12 Measles

Measles vaccine introduced into National Immunisation Schedule -1985
MMR vaccine introduced-1988

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics (SmPC) 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

12.1. Introduction

Measles is an acute viral illness caused by a morbillivirus of the paramyxovirus family. There is only one antigenic type, with a number of genotypes. Measles is one of the world's most contagious diseases; one case of measles can infect 12-18 unvaccinated people. Even in high-resource countries, complications result in hospitalisation in up to a quarter of cases, and can lead to lifelong disability, from brain damage and blindness to hearing loss.

Humans are the only known host. Both infection and appropriate immunisation confer long-lasting and lifelong immunity in most people.

Worldwide, measles vaccination resulted in an 80% decline in measles deaths between 2000 and 2018, preventing an estimated 23 million deaths. Even though a safe and cost-effective vaccine is available, in 2017, there were 110,000 measles deaths globally, mostly among children under the age of five.

12.2. Epidemiology

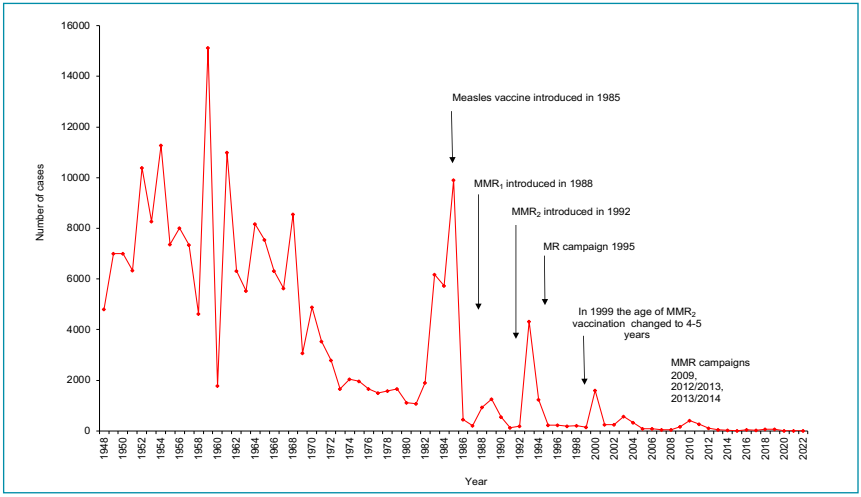
Globally, the number of measles cases has risen significantly since 2016. Many countries are in the midst of sizeable measles outbreaks, with all regions of the world experiencing sustained rises in cases. Between January 2016 and March 2019, 44,047 cases were reported from 30 EU/EAA countries, with a fourfold increase in cases noted between 2016 and 2017. Outbreaks have occurred in countries with high overall vaccination coverage, including Ireland.

In Ireland, between 1948 and 1984 an average of over 5,000 cases were reported annually. The incidence declined dramatically after the introduction of monocomponent measles vaccine in 1985, from 10,000 cases in in 1985 to 201 cases in 1987.

An outbreak of measles in 1993 affected more than 4,000 people and in 2000 over 1,600 cases of measles were reported, with three associated deaths. Additional local and national outbreaks have occurred since then, predominantly affecting subgroups of the population with low vaccination coverage (Figure 12.1).

Figure 12.1 Number of measles notifications in Ireland, 1948-2022

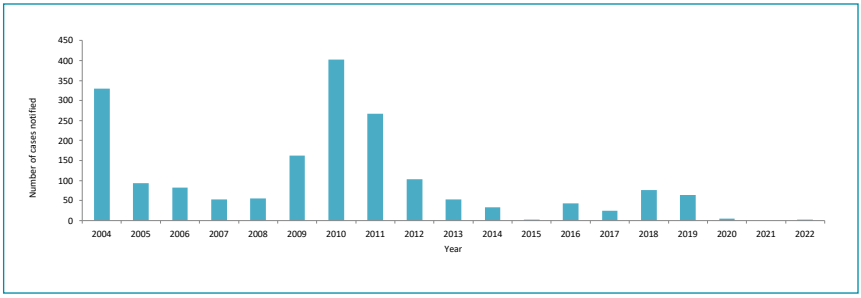
Source: HPSC



From 2004-2022 there were 1,851 cases of measles notified in Ireland. Incomplete vaccine coverage combined with a pool of susceptible unvaccinated older children resulted in rapid spread of the infection during these outbreaks (Figure 12.2). However, there seems to be a reduction of cases following the MMR campaigns in schools in 2009 and 2012-2014.

Figure 12.2 Number of measles notifications in Ireland, 2004-2022

Source: CIDR HPSC



Transmission

Transmission of measles is by airborne or droplet infection. It is spread by coughing and sneezing, close personal contact or direct contact with infected nasal or throat secretions.

The virus remains active and contagious in the air or on infected surfaces for up to two hours.

Incubation period
The incubation period averages 10-12 days, and exposure to rash onset averages 14 days (range 7-21 days). The prodrome (before rash onset) usually lasts 2-4 days (range 1-8 days).

Infectious period
The infectious period is from four days prior to the onset of the rash to four days after the rash erupts.

12.3. Effects of measles

The prodrome phase is characterised by fever, significant malaise, anorexia, rhinitis, conjunctivitis and cough. The severity of conjunctivitis is variable and may be accompanied by photophobia. Respiratory symptoms result from mucosal inflammation due to viral infection of epithelial cells. Fever is typically present and may be as high as 40ºC. The prodromal symptoms typically intensify a few days before the rash appears.

The erythematous, maculopapular rash first appears behind the ears and spreads to the face, trunk and limbs over 3-4 days. The rash may become confluent in places. After 3-4 days, the rash begins to fade, in the order that it appeared, leaving a temporary brownish discolouration. Koplik spots (small red spots with white centres) may appear on the buccal mucosa near the exit of the parotid duct, from 1-2 days before to 1-2 days after the rash appears.

Clinical improvement usually begins within 48 hours of the appearance of the rash. The cough may persist for 1-2 weeks. Fever lasting longer than 3-4 days after rash onset suggests the presence of a measles-associated complication.

Approximately 30% of measles cases have one or more complications, which are more common in those aged <5 and >20 years of age. These complications include otitis media (1/10-15 cases), diarrhoea (1/16), pneumonia (1/15), convulsions (1/200), death (1/500-800) encephalitis (1/1,000) and subacute sclerosing panencephalitis (1/25,000).

Measles infection induces transient immune compromise with decreased numbers of CD4 T cells in lymphoid tissue for weeks and leucopoenia for about a week following infection. This contributes to the susceptibility to serious bacterial infection that may follow measles.

There are three types of measles encephalitis:

1. Measles inclusion body encephalitis occurs in 1-3/1,000 children concurrent with measles infection. It is characterised by acute neurological compromise, loss of consciousness, seizures and progressive neurological damage. Ten to 15% of these children die and 25% have permanent neurological damage.
2. Acute demyelinating encephalomyelitis occurs about one week after the onset of the rash in approximately 1/1,000 cases, has a mortality of about 15% and results in residual neurological sequelae in 20-40% of survivors.
3. Sub-acute sclerosing panencephalitis (SSPE), a degenerative CNS disease presenting usually 7-10 years after infection and progressing to death, occurs in 1/25,000 infected people. If measles infection occurs in children under five years of age the rate of SSPE is 1-3/3,000. If infection occurs in children under one year of age, the rate is 1/600, which is 16 times greater than with infection occurring over five years of age.

The risk of encephalitis following administration of MMR vaccine (<1/10 million doses) is far below the risk of encephalitis caused by natural disease. Complications and mortality rates from measles are high in the immunocompromised, the malnourished and in those with vitamin A deficiency. Severe complications may occur in up to 80% of these individuals, with case-fatality rates of 70% in those with cancer.

The case fatality rate is highest in children under one year of age, lowest in those aged 1-9 and rises again in teenagers and adults. Pneumonia accounts for 56-86% of measles-associated deaths. Death occurred in 1 in 500 notified cases in Ireland in the outbreak of 2000.

Modified measles

Modified measles occurs primarily in those who receive immunoglobulin as post-exposure prophylaxis or in infants with residual maternal antibodies.

It is characterised by a prolonged incubation period, mild prodrome and a sparse, discrete rash of short duration. A similar illness has been reported in previously vaccinated persons who develop measles.

12.4. Measles vaccines

Monocomponent measles vaccine was introduced in Ireland in 1985. In 1988 a combined measles, mumps and rubella vaccine (MMR) was introduced for children aged 15 months. 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.

The WHO declared measles eliminated in Ireland in 2017. Since then, any measles cases have been associated with imported measles cases.

> Uptake rate of at least 95% with two doses of MMR vaccine at ≥12 months of age and at least four weeks apart is required to halt endemic transmission of the virus and thus eliminate measles.

Measles 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.

Measles vaccine effectiveness
Approximately 95-98% of recipients develop immunity to measles after one dose of MMR vaccine. Over 99% of those who receive two doses of measles vaccine ≥12 months of age and ≥4 weeks apart will develop measles immunity which is lifelong in most people. Breakthrough infections are very rare and are generally milder than in unvaccinated persons. 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 shows no association between the MMR vaccine and autism or inflammatory bowel disease.

12.5 Recommendations

12.5.1 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.

2.5.2 Catch up childhood vaccination

Any child under 18 years who has not received two doses of MMR vaccination should be opportunistically vaccinated with one or two doses of MMR vaccine as required to bring them up to date. This includes migrants, ethnic minority groups and those coming from low resource countries.

12.5.3 Vaccination of adults

Adults in the following groups who are partially vaccinated, unvaccinated or unsure about their vaccination status should receive one or two doses of MMR vaccine as indicated by their vaccination history:

a) All adults aged under 25 years of age, a recent seroprevalence study showed those born 1998-2004 had the highest seronegativity for measles.

b) Adults considered at high risk of exposure to measles (e.g., those living in congregate settings or members of underserved communities).

c) Adults living with people who are vulnerable to severe consequences of measles infection. (e.g., non-immune pregnant women, severely immunocompromised people, and infants under one year of age).

d) Migrants from low resource settings (migrants from low resource settings are less likely to have been vaccinated with MMR and should be offered two doses of MMR vaccine unless documented evidence of vaccination).

e) Adults of all ages who are planning to travel to an area where measles is endemic or where outbreaks are occurring.

It is estimated that at least 90% of people born in Ireland before 1978 are likely to have had measles infection and are thus immune to measles. Where there is uncertainty about measles status, the MMR vaccine should be offered on request to individuals born in Ireland before 1978 particularly if they are considered at high risk of exposure or disease as outlined in b) and c) above.

12.5.4 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 **measles** includes at least one of the following:

- written documentation of vaccination with two doses of MMR vaccine at least four weeks apart

or

- serological evidence of measles immunity (i.e., detectable measles specific IgG from an INAB accredited laboratory or equivalent*)

or

- birth in Ireland before 1978. It is estimated that at least 90% of adults born in Ireland before 1978 are likely to have had measles infection. MMR vaccine should be offered to such individuals on request if they are considered at high risk of exposure.

*Acceptable laboratories to be determined by local occupational health and/or public health teams. Only international laboratories that are accredited to the same international standard (ISO15189) as INAB should be accepted.

All HCWs born outside of Ireland (regardless of age) or born in Ireland after 1978, without evidence of two doses of MMR vaccine or measles immunity (i.e., detectable measles specific IgG from an INAB accredited laboratory or equivalent*) should be offered one or two doses of MMR vaccine as required at least four weeks apart so that a total of two doses are received.

In the case of an outbreak or close contact with a measles case in a healthcare setting, either written documentation of vaccination with two doses of MMR vaccine at least four weeks apart or serological evidence of measles immunity (i.e., detectable measles specific IgG from an INAB accredited laboratory or equivalent*) are acceptable evidence of confirmed measles immunity. Presumptive immunity by birth before 1978, should not be used to confirm immunity in those identified as close contacts with a measles case.

12.5.5 Vaccination during measles outbreaks

Outbreaks of measles may be controlled by immunising all susceptible individuals within 3 days of contact, as vaccine-induced immunity develops more rapidly than that following measles infection. Presumptive immunity by birth before 1978, should not be used to confirm immunity in those identified as close contacts with a measles case.

> When measles outbreaks occur, susceptible persons aged ≥6 months should be given MMR vaccine within 72 hours of contact with a case.

When measles outbreaks occur, susceptible persons should be given MMR vaccine, unless contraindicated, within 72 hours of contact with a case.

A person should be considered susceptible if they have not received two doses of MMR vaccine or do not have serological evidence of measles immunity (i.e., detectable measles specific IgG from an INAB accredited laboratory or equivalent*).

If there is uncertainty about vaccination status, MMR vaccine should be given as MMR vaccine can be safely given to those who are immune. If vaccination within 72 hours of exposure is not achievable, MMR vaccine should still be offered to susceptible persons as this is a good opportunity to vaccinate previously unvaccinated individuals.

During an outbreak, particularly if there are high attack rates in younger infants, MMR vaccine may be given as young as 6 months of age. However, maternal antibodies may compromise the response to the vaccine. Therefore, infants vaccinated before their first birthday should have a repeat vaccination at 12 months of age, at least four weeks after the first vaccine, with a further dose at 4-5 years of age.

When protection is urgently required for those aged 12 months and older, a second dose of MMR vaccine can be given as early as four weeks after the first dose. This is a valid dose and no further doses are required if both doses were given after 12 months of age.

Some susceptible persons may require Human Normal Immunoglobulin (HNIG) (see below).

12.5.6 Vaccination for those travelling to areas where measles is endemic or where outbreaks are occurring:

- **Infants aged six months to less than 12 months of ag**e
  These should receive one dose of MMR vaccine. A dose given at less than 12 months of age does not replace the dose recommended at 12 months of age. If a dose of MMR vaccine is given before the first birthday, either because of travel to an endemic country or because of a local outbreak, two further doses should be given at 12 months of age or older (at least four weeks after the first dose) and at 4 to 5 years of age.

- **Children aged 12 months and older**
  a. if unvaccinated should receive two doses of MMR vaccine separated by at least four weeks. To ensure optimal protection, the second dose should be given two or more weeks prior to travel.
  b. who have received one dose of MMR vaccine should receive a second dose four or more weeks later and ideally two or more weeks prior to travel.

- **Teenagers and adults without evidence of measles vaccination**
  These should receive two doses of MMR vaccine separated by at least four weeks.

Serological testing after routine MMR vaccination is not recommended.

Serological testing is not recommended before or after receiving measles-containing vaccine. If serology is inadvertently done subsequent to appropriate measles immunisation and does not demonstrate immunity, measles re-immunisation is not necessary.

Contraindications

1. Anaphylaxis to a previous dose of MMR or to any of the vaccine constituents.
2. Severely 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 or increase in other teratogenic effects in women inadvertently given MMR vaccine. However, pregnancy remains a contraindication to its administration.

12.6 Post exposure prophylaxis of measles

Note: *In this section the term 'exposure' refers to 'significant' exposure.*

12.6.1 Exposure to measles is considered significant if:

a susceptible individual is exposed to a confirmed or probable case of measles during the infectious period (four days before to four days after rash onset) in any of the following ways:

- Face-to-face contact of any duration.
- An immunocompetent individual is in a room with the case for more than 15 minutes. This includes those who, within the preceding six days, may have been exposed to measles in the setting of an emergency department or an outpatient clinic where the intensity of such exposure cannot accurately be judged.
- An immunocompromised person is in a room with the case for any duration or enters a room vacated by a case within two hours of the case leaving the room.

12.6.2 Groups at increased risk for severe illness and complications include:

- Infants younger than 12 months of age.
- Pregnant women without measles immunity.
- Those who are immunocompromised (see Chapter 3).

Household contacts of a case have higher intensity exposure and an increased risk of more severe disease than non-household contacts.

Most Irish-born mothers, born after 1985 (when routine measles vaccination was introduced), are unlikely to have had measles infection. The levels of transplacentally acquired antibodies in infants born to vaccinated mothers tend to be lower than in infants of mothers who had natural infection and to wane more rapidly, usually declining within weeks of birth. If mothers have had measles infection, maternal antibodies may protect the infant for a few months after birth.

Immunity to measles from MMR vaccine develops more rapidly than immunity from infection and thus MMR vaccine can be successfully used to prevent measles infection following exposure. When used for prophylaxis, MMR vaccine should be given within three days of exposure.

Antibody response to the mumps and rubella components of the MMR vaccine does not develop quickly enough to provide effective prophylaxis after exposure to suspected mumps or rubella.

Maternal antibodies can interfere with an infant's response to MMR vaccine for up to 12 months of age. Thus, Infants who receive MMR vaccine <12 months of age need two additional doses of MMR vaccine, at ≥12 months (at least 4 weeks after first dose) and at 4-5 years of age, in accordance with the national schedule.

Human normal immunoglobulin (HNIG) is prepared from pooled plasma derived from blood donations and contains sufficient anti-measles antibodies to prevent or ameliorate infection in susceptible persons. There are two types of preparation available those for intramuscular or subcutaneous use (human normal immunoglobulin, HNIG IM/HNIG SC) and those for intravenous use (intravenous immunoglobulin IVIG). Ideally HNIG should be given within three days of exposure, but it may provide some protection if given within six days of exposure.

12.6.3 Post exposure prophylaxis of vulnerable contacts following significant exposure:

12.6.3.1 Infants (see Table 12.1)

- ***aged <6 months***

  i. Household or household type exposure:
  Contacts should receive HNIG, ideally within three days of exposure. It can be given with potential benefit up to six days following exposure.

  ii. Non-household exposure:
  This includes those who, within the preceding six days, may have been exposed to measles in the setting of an emergency department or an outpatient clinic where the intensity of such exposure cannot be accurately judged

  - If the infant's and mother's measles IgG status can be ascertained within three days and is positive, HNIG is not indicated. If the measles IgG result is weakly positive, equivocal or unknown, HNIG is recommended, and should be given within three days. It can be given with potential benefit up to six days following exposure.

- **aged 6 to <9 months**

i. Household or household type exposure:

- **exposure within the preceding three days** - give MMR vaccine.

- **exposure between 3-6 days previously** (i.e., days 4-6 post exposure) and MMR vaccine has not been given within three days of exposure - give HNIG if practicable.

Those who have received HNIG should wait at least six months before receiving routine MMR vaccination (See Chapter 2 Table 2.6 for specific intervals).

ii. Non-household exposure:
These infants are less likely to have the intensity of exposure to develop severe disease. They should receive MMR vaccine within three days of exposure. If MMR vaccine cannot be given within three days of exposure, HNIG should be considered up to six days.

- ***aged 9 months or older***

Household or non-household exposure
These contacts should receive MMR vaccine. Ideally the vaccine should be administered within three days; it should still be offered at any interval following exposure in order to offer protection from future exposure.

Table 12.1. Management of infants with significant exposure to measles

Age	Management	
	Household or household type exposure	Non household exposure
< 6 months	Give HNIG within 3 days (can be given up to 6 days after exposure)	Give HNIG within 3 days (can be given up to 6 days after exposure), unless infant and mother have positive measles IgG serology. *If the Measles IgG result is equivocal, weakly positive or unknown, HNIG is recommended.*
6 – <9 months	Give MMR vaccine within 3 days. Give HNIG if within 3-6 days of exposure.[1]	Give MMR vaccine within 3 days. If not possible, consider HNIG up to 6 days post exposure[2]
≥ 9 months	Administer MMR vaccine, ideally within 3 days of exposure.[3]	

[1] Following HNIG, wait at least six months before MMR vaccination (see Chapter 2 Table 2.6).

[2] If MMR vaccine is given <12 months of age, two further doses are required, at ≥12 months and at least 4 weeks apart.

[3] If exposure may be ongoing (e.g., a single case in a nursery or during a community outbreak), MMR vaccination >3 days may provide protection from subsequent exposures. HNIG is not routinely recommended for this age group in the absence of other indications (e.g., immunocompromise).

12.6.3.2 Pregnancy

HNIG should be administered to pregnant women without evidence of measles immunity who have had significant exposure to measles. Ideally it should be given within three days of exposure but can be given up to six days. Women with measles IgG titres reported as 'positive' or 'weak positive' are likely to have measles vaccine or infection induced immunity and do not need HNIG.

12.6.3.3 Immunocompromised persons (see Chapter 3)

Most immunosuppressed individuals can maintain protective antibodies from prior vaccination or natural infection and can be managed based on a history of natural infection or prior measles antibody test results.

If prior documentation of measles immunity is available, post exposure prophylaxis is not required. If no such documentation is available, urgently assess serologic status and give post exposure IVIG prophylaxis to exposed individuals who are antibody negative. IVIG should ideally be given within three days of exposure but can be given up to six days.

Those who are severely immunocompromised may not maintain adequate antibody levels following past exposure or vaccination. This includes patients with leukaemia, lymphoproliferative disorder, post solid organ transplant, patients who are ≥12 months post haematopoeitic stem cell transplant (HSCT), or receiving or within six months of completion of biologic therapies or a diagnosis of AIDS. These patients should be urgently assessed for measles immunity at the time of exposure *regardless of past vaccination history or previous serologic test result*. If measles IgG is detected, post exposure prophylaxis is not required. If seronegative, offer post exposure prophylaxis with IVIG.

Severely immunocompromised patients who have received a HSCT within the preceding 12 months and those with severe primary immunodeficiency, should receive IVIG, regardless of immunologic or vaccination status.

Immunocompromised patients who are regular recipients of immunoglobulin therapy do not require additional prophylaxis if they have received a dose of IVIG within three weeks prior to exposure.

NB: Post exposure prophylaxis with immunoglobulin or MMR vaccine is not always fully effective in preventing measles infection. Therefore, exposed persons who receive post exposure prophylaxis remain an infection control

risk. They should be managed in accordance with usual infection control procedures following a measles exposure.

12.7 Human normal immunoglobulin (HNIG) preparations, dose and administration

Although HNIG products are not licensed for post exposure prophylaxis, their use has proven effective in preventing or attenuating measles if given within six days of exposure.

Peak levels of HNIG are obtained within minutes of IV administration, approximately two days after IM injection and 2-3 days after SC administration. HNIG should ideally be given within 72 hours of exposure to a case of measles, from 4-5 days before to four days after the measles rash appears. There is no consistent evidence regarding the efficacy of SC HNIG received 4-6 days after exposure to a case of measles, and its use is primarily to reduce the severity of disease in vulnerable contacts.

HNIG can be given up to six days after exposure, allowing time for assessment of immunity status in most instances.

Preparations

Subcutaneous use (Table 12.2)

Four HNIG products are licensed and available in Ireland for subcutaneous (SC) administration - **Cuvitru** (20%), **Gammanorm** (16.5%), **Hizentra** (20%), and **HyQvia** (10%). Following SC administration, peak serum IgG levels are reached by **Hizentra** in approximately two days, by **Cuvitru** in three days, by **HyQvia** in 3-5 days and by **Gammanorm** in 4-6 days.

When available, either Cuvitru or Hizentra are recommended, because of the smaller volume required, and the earlier peak serum levels achieved compared to lower concentration products. These preparations should be given at an initial rate of not more than 10ml/hour/infusion site. More than one pump can be used simultaneously, to shorten the infusion time. If tolerated, the rate can be increased at intervals of ≥10 minutes to a maximum of 20ml/hour/site. The infusion site can be changed every 5-10ml.

Cuvitru may also be administered manually (as a slow push). The recommended infusion rate is 1-2ml/minute. Always refer to product SPC before use.

Intramuscular use
This route may be used if SC or IV administration is not practicable. Gammanorm is the only HNIG preparation licensed for IM administration.

If SC or IM HNIG is not available, IVIG can be substituted.

Intravenous use
A number of IVIG products (e.g., Kiovig, Flebogamma, Intratect) are available through hospital pharmacies. IVIG is recommended for use in immunocompromised contacts (see Chapter 3).

12.7.2 Dose and route for measles prophylaxis

Dose recommendations for post exposure prophylaxis against measles are not well established. Based on available evidence the following doses are recommended:

Table 12.2. Dose of subcutaneous HNIG recommended for measles contacts aged <9 months.

Infant weight (kg)	20% HNIG (Cuvitru Hizentra)
3-<4	3ml
4-<5	3.5ml
5-<6	4.5ml
6-<7	5ml
7-<8	6ml
8-<9	6.5ml
9-<10	7.5ml
10-<11	8ml
11-<12	9ml
12 -<14	10ml

Dose of HNIG for measles contacts ≥9 months where indicated (see Table 12.1):

- HNIG SC or HNIG IM: 200mg/kg
- IVIG: 400mg/kg.

Re-exposure
If there is significant ongoing or re-exposure to measles following the administration of HNIG SC, the administration of HNIG SC should be repeated at two weekly intervals. If there is significant ongoing or re-exposure to measles following the administration of IVIG, the administration of IVIG should be repeated at three weekly intervals.

Administration
Always consult the SmPC for information about product usage, administration, adverse events etc.

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