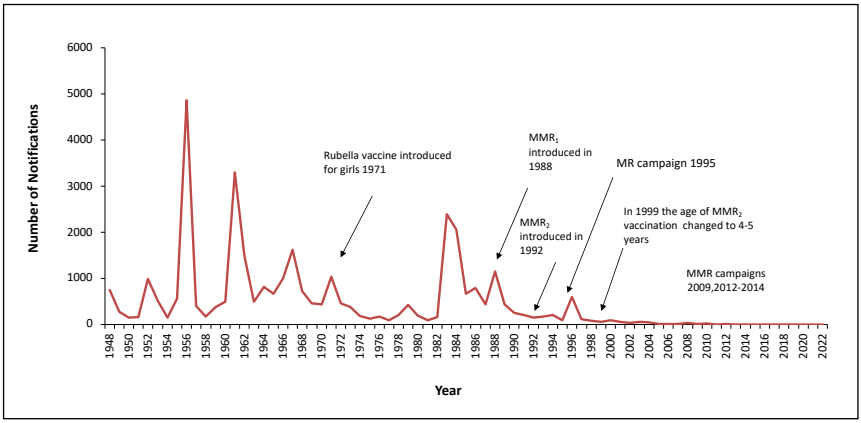
20.1 Introduction

Rubella is a mild disease caused by a toga virus whose only host is humans. Up to 50% of infections are asymptomatic. Its most serious effects are on the fetus, and prevention of the congenital rubella syndrome (CRS) is the main aim of rubella vaccination.

20.2 Epidemiology

Prior to the introduction of Rubella vaccine, most infections occurred in winter or early spring. Since the introduction of rubella vaccine in 1971, notifications of rubella have decreased (Figure 20.1). There is a longer interval between outbreaks and the numbers infected are smaller. In order to prevent rubella transmission all children are recommended vaccination with a rubella containing vaccine. In Ireland rubella vaccine is only available as part of the combined measles, mumps and rubella (MMR) vaccine.

Figure 20.1 Number of rubella notifications in Ireland, 1948-2022.
Source: HPSC



In April 2016 WHO announced that rubella transmission has been interrupted and Ireland is now considered free of endemic rubella. Although each year suspect rubella cases are notified, only one case (an imported case in 2020) has met the case definition for confirmed case since 2009. However, the risk of transmission, if the virus is re-introduced, still exists. Rubella continues to occur in other countries. Worldwide, over 100,000 babies are born with congenital rubella syndrome (CRS) every year.

Transmission
Rubella is spread by droplet transmission.

Incubation period
The incubation period is 14-21 days, with most developing a rash 14-17 days after exposure.

Infectious period
Individuals with rubella are most infectious from one week before to one week after onset of the rash. Infants with congenital rubella may shed high titres of virus from their nasopharynx or in their urine for over one year

20.3 Effects of rubella

When symptoms occur, they are generally mild. In children, rash is usually the first manifestation and a prodrome is rare. In older children and adults there is often a prodromal illness with low-grade fever, malaise, coryza and mild conjunctivitis. Lymphadenopathy involving post-auricular and sub-occipital glands may precede the rash. The rash is an erythematous maculopapular rash which initially occurs on the face and neck. The rash is short-lived and is not specific to rubella. Where clinical features are suggestive of rubella laboratory confirmation is recommended

Arthralgia and arthritis, which may last for up to one month, occur frequently in adult females (up to 70%) but are rare in adult males and children. Fingers, wrists and knees are usually affected.

Post-infectious encephalitis occurs in 1 in 6,000 cases, more often in adult females. Haemorrhagic manifestations occur in approx. 1 in 3,000 cases, more commonly in children and are due to thrombocytopenia or vascular damage. Cerebral, gastrointestinal or renal haemorrhage may rarely result. Effects may last from days to months, but most patients fully recover.

Congenital rubella syndrome (CRS) (notifiable)
Maternal rubella infection in pregnancy may result in fetal loss or major defects affecting almost all organ systems. Some manifestations may be delayed for up to four years. The congenital rubella syndrome (CRS) comprises eye, ear, heart and CNS defects. Deafness is the most common and sometimes the only manifestation, especially when infection occurs after 16 weeks' gestation. Cardiac defects include patent ductus arteriosus,

pulmonary stenosis, septal defects and coarctation of the aorta. Eye defects include cataracts, microphthalmia, pigmentary retinopathy and glaucoma. Neurological problems include encephalitis, microcephaly, mental handicap, and behavioural problems. Other abnormalities include hepatitis, splenomegaly, thrombocytopenia and growth retardation.

Diabetes mellitus occurs frequently in later childhood in those with the CRS. Reinfection with rubella may occur, as impaired cell-mediated immunity has been demonstrated in some children with CRS.

The overall risk of CRS depends on the stage of pregnancy. Up to 85% of infants infected in the first 12 weeks of pregnancy will be affected. The risk of fetal damage is about 50% when infection occurs between 12-<16 weeks and 25% (mainly deafness) when infection occurs between from 16-20 weeks' gestation. Congenital anomalies are rare after 20 weeks' gestation.

Preconception testing for rubella immunity is recommended.

Assessment of immunity

Satisfactory evidence of protection against rubella includes documentation of having received at least one dose of a rubella-containing vaccine or a positive antibody test for rubella. It has been reported that viraemic infection can occur in vaccinated persons who have low levels of detectable antibody. On very rare occasions, clinical re-infection and resulting fetal infection have been reported and CRS has occurred in infants born to women with serological evidence of rubella immunity prior to reinfection.

20.4 Rubella vaccines

Rubella vaccine was introduced for girls aged 10-14 years in 1971. In 1988 a combined measles, mumps and rubella vaccine (MMR) was introduced for children aged 15 months and replaced the rubella vaccine for girls aged 10-14 years. In 1992 a second dose of MMR vaccine was recommended for boys and girls at 10-14 years of age. In 1995 a measles and rubella (MR) vaccination catch- up campaign was carried out.

In 1999 the age for the second dose of MMR vaccine was reduced to 4-5 years and in 2000 the age for first dose was reduced to 12-15 months. In 2009 an MMR vaccination catch-up campaign for children in the senior

cycle (last three years) of second level schools was undertaken in response to a national mumps outbreak. In 2012-2014 MMR catch-up vaccination campaigns were carried out in second level and primary schools in response to suboptimal vaccine uptake in these age groups.

Rubella vaccine is only available as MMR (Measles, Mumps and Rubella vaccine). The vaccines contain live attenuated measles, mumps and rubella viruses that are cultured separately and combined.

Two vaccines are available in Ireland:

MMRvaxPRO (MSD)

Priorix (GSK).

Storage

MMR vaccines must be kept refrigerated at +2 to +8°C and protected from light. If a vaccine has been frozen it should not be used. MMR vaccine does not contain thiomersal or any other preservatives. They should be used within one hour of reconstitution.

Failure to adhere to these recommendations can result in loss of vaccine potency and diminished effectiveness.

Licensed indications

Active immunisation of children aged nine months or older, adolescents, and adults against measles, mumps and rubella.

Rubella vaccine effectiveness

Over 95% of recipients are likely to develop lifelong immunity to rubella after a single dose of a rubella containing vaccine. Lower rates of seroconversion occur in those under 12 months of age, because of maternal antibodies.

Laboratory investigation to determine vaccine response is not routinely recommended.

An up-to-date list of licensed vaccines can be accessed on the HPRA website www.hpra.ie

A list of the vaccines currently available from the National Cold Chain Service can be found at www.immunisation.ie

There is no evidence to recommend the use of single vaccines against measles, mumps and rubella instead of the combination MMR vaccine. No single antigen vaccines are licensed in Ireland.

Dose, route of administration and schedule

The dose is 0.5 ml by intramuscular injection (IM) into the deltoid or the anterolateral thigh. It may be given subcutaneously (SC) to those with significant thrombocytopenia or bleeding disorder.

Alcohol swabbing of the injection site should be avoided as alcohol can inactivate the MMR vaccine. If an alcohol swab is used, injection should be delayed for 30 seconds to ensure the alcohol will have evaporated.

MMR vaccine can be given at the same time as any other live vaccine except yellow fever vaccine. If not given on the same day, they must be separated by at least four weeks*.

There must be an interval of four weeks between the administration of MMR and varicella or zoster vaccines if they are not given at the same time.

*Co-administration of MMR and yellow fever vaccines can lead to suboptimal antibody responses to mumps, rubella and yellow fever antigens. If rapid protection is required, the vaccines may be given at any interval and an additional dose of MMR given at least four weeks later.

Scientific evidence confirms that there is no causal relationship between the MMR vaccine and autism or inflammatory bowel disease.

20.5 Recommendations

20.5.1 Routine childhood vaccination:

All children at 12 months of age should receive an MMR vaccine, with a second dose at 4-5 years of age. *If protection is urgently required*, the second dose can be given four weeks after the first.

Children receiving their first dose of MMR vaccine ≥ 4-5 years of age should be given a second dose four weeks later.

MMR vaccine can be given to those who have a history of measles, mumps or rubella infection.

20.5.2 Migrants, ethnic minority groups and those coming from low resource countries

These groups are less likely to have been vaccinated with MMR. Without documented evidence of rubella vaccination, they should be offered one dose of MMR vaccine. Two doses may be needed for protection against measles and mumps.

20.5.3 Rubella seronegative women of child-bearing age

All rubella seronegative women of child-bearing age should be offered one dose of MMR vaccine. Satisfactory evidence of protection is documentation of having received at least one dose of rubella containing vaccine or a positive rubella antibody test (IgG level ≥10 IU/ml).

If a woman has documented evidence of having received one dose of a rubella-containing vaccine, *irrespective of rubella serology*, no further rubella (MMR) vaccine is necessary.

Two doses may be needed for protection against measles and mumps.

20.5.4 Healthcare workers

All healthcare workers, both clinical and non-clinical, who have direct patient contact should be immune to measles, mumps and rubella. This applies to roles in which:

- their work requires face to face contact with patients, or
- their normal work location is in a clinical area such as a ward, emergency department or outpatient clinic, or
- their work frequently requires attendance in clinical areas.

Acceptable presumptive evidence of immunity against **rubella** includes at least one of the following:

- written documentation of vaccination with one dose of live rubella or MMR vaccine

or

- serological evidence of rubella immunity (serum rubella IgG level ≥10 IU/ml) from an INAB accredited laboratory. Equivocal results should be considered negative.

HCWs without evidence of at least one dose of MMR vaccine or serological evidence of rubella immunity should be offered one dose of MMR vaccine. For protection against measles and mumps two doses may be required.

If an outbreak of rubella occurs in an institution or an area served by an institution, HCWs without evidence of serological immunity to rubella, or without documented evidence of having received at least one dose of a rubella containing vaccine should be given a dose of MMR. This is to prevent ongoing spread to susceptible staff during the outbreak.

Protection is important both for themselves and in the context of their ability to transmit rubella to vulnerable groups.

Antibody response to the rubella component of the MMR vaccine does not develop quickly enough to provide effective prophylaxis after exposure to suspected rubella. However, the vaccine can provide protection against future infection. Therefore, contact with suspected rubella provides a good opportunity to offer MMR to previously unvaccinated individuals. If the individual is already incubating rubella, MMR vaccination will not exacerbate the symptoms.

Human normal immunoglobulin is not recommended for post-exposure protection from rubella since there is no evidence that it is effective.

Contraindications

1. Anaphylaxis to a previous dose of MMR or to any of the vaccine constituents.
2. Significantly immunocompromised persons (see Chapter 3), e.g., primary immunodeficiency or acquired immunodeficiency (from disease (including HIV/AIDS), or immunosuppressive therapy (including biologics)).
3. Pregnancy. Furthermore, pregnancy should be avoided for one month after MMR.

The following are NOT contraindications to MMR vaccine

1. Allergy to egg including anaphylaxis following egg. MMR vaccines do not contain significant amounts of egg cross-reacting proteins and recent data suggest that anaphylaxis following MMR is not associated with hypersensitivity to egg antigens but to other vaccine components (gelatin or neomycin).
2. Breastfeeding.
3. People living with HIV who are not severely immunocompromised (see Chapter 3).
4. Personal or family history of convulsions.
5. Close contacts of immunosuppressed individuals should be fully immunised with MMR, as there is no evidence of harm from the transmission of measles, mumps and rubella viruses from recent vaccinees.
6. Uncertainty as to whether a person has had two previous MMR vaccines.
7. Recent injection of anti-RhD immunoglobulin.
8. Hereditary fructose intolerance.
9. Use of topical tacrolimus does not affect the immunogenicity of the MMR vaccine.
10. Priorix contains 334 micrograms of phenylalanine per 0.5ml dose. Though phenylalanine may be harmful to individuals with phenylketonuria (PKU) the amount of phenylalanine contained in Priorix is negligible and vaccination with Priorix is advised in individuals with PKU.

Precautions

1. Acute severe febrile illness, defer until recovery.
2. Injection with another live vaccine within the previous four weeks. Two live vaccines can be administered on the same day without causing interference e.g., MMR and Varicella. However, MMR vaccine should not be routinely administered on the same day as yellow fever vaccine as co-administration of these two vaccines can lead to suboptimal antibody responses to yellow fever, mumps and rubella antigens. If rapid protection is required, the vaccines should be given on the same day or at any interval and an additional dose of MMR should be given at least four weeks later.

3. Family history of primary immunodeficiency (e.g., severe combined immunodeficiency syndrome (SCID)) defer vaccination until immune status is determined.
4. Recent administration of blood, blood products, HNIG or specific immunoglobulin could prevent vaccine virus replication. MMR should be deferred for specific intervals depending on product received as outlined in Chapter 2 Table 2.6.
5. Tuberculin skin testing should be deferred for at least four weeks after MMR vaccine as the vaccine can reduce the tuberculin response and could give a false negative result.
6. Patients who developed thrombocytopaenia within six weeks of their first dose of MMR should undergo serological testing to decide whether a second dose is necessary. The second dose is recommended if the patient is not fully immune to the three component viruses.
7. Live vaccines should not be given to infants after *in utero* exposure to infliximab for 12 months after birth. However, administration of MMR vaccine may be considered before 12 months where there is a clear clinical indication and clear benefit, if infant infliximab serum levels are undetectable or if infliximab administration was limited to the first trimester of pregnancy.
8. Infants of breastfeeding mothers receiving monoclonal antibody treatment (including infliximab) post-partum should be immunised with MMR vaccines according to routine schedule. If there is any doubt as to whether an infant due to receive a live attenuated vaccine such as MMR may be immunosuppressed due to the mother's therapy, specialist advice should be sought.

Adverse reactions

Local: very common: erythema at injection site.
common: soreness, swelling.
General: common: rhinitis, rash.

"Mini-measles" may occur 6-10 days after immunisation and consists of mild pyrexia and an erythematous rash.

'Mini-mumps' with salivary gland swelling may rarely occur during the third week after immunisation.

The rubella component may occasionally produce a rash, mild arthralgia, and lymph-node swelling 2-4 weeks post-vaccination, particularly in post-pubertal females (up to 25% of recipients). The incidence is lower than after natural disease.

Febrile convulsions occur rarely (<1/1,000 children).

Very rarely, erythema multiforme, thrombocytopenia and nerve deafness have been reported.

There is no evidence of congenital rubella syndrome (CRS) or increase in other teratogenic effects in women inadvertently given MMR vaccine. However, pregnancy remains a contraindication to its administration.

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