

Measles is an acute, viral, infectious disease. References to measles can be found from as early as the 7th century. The disease was described by the Persian physician Rhazes in the 10th century as “more to be dreaded than smallpox.”

In 1846, Peter Panum described the incubation period of measles and lifelong immunity after recovery from the disease. John Enders and Thomas Chalmers Peebles isolated the virus in human and monkey kidney tissue culture in 1954. The first live, attenuated vaccine (Edmonston B strain) was licensed for use in the United States in 1963. In 1971, a combined measles, mumps, and rubella (MMR) vaccine was licensed for use in the United States. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed.

Before a vaccine was available, infection with measles virus was nearly universal during childhood, and more than 90% of persons were immune due to past infection by age 15 years. Measles is still a common and often fatal disease in developing countries. The World Health Organization estimates there were 142,300 deaths from measles globally in 2018. In the United States, there have been recent outbreaks; the largest occurring in 2019 primarily among people who were not vaccinated.

## Measles Virus

The measles virus is a paramyxovirus of the genus *Morbillivirus*. It is 120 to 250 nm in diameter, with a genome of single-stranded, negative sense RNA, and is closely related to the rinderpest and canine distemper viruses. Two membrane envelope proteins are important in pathogenesis. They are the F (fusion) protein, which is responsible for fusion of virus and host cell membranes, viral penetration, and hemolysis, and the H (hemagglutinin) protein, which is responsible for binding of virus to receptors on host cells.

There is only one antigenic type of measles virus. Although studies have documented antigenic changes in the H protein, these changes do not appear to be epidemiologically important (i.e., no change in vaccine efficacy has been observed).

Measles virus is rapidly inactivated by heat, sunlight, acidic pH, ether, and trypsin.

## Pathogenesis

Measles is a systemic infection. The primary site of infection is alveolar macrophages or dendritic cells. Two to three days after replication in the lung, measles virus spreads to regional lymphoid tissues followed by a systemic infection. Following further viral replication in regional and distal reticuloendothelial

### Measles

- Acute viral infectious disease
- First described in 7th century
- Vaccines first licensed include measles in 1963, MMR in 1971, and MMRV in 2005
- Infection nearly universal during childhood in prevaccine era
- Still common and often fatal in developing countries

### Measles Virus

- Paramyxovirus (RNA)
- F (fusion) protein fuses virus and host cell membranes and H (hemagglutinin) protein binds virus to host receptors
- One antigenic type
- Rapidly inactivated by heat, sunlight, acidic pH, ether, and trypsin

### Measles Pathogenesis

- Primary site of infection is alveolar macrophages or dendritic cells
- Primary viremia 2 to 3 days after replication
- Secondary viremia 5 to 7 days after exposure

## Measles Clinical Features

- Incubation period 11 to 12 days
  - Exposure to rash onset averages 14 days (range, 7 to 21 days)
- Prodrome lasts 2 to 4 days (range, 1 to 7 days)
  - Stepwise increase in fever to 103°F–105°F
  - Cough, coryza, and conjunctivitis
  - Koplik spots (on mucous membranes)
- Rash
  - Persists 5 to 6 days
  - Begins at hairline, then involves face and upper neck
  - Proceeds downward and outward to hands and feet
  - Severe areas peel off in scales
  - Fades in order of appearance

## Measles Complications

- Diarrhea, otitis media, pneumonia, encephalitis, subacute sclerosing panencephalitis, death
- Most common among children younger than age 5 years and adults

sites, a second viremia occurs 5 to 7 days after initial infection. During this phase, infected lymphocytes and dendritic cells migrate into the subepithelial cell layer and transmit measles to epithelial cells. Following amplification in the epithelia, the virus is released into the respiratory tract.

## Clinical Features

The incubation period of measles from exposure to prodrome averages 11 to 12 days. The time from exposure to rash onset averages 14 days, with a range of 7 to 21 days.

The prodrome lasts 2 to 4 days, with a range of 1 to 7 days. It is characterized by fever, which increases in a stepwise fashion often peaking as high as 103°F to 105°F, cough, coryza, and conjunctivitis.

Koplik spots, present on mucous membranes, are considered to be unique to measles. They occur 1 to 2 days before the measles rash (i.e., during the prodromal period), and appear as punctate blue-white spots on the bright red background of the buccal mucosa.

The measles rash is a maculopapular eruption that usually lasts 5 to 6 days. It begins at the hairline, then involves the face and upper neck. During the next 3 days, the rash gradually proceeds downward and outward, reaching the hands and feet. The maculopapular lesions are generally individually distinct but may run together, particularly on the upper body. Initially, lesions blanch (become white or pale) with fingertip pressure. By 3 to 4 days, most do not blanch with pressure. The lesions peel off in scales in more severely involved areas. The rash fades in the same order that it appears, from head to extremities.

Other symptoms of measles include anorexia and generalized lymphadenopathy.

## Complications

Approximately 30% of measles cases in the United States from 1987 to 2000 were reported to have one or more complications. Complications include diarrhea, otitis media, pneumonia, encephalitis, subacute sclerosing panencephalitis, and death. Complications of measles were most common among children younger than age 5 years and adults.

## Laboratory Testing

The most widely used methods for laboratory confirmation of measles are detection of measles virus RNA in nasopharyngeal aspirates, throat swabs, or urine by reverse transcriptase polymerase chain reaction (RT-PCR) or detection of measles specific IgM in serum samples by enzyme immunoassay (EIA).

Collection of both a throat swab specimen for RT-PCR and a serum specimen for IgM detection is recommended from all patients with clinical features compatible with measles.

Clinical specimens for viral detection should be collected at the same time as samples taken for serologic testing. In addition to RT-PCR for diagnosis, viral genotyping performed by state public health laboratories or CDC can help to track the transmission pathways of measles virus. Specimens for viral detection should be shipped to a state public health laboratory or CDC (at the direction of the state health department).

Laboratory testing can confirm the presence of measles vaccine virus in a recently vaccinated and potentially exposed individual.

## Epidemiology

### Occurrence

Measles occurs throughout the world. Interruption of indigenous transmission of measles was declared in the United States in the year 2000 and in other parts of the Western Hemisphere in 2016. However, outbreaks with sustained measles virus transmission have recently occurred in Venezuela and Brazil, leading to re-establishment of endemic transmission in these countries and loss of measles elimination in the Americas.

### Reservoir

Measles is a human disease. There is no known animal reservoir, and an asymptomatic carrier state has not been documented.

### Transmission

Measles transmission occurs person-to-person via large respiratory droplets and via airborne transmission of aerosolized droplet nuclei in closed areas (e.g., an office examination room) for up to 2 hours after a person with measles occupied the area.

### Temporal Pattern

In endemic, temperate areas, measles disease occurs primarily in late winter and spring.

### Communicability

Measles is highly communicable, with more than 90% secondary attack rates among exposed susceptible persons in close-contact settings. Measles is considered transmissible from 4 days before through 4 days after rash onset.

#### Measles Epidemiology

- Reservoir
  - Human
- Transmission
  - Person-to-person via large respiratory droplets
  - Airborne in closed areas for up to 2 hours
- Temporal pattern
  - Primarily late winter and spring
- Communicability
  - 4 days before through 4 days after rash onset

## Measles Secular Trends in the United States

- About 500,000 reported cases and 500 deaths annually before vaccine
  - Actual cases estimated at 3 to 4 million
- Following vaccine licensure in 1963, incidence decreased by over 95%
- Measles occurrence among vaccinated school-aged children in the 1980s led to recommendations for a second dose
- In 2019, 13 outbreaks reported; underimmunized communities accounted for 88% of cases

## Secular Trends in the United States

Before 1963, approximately 500,000 cases and 500 measles deaths were reported annually, with epidemic cycles every 2 to 3 years. However, the actual number of cases was estimated at 3 to 4 million annually. More than 50% of persons had measles by age 6 years, and more than 90% by age 15 years. In the years following licensure of vaccine in 1963, the incidence of measles decreased by more than 95%, and 2- to 3-year epidemic cycles no longer occurred. From 1985 through 1988, 68% of cases in school-aged children (age 5 to 19 years) occurred among those who had been appropriately vaccinated – i.e., had received a single dose of measles vaccine as recommended. The occurrence of measles among previously vaccinated children (i.e., vaccine failure) led to a recommendation for a second dose in this age group in 1989.

In 2019, 13 outbreaks of measles were reported, accounting for 663 cases; six were associated with underimmunized close-knit communities and accounted for 88% of all cases. Before 2019, the highest number of measles cases following elimination in the United States occurred in 2014 when 667 cases were reported. Increasing incidence of measles globally contributes to increased opportunities for measles importation into the United States. Fortunately, public health measures and a long-standing vaccination program has prevented outbreaks from imported cases.

Among children born during 2016–2017, 90.7% received measles, mumps, and rubella-containing vaccine by age 24 months; this was not statistically significantly different from the coverage of 90.3% for children born during 2014–2015.

## Measles Vaccines

- MMR (MMR-II)
- MMRV (ProQuad)

## Measles Vaccines

In 1963, both an inactivated (“killed”) and a live, attenuated (Edmonston B strain) measles vaccine were licensed for use in the United States. The inactivated vaccine was withdrawn in 1967 because it did not protect well against measles. The original Edmonston B vaccine was withdrawn in 1975 because of a relatively high frequency of fever and rash in recipients. A live, further attenuated (Schwarz strain) vaccine was first introduced in 1965, but also is no longer used in the United States. Another live, further attenuated strain (Edmonston-Enders strain) vaccine was licensed in 1968. These further attenuated vaccines caused fewer reactions than the original Edmonston B vaccine. In 1971, measles vaccine was licensed as a combined measles, mumps, and rubella (MMR) vaccine. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed.

Measles vaccine is available as measles, mumps, and rubella vaccine (MMR [MMR-II]) and measles, mumps, rubella, and varicella vaccine (MMRV [ProQuad]). Both MMR and MMRV

vaccine contain live, attenuated viruses. Single-antigen measles vaccine is not available in the United States. The Advisory Committee on Immunization Practices (ACIP) recommends that MMR or MMRV vaccine be used when any of the individual components is indicated.

## Characteristics

MMR vaccine is a lyophilized preparation of measles virus vaccine live, an attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; mumps virus vaccine live, the Jeryl Lynn strain of mumps virus propagated in chick embryo cell culture; and rubella virus vaccine live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts. MMRV vaccine contains measles, mumps, and rubella virus of equal titer and identical to those in the MMR vaccine. The titer of Oka varicella zoster virus is higher in MMRV vaccine than in single-antigen varicella vaccine, a minimum of 9,772 plaque-forming units (PFU) versus 1,350 PFU, respectively. MMR and MMRV vaccines are supplied as a lyophilized (freeze-dried) powder and are reconstituted with sterile, preservative-free water. Both vaccines contain gelatin. MMR and MMRV vaccines are administered by the subcutaneous route. Each dose of MMR and MMRV vaccine contains neomycin as an antibiotic. It contains no adjuvant or preservative.

## Vaccination Schedule and Use

MMR vaccine or MMRV vaccine can be used to implement the vaccination recommendations for prevention of measles, mumps, and rubella. MMR vaccine is licensed for use in persons age 12 months or older. MMRV vaccine is licensed for use in persons age 12 months through 12 years; MMRV vaccine should not be administered to persons age 13 years or older.

Two doses of MMR vaccine, separated by at least 4 weeks, are routinely recommended for children age 12 months or older. Dose 1 of MMR vaccine should be given at age 12 through 15 months. A second dose of MMR vaccine is recommended based on previous observations of the failure of some to generate an immune response to measles following dose 1. Dose 2 is routinely given at age 4 through 6 years, before a child enters kindergarten or first grade. All students entering school should receive 2 doses of MMR vaccine (with the first dose administered at age 12 months or older) before enrollment. Dose 2 of MMR vaccine may be administered as soon as 4 weeks after dose 1.

The minimum interval between doses of MMRV vaccine is 3 months, although when dose 2 is administered 4 weeks following dose 1, it can be considered valid. For the first dose of measles, mumps, rubella, and varicella vaccines at age 12

### Measles Vaccine Characteristics

- Live, attenuated vaccine
- Available as lyophilized powder and reconstituted with sterile, preservative-free water
- Administered by subcutaneous injection
- Contains gelatin
- Contains neomycin

### Measles Vaccination Schedule

- 2-dose series at age 12 through 15 months and at age 4 through 6 years
- Minimum age for dose 1 is 12 months
- Minimum interval from dose 1 to 2 is 4 weeks for MMR and 3 months for MMRV (although a 4-week interval is valid)
- Discuss risks and benefits of MMRV versus separate MMR and VAR
  - Separate MMR and VAR vaccines preferred for dose 1 in ages 12 through 47 months
  - MMRV preferred for dose 2 and dose 1 at age 48 months or older

## MMR Vaccination of Adults

- Certain persons without acceptable presumptive immunity:
  - At least 1 dose MMR for unvaccinated adults
  - 2 doses MMR for students entering colleges, universities, technical and vocational schools, and other post-high-school educational institutions
  - 2 doses MMR for measles and mumps and 1 dose MMR for rubella for healthcare personnel
- Healthcare personnel during an outbreak
  - 2 doses MMR for measles or mumps outbreak and 1 dose MMR for rubella outbreak

through 47 months, either separate MMR and varicella (VAR) vaccines, or MMRV vaccine, may be used. However, the risk of febrile seizures is about twice as high for children receiving MMRV vaccine versus separate MMR and VAR vaccines. Providers who are considering administering MMRV should discuss the benefits and risks of both vaccination options with the parents. Unless the parent or caregiver expresses a preference for MMRV, separate MMR vaccine and VAR vaccine should be administered for the first dose in this age group. For the second dose of measles, mumps, rubella, and varicella vaccines at any age and for the first dose at age 48 months or older, the use of MMRV generally is preferred over separate injections of its equivalent component vaccines (i.e., MMR vaccine and VAR vaccine).

## Vaccination of Adults

Adults born in 1957 or later should receive at least 1 dose of MMR vaccine unless they have documentation of vaccination with at least 1 dose of measles, mumps, and rubella-containing vaccine or other acceptable presumptive evidence of immunity to these three diseases. Except for health care personnel who should have documented immunity, birth before 1957 generally can be considered acceptable evidence of immunity to measles, mumps, and rubella.

Colleges and other post-high-school educational institutions are potential high-risk areas for measles, mumps, and rubella transmission because of large concentrations of persons. Prematriculation vaccination requirements for measles immunity have been shown to significantly decrease the risk of measles outbreaks on college campuses where such requirements are implemented and enforced. All students entering colleges, universities, technical and vocational schools, and other institutions for post-high-school education should receive 2 doses of MMR vaccine or have other acceptable evidence of measles, mumps, and rubella immunity before entry.

For unvaccinated health care personnel born before 1957 who lack laboratory evidence of measles, mumps, or rubella immunity or laboratory confirmation of disease, health care facilities should have policies that offer 2 doses of MMR vaccine at the appropriate interval for measles and mumps and 1 dose of MMR vaccine for rubella, respectively. Health care facilities should also have policies for such personnel that recommend 2 doses of MMR vaccine during an outbreak of measles or mumps and 1 dose during an outbreak of rubella. This recommendation is based on serologic studies indicating that among hospital personnel born before 1957, 5% to 10% had no detectable measles, mumps, or rubella antibody. Adequate vaccination for health care personnel born during or after 1957 consists of 2 appropriately spaced MMR doses for measles and mumps, and at least 1 dose of MMR for rubella.

Persons who travel outside the United States are at increased risk of exposure to measles. Measles is endemic or epidemic in many countries throughout the world. Although proof of immunization is not required for entry into the United States or any other country, persons traveling or living abroad should have evidence of measles immunity. Adequate vaccination of persons who travel outside the United States is 1 dose of MMR vaccine for children age 6 through 11 months and 2 doses of an age-appropriate measles-, mumps-, and rubella-containing vaccine for children age 12 months and older and adults.

## Revaccination

Revaccination is recommended for certain persons. The following groups should be considered unvaccinated and should receive at least 1 dose of measles vaccine: 1) persons vaccinated before their first birthday, 2) persons vaccinated with killed measles vaccine, 3) persons vaccinated from 1963 through 1967 with an unknown type of vaccine, 4) persons who received immune globulin (IG) in addition to a further attenuated strain or vaccine of unknown type, and 5) persons with perinatal human immunodeficiency virus (HIV) infection who were vaccinated before establishment of effective antiretroviral therapy (ART) and who do not have evidence of current severe immunosuppression.

Measles-, mumps-, or rubella- virus-containing vaccine administered prior to age 12 months (e.g., for international travel) should not be counted as part of the 2-dose series. Children vaccinated before age 12 months should be revaccinated with 2 doses of appropriately spaced MMR or MMRV vaccine, the first dose administered when the child is age 12 through 15 months (12 months if the child remains in an area where disease risk is high) and the second dose at least 4 weeks later.

Persons who experienced perinatal HIV infection who may have received MMR vaccine prior to the establishment of effective combined antiretroviral therapy (cART) should be revaccinated with 2 appropriately spaced doses of MMR (i.e., the dose does not count) unless they have other acceptable current evidence of immunity. MMR series should be administered once effective cART has been established for at least 6 months and there is no evidence of severe immunosuppression.

## Measles Immunity

Generally, persons can be considered immune to measles if they were born before 1957, have serologic evidence of measles immunity (equivocal test results should be considered negative), or laboratory confirmation of disease, or have documentation of adequate vaccination for measles.

### MMR Vaccination of Travelers

- Adequate vaccination for persons traveling outside the United States
  - 1 dose MMR for children age 6 through 11 months
  - 2 doses of age appropriate MMR or MMRV for children age 12 months and older and adults

### Measles Immunity

- Born before 1957
- Serologic evidence of measles immunity (equivocal tests are considered negative)
- Laboratory confirmation of disease
- Documentation of adequate vaccination for measles

## Measles Vaccine Efficacy

- Antibodies develop in approximately 95% of children vaccinated at age 12 months and over 99% of children who receive 2 doses
- Immunity long-term and probably lifelong in most persons

## Immunogenicity and Vaccine Efficacy

Measles antibodies develop in approximately 95% of children vaccinated at age 12 months. Seroconversion rates are similar for single-antigen measles, MMR vaccine, and MMRV vaccine. Approximately 2% to 7% of children who receive only 1 dose of MMR vaccine fail to respond to it, i.e., they experience primary vaccine failure. MMR vaccine failure can occur because of passive antibody in the vaccine recipient, immaturity of the immune system, damaged vaccine, or other reasons. Most persons who fail to respond to the first dose will respond to a second dose. Studies indicate that more than 99% of persons who receive 2 doses of measles vaccine (with the first dose administered no earlier than the first birthday) develop serologic evidence of measles immunity.

Although the titer of vaccine-induced antibodies is lower than that following natural disease, both serologic and epidemiologic evidence indicate that vaccine-induced immunity appears to be long-term and probably lifelong in most persons. Most vaccinated persons who appear to lose antibody show an anamnestic immune response upon revaccination, indicating that they are probably still immune.

Although revaccination can increase antibody titer in some persons, available data indicate that the increased titer may not be sustained. Some studies indicate that waning immunity may occur after successful vaccination, but this appears to occur rarely and to play only a minor role in measles transmission and outbreaks.

## Contraindications and Precautions to Vaccination

As with other vaccines, a history of a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose is a contraindication to further doses. Moderate or severe acute illness (with or without fever) in a patient is considered a precaution to vaccination, although persons with minor illness may be vaccinated.

MMR and MMRV vaccines both contain minute amounts of neomycin and gelatin. Persons with alpha-gal allergy may wish to consult their physician before receiving a vaccine that contains gelatin.

Severe immunocompromise (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy or patients with HIV infection who are severely immunocompromised) is a contraindication for MMR and MMRV vaccination. If the person's level of immunocompetence is uncertain, the decision to vaccinate should be made by the health care provider that prescribed the immunosuppressive medication for those

## Measles Vaccine Contraindications

- Contraindication
  - Severe allergic reaction to vaccine component or following a prior dose
  - Severe immunocompromise
  - Systemic high-dose corticosteroid therapy for 14 days or more
  - HIV infection, regardless of immunocompetence status\*
  - Family history of congenital or heredity immunodeficiency in first-degree relatives
  - Pregnancy

\*MMRV only



patients whom immunocompromise is due to medication. Patients who have not received chemotherapy for at least 3 months, whose disease remains in remission, and who have restored immunocompetence, may receive MMR or MMRV vaccine. Healthy, susceptible close contacts of severely immunocompromised persons should be vaccinated.

Persons receiving systemic high-dose corticosteroid therapy (2 milligrams per kilogram of body weight or more per day or 20 milligrams or more per day of prednisone) for 14 days or more should not receive MMR or MMRV vaccine because of concern about vaccine safety. MMR or MMRV should not be administered for at least 1 month after cessation of systemic high-dose corticosteroid therapy. Although persons receiving high doses of systemic corticosteroids daily or on alternate days for less than 14 days generally can receive MMR or MMRV immediately after cessation of treatment, some experts prefer waiting until 2 weeks after completion of therapy.

Available data indicate that vaccination with MMR has not been associated with severe or unusual adverse reactions in HIV-infected persons who are not severely immunosuppressed, although antibody responses have been variable. MMR vaccine is recommended for susceptible HIV-infected persons age 12 months or older with no evidence of current severe immunosuppression ("no evidence of current severe immunosuppression" is defined as CD4 percentages greater than or equal to 15% for 6 months or longer for persons age 5 years or younger; and CD4 percentages greater than or equal to 15% and CD4 count greater than or equal to 200 cells/mm<sup>3</sup> for 6 months or longer for persons older than age 5 years). MMR vaccine is not recommended for HIV-infected persons with evidence of severe immunosuppression.

MMRV is not approved for and should not be administered to a person known to be infected with HIV.

A family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings) is a contraindication for MMR or MMRV vaccine, unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory.

A history of thrombocytopenic purpura or thrombocytopenia is a precaution for MMR and MMRV vaccine. Such persons may be at increased risk for developing clinically significant thrombocytopenia after MMR or MMRV vaccination.

Simultaneous use of aspirin or aspirin-containing products is a precaution for MMRV vaccine due to the varicella component. The manufacturer recommends that vaccine recipients avoid the use of salicylates for 6 weeks after receiving MMRV vaccine because of the association between aspirin use and Reye syndrome following chickenpox.

### Measles Vaccine Precautions

- Precaution
  - Moderate or severe acute illness
  - Alpha-gal allergy (consult with physician)
  - Receipt of antibody-containing blood products (wait 3 to 11 months to vaccinate)
  - History of thrombocytopenic purpura or thrombocytopenia
  - Need for tuberculin skin testing or interferon-gamma release assay testing
  - Simultaneous use of aspirin or aspirin-containing products\*
  - Personal or family history of seizures of any etiology\*
  - Receipt of specific antiviral drugs 24 hours before vaccination\*

\*MMRV only

A personal or family (i.e., sibling or parent) history of seizures of any etiology is a precaution for MMRV vaccine but not MMR. Children with a personal or family history of seizures of any etiology should ideally be vaccinated with separate MMR and VAR vaccines because the risks for using MMRV vaccine in this group of children generally outweigh the benefits.

MMR vaccine may be administered to egg-allergic persons without prior routine skin testing or the use of special protocols.

## Spacing Considerations

The effect of the administration of antibody-containing blood products (e.g., immune globulin, whole blood or packed red blood cells, or intravenous immune globulin) on the response to MMR or MMRV vaccine is unknown. Because of the potential inhibition of the response to vaccination by passively transferred antibodies, neither MMR vaccine nor MMRV vaccine (nor VAR vaccine) should be administered for 3 to 11 months after receipt of antibody-containing blood products. The interval between the antibody-containing blood product and receipt of MMR or MMRV vaccine is determined by the type of product administered. Antibody-containing products should not be given for 2 weeks following vaccination unless the benefits exceed those of the vaccine. In such cases, vaccine recipients should either be revaccinated later at the appropriate intervals (ranging 3 to 11 months) or tested for immunity and revaccinated if seronegative.

Need for tuberculin skin testing or interferon-gamma release assay (IGRA) testing is a precaution for MMR and MMRV vaccine. Measles vaccine (and possibly mumps, rubella, and varicella vaccines) may transiently suppress the response to tuberculin skin test (TST) in a person infected with *Mycobacterium tuberculosis*. TST and measles-containing vaccine may be administered at the same visit if necessary. Simultaneously administering TST and measles-containing vaccine does not interfere with reading the TST result at 48 to 72 hours and ensures that the person has received measles vaccine. If the measles-containing vaccine has been administered recently, TST screening should be delayed for at least 4 weeks after vaccination.

Receipt of specific antiviral drugs (e.g., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination is a precaution for MMRV vaccine due to the varicella component. These drugs should be avoided for 14 days after vaccination.

## Vaccination in Pregnancy

Pregnancy is a contraindication for MMR or MMRV vaccine. Pregnancy should be avoided for 4 weeks following MMR or MMRV vaccine. Close contact with a pregnant woman is not a contraindication to MMR or MMRV vaccination of the contact.

If a pregnant woman inadvertently receives MMR or MMRV vaccine, termination of pregnancy is not recommended because the risk to the fetus appears to be extremely low. Instead, individual counseling for these women is recommended.

## Vaccine Safety

Studies have shown MMR and MMRV vaccines are safe and well-tolerated. The National Academy of Medicine, formerly called the Institute of Medicine, reviewed the evidence between MMR vaccination and certain adverse events. The experts determined that evidence supports a causal relation between MMR vaccination and anaphylaxis, febrile seizures, thrombocytopenic purpura, transient arthralgia, and measles inclusion body encephalitis in persons with demonstrated immunodeficiencies.

Most adverse events reported following MMR vaccination (such as fever and rash) are attributable to the measles component. After MMR vaccination, 5% to 15% of susceptible persons develop a temperature of 103°F (39.4°C) or higher, usually occurring 7 to 12 days after vaccination and generally lasting 1 or 2 days. Most persons with fever do not have other symptoms. MMR vaccine is associated with a very small risk of febrile seizures; approximately one case for every 3,000 to 4,000 doses of MMR vaccine administered. The febrile seizures typically occur 6 to 14 days after vaccination and do not appear to be associated with any long-term sequelae. Children with a personal or family history of febrile seizures or family history of epilepsy might be at increased risk for febrile seizures after MMR vaccination.

MMR vaccine may cause a transient rash in approximately 5% of vaccine recipients, usually appearing 7 to 10 days after vaccination. Laboratory testing can confirm the presence of measles or mumps vaccine virus in a recently vaccinated and potentially exposed individual.

Allergic reactions following the administration of MMR vaccine are rare. Most of these are minor and consist of a wheal and flare or urticaria at the injection site. Immediate, anaphylactic reactions to MMR vaccine occur in 1.8 to 14.4 cases per million doses.

Arthralgias and other joint symptoms are reported in up to 25% of adult women following MMR vaccination and are associated with the rubella component. Transient lymphadenopathy sometimes occurs following receipt of MMR or other rubella-containing vaccine, and parotitis has been reported rarely (less than 1%) following receipt of MMR or other mumps-containing vaccine.

Rarely, MMR vaccine may cause thrombocytopenia within two months after vaccination. The clinical course of these

### Measles Vaccine Safety

#### MMR

- Fever of 103°F (39.4°C) or higher
  - 5%–15%
- Rash
  - 5%
- Febrile seizures
  - 1 in every 3,000 to 4,000 doses
- Anaphylactic reactions
  - 1.8 to 14.4 cases per million doses
- Arthralgias and other joint symptoms
  - 25% (adult women)

#### MMRV

- Fever of 102°F or higher
  - 21.5%
- Febrile seizures
  - 1 additional per 2,300 to 2,600 children age 12 through 23 months

cases is usually transient and benign, although hemorrhage occurs rarely. Based on case reports, the risk for MMR vaccine-associated thrombocytopenia may be higher for persons who have previously had immune thrombocytopenic purpura, particularly for those who had thrombocytopenic purpura after an earlier dose of MMR vaccine.

Measles inclusion body encephalitis has been documented after measles vaccination in persons with immune deficiencies. The illness is also known to occur within 1 year after initial infection with wild-type measles virus and has a high death rate. In the cases after MMR vaccination, the time from vaccination to development of measles inclusion body encephalitis was 4–9 months, consistent with development of measles inclusion body encephalitis after infection with wild-type measles virus.

In MMRV vaccine prelicensure studies conducted among children age 12 to 23 months, fever (reported as abnormal or elevated greater than or equal to 102°F oral equivalent) was observed 5 to 12 days after vaccination in 21.5% of MMRV vaccine recipients compared with 14.9% of MMR vaccine and VAR vaccine recipients. Two postlicensure studies indicated that one additional febrile seizure per 2,300 to 2,600 children age 12 through 23 months occurred 5 to 12 days after the first dose of MMRV vaccine, compared with children who had received the first dose of MMR vaccine and VAR vaccine administered as separate injections at the same visit. Data from postlicensure studies do not suggest that this increased risk exists for children age 4 to 6 years receiving the second dose of MMRV vaccine.

Multiple studies, as well as a National Academy of Medicine Vaccine Safety Review, refute a causal relationship between autism and MMR vaccine or between inflammatory bowel disease and MMR vaccine.

## Vaccine Storage and Handling

For MMR-II and Proquad storage and handling specifics, refer to the manufacturer. For complete information on storage and handling best practices and recommendations, please refer to CDC's Vaccine Storage and Handling Toolkit, [www.cdc.gov/vaccines/hcp/admin/storage/toolkit/storage-handling-toolkit.pdf](http://www.cdc.gov/vaccines/hcp/admin/storage/toolkit/storage-handling-toolkit.pdf).

## Surveillance and Reporting for Measles

For information on guidance for state and local health department staff who are involved in surveillance activities for vaccine-preventable diseases, please consult the Manual for the Surveillance of Vaccine-Preventable Diseases, [www.cdc.gov/vaccines/pubs/surv-manual/chapters.html](http://www.cdc.gov/vaccines/pubs/surv-manual/chapters.html).

## Acknowledgements

The editors would like to acknowledge Jennifer Hamborsky and Valerie Morelli for their contributions to this chapter.

## Selected References

American Academy of Pediatrics. Measles. In: Kimberlin D, Brandy M, Jackson M, et al., eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics;2018:537–50.

Atkinson W, Orenstein W, Krugman S. The resurgence of measles in the United States, 1989–1990. *Ann Rev Med* 1992;43:451–63.

Bellini W, Rota P. Genetic diversity of wild-type measles viruses: implications for global measles elimination programs. *Emerg Infect Dis* 1998;4(1):29–35.

Bellini W, Rota J, Lowe L, et al. Subacute sclerosing panencephalitis: more cases of this fatal disease are prevented by measles immunization than was previously recognized. *J Infect Dis* 2005;192(10):1686–93.

CDC. Global measles mortality, 2000–2008. *MMWR* 2009;58(47):1321–6.

CDC. Immunization of health-care personnel. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2011;60(RR-7):1–45.

CDC. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1998;47(No. RR-8):1–57.

CDC. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2013;62(No. RR-4):1–34.

CDC. Recommendations of the Advisory Committee on Immunization Practices for use of a third dose of mumps virus-containing vaccine in persons at increased risk for mumps during an outbreak. *MMWR* 2018;67(1):33–8.

CDC. Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2010;59(No. RR-3):1–12.

Clemmons N, Wallace G, Patel M, et al. Incidence of Measles in the United States, 2001–2015. *JAMA* 2017;318(13):1279–81.

## NOTES

