10 Measles

10.1 Introduction

The earliest written description of measles is classically attributed to the Persian-born physician Abu Becr (Rhazes) in the 10th century. Rhazes was the first to differentiate measles from smallpox and considered the former to be more dreaded. Although he recognised both the cyclical and seasonal nature of the disease, it was not until the 17th century that Thomas Sydenham of London identified the infectious nature of measles. The studies of Peter Panum in the Faroe Islands in 1846 showed that the disease was acquired solely by direct transmission.

Outbreaks of measles occurred for the first time in the South Pacific during the mid and late 19th century, with devastating results among the Fijians and New Zealand Māori. In 1954 Enders and Peebles in the US reported the first successful isolation and propagation of the measles virus in human and monkey kidney cells. This led to the production of a live attenuated measles vaccine, which was first licensed for use in the US in 1963.

10.2 The illness

Measles is transmitted by direct contact with infectious droplets, or, less commonly, by airborne spread. Measles is one of the most highly communicable of all infectious diseases. There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik spots on the buccal mucosa. The characteristic maculopapular rash appears first behind the ears on the third to seventh day, spreads over three to four days from the head and face over the trunk to the extremities. It lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is usually 10 to 12 days, but may range up to 18 days, and is prolonged in the immune suppressed. Measles is highly infectious from the beginning of the prodromal phase until four days after the appearance of the rash. Complications are common, occurring in 10 percent of cases (see Table 10.1 in section 10.6), and include otitis media, pneumonia, croup or diarrhoea. Encephalitis has been reported in 1 in every 1000 cases, of whom some 15 percent die and a further 25 to 35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and immune thrombocytopenic purpura (ITP or thrombocytopenia).

Sub-acute sclerosing panencephalitis, a rare degenerative central nervous system disease resulting from persistent measles virus infection, is fatal. This complication has virtually disappeared where there is widespread measles immunisation.
The case fatality rate for reported cases of measles in the US is 1–3 per 1000. Measles is particularly severe in the malnourished and in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash, and have a much higher case fatality rate.

Measles is also serious in healthy children: over half of all the children who died from measles in the UK between 1970 and 1983 were previously healthy.¹ No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

Vitamin A deficiency, common in developing countries, is associated with more severe disease. In general, vitamin A treatment/supplementation is not necessary for children with measles in developed countries. However, it is recommended for children who are hospitalised with measles, and other children with risk factors such as immune deficiency or malabsorption, and should be considered for children recently arrived from developing countries (see section 10.8).

**Diagnosis**

The standard case definition for measles is ‘any person with fever 38°C or higher, generalised maculopapular rash lasting three or more days and cough or coryza or conjunctivitis or Koplik’s spots.’ However, because many viral infections can mimic measles, it is important that the diagnosis is laboratory confirmed.

In the first instance, blood should be taken for serological confirmation and a nasopharyngeal and throat swab taken for viral identification by PCR (see Appendix 10 for details). Further specimens for viral culture, detection of measles virus by PCR or further serological tests should be taken in consultation with the laboratory. The timing and choice of samples in relation to the onset of symptoms is important.

For further information contact the local medical officer of health or infectious disease physician. More detailed information is available from the National Measles Laboratory (http://www.cdhb.govt.nz/measles/).

**10.3 Epidemiology**

Measles is the most common vaccine-preventable cause of death among children throughout the world. The Global Burden of Disease Study ranked measles eighth, both as a cause of death and as a cause of disability-adjusted life years (DALYs) lost, in the global population (all ages combined) in 1990.² Among children aged 0–4 years in non-developed countries, measles ranked fourth as a cause of DALYs lost, and was the infectious agent with the highest burden of disease. In 1989 the WHO Expanded
Programme on Immunization estimated that 1.5 million children died annually from measles or its complications. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year. A 1951 outbreak of infection in southern Greenland, a country that had not previously experienced measles, resulted in an almost 100 percent infection rate of adults and children. Natural measles infection results in long-term immunity. This is exemplified by Peter Panum’s description of measles in the Faroe Islands, which affected people of all ages who had not been affected during the previous epidemic 65 years before.\(^3\)

The US reported\(^4\) that of the 251 cases of measles reported from 2001 to 2004, 177 (71 percent) were in US residents, and of these 100 were preventable. Forty-three percent of these preventable cases were associated with international travel; the rest acquired the disease in the US. Preventable cases are those that would not occur had the person received the recommended immunisation schedule, including MMR vaccination at 6–11 months if the infant is travelling outside the US. The 77 non-preventable cases had received a measles-containing vaccine, or were expected to be protected because of their age; of these, 16 percent were associated with travel. Because international travel is an important factor in reintroducing measles into a country, a measles-containing vaccine should be considered for those travelling overseas, if they have not been previously vaccinated.

Indigenous cases of measles, mumps and rubella have been eliminated from Finland over a 12-year period using a two-dose measles, mumps and rubella vaccine (MMR) schedule given between 14 and 16 months and at age six years.\(^5\)

In October 2005 the Regional Health Assembly of the Western Pacific Region of WHO endorsed a target that by 2012 measles would be eliminated from the Western Pacific Region. To reach this target, all countries in the region will need to have ongoing high levels of measles immunisation coverage with two doses of vaccine, including at least one dose after the age of one year. All countries will need a surveillance system for measles, and in order to monitor progress every suspected case of measles will need laboratory confirmation at a national measles reference laboratory. The New Zealand National Measles Laboratory, set up in 2005, is at Canterbury Health Laboratories (see Appendix 10). Positive viral cultures are sent to the regional laboratory in Melbourne, Australia, for detailed analysis of the virus.

**New Zealand epidemiology**

Despite the introduction of the measles vaccine in 1969, measles occurred every year until 1980, with a pattern of ‘low’ years (an average of approximately 100 hospitalisations per year) alternating with ‘high’
or ‘epidemic’ years (an average of approximately 300 hospitalisations per year). Increased uptake of the measles vaccine, which is thought to have reached 70 percent or more by 1980, resulted in this epidemic cycle becoming more accentuated. Measles virtually disappeared between epidemic years, which occurred less frequently (1984/85, 1991 and 1997), but the epidemics were of increased size, with 400 hospitalisations in 1984/85 (see Figure 10.1 for hospital discharges, notifications of measles and laboratory-confirmed cases). A shift in the age distribution of cases towards older ages was also noted. This effect was most evident in the 1991 epidemic, and was seen more in European than in Māori or Pacific children.

The 1991 and 1997 epidemics resulted in a total of 943 hospitalisations with a principal or secondary diagnosis of measles. In the second half of the 1991 epidemic, reports of measles were requested and 10,000 were received; on this basis it was estimated that the epidemic involved 40,000 to 60,000 cases. In the 1997 epidemic, 2169 cases were identified via notification, laboratory and hospitalisation data. The 1997 epidemic was predicted and an immunisation campaign was planned to prevent it. However, the epidemic began three months before the start of the campaign, which was then brought forward and it is estimated that 90–95 percent of cases were prevented. During the 1991 epidemic the deaths of four unimmunised children were reported, but mortality records revealed a total of seven deaths. There were no deaths in the 1997 epidemic. There were 10 hospitalised cases of measles encephalitis in 1991 and one case in 1997.

Between 2005 and 2010 a total of 369 cases of measles were notified, 161 (44 percent) of which were laboratory confirmed. In 2009, 248 cases of measles were notified with 205 cases being attributed to three outbreaks. The largest of these was the community-based outbreak that involved the Canterbury Health District (170 cases). The highest age-specific rate was seen in those aged less than one year (46.0 per 100,000 population, 29 cases) followed by those aged one to four years (31.3 per 100,000, 76 cases) and those aged 10–14 years (17.8 per 100,000, 53 cases). Of the 253 measles cases, 243 (96 percent) had a known vaccination status. One hundred and forty-three cases were not vaccinated, including 35 cases aged less than 15 months and therefore not eligible for vaccination. Fifty-nine cases had received one dose of vaccine, including five cases aged less than 15 months who had received their first dose (due at 15 months) early and 38 cases aged 15 months to three years who were only eligible for one dose of vaccine. Twenty-eight cases were reported to have completed measles vaccination.

Large-scale measles epidemics occur when the number in the susceptible population increases and the immunisation coverage is low. It has been estimated that to prevent recurrent outbreaks of measles, 95 percent of
the population must be immune. Since measles vaccine efficacy is 90–95 percent and not all children receive the first scheduled dose, the only way to achieve this level of immunity is by implementing a two-dose immunisation strategy, as is now recommended.

In 2000 a mathematical model was developed to estimate the future timing of measles epidemics in New Zealand. The model included MMR immunisation coverage, the number of notified cases of measles and the MMR coverage in the 1997 MMR campaign. The results suggested that if no changes were made to the MMR schedule of 15 months and 11 years, the next measles epidemic would be between 2002 and 2004. However, if the Schedule were changed to give MMR at 15 months and at four years, before school entry, the length of time between epidemics would increase and eventually measles might be eradicated, if coverage were high.

As a result, from January 2001 the Schedule was changed to give the first dose of MMR at age 15 months and the second dose at age four years, prior to school entry. During 2001 there was an MMR school catch-up programme throughout the country for all children aged 5 to 10 years who would not receive MMR in Year 7 (Form 1) because of the 2001 Schedule change.

During the 2001 MMR school catch-up programme it is estimated that 71 percent of all children received a first or second dose of MMR, or reported they had already received two doses of a measles-containing vaccine. An additional 10 percent of children reported they would be going to their general practitioner for an MMR vaccine, so that an estimated total of about 81 percent of children were immunised.

In 2005 the measles mathematical model was updated to calculate the effect of the measles catch-up in 2001 and to estimate the effect of changing the Schedule to give MMR at age 15 months and at age four years before school entry. Because there were no accurate immunisation coverage data until the National Immunisation Register (NIR) became fully operational, the model relies on estimates of coverage. The model shows that if the MMR immunisation coverage at 15 months is 85 percent, and at age four years is 80 percent, then New Zealand would not expect an epidemic of measles for another 10–20 years. If immunisation coverage were higher, a longer time interval between epidemics would be likely.

Although MMR coverage of 85 percent of both doses is likely to prevent further epidemics, because areas of low coverage can exist within any population the model suggests that New Zealand needs to achieve a coverage level of 90 percent for both doses of MMR at ages 15 months and four years to eliminate epidemics. If MMR coverage of 90 percent or higher for both doses of MMR is achieved and maintained, the length of time between epidemics will increase and may lead to the eradication of measles.
The 2009 outbreak was probably stopped and an epidemic prevented by the enhanced immunisation programme that was implemented. This involved active recall and MMR vaccination of unimmunised children and young people aged 12 months to 20 years, ensuring all children received their second MMR vaccination on time, offering MMR vaccine to any adults born after 1969 who had no documented history of receiving one dose of MMR vaccine, and improved immunisation coverage. Figure 10.1 shows hospital discharges, notifications of measles and laboratory-confirmed cases.

**Figure 10.1  Hospital discharges from measles, 1970–2010, notifications, 1996–2010, and laboratory-confirmed cases, 1984–2010**

Source: Ministry of Health and the Institute of Environmental Science and Research

Small numbers of cases of measles are notified each year, and as the number of cases reported decreases it is important that all cases of suspected measles be laboratory investigated. In response to a confirmed case an enhanced measles immunisation programme may need to be implemented.

As the incidence of measles decreases in New Zealand, it is also important to achieve high MMR immunisation coverage to lower the risk of imported measles causing outbreaks. Contact the local medical officer of health to discuss suspected cases before laboratory confirmation and characterisation, so that public health control measures can be put in place.
History of the New Zealand Immunisation Schedule

The measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those less than 10 years at special risk. In 1974 the recommended age for measles vaccine was changed from 10 months to 12 months, and in 1981 it was changed to age 12–15 months. These changes attempted to achieve a balance between too early immunisation, where the vaccine is neutralised by maternally acquired antibody, and the requirement to protect the very young during an epidemic.

MMR vaccine was introduced in 1990 to be given at age 12–15 months in place of the measles vaccine. The dose at age 11 years was introduced in 1992. In 1996 the timing of the first dose of MMR was changed to age 15 months, to be given at the same time as the booster dose of diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b (DTwPH) vaccine.

At the start of the 1997 epidemic, the measles immunisation campaign, using MMR, targeted all children aged less than 10 years. During the campaign the recommended time for the first dose was brought forward to age 12 months, and in Auckland a dose was recommended for children age 6 to 11 months, to be repeated at 15 months of age.\(^\text{10}\) The national coverage achieved in the campaign is not known, but estimates for the school-aged population range from 55 percent for Auckland to 85 percent for the Wellington region.

In 2001 the Schedule was changed to give the first dose of MMR at age 15 months and the second dose at four years. There was a school catch-up programme for the second MMR dose for children aged 5 to 10 years. This schedule of two doses of MMR at 15 months and four years continues.

Vaccine-derived maternal antibody, which protects young infants is lower and wanes earlier than antibody derived from natural infection. It is likely that in due course the age of the first dose of measles-containing vaccine will be changed to age 12 months.

10.4 Vaccines

The measles vaccine is only available as one of the components of MMR vaccine. (See below for administration in infants aged less than 12 months.) The MMR II (MSD) vaccine used and funded is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses. It must be reconstituted only with the diluent supplied by the manufacturer.
MMR vaccine viruses have been regarded as being non-transmissible from vaccinees. There are two poorly documented case reports of transmission: one of rubella and one of a mumps vaccine strain from a vaccine that is no longer in production.\textsuperscript{11} Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.\textsuperscript{12,13} There have been no confirmed cases of disease transmission from vaccine virus. The measles and mumps vaccines are grown in chick embryo cell cultures and rubella vaccine in human diploid cell culture.

MMR vaccine funded as part of the Schedule is MMR II (MSD), a sterile lyophilised preparation of:

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

Another MMR vaccine approved for use and available for distribution in New Zealand is:

- **Priorix** (GSK), which contains Schwartz strain measles, RA 27/3 rubella, and RIT 4385 mumps strain derived from the Jeryl Lynn strain.

Quadrivalent measles, mumps, rubella and varicella vaccines (MMRV, see chapter 18) approved for use and available for distribution in New Zealand are:

- **ProQuad** (MSD), which contains further attenuated Enders’ Edmonston (Moraten) strain measles, RA 27/3 rubella, Jeryl Lynn mumps and Varicella Virus Vaccine Live (Oka/Merck)
- **Priorix-Tetra** (GSK), which contains Schwartz strain measles, RA 27/3 rubella, RIT 4385 mumps strain derived from the Jeryl Lynn strain and Oka varicella strains of viruses.

**Efficacy and effectiveness**

Seroconversion to all three viruses of MMR vaccine occurs in 85–100 percent of recipients. ‘Primary vaccine failure’ refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate
an immune response. This occurs in 5–10 percent of recipients after the first
dose and is rare after a second dose.

Even though antibody levels decline over time, secondary vaccine failure (ie,
vaccine failure due to waning of protective immunity) has only rarely been
documented for any of the three components of the vaccine, most commonly
mumps. A meta-analysis of the measles vaccine found no evidence of
secondary vaccine failure in the US-manufactured vaccine currently used in
New Zealand.14

More recent data from Finland, where there is high coverage with two
doses of MMR using the same vaccine as used in New Zealand, suggest
that immunity to rubella is secure after 20 years, that 95 percent of people
remain sero-positive for measles and that immunity to mumps is declining
with 74 percent being sero-positive.15 Similar data on the persistence of
rubella and measles immunity are available from Luxembourg.16 A recent
significant outbreak of mumps has been seen in the US17 and a mumps
epidemic occurred in the UK in 2004–2005.18

New Zealand will have to consider the possibility that further doses of
MMR in adults may be required in the future. Information from Finland and
elsewhere will assist decision-making as to whether adult booster doses of
MMR are required.

See chapter 18 for efficacy data on the varicella vaccine.

**Dosage and administration**

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL)
administered by subcutaneous injection in the deltoid area of the upper arm,
to all age groups (see section 2.4).

MMR must be stored in the dried state at +2°C to +8°C and protected
from light. It must be reconstituted only with the diluent supplied by the
manufacturer, refrigerated at +2°C to +8°C and used within eight hours or
discarded.

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.
10.5 Recommended immunisation schedule

Children

Measles vaccine is recommended as MMR at age 15 months and at age four years, prior to school entry. Two doses of measles vaccine are recommended because the 5–10 percent who fail to be protected by the first dose will nearly all be protected by the second. The second dose of measles vaccine can be given as soon as four weeks after the first dose. Children who in an outbreak receive MMR vaccine when aged less than 12 months require two further doses administered after age 12 months. MMR vaccine may be given to children age 12 months or older whose parents/guardians request it, and no opportunity should be missed to achieve immunity.

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

Adults

MMR is recommended and funded for any adult who is known to be susceptible to one or more of the three diseases.

Adults born before 1969

Adults born before 1969 should be considered to be immune to measles.

Adults born between 1969 and 1981

Adults born between 1969 and 1981 should have one dose of MMR administered if they fulfil one of the following criteria:

- a student in post-secondary education
- a health care worker with patient contact – all should be immune to measles, mumps, rubella and varicella, but if a health care worker does not have a documented history of two doses of a measles-containing vaccine they should receive a single dose of MMR (see also chapter 18 for varicella recommendations)
- those in institutional care and those who care for them
- a susceptible international traveller visiting a country in which measles is endemic.

Note: Some adults may have received one dose of measles vaccine and MMR during one of the catch-up campaigns (eg, the 1997 campaign when
all those aged up to 10 years were offered MMR vaccine). They will have therefore received the recommended two doses of measles, but only one of mumps and rubella. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended and funded. These individuals can receive a second dose of MMR (ie, a third dose of measles vaccine) without any concerns. It is important that women of child-bearing age are immune to rubella (see chapter 12).

Immune suppression

MMR is contraindicated in children who are immune-suppressed (see section 1.8). 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 immune-compromised individual.

MMR vaccination at 12 months of age is recommended for children with HIV infection who are asymptomatic and who are not severely immune compromised.

MMR is contraindicated in children with severe immune suppression from HIV because vaccine-related pneumonitis (from the measles component) has been reported. Discuss vaccination of children with HIV infection with their specialist.

MMR vaccine aged less than 12 months

MMR may be recommended to infants aged 6 to 12 months during measles outbreaks if cases are occurring in the very young (see section 10.8). These children still require MMR at ages 15 months and four years because their chance of protection from measles is lower when the vaccine is given at aged less than 12 months. Any recommendations will be made by the medical officer of health and the Ministry of Health based on the local epidemiology.

10.6 Expected responses and adverse events following immunisation (AEFI)

Expected responses

It is reported that 5–15 percent of children experience a fever of 39.5°C or more and 5 percent a rash 6–12 days post-immunisation. A placebo-controlled study has shown that fever and/or rash in most cases are unrelated to immunisation, and only rash in only 1.6 percent and high fever in 1.4 percent of cases could be attributed to MMR; these fevers were most
likely 9 or 10 days after immunisation and the rash occurred in the second week.\textsuperscript{20}

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccinees, most often 10–14 days after immunisation. The rubella vaccine can cause a mild rash, fever and lymphadenopathy between two and four weeks after immunisation. There were no persisting sequelae associated with the administration of three million doses of MMR to 1.5 million children in Finland.\textsuperscript{20,21}

Febrile seizures occur in approximately 1 in 3000 children, 6–12 days after immunisation. Parents/guardians should be advised they can give the child an age-appropriate dose of paracetamol if there is fever > 39°C (see section 2.4 for more detail on the use of paracetamol and other antipyretics). Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response.

Arthritis or arthralgia occurs after both the rubella disease and vaccine, especially in adults. About 15 percent of adult women and less than 1 percent of children get joint symptoms about two to four weeks after immunisation. There is no evidence to suggest that rubella vaccine leads to chronic long-term arthritis: two large controlled studies found no evidence,\textsuperscript{22,23} while another study did find a slight increase in arthritis risk following rubella vaccine, but this was of borderline statistical significance.\textsuperscript{24} A review of the available evidence concluded that rubella vaccine does not cause chronic arthritis.\textsuperscript{25}

After reimmunisation, reactions are expected to be clinically similar but much less frequent, since most vaccine recipients are already immune. No unusual reactions have been associated with MMR reimmunisation.\textsuperscript{20}

**Adverse events following immunisation**

ITP occurs in approximately 1 in 30,000 doses, 15–35 days after immunisation. If this occurs, measles, mumps and rubella serology should be measured, and if the individual is immune to all three infections, a second dose is not required. However, if the individual is susceptible to any of the three infections, a second dose should be administered.\textsuperscript{26–29}

Central nervous system symptoms following measles vaccine are reported to occur in 1 in 1 million children. In most cases this seems to be a chance occurrence that is not caused by the vaccine. An analysis of claims for encephalitis following measles vaccine in the US found clustering of events at eight to nine days after immunisation.\textsuperscript{30} This clustering supports, but does not prove, the claim that the vaccine causes encephalitis, albeit rarely and at a lower rate than the wild virus illness. For comparison, the rate of encephalitis following measles disease is 1 in 1000.
MMR containing the Urabe strain of mumps was withdrawn in 1992 following a UK study that found a 1 in 11,000 risk of mumps vaccine meningitis. MMR containing the Urabe strain was used in New Zealand from 1991 until it was withdrawn in 1992. Aseptic meningitis occurs in 1 in 800,000 doses following administration of the Jeryl Lynn strain of mumps vaccine,\(^{31,32}\) which is used in New Zealand. For comparison, aseptic meningitis occurs in 15 percent of cases of mumps.

**Adverse outcomes not linked to MMR**

There have been several epidemiological studies published from the UK,\(^{33}\) Finland\(^{34}\) and elsewhere\(^{35,36}\) confirming there is no link between MMR vaccine and the development of autism in young children. The concern arose because in 1995 a group of researchers from the Royal Free Hospital in London published a study comparing children who took part in the 1964 UK Medical Research Council measles vaccine trial and received the measles vaccine at ages 10–24 months, with a cohort of their unvaccinated partners and with a longitudinal birth cohort from the National Child Development study born in 1958.

The researchers looked at the history of inflammatory bowel disease (IBD; ie, Crohn’s disease and ulcerative colitis) in all three groups and found that the group receiving the measles vaccine had an increased risk of Crohn’s disease (with a relative risk [RR] of 3.01; and 95% CI: 1.45–6.23%) and of ulcerative colitis (RR 2.53; 95% CI: 1.15–5.58%) compared with the birth cohort. The researchers suggested this indicated that the measles virus might play a part in the development of Crohn’s disease and ulcerative colitis.\(^{37}\)

In 1998\(^{38}\) the researchers found that in a series of 12 children with chronic bowel disease and a regressive developmental disorder, parents thought the onset of neurological symptoms was associated with MMR in 8 of the 12 children, measles infection in one child and otitis media in one child. In nine of the children the neurological syndrome was classified as autism. All the children had intestinal abnormalities of chronic colitis, and 11 children had lymphoid nodular hyperplasia. It was suggested by the researchers that there was an association between IBD, autism and MMR vaccine.

The conclusions the researchers reached in this study were criticised\(^{39}\) because of the small number of cases in the series, and selection bias. There was also concern that the report was based on cases referred to a group known to be interested in the relationship between MMR vaccine and IBD rather than based on a population study. Finally, were no controls to compare events following immunisation, and there was no clear case definition.
There are no other reports suggesting an association between IBD and behavioural syndromes or autism following MMR or measles vaccine in the millions of doses of vaccine used worldwide since the 1960s.\textsuperscript{20,21,40,41} Members of the original study group proposing the association have now withdrawn their claims.\textsuperscript{42}

The hypothesis was also examined in studies by other researchers and in other countries. A study from Finland\textsuperscript{21} followed up those children who developed gastrointestinal disease after MMR. At the end of 1996 three million doses of MMR vaccine had been delivered with 31 children reported with gastrointestinal symptoms, none of whom developed either IBD or autism. A population-based study from the UK, which examined the incidence of autism after the introduction of MMR,\textsuperscript{40} also failed to find any association or increase in the incidence of autism. In this study a community child health system was used to identify children diagnosed with autism born since 1979. The records showed no increase in incidence following the introduction of MMR and no difference in the age at diagnosis of cases who had received MMR before or after 18 months, compared with those never vaccinated with MMR.

The Institute of Medicine in the US reviewed this issue\textsuperscript{41} and concluded in their report that the evidence does not support, at the population level, a link between MMR vaccine and autistic spectrum disorder (ASD). The Immunization Safety Review Committee did not exclude the possibility that MMR could contribute to ASD in a small number of children, because it is difficult to assess a rare occurrence and biological models have not been disproved. The Committee recommended no change or review of MMR licensure, or change to the US MMR programme. No recent data have emerged to change these recommendations\textsuperscript{43–45} (see section 21.2 for further discussion on this issue).

Table 10.1 shows the complications associated with contracting measles, mumps and rubella, and from receiving MMR vaccine.
Table 10.1 Complications from contracting measles, mumps and rubella, and MMR vaccine adverse effects

<table>
<thead>
<tr>
<th>Measles complications</th>
<th>Mumps complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Otitis media, pneumonia, diarrhoea</td>
<td>Meningitis 1/7</td>
</tr>
<tr>
<td>Encephalitis, probably resulting in brain damage 1/1000</td>
<td>Orchitis 1/5 post-pubertal males</td>
</tr>
<tr>
<td>Death 1/1000</td>
<td>Nerve deafness 1/15,000</td>
</tr>
<tr>
<td></td>
<td>Death 1.8/10,000</td>
</tr>
</tbody>
</table>

Rubella complications

Congenital rubella: cataracts, deafness, cardiac malformations and brain damage. Some abnormality of the fetus will be detectable in 85 percent of women infected in the first eight weeks of pregnancy (see Table 12.1).

Vaccine adverse effects

<table>
<thead>
<tr>
<th>Rashes, fever, local reactions, parotid swelling</th>
<th>1/7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Febrile seizures</td>
<td>400/1,000,000</td>
</tr>
<tr>
<td>Transient joint symptoms – children</td>
<td>1/35</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>33.3/1,000,000</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>1/1,000,000</td>
</tr>
<tr>
<td>Aseptic meningitis</td>
<td>&lt; 1/100,000</td>
</tr>
</tbody>
</table>

Adverse events should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442, or via online reporting at http://otago.ac.nz/carm (see ‘AEFI reporting process’ in section 2.5).

10.7 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR vaccines (eg, children with an acute febrile illness should have their immunisation deferred; see section 1.8).

Anaphylaxis following a previous dose of MMR vaccine is a contraindication to a further dose of MMR.

Children who have anaphylaxis after MMR should be serologically tested for immunity and referred to, or discussed with, a paediatrician if non-immune to rubella or measles. Children who have a hypersensitivity reaction after MMR should be serologically tested for immunity, and if non-immune referred to a paediatrician for evaluation before receiving a second dose of MMR.
Individuals in which MMR is contraindicated include:

- individuals with proven anaphylaxis (but not contact dermatitis) to neomycin

- children with immune suppression (ie, children with significantly impaired cell-mediated immunity, including those with untreated malignancy, altered immunity as a result of drug therapy, including high-dose steroids, or receiving high-dose radiotherapy) (see section 1.7)

- children who have received another live vaccine, including Bacillus Calmette-Guérin (BCG), within the previous four weeks (see chapter 14)

- pregnant women

- women of childbearing age, who should be advised to avoid pregnancy for the next 4 weeks\textsuperscript{46} after MMR vaccine (see chapter 12)

- individuals who have received immunoglobulin or a blood transfusion during the preceding 11 months (see Table 1.5 for the length of time to defer measles vaccine after specific blood products)

- children with HIV infection who are severely immune compromised.\textsuperscript{19}

Precautions

Children with current ITP should have the timing of vaccination discussed with the specialist responsible for their care.

Tuberculin skin testing is not a prerequisite for measles vaccination. Antituberculous therapy should be initiated before administering MMR vaccine to people with untreated tuberculous infection (latent) or disease (active). Tuberculin skin testing, if otherwise indicated, can be done on the day of vaccination. Otherwise testing should be postponed for four to six weeks, because measles vaccination may temporarily suppress tuberculin skin test reactivity.

Egg allergy

Egg allergy is no longer considered a contraindication to measles-containing vaccines. Various studies have confirmed these children can be vaccinated safely.\textsuperscript{47–49} Other components of the vaccine (eg, gelatin)\textsuperscript{50} may be responsible for allergic reactions. It is, however, recommended that any child who has a history of anaphylaxis to eggs be vaccinated under close medical supervision.
10.8 Control measures

**It is a legal requirement that all cases of measles be notified immediately on suspicion to the local medical officer of health.**

A single case of measles should be considered an outbreak and result in a suitable outbreak response. Whilst practitioners should have a low index of suspicion for notification it is important that all suspected clinical cases are laboratory confirmed. An exception to this approach requiring laboratory confirmation may occur in an established outbreak.

The standard clinical case definition for measles is ‘any person with fever 38°C or higher, generalised maculopapular rash lasting three or more days and cough or coryza or conjunctivitis or Koplik’s spots.’

However as many viral infections can mimic measles it is important that the diagnosis is laboratory confirmed. In the first instance blood should be taken for serological confirmation and a nasopharyngeal and throat swab for viral identification by PCR (for instructions on specimen collection, see Appendix 10).

Further specimens for viral culture, detection of measles virus by PCR or further serological tests should be taken in consultation with the laboratory. The timing and choice of samples in relation to the onset of symptoms is important. For further information contact your local medical officer of health or infectious disease physician. More detailed information is available from the National Measles Laboratory (http://www.cdhb.govt.nz/measles).

Although serological or virological diagnosis of the early cases is essential, outbreak control planning and response should not be delayed. All children who could become infected during the outbreak and have not received two doses of measles-containing vaccine should be offered MMR, ideally within three days of diagnosing the index case. The vaccine, if given within 72 hours of measles exposure, will provide protection in some cases, so prompt immunisation may protect those who are susceptible.

If there is doubt about the state of immunity, the vaccine should be given because there are no ill effects from vaccinating an individual who is already immune. Particular attention should be paid to individuals born during 1969 to 1975. At that time the measles vaccine was given at age 10 months. There is now good evidence that the vaccine is less effective at that age because of residual maternally acquired passive immunity, and so these people are less likely to be protected.

In an outbreak affecting infants, the use of MMR vaccine for infants aged 6 to 14 months should be considered. If MMR vaccine is given to infants aged less than 12 months, it should still be given at ages 15 months and four years.
This is because the seroconversion rate is lower when MMR is administered to an infant aged less than 12 months.

**Normal Immunoglobulin (IG) prophylaxis for contacts**

Normal immunoglobulin is recommended for measles-susceptible individuals in whom the vaccine is contraindicated (see section 10.7) and susceptible pregnant contacts. For these individuals, IG is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure.

Normal immunoglobulin is recommended for the following contacts of measles cases as soon as possible after exposure:

- immune-compromised or immune-deficient children
- pregnant women
- immune competent children aged less than 15 months beyond 72 hours after exposure
- people outside the 72 hour window for MMR who have not had a history of measles infection or vaccination.

The recommended doses of IG are:

- immune competent infants aged less than 15 months should receive 0.6 mL/kg intramuscularly, to a maximum volume of 5 mL
- pregnant women, immune competent adults and immune-compromised or immune-deficient children should receive 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, recommended as three 5 mL injections.

**Prophylaxis with intravenous immunoglobulin**

Intravenous immunoglobulin (Intragam P) can be considered for immune-suppressed and immune-deficient measles contacts (who may, for example, have a central venous catheter), individuals with reduced muscle bulk, or in those people for whom large doses are required.

The recommended dose of intravenous immunoglobulin is 0.15 g/kg. See the revised guidance from the Health Protection Agency for further information (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587).

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

Parents/guardians should be advised that children who are measles cases should be excluded from early childhood services, school or community gatherings until at least four days after the appearance of the rash. Immunised contacts (ie, who have received two doses after their first birthday) need not be excluded from these settings. Non-immune contacts should be excluded because of the risk of catching the disease themselves, and the risk of passing on the disease during the prodromal phase to other susceptible children. Seek medical officer of health advice on the possible exclusion of recently vaccinated individuals during a measles outbreak.

Non-immune is defined as:

- an individual born after 1969 with no documented history of two doses of measles-containing vaccine after age 12 months
- an individual with no documented measles IgG antibody.

Note: Individuals born between 1969 and 1974 may be susceptible because a single dose of measles vaccine was scheduled at age 10 months.

Individuals born between 1975 and 1981 may be susceptible because only a single dose of measles-containing vaccine was scheduled at age 12–15 months.

The recommended period during which absence from an early childhood service or school is advised is from diagnosis of the first case until 14 days after the appearance of the rash in the last case.

Recommendations for vitamin A for infants and children with measles infection

In developing countries the use of vitamin A has been associated with decreased morbidity and mortality.51,52 The Ministry of Health recommends53 that all infants and children hospitalised with measles receive vitamin A (subject to its availability). Measles may occur in children recently arrived from developing countries, where vitamin A deficiency may be more prevalent than in New Zealand. If a child with measles has a condition causing fat malabsorption (cystic fibrosis, short bowel syndrome and cholestasis), an immune deficiency or malnutrition (including adolescents with eating disorders), the case should be discussed with a paediatrician and vitamin A may be recommended.

Vitamin A is administered once daily for two days at the following doses:

- 200,000 IU for children aged 12 months or older
- 100,000 IU for infants 6–11 months of age
- 50,000 IU for infants aged less than 6 months.
In children with clinical signs of vitamin A deficiency, a third dose should be given four to six weeks following the diagnosis of measles.

For more details on control measures, refer to the *Communicable Disease Control Manual 2011* or the *Control of Communicable Diseases Manual*.

References


