Measles


Edited by Mike Sharland, Karina Butler, Andrew Cant, Ron Dagan, Graham Davies, Ronald de Groot, David Elliman, Susanna Esposito, Adam Finn, Manolis Galanakis, Carlo Giaquinto, Jim Gray, Paul Heath, Terho Heikkinen, Ulrich Heininger, Philipp Henneke, Irja Lutsar, Hermione Lyall, Federico Martinon Torres, Andrew Pollard, Mary Ramsay, Andrew Riordan, Fernanda Rodrigues, Emmanuel Roilides, Pablo Rojo, Delane Shingadia, Steve Tomlin, and Maria Tsolia

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Name and nature of organism

- Measles (also known as rubeola) virus causes an acute illness, characterized by rash, fever, and respiratory symptoms.
- Caused by *Paramyxoviridae* virus of the genus *Morbillivirus*.
- An enveloped single-stranded RNA virus. The genome encodes eight proteins, including haemagglutinin (H) and fusion (F) proteins.
- The complete measles genome has been sequenced, allowing the differentiation of various wild (24 so far, though not all in circulation this century) and vaccine genotypes.

Epidemiology

- Only found in humans.
- Highly infectious. In the pre-vaccination era, >90% of individuals had a symptomatic infection by the age of 10 years.
- In temperate areas, it is commonest in late winter and early spring, whereas, in the tropics, it is commonest in the dry season.
- Where infection is common, epidemics occur every 2 years.
- WHO estimates that worldwide deaths fell from 562,000 in 2000 to 122,000 in 2012.
  - In the EU and EEA/European Parliamentary Technology Assessment (EPTA) in 2006, there were 2723 reported cases and six deaths. This rose to 10,271 cases and three deaths in 2013, with eight cases of measles encephalitis. Five countries (the Netherlands, Italy, the UK, Germany, and Romania) accounted for 91% of cases. The majority of affected children were unimmunized, with only 20% of the 1–4 year olds immunized. The highest notification rate was in those under 1 year old.
  - In England and Wales, confirmed cases increased from a low of 56 in 1998 to over 2000 cases in 2013, with one death in each of 2006, 2008, and 2013.
  - In the first 5 months of 2014, there were 334 cases, more than in any complete year since measles was eliminated from the US in 2000.
- Immunity after natural infection is usually lifelong, due to both neutralizing antibody to the H protein and cell-mediated immunity.

Transmission and incubation period

- Highly infectious, up to 90% of susceptible contacts are infected.
- Spread from person to person via respiratory droplets, which may persist in the air for several hours.
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- Can survive on surfaces for up to 2 hours, but its lipid envelope is destroyed by ethanol-based handscrubs.
- Incubation period is from 6 to 19 days (median 13 days). There is a short 1° viraemia from the pharynx to local nodes, with a main 2° viraemia around a week after infection, leading to URTI symptoms, then a rash.
- Virus is shed from 2 days before to 3 days after symptoms appear.
- The period of infectiousness is not known but is thought to be 1–2 days prior to the appearance of the rash to 4–5 days after.

Clinical features and sequelae

- Prodrome of high fever, cough, coryza, and conjunctivitis.
- Maculopapular rash appears next around 2–4 days later, first behind the ears, then spreads down the body; generally the more rash, the more unwell the child is—the rash can look almost haemorrhagic.
- Koplik spots (small 1mm bluish white spots on the buccal mucosa) are present about 1–3 days before the onset of the rash and are characteristic of measles, though not found in all cases.
- Three days after the rash appears, children improve and are usually fully recovered 7–10 days after the onset of illness.
- Complications occur in 6–7% of otherwise healthy individuals in developed countries.
- Complications include otitis media, measles pneumonitis, or 2° bacterial pneumonia—difficult to distinguish clinically (38/1000), convulsions (5/1000), encephalitis (1.2/1000), idiopathic thrombocytopenic purpura (1 in 2000–3000), and diarrhoea.
- Acute encephalitis occurs around 2–5 days after the onset of rash; CSF shows lymphocytosis with elevated protein—may be PCR-positive. Most children recover. A severe fulminant encephalitis has been reported.
- SSPE occurs in 4/100 000 overall, but 18/100 000 in children infected with measles under a year old. SSPE presents with gradual neurological deterioration around 5–10 years after measles; proceeds to myoclonic epilepsy, coma, and death. Diagnosis is based on classic EEG pattern of bilateral, high-amplitude, periodic complexes and monoclonal measles antibody titres in the CSF.
- In those malnourished, especially if vitamin A-deficient, or immunocompromised, there is a higher morbidity and mortality. There may be no rash in the immunocompromised who present with unexplained pneumonia or encephalitis.
- Mortality is greatest in infants and adults. Overall, it is about 1 in 1000–3000 in industrialized nations.
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- Globally, up to 5% of deaths in the <5 year olds are still due to measles.

Diagnosis

- As the disease has become less common, the accuracy of clinical diagnosis, especially of sporadic cases, has become poor, with as few as 1–2% of suspected cases being confirmed. The differential diagnosis includes adenovirus, rubella, enterovirus or EBV infection, streptococcal disease, and Kawasaki disease.
- Laboratory diagnosis used to depend on the finding of measles-specific IgM or a 4-fold rise in IgG in blood.
- Diagnosis is now possible by salivary measles-specific IgM.
- Using RT-PCR, viral RNA can also be found in saliva, allowing genotyping and epidemiological mapping. Oral fluid is the best sample—ideally collected using special kits.

Management and treatment

- Treatment of individual cases is symptomatic, with complications being managed individually as they arise. Antibiotics are only needed for 2° bacterial pneumonia.
- WHO recommends that all cases should be treated with vitamin A and that, even in countries where measles is not usually severe, a dose of vitamin A at diagnosis, and another a day later, should be given to all severe cases. There is little evidence that this is efficacious in patients not deficient in vitamin A.
- The daily dose of vitamin A is 50,000IU for infants <6 months old, 100,000IU for infants aged 6–11 months, and 200,000IU for those ≥12 months. A recent Cochrane analysis reported a fall of over 60% in pneumonia mortality associated with high-dose vitamin A use.
- Patients should be isolated until 4 days after the onset of rash.
- Contacts should be traced, and consideration given to vaccination or administration of immunoglobulin, depending on their age and immunization status and the interval elapsed after contact with the index case (see Prevention, p.[link]-[link] for more details).

Prevention

- Measles vaccines have been available for almost 50 years.
- Initially, both live and killed vaccines were used. The latter caused many cases of a severe atypical infection and rapidly gave way to the live attenuated vaccines, which are the only ones now available.
The measles virus strains in commonest use are derived from the Edmonston strain (named after the boy from whom the measles virus strain was isolated). There is little to choose between them.

A single dose of a measles-containing vaccine protects 90–95% of recipients, if given to children ≥12 months old.

To attain herd immunity, it is necessary to give two doses.

When given to children <12 months old, the efficacy is less, in large part due to the presence of maternal antibodies.

In countries where measles is a major problem in infants, measles vaccine may be given to individuals as young as 9 months. In outbreak situations, the vaccines may be used in children as young as 6 months.

High-titre vaccines were produced in an attempt to protect infants, but they are not in use due to evidence of higher non-measles death rates in recipients.

Most affluent countries give measles vaccine as part of the combined MMR vaccine. Two doses are given: one at 12-15 months, and the other at anything between 2 and 10 years later, with a few countries giving it earlier.

Side effects of the vaccine usually occur in the second week after vaccination and include a transient rash (2%), fever and other symptoms of measles (5–10%), febrile convulsions (1 in 3000), and idiopathic thrombocytopenia (1 in 30 000). These reactions are much less common after the second dose.

The relative incidence of febrile seizures following MMR is higher in children vaccinated between 16 and 23 months, compared with 12 and 15 months.\(^1\)

Anaphylaxis after the vaccine occurs in 1 in 100 000 or fewer recipients.

The vaccine is contraindicated in pregnancy and in individuals who are significantly immunocompromised (HIV is an exception where it may sometimes be given).

In the UK, after spurious reports of an association of MMR with autism, immunization rates fell markedly. Following clear evidence of absolutely no link between MMR and autism, national immunization rates rose again and now exceed pre-scare levels among 2-year-old children.\(^2\) Of UK children reaching 2 years old at the end of 2013, 93.3% have received one dose of MMR, and 89.6% of 5 year olds have received two doses. Uptake in the rest of Europe and across the US varies.

It may be possible to prevent disease in susceptible contacts:

Immunosuppressed individuals, whose last contact was within 6 days, should have an urgent assessment of antibody levels and given human normal immunoglobulin (HNIG) if negative or equivocal. If urgent testing is not possible, immunoglobulin as HNIG should be given. The dose recommended is 0.6mL/kg.
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- subcutaneously or 0.15g/kg IV. Infants <1 year should be given 0.6mL/kg IM, up to a maximum of 5mL.3

- As the incubation period of the vaccine virus is shorter than that of wild measles virus (7, as opposed to 10, days), if given within 3 days of exposure, MMR or measles vaccination reduces the risk of development of measles.

- A combined MMRV (measles, mumps, rubella, and varicella) vaccine is available in some countries. When the first dose is given at or below 47 months of age, there is an increased risk of fever, febrile convulsions, and rash, when compared with MMR and varicella vaccines given separately, but on the same occasion. For this reason, in the US, it is advised that, when the first dose of MMR is given at or below 47 months, it should not be given as part of MMRV.

Future research

- Why does a small proportion of the population not become immune after a single dose of measles vaccine?

- Should the age for vaccination be reduced in countries where maternal immunity is vaccine-based?

Key references

